Morbid Obesity

Peri-operative Management

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MORBID OBESITY

PERI-OPERATIVE MANAGEMENT

Dr Adrian O. Alvarez is at present one of the most recognized experts in the anesthetic management of the morbidly obese patient in the world. Being an anesthesiologist and also general surgeon he early recognized the importance of the multidisciplinary approach to these kind of individuals. He has been working in this scenario in close relationship with experts of other fields (bariatric surgeons, internists, nutritionists) since many years ago, and this spirit is clearly reflected in this work "Morbid Obesity, Perioperative Management".

MORBID OBESITY
PERI-OPERATIVE MANAGEMENT

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FOREWORD

In the last 25 years, overweight (body mass index, BMI $> 25\,kg/m^2$) and obesity (BMI $>30\,kg/m^2$) have developed into a global epidemic. This increase in obesity cannot be attributed to genetics alone; rather, complex fast-food and nutritional causes, lifestyle changes and physical inactivity have become important factors.

The severe form of obesity, called *morbid obesity*, occurs in patients with BMI > 40 (or $>35\,kg/m^2$ with severe co-morbidities) and is associated with serious, debilitating and progressive sequelae.

Morbid obesity and super-obesity (BMI $> 50\,kg/m^2$) have significant co-morbidities – type 2 diabetes, cardiovascular disease, hypertension, deep vein thromboses and pulmonary embolism, debilitating arthritis of weight-bearing joints and low back, an increased incidence of certain cancers, alveolar hypoventilation (Pickwickian) and/or obstructive sleep apnea, foul intertrigos under skin folds, abdominal and hiatal hernias, gastroesophageal reflux disease, stasis leg ulcers, accident proneness, plethora and diaphoresis, immobility, gallbladder disease, amenorrhea, increased incidence of Caesarian section, urinary stress incontinence in females, psychosocial and economic problems, etc.

These patients require medical assistance by multiple allied health fields – internal medicine, endocrinology, pulmonology, psychiatry and psychology, eating disorder specialists, nutritionists and dietitians, specialized nursing care, plastic surgery, intensive care specialists, social workers and governmental assistance for disability, among others. Specific operations (known as bariatric surgery) have been the only means of achieving significant sustained weight loss in these unfortunate individuals. Weight loss is associated with reversal of these serious co-morbidities.

The morbidly obese population especially presents a challenge for the anesthesiologist during surgery. Their multiple associated diseases are integrally dependent on specialized expertise of the anesthesiologist to undergo this surgery, as well as the multidisciplinary care from the allied health professionals.

The practice of anesthesia must keep abreast with the surgery which has developed and is necessary for these special individuals.

Dr. A.O. Alvarez being an anesthesiologist and general surgeon also, understood early the importance of the close relationship between surgeons and anesthesiologists in the difficult task of managing these patients. He has an important experience in this field, and the spirit of the multidisciplinary approach to the morbidly obese has been reflected during Sao Paolo International Federation for the Surgery of Obesity (IFSO) World Congress, in which for the very first time, surgeons and anesthesiologist (represented by Dr. A.O. Alvarez) got together in a special experts table.

Dr. A.O. Alvarez has also undertaken a major accomplishment by this book with chapters by renowned contributors.

The anesthetic challenges, poor veins, potentially difficult intubation, the premedication, the various techniques and means of anesthetic and analgesic delivery, the positioning, thromboprophylaxis, monitoring, the post-anesthetic surveillance and intensive care, the ability of the hospital personnel to move these individuals, potential atelectasis, wound care, are all challenges for the anesthetic and allied hospital staff. These aspects are covered in this monumental volume. We applaud Dr. A.O. Alvarez for undertaking this original and necessary project.

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PREFACE

There is a global epidemic threatening the health of people throughout the world. That epidemic is "obesity". Whereas at one time the problems of obesity were confined to only wealthy industrialized countries, today the incidence of obesity is rising in both developed and developing countries. Obesity-related medical problems are now even affecting the children of those countries. The International Obesity Task Force (IOTF), a collaborative program of the International Association for the Study of Obesity (IASO) and the World Health Organization (WHO) recently estimated that over 1.7 billion people are either overweight (body mass index, BMI $> 25\,kg/m^2$) or obese (BMI $> 30\,kg/m^2$).

Obesity is associated with many medical co-morbidities including type 2 diabetes, hypertension and cardiovascular disease, respiratory problems and obstructive sleep apnea, arthritis on weight-bearing joints, liver and gallbladder disease, and several types of cancer. In addition there are "quality of life" issues that are of great importance but which cannot be quantified.

These obesity-related health problems have major implications for the individual, and have an enormous impact on the health resources of every country. The costs of obesity are staggering and threaten to overwhelm health services everywhere. The incidence of obesity in the adult population of the US rose from 14.25% in 1978 to over 31% in 2000. One in five Americans now has a BMI $> 30\,kg/m^2$, and at the current rate that figure is expected to double to 40% by 2025. In 1990 it was estimated that 46 billion dollars, or 6.7% of all healthcare costs, were spent on obesity-related health problems in the US. Today, those costs are much higher.

The precursors of obesity are multifactorial. They include genetic tendency, environmental effects, education, sex, race and socioeconomic status. There is no precise definition of when obesity begins. A person is usually considered to be obese when the amount of their body fat increases beyond the point where physical health deteriorates. Extreme obesity, that is, obesity that if untreated significantly shortens the individual's life expectancy is termed "morbid obesity". In the US one out of 16 women is "morbidly obese". The World Health Report for 2002 estimated that there were more than 2.5 million annual deaths due to weight-related problems, with 220,000 of those deaths in Europe and more than 300,000 obesity-related deaths in the US.

The obesity epidemic reflects changes in behavioral patterns, including decreased physical activity and overconsumption of high-fat foods. There are simple solutions to the problem – early education, sensible long-term diets, increased physical activity and exercise, and in some cases medications. Unfortunately, these easy answers are usually not practical. Therefore, healthcare providers must turn to the only treatment of extreme obesity that is effective – bariatric surgery.

The United States National Institutes of Health Consensus Panel (Gastrointestinal Surgery for Severe Obesity. Consensus Development Conference Panel) convened surgeons, gastroenterologists, endocrinologists, psychiatrists, nutritionists and other healthcare professionals in 1991 to consider the treatment options for severe obesity. That panel recommended that patients first be treated in a program that integrates a dietary regimen, appropriate exercise, behavior modification and psychological support. If these non-surgical interventions failed, as they usually do, then vertical banded gastroplasty and gastric bypass should be considered. Bariatric surgery today with a wider range of acceptable procedures remains the only effective treatment for patients with morbid obesity.

Bariatric surgery is a cost-effective alternative to no treatment. Surgery is associated with sustained weight loss for patients who uniformly fail non-surgical treatment. Following the weight loss there is a high cure rate for diabetes and sleep apnea, with significant improvement in other complications of obesity, such as hypertension and osteoarthritis. It is estimated that nearly 200,000 bariatric surgical procedures will be performed in the US in 2004.

Everyday, every anesthesiologist must be ready to deal with morbidly obese surgical patients. Since morbid obesity is present in such a high percentage of the general population, it is also not unusual to be presented with

them for non-bariatric surgical procedures. In my own practice at a major university medical center, I estimate that at least 25% of our routine surgical patients are obese and at least 10% of all patients are morbidly obese.

The global nature of the problem is reflected in the worldwide growth of interest in this problem. The International Federation for the Surgery of Obesity (IFSO) now holds a well-attended annual meeting, and the organization has a membership that includes over 30 national bariatric surgical organizations and members from 53 countries. The journal *Obesity Surgery*, now in its second decade, is dedicated to the field of bariatric surgery. So why have we not had a book on the anesthetic management of these patients?

The risks associated with anesthesia and surgery are believed to be higher for obese patients than for normal weight patients. Every anesthesiologist and surgeon must be prepared to safely manage these patients. That requires an understanding of the pathophysiology of obesity and its associated medical problems. The only book I could find dedicated solely to the anesthetic management of obesity is a small monograph (*Anesthesia and the Obese Patient* in the *Contemporary Anesthesia Practice Series*) edited by Brown and Vaughan and published over 20 years ago. Obviously, the techniques of anesthesia and surgery (laparoscopy, epidural opioids, total intravenous anesthesia, etc.) have changed markedly over the past two decades.

When Dr. Alvarez first approached me and asked me to contribute to this book, I was both pleased and honored. A comprehensive book dealing with the anesthetic management of the morbidly obese patient is long overdue. This book covers all areas of anesthesia for the morbid obese surgical patient, from pre-operative evaluation and preparation to intra-operative and post-operative management. The authors, all experts in their respective areas, present the most up-to-date information in their chapters. The international group of the contributors emphasizes the international scale of the obesity epidemic. The reader is encouraged to use this book as a guide and a reference, and continue to follow the medical journals and the Internet for the rapidly developing changes in the field of anesthesia for the obese patient.

We are all indebted to Dr. A.O. Alvarez for bringing this important project to fruition.

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December 2003

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To my wife Gabriela for her love, patience and support.

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Finally to my partners in this unique experience of working in a bariatric team, Dr. Albarracin Silvio and Dr. Antonio Cascardo who shared with me all the exceptional emotional experiences of this monumental task, the peri-operative management of the morbidly obese patient.

A.O. Alvarez
Buenos Aires
April 2004

"*En la vida existe un valor que permanece muchas veces invisible para los demás, pero que el hombre escucha en lo hondo de su alma; es la fidelidad o traición a lo que sentimos como un destino o una vocación a cumplir.*"

Ernesto Sábato
Mayo del año 2000

"*There exists in life a value which, while often invisible to all others, an individual feels deep within his soul: it is an acceptance or rejection of a calling to what they feel is their destiny or vocation*."

Ernesto Sabato
May 2000

GENERAL ASPECTS

SECTION 1

INTRODUCTION TO PERI-OPERATIVE MANAGEMENT: REASONS FOR A MULTIDISCIPLINARY APPROACH

1

A.O. Alvarez & A. Baltasar

1.1 Introduction

Morbid obesity has always been a challenge to the anesthesiologist and surgeon. In the past, it was frequent to avoid any surgical procedure due to the increased risk observed among these subjects. It was common to hear, "if you do not lose weight you cannot be operated …".

But this situation have changed, mainly in the last two decades.

Morbid obesity is actually one of the most prominent medical problems in the world. Two aspects support this concept: **quantitative** and **qualitative**.

Quantitative

Obesity prevalence is increasing. It has been recently reported that the incidence of all classes of obesity, those with body mass indexes (BMI) of 30, 40, or 50 kg/m^2 have shown a dramatic growth from 1986 to 2000. One in five patients has a BMI over 30, one in 50 over 40, and one in 400 has a BMI over 50.[1]

Similar incidence and tendency have been observed in the rest of the world.

Qualitative

Morbid obesity is a life-threatening situation in the long term. BMI over 40 if not treated, significantly shortens the individual's life expectancy. Apart from the increased morbidity associated with obesity, the excess mortality is substantial. It is principally caused by death from coronary heart disease, stroke, and diabetes mellitus, although sudden unexplained death, malignancies, and fatal accidents are also more prevalent in the obese. It has been shown that there is a 12-fold excess mortality in men in the age group 25–34 years and a 6-fold in those aged 35–44 years. In addition, the prevalence and severity of co-existing diseases has shown a clear correlation with the duration

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of obesity; therefore, it is advisable to provide a successful weight reduction treatment as early in the patient's life as possible.[2,3]

1.2 Weight reduction therapies, results

Unfortunately, medically supervised weight-control programs have been ineffective because patients cannot maintain pronounced long-term weight loss. In contrast, current operative methods have been proved to be effective in helping patients achieve and maintain permanent weight reduction. Several operations have being designed and assessed; with these procedures, weight loss is achieved by inducing malabsorption, early saciety, or a combination of these outcomes. Although these operations have associated side effects and limitations, the expected benefits outweigh the risks. For optimal results, patients must be carefully selected and treated by a multidisciplinary group.[4]

The National Institutes of Health Consensus Conference in 1991 recommended that obesity surgery is an appropriate treatment for patients with BMI over 40 who had failed in attempts at medical treatment and for patients with a BMI over 35 with severe complications of obesity. Bariatric surgery remains the most reasonable treatment option for most morbidly obese patients. Vertically banded gastroplasty and Roux-en-Y gastric bypass were the two operations recommended because of their relative safety and effectiveness.[5] Both the techniques induce an impressive loss of weight, and are surprisingly well tolerated, even by severely obese persons. The usual 50–75% reduction of initial weight excess, is followed by a clear-cut reduction, or even disappearance of, obesity-related co-morbidity, such as hypertension, diabetes mellitus, or obstructive sleep apnea syndrome (OSAS).[6]

1.3 Morbid obesity, implications in the anesthesiological practice

Consequently, everyday, we frequently find a morbidly obese in the operating room, but, not only for bariatric surgery, also for any other surgical procedure. In fact the American Society of Bariatric Surgery (ASBS) estimates that nearly 200,000 bariatric surgical procedures will be performed just in the US in 2004.

If it is considered that other pathological surgical processes are more frequent between the obese, such as gallbladder disease, several types of cancer and arthritis on weight-bearing joints, the magnitude of the problem is more than clear.[7]

The risks associated with anesthesia and surgery are believed to be higher for the obese patients than for normal weight patients. Obesity is also associated with higher resource utilization (more peri-operative days in the hospital) and greater peri-operative morbidity and mortality.[8–11]

Pathophysiological changes induced by overweight (cardiac, respiratory, metabolic, and digestive functions between others) and frequent co-morbidities (diabetes, arterial hypertension, sleep apnea, etc.) are involved.[12–22]

Nevertheless the main concerns for the anesthesiologist have been the same for over three decades; derangements of the cardiopulmonary system.[23,24]

1.4 Multidisciplinary approach of the morbidly obese individual

So it is not surprising that, multidisciplinary approach, and a better and more profound knowledge about pathophysiology involved in these treatments have contributed to improve the outcomes. Improved management should ultimately influence the negative selection bias that has excluded obese patients from elective surgery for fear of complications, potentially resulting in emergency procedures in those already compromised patients. Over the long term, if adequate medical policies are taken, morbidity and mortality in obese patients should be expected to decrease as well as resources utilization and costs.

Morbidly obese surgical–anesthetic management should be conceived as a continuous and indivisible process that begins with surgical indication and ends at institution discharge. In this process, the multidisciplinary team has to work not as isolated professionals over a unique patient:

> *Multidisciplinary group have to plan the procedure, take the actions and re-plan every decision in a continuous interdependent manner.*

In this scenario, the relationship between surgeon and anesthesiologist has to be extremely close, because during surgery and anesthesia is when obese patient's body usually is challenged at the highest point.[25]

1.5 The bariatric multidisciplinary team

The number of professionals and specialties involved in the multidisciplinary approach may vary from one

institution to another. It is advisable to count at least with three surgeons, two anesthesiologists (with experience in difficult airway and hemodynamic management), a cardiologist, a pulmonologist, a nutritionist, and a psychologist, all of them with experience in managing morbidly obese patients and related disorders.

At this moment, it could be assumed that bariatric surgery is the best procedure for the morbidly obese, but professionals and patients involved have to be aware that this is not an esthetic procedure exeunt of complications. *This is a major surgical procedure in a risky surgical population*. This is important not only for clinical reasons but also regarding legal aspects and it has to be taken into account when obtaining the informed consent.[26]

1.6 Peri-operative management in morbid obesity: philosophical approach

In order to be able to face this complex situation, and even if it is an artificial simplification, this book has been developed in sequential sections and chapters with the intention to guide the readers to follow a comprehensive line of thoughts. Through a careful reading of the paragraphs ahead, it will be understood why the cooperation of different disciplines is necessary and how morbidly obese patient should be focused by the anesthesiologist.

1.6.1 Pathophysiological considerations

Morbid obesity induced many physiological alterations. All of them have to be deeply understood in order to decide which procedure could be more suitable for every clinical situation. Respiratory, cardiac, digestive, and metabolic are the systems more frequently altered in the obese and they are treated in depth in separate chapters. All of them could have a significant impact during surgical-anesthetic process.

Respiratory system

Functional residual capacity is reduced in the obese. It could be even lower than the closing capacity. This means that during tidal ventilation, some areas of pulmonary parenchyma are collapsed and not ventilated. It has been observed that there is an increased pulmonary shunt and significant ventilation/perfusion mismatch between the obese. In addition, it has been informed that a higher incidence of difficult tracheal intubation and mask ventilation was found specially in those patients with OSAS.[27–31] This combination could lead to a dangerous situation, because, airway management could be longer in time, in a patient that quickly develops hypoxemia due to respiratory alterations and in whom pre-oxygenation is less effective.[32,33] It is clear why, in selected cases, special pneumonological and even laryngological or echographic evaluation could be extremely helpful to choose the best procedure. In addition, during post-operative period, mainly in upper abdominal surgery, ventilatory function could be significantly affected. A proper pre-operative evaluation between anesthesiologist and *pulmonologist* could help to know pulmonary performance in depth, and to decide if any pre-operative or post-operative treatment would be necessary. Patients with OSAS, obesity hypoventilation syndrome (OHS), chronic obstructive pulmonary disease (COPD), smokers, or with asthma or asthma-like states could benefit from peri-operative bronchodilatators, continuous positive airway pressure (CPAP) or bi-level positive airway pressure (Bi PAP) therapy. In fact OSAS is a frequent co-morbidity observed among these individuals.[34–36]

But if it is taken into account that face mask adaptation could be problematic in the obese due to anatomical reasons, and that a training period is frequently necessary for the patient to be comfortable with CPAP or Bi PAP, it may be wise to define pre-operatively which mask and which pressures are the best for every individual. Trying to use for the very first time Bi PAP or CPAP in the immediate post-operative period should not be recommended and frequently will be impossible. In fact patients should bring their own masks, and anesthesiologist should know from the beginning the pressures that help to obtain the best results in every individual case.

In a recently published study, the overall rate of critically respiratory events in obese patients was 3%, much higher than in lean population.[37] But in another retrospective study, the importance of the full and early recovery of consciousness was evident, showing that no significant increase of adverse peri-operative events in patients with polysomnographically confirmed OSAS when the levels of wakefulness are carefully maintained.[38] Consequently, quick and full recovery of consciousness should be considered as an essential anesthetic target.

Deep vein thrombosis with pulmonary embolism is a dramatic complication associated with the morbidly obese patient.[39–45]

It is considered as the most frequent cause of death during the first 30 post-operative days, after bariatric surgery (more than three times greater than anastomotic leak and subsequent sepsis) therefore all efforts have to be made in order to diminish its incidence. Early recovery of consciousness, ambulating capacity, pharmacological prevention, and mechanical devices

may reduce its occurrence. This topic will be analyzed in detail throughout the book.[46]

Cardiac

The incidence of pre-existing, often severe, cardiovascular disease in obese patients scheduled for elective bariatric surgery is claimed to be as great as 20% in some series.[47,48]

Morbid obesity induced an enhance in blood volume, in order to satisfy metabolic requirements of increased corporal tissue. Also blood viscosity could be higher, due to chronic hypoxemia that produces an increment in plasmatic eritropoyetin levels and consequently polycythemia. The enhanced blood volume and viscosity are responsible for a significant over-demand in ventricular work. This is the reason why morbidly obese are not frequently capable to respond appropriately to acute hemodynamic stress situations.[12–16]

It has been said that obesity is similar to exercise, but it is a constant state of "exercise".

Incidence of arterial blood hypertension is higher in the obese compared with normal weighted adults.[49–53]

Also vascular disease is more frequent, due to arterial blood hypertension and/or diabetes. Consequently it has to be considered that morbidly obese could suffer an impairment in myocardial oxygenation as a result of an increased oxygen consumption (higher preload and afterload, ventricular hypertrophy, and chamber dilation) and a reduced oxygen offer (coronary vascular disease or respiratory dysfunction). In addition there is a strong relationship between obesity and coronary artery disease (CAD).[54–61] Cardiac arrythmias and alterations in electrocardiography are also common.[62–65]

Many times diagnostic resources involved in the cardiological evaluation of these subjects could be different and controversial compared with normal weighted patients. It is also questioned when invasive hemodynamic monitoring should be applied.[66–68]

Therefore, it is clear that if necessary, *cardiologists* with experience in managing obese patients, may provide an essential contribution in the multidisciplinary team.

Digestive

Regarding digestive system, gastric aspiration could be more frequent due to a higher incidence of incompetent esophageal sphincter function with or without hiatal hernia. In addition, intra-abdominal pressure is enhanced, and residual gastric content is greater and more acidic.[69]

If it is considered that, during induction, it is possible that proper airway protection (tracheal tubing with insufflated cuff) could be delayed because of difficulties during laringoscopy,[47] a dangerous situation may appear; for example, larger gastric acid content, diminished sufficiency of anti-reflux mechanisms, abolished laryngeal protective reflexes, and long period until proper protection is established (tracheal intubation). For this contingency, mainly if predicted difficult airway was detected during pre-operative evaluation, a *professional highly skilled in fiberoscopic awake intubation* could be necessary.[70]

It also has to be noticed that mask ventilation could be problematic, and that morbidly obese could present a significant reduction in the time for oxyhemoglobin desaturation after apnea. Facing this situation, intubation with patent airway and spontaneous ventilation should be considered in order to diminish undesirable and life-threatening respiratory misadventures. Precautions regarding difficult tracheal intubation and mask ventilation have to be taken during all perioperative period not just for induction of general anesthesia, but also if regional anesthesia is provided, because it could be necessary to perform an emergent tracheal intubation during post-operative period specially in patients with severe respiratory disorders, therefore all technological and human resources have to be available immediately.[71]

Metabolic

Obviously, body composition is quite different in the morbidly obese. Increased fat tissue, proportionally lower water content, and greater lean body mass do affect pharmacokinetics. In respective chapters it will be analyzed how this impacts in dosing and drugs selection.

Diabetes mellitus or insulin resistance states are frequent co-morbidities, and it is not unusual to be in front of a patient who may need peri-operative requirements of insulin and glucose.[72–76] In these cases the contribution of an *endocrinologist* could be useful.

Psychological issues

Morbid obesity is frequently associated with psychological disorders. Depression, alterations in self-esteem, eating disorders, incidence of suicide attempts and others are common among these subjects. In addition it is essential that the patient deeply understand, the risks and reasonable expectations of the procedure, prior to take any decision regarding bariatric surgery. This fact has a prominent impact, not only in clinical results, but also concerning eventual legal

claims. Besides, an appropriate pre-operative psychological evaluation could help the surgeon to decide what kind of bariatric procedure could be more suitable for each patient. Psychological attitude and preparation of the patient is usually the most welcomed and important to the surgeon. For it is the psychological readiness of each patient and that patient's commitment to outcome after this operation that appears to determine its long-term worth for that patient. Finally pre-operative psycho-prophilaxis would help to reduce anxiety and to improve confidence between patient and surgical team. This could be reflected in a higher adherence to the treatment after surgery. Consequently in my opinion, and based on our own experience, a *psychologist* should be part of every bariatric team.

Nutritional state

It is important to recognize patients with nutritional compromise in the face of their obesity. The majority of extremely obese patients have a greater absolute cell mass than the normal weight population. Even though the modalities of diet and exercise are generally unsuccessful in treating obesity per se, they are invaluable adjuncts in preparing the obese patient for surgery. Pre-operative weight loss is obviously beneficial to ameliorate many of the complicating conditions afflicting the obese especially regarding respiratory function and metabolism. Even though weight reduction immediately before surgery has not been shown to reduce peri-operative morbidity and mortality, it may reverse some of the pathophysiological changes in the obese patient, and mild weight reduction before surgery may reduce liver size thus facilitating surgical approach to diaphragmatic hiatus.[77] In addition, also intra-abdominal pressure could decrease and concomitantly impaired diaphragmatic impedance, thus improving conditions for mechanical ventilation.

But if weight reduction is achieved before surgery, however, it is important that the loss not occur at the expense of lean body mass and that sufficient protein (1.5 g/kg of ideal body weight per day) be provided. Diets in the pre-operative period have to be deeply considered, because they can influence dangerously in the peri-operative outcomes. Starvation diets, low and very low calorie diets, and protein-sparing modified fasting diets could develop severe cardiac arrythmias and even sudden death.[78–83] Anyway, reduction in simple carbohydrates reduces glycemia and lipogenesis, and should be recommended routinely.

A subgroup of obese patients has reduced body cell mass with concomitant elevated extracellular water, making them less able to withstand operative stress and post-operative catabolism. A particularly compromised group is patients who have had prior surgery for obesity. They must always be considered to have latent malnutrition and thus present a greater risk for the development of post-operative complications. This is especially true for patients who have had malabsorptive operations. They may require pre-operative total parenteral nutrition to improve their nitrogen balance. It is clear why the cooperation of a highly skilled *nutritionist* is essential in the multidisciplinary team.

Physical therapy

An important adjunct to dietary management is implementation of an exercise program whenever feasible, since the majority of obese patients are sedentary, and exercise improves glucose tolerance and respiratory capacity, and helps maintain lean body mass.

Chest physical therapy with breathing exercise and instruction of the incentive spirometer should be routine in obese patients in order to improve peri-operative oxygenation and reduce post-operative atelectasis. A course of CPAP or Bi PAP can dramatically improve the pulmonary function of an obese patient and it can be implemented even in patients with gastric sutures, without increasing the risk of developing post-operative anastomotic leaks.[84–86]

1.6.2 Risks and frequent complications associated with obesity

According to pathophysiological alterations, peri-operative risks are believed to be higher among obese patients. All professionals involved in the treatment have to be aware of them to take appropriated precautions. Risks and frequent complications associated with the anesthetic care of the obese will be discussed in a separate chapter in order to allow the reader to have a general overview about the magnitude of the problem.

1.6.3 Legal aspects

According to increased risks and complications, surgical treatment in the morbidly obese could lead to devastating legal claims. Despite all medical precautions and proper management, all data have to be clearly and completely reported in the correspondent medical document.[26] But even if the whole treatment has been performed according to the highest standards of medical care, if a well-designed legal consent is not present, legal situation could seriously compromise the professionals involved. In a special chapter, all information regarding legal aspects is deeply developed.

1.6.4 Pre-operative evaluation

Up to the present moment, no randomized controlled trials have been performed to analyze if a proper pre-operative evaluation and preparation may reduce significantly patient's morbidity and mortality between the morbidly obese population. Nevertheless, there exists much evidence in other kind of patients indicating that such evaluation makes the peri-operative period more efficient. In fact during the pre-operative assessment it is possible to detect risk factors, pathophysiological impairments and other situations that could and should be deeply considered and eventually treated before surgery thus improving patient's condition to better face surgical stress. In addition, it gives the chance for developing a closer relationship and confidence between the patient and the bariatric team. Pre-operative evaluation and preparedness has to be considered as an essential component of any surgical-anesthetic procedure between the morbidly obese population.

1.6.5. Peri-operative management focused to reduce co-morbidities' impact

According to the higher risks observed among obese individuals and facing the fact that many peri-operative complications are common, it is logical to take some preventive measures in order to reduce their incidence or severity. Peri-operative management of the most important co-morbidities and complications will be treated in separate chapters (deep vein thromboses, diabetes mellitus, peri-operative infections, cardiovascular associated diseases, and peri-operative renal function). All professionals eventually involved (infectologists, nephrologists, endocrinologists, pulmonologists, cardiologists, surgeons, anesthesiologists, intensivists, and some others) should conceive a rational and coherent plan to be applied in a continuous fashion. It is not logical that a clinician takes care of pre-operative evaluation and treatment, an anesthesiologist provides anesthesia, and an internist or intensivist follows the post-operative period if they do not use the same pathophysiological and therapeutic concepts and goals. In this complex scenario the anesthesiologist should be the one to agglutinate and supervise all the therapeutic resources applied to the patient.

1.6.6 Pharmacological implications of morbid obesity

Alterations in body composition and mechanisms implied in drugs absorption, distribution, availability, inactivation, or elimination have an enormous impact in the anesthetic management of the morbidly obese.[87–92] Drugs dosing is yet a controversial and difficult task to manage in this population. Pharmacokinetics and pharmacodynamics will be deeply discussed not only in a specific chapter but almost throughout the entire book. Since opioid administration could become highly dangerous in some cases such as patients with OSAS or OHS, remifentanil properties and clinical applications will be deeply developed to understand how its use in the morbidly obese could be beneficial.[92]

1.6.7 Intra-operative care

The higher morbidity and mortality observed in the bariatric patient depends mainly on perianesthetic complications rather than surgical ones. Many special situations such as position-related physiological alterations and/or complications, advantages, or disadvantages of different anesthetic techniques (total intravenous anesthesia and inhalational anesthesia) and difficulties in monitoring even basic physiological parameters such as not invasive arterial blood pressure become of essential importance in some morbidly obese subjects. Not taking care of a meticulous positioning a padding could result in severe injuries affecting plexus, nerves, eyes, and even developing acute renal failure and death.[93–95] This is the reason why, all these topics are carefully considered among the work. Even though this book is mainly related to the peri-operative management of the morbidly obese bariatric patient, it could not be excluded the very particular and difficult task of providing anesthesia to the obese parturient.

Special attention to pharmacodynamic monitoring (anesthesia depth or central nervous system (CNS) electrical activity) have being paid, considering the problematic pharmacological management of the obese, and the eventual advantages that anesthesia depth monitoring could provide, facing the possibility of devastating complications that may result as a consequence of inadequate drug dosing in these patients.[96–99]

1.6.8 Post-operative management

Post-operative care of a morbidly or superobese patient with OSAS, severe co-existing cardiac disease, diabetes mellitus, and smoking habit, after 5 or 6 h of a major upper abdominal open surgical procedure could challenge the professional involved in his health care, and this clinical situation is not infrequent for anesthesiologists involved in a bariatric team:

> *Is precisely in this particular patient where the coherent, rational, continuous, and combined work of the multidisciplinary bariatric team can make the difference in the quality of outcomes.*

Post-anesthesia care unit (PACU), intensive care unit (ICU), nursing, and post-operative pain management

are prominent topics to know in detail in order to achieve successful results.

1.7 Conclusion

Once the reader has carefully gone through all the contents of the book, he/she could realize that still there is a long way to go. Many randomized controlled trials have to develop in order to bring some clearness in several controversial topics. In the final chapter the actual situation regarding peri-operative management of the surgical morbidly obese patient, and the eventual actions that should be taken in my opinion to have better chances of improvement in this challenging field will be discussed.

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PERI-OPERATIVE RISKS AND FREQUENT COMPLICATIONS

2

L. Brusco Jr.

2.1 Introduction

Obesity is a major health care problem, and the prevalence is increasing. A recent report[1] showed that the incidence of obesity in all classes of obesity, those with body mass indexes (BMI) of 30, 40, or 50 kg/m^2 have shown dramatic increases from 1986 to 2000. One in five patients has a BMI over 30, one in 50 over 40, and one in 400 has a BMI over 50. Thus, the chances that an anesthesiologist or surgeon will be dealing with a patient who is morbidly obese is increasing, even if you do not have a bariatric surgery program.

This increase in the incidence of morbid obesity, combined with the fact that the number of bariatric surgery procedures per year is estimated to be over 100,000 in 2003 and increasing rapidly,[2] means that anesthesiologists are more and more often encountering patients with morbid obesity, and in many cases these are patients who would not have been considered for any type of operation 20 years ago. In addition, studies showing efficacy in older patients have caused more older patients with more co-morbidities to have bariatric surgery.[3,4] Finally, increased success and familiarity taking care of these patients lead more patients as more obese patients to be considered for surgery of all types. Being able to comfortably take care of patients like this is essential to good anesthetic practice.

Much of the literature and the discussion of the perioperative care of the morbidly obese concerns bariatric surgery; however, like literature on patients with cardiac disease, much of it is relevant to non-bariatric surgery in patients with morbid obesity.

2.2 Pre-operative considerations

Patients with morbid obesity have a long list of co-morbidities of concern to the anesthesiologist[5–10] (see also Chapter 9). The incidence of cardiac and pulmonary disease is increased, as is the incidence of

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Table 2.1 Medical problems associated with obesity

System	Disease
Cardiac	Arterial hypertension Atherosclerosis
Pulmonary	Sleep apnea Asthma Pulmonary embolism Pulmonary hypertension Obesity hypoventilation syndrome
Endocrine	Diabetes mellitus
Hepatic	Hepatic steatosis Cholelithiasis
Vascular	Deep venous thrombosis Varicose veins
Skeletal	Degenerative arthritis
Oncology	Carcinoma of the endometrium Carcinoma of the prostate Carcinoma of the breast Carcinoma of the colon

From: Ref [11].

diabetes mellitus (DM) and other medical problems (Table 2.1).[11] It is often difficult to assess the physiological impact of these conditions, especially cardiac and pulmonary diseases, because exercise tolerance is usually diminished due to obesity. Also, many co-morbidities are undiagnosed.[5] Thus, at some point before the morbidly obese patient undergoes surgery, it is imperative to take a thorough history to pinpoint those conditions that may have not been diagnosed. Chief among these is a history of symptoms of DM (polyuria, polydipsia, or nocturia; frequent fungal skin infections and recurring skin, gum, or urinary tract infections; irritability and mood changes; blurred vision and tingling or numbness in the legs, feet, or fingers; slow healing of cuts and bruises). These symptoms may be more suggestive of DM in the morbidly obese than other symptoms of DM that may be present simply because of the presence of morbid obesity (excessive hunger, fatigue, and drowsiness) or are unlikely to be chronically present in the morbidly obese (weight loss, nausea, and vomiting). Others, as seen below, include heart disease and sleep apnea. Physical examination needs to look for signs of overt left or right ventricular heart failure, wheezing or rales, peripheral edema, and cyanosis. We will discuss the airway examination below. While most co-existing conditions are managed as they would be in any other patient, cardiac and pulmonary conditions raise unique concerns in the morbidly obese patient and deserve some discussion.

2.3 Pre-operative considerations: cardiac disease

Along with pulmonary disease, most anesthesiologists who take care of patients with morbid obesity are very concerned with whether the patient has cardiac disease (see also Chapters 5, 6, and 11). There is good reason for this – patients usually have poor exercise tolerance, which does not allow them to reveal their lack of physiological reserve on an everyday basis. Patients with morbid obesity have an increased incidence of DM, hypertension, hypercholesterolemia, and usually have a family history of heart disease, and, thus, have an increased risk of heart disease.[12] The abnormalities range from narrowing and obstruction of the coronary circulation, dysfunction of either the contraction or relaxation phases of the heart muscle, hypertrophy of the cardiac muscle, and valvular degeneration. Some of these can be modified pre-operatively, some cannot. It is imperative to assess the severity of these conditions, decide on whether or not any therapeutic measures can be taken prior to surgery, and to decide if any extra intra- or post-operative monitoring is indicated.

A usual starting place is the evaluation for ischemic disease. A place to start is the American College of Cardiology/American Heart Association *Guidelines on Peri-operative Cardiovascular Evaluation for Non-cardiac Surgery*.[13] Key in using these guidelines is having an estimate of the reported cardiac risk. For gastric bypass, for example, the risk falls into the intermediate category with cardiac risk $<5\%$ would put it into high risk. Then the patient's exercise tolerance needs to be assessed. If the patient can perform at four metabolic equivalents (METs), which is the ability to walk up a flight of stairs or up a hill, they are considered to have at least moderate exercise tolerance; if not, they are considered to have poor exercise tolerance. Then the patient's co-morbidities must be considered to see what clinical predictors of cardiac disease they have. The most common of these, DM, puts the patient into the intermediate clinical predictors category, as would mild angina pectoris, prior myocardial infarction, compensated or prior congestive heart failure (CHF), or renal insufficiency. While it would be rare to have a patient coming for elective surgery with the factors that are major clinical predictors (unstable coronary syndromes, decompensated CHF, severe valvular disease, or significant arrythmias), they may present for emergency surgery.

If the patient is having gastric bypass surgery (intermediate-risk surgery) and has both poor exercise tolerance (very common) and intermediate clinical

predictors, then they need to have a non-invasive evaluation prior to such surgery. If they have either only minor clinical predictors or moderate or better exercise tolerance, then they do not. Care should be taken to get current exercise tolerance; patients many times will overestimate their exercise tolerance, or give what it was a time in the past at a lower weight. For other operations, the risk of that particular procedure must be taken into account, as well as the patient's history or previous cardiac interventions and testing.

When it comes to the type of testing, there is no consensus on which type is best. The first decision would be whether or not the patient can exercise sufficiently to get to 85% of the predicted maximal heart rate. If they cannot, then a pharmacological stress test would be indicated. The choice among the various non-invasive tests must be made on a local basis, depending on which one at a given institution is better regarded. Also, the patient's weight must be taken into account. For example, for nuclear scanning, the weight limits of the table used for the scanning must be considered; frequently, it is 350–375 lb. The patient's weight will interfere both with stress echocardiography and nuclear stress testing. While transesophageal stress echocardiography is safe and effective, it is cumbersome, uncomfortable, and is not in widespread use.[14] Overall, non-invasive testing is less sensitive and even less specific than in patients with lower weight, reflecting a higher incidence of false positives.[15] Close discussion with the cardiology service is mandatory before ordering non-invasive testing.

If the non-invasive test is positive, then a cardiac catheterization is usually indicated. Weights can be even more limiting for cardiac catheterization, as some tables have weight limits as low as 300 lb, although they can go as high as 450 lb and higher. Cardiac catheterization is safe in these patients, and if it is possible to be done and is required, it should be considered. Cardiac catheterization could lead to a negative result (55% of the time),[15] or it could lead to a positive result that could lead to medical management, interventional cardiology therapy or even cardiac bypass surgery. Percutaneous transluminal coronary angioplasty interventional procedures (PTCA), such as coronary angioplasty or stent placement, can be technically difficult in morbidly obese patients, and there may be some reluctance on the part of interventional cardiologists to perform PTCA on a morbidly obese patient. This decision has to rest on the relative skills of the interventionalists caring for the patient. However, the literature is mixed on the impact of BMI on outcome after PTCA. Patients with BMI $\geqslant 35\,kg/m^2$ have been shown to have a mortality rate higher than that of patients with BMI of 26–34 kg/m^2 and similar to that of patients with BMI $\leqslant 25\,kg/m^2$.[16] However, in other, larger studies, patients with higher BMIs had a lower incidence of major in-hospital events, such as death, myocardial infarction, stroke, and coma.[17,18] This in spite of the fact that the obese patients in these studies consistently have higher incidence of such things as hypertension, diabetes, hypercholesterolemia, and smoking history. Obese patients undergoing cardiac bypass surgery do not have a higher incidence of in-hospital mortality, stroke, myocardial infarction, re-exploration for bleeding, and renal failure following surgery. However, they do have a higher incidence of sternal wound and donor site infections, atrial arrhythmias, prolonged mechanical ventilation, and post-operative stays.[19,20] In another study, however, patients with BMI $> 40\,kg/m^2$ had an increased incidence of in-hospital mortality and renal failure, as well as the findings from the previous studies.[21] It is clear that there may not be an increased risk to coronary revascularization in obese patients, and, if there is, it is not a prohibitive increase in risk. Morbidly obese patients who need an ischemic cardiac work-up prior to surgery and anesthesia should have it done.

Morbidly obese patients also have increased incidence of cardiac dysfunction, whether on the basis of valvular disease, poor function of cardiac muscle, or cardiac hypertrophy. This is even in the absence of systemic hypertension and underlying organic heart disease. Cardiac output is increased as well as blood volume proportional to weight gained.[22] This can lead to hypertrophy of the left ventricle from ventricular dilation, which can lead to diastolic dysfunction. If the wall thickening does not keep pace with dilation, the myocardium can develop dysfunction at systole also. This disorder is obesity cardiomyopathy.[23] In addition, if obese patients have hypertension, this may also facilitate the left ventricular dilation and hypertrophy, which can lead to CHF, which may be due to either diastolic or systolic dysfunction or both. Depending on the presence or absence of such symptoms, pre-operative echocardiography may be indicated apart from the ischemia evaluation mentioned above. While routine invasive hemodynamic monitoring may not be indicated routinely just based on the presence of morbid obesity,[24] it would be indicated for patients with known CHF, renal insufficiency, or severe pulmonary hypertension (Pulmonary artery systolic $>$ 60–70 mmHg), or for procedures with large fluid shifts either pre- or post-operatively. A pre-operative echocardiogram may help make this decision and indicate a greater or lesser need for invasive hemodynamic monitoring.

2.4 Pre-operative considerations: pulmonary diseases

Along with cardiac disorders, of concern to anesthesiologists are the various pulmonary disorders that patients with morbid obesity have (see also Chapter 4). Most common among these are asthma, obstructive sleep apnea (OSA), obesity hypoventilation syndrome (OHS), and cor pulmonale. In addition, patients with morbid obesity usually have decreased pulmonary reserve, even if they do not have a specific pulmonary disorder. For example, patients with morbid obesity have a greater degree of post-operative atelectasis after laparoscopic procedures than non-obese patients.[25] Patients with obesity also have an increased incidence and degree of a restrictive component to their pulmonary function.[26] While the consequences of these pulmonary disorders in the morbidly obese may not have the same severe consequences as the above-mentioned cardiac disorders, they tend to manifest more commonly. Different from cardiac disorders, the pre-operative evaluations that are available for pulmonary disorders less often lead to definitive and effective pre-operative therapy. Again, as with cardiac disorders, elements of the history and physical examination can be as important as pre-operative testing. Routine pre-operative screening spirometry has not been shown to be helpful.[27]

2.4.1 Respiratory function in the pre-operative period

Morbidly obese patients have impairment of both lung volumes and lung mechanics. Patients who have obesity uncomplicated by upper or lower airway obstruction leading to hypoventilation syndrome, sometimes referred to as "simple obesity", usually have only mild respiratory compromise, if at all, as total lung capacity (TLC), forced vital capacity (FVC), and functional residual capacity (FRC) are usually within normal limits.[28] At the wider extremes of obesity, with higher BMI ($>40\,kg/m^2$) patients have reductions of FVC, FRC, and TLC with a decreased expiratory reserve volume (ERV), as well as increased respiratory resistance resulting from the reduction in lung volumes related to being overweight.[29] Due to this, some degree of pulmonary insufficiency is present in almost all morbidly obese patients. These changes are of particular interest to the anesthesiologist, because of the added decreases in these values that anesthesia, the supine position, and post-operative pain cause on their own, which would be additive in the morbidly obese. In addition, morbidly obese patients have a decrease in respiratory system compliance, due in part to a reduction of chest wall compliance due to the increase and to the distribution of adipose tissue.[30] Both of these changes in respiratory function cause morbidly obese patients to have a decreased pulmonary reserve, have faster desaturations, and make them more difficult to ventilate with positive pressure ventilation.

2.4.2 Asthma

Of particular importance for pulmonary disorders is the presence or absence of wheezing. Patients with obesity have a higher incidence of asthma.[31,32] While some may believe that this may be due to a decrease in exercise in asthmatics leading to obesity, studies indicate that this may not be the case.[33] Importantly, the impact of obesity is much stronger in females than in males.[34] Add to this the over diagnosis of asthma in patients with audible wheezing which is actually upper airway sounds from obesity. There are several mechanisms by which obesity could cause either respiratory symptoms or more fundamental changes in the airways leading to asthma. In obese people, symptoms of breathlessness and wheezing may be due to increased work of breathing.[35] Alternatively, obesity may have a direct effect on the mechanical behavior of the respiratory system by altering lung volume, airway caliber, or respiratory muscle strength.[36]

It is clear that at least some of the wheezing that is heard in obese patients is not related to classic bronchoconstriction that is responsive to bronchodilators. The only way to definitively tell if a patient's wheezing is indeed responsive to bronchodilators is to do pulmonary function testings (PFTs) before and after the administration of bronchodilators. If a patient has had PFTs, then it is helpful to review the results prior to elective surgery. However, if they have not been done, it may not be necessary to do them prior to surgery. There are no studies showing a benefit to pre-operative PFTs in obese patients. It is most important to show that the patient is at their optimal state of health at the time of the operation. For the rare patients with steroid-dependent asthma, it may be helpful to perform PFTs to show optimization, but most often optimization can be determined by taking a careful history of the occurrence of bronchodilators and steroid use, emergency room visits, hospitalizations, and intubations. In some instances, discussion with a pulmonologist who has been following the patient for a prolonged period of time will be helpful. Rarely, if ever, are PFTs helpful in this situation.

Many obese patients who are diagnosed with asthma will present pre-operatively with a history of intermittent use of bronchodilators, rare emergency room visits

and no hospitalizations, steroid requirement, or intubations. These patients are best managed by pre-operative administration of bronchodilators, starting anywhere from immediately pre-induction to 48 h pre-operatively. Otherwise, patients who are obese with asthma can be managed just as any other asthmatic.

2.4.3 Obstructive sleep apnea

Patients with morbid obesity have an incidence of OSA that is 12–30-fold higher than in the general population.[37] In one study, 10–15% of patients presenting for bariatric surgery have either OSA or OHS,[38] and operative mortality may be higher in this group of patients (3.4% – 2 of 59 patients).[39] The presence of OSA indicates a high chance of having a number of other sequelae. In one study, 60% of patients with OSA suffer from hypertension[40] as well as left and right ventricular hypertrophy (LVH and RVH, respectively). The LVH is caused by the hypertension, and the RVH is caused by pulmonary hypertension, which is triggered by chronic hypoxia during apnea episodes.[41] The RVH can lead to the most serious of the sequelae of OSA – cor pulmonale and, in end stages, right and left ventricular failure.[42,43] Patients with OSA are also at higher risk for sudden death,[44] possibly related to the above-mentioned cardiac changes. Also, during apneas, there is a reduction of cerebral blood flow, indicating disordered cerebral blood flow autoregulation.[45] There is a compensatory increase in blood pressure, but the decrease in cerebral perfusion along with the hypoxia from the apneas can combine to cause intermittent cerebral ischemia.

The diagnosis is made based on polysomnography, also commonly known as sleep studies.[46] The patient is monitored during sleep via electroencephalography, electromyography, and electro-oculography (detection of eye movements), which determine the level of sleep. Then the patient is observed for episodes of apnea and hypopnea by monitoring airflow or tidal volume and oxygen saturation. An apnea or hypopnea is often accompanied by a decrease in oxygen saturation and terminated by an arousal (awakening of the patient for at least 3 s). In addition, other things such as breathing and limb movements and an electrocardiographic (ECG) lead are monitored. Full sleep studies can take a full night for diagnosis, then another night to test the efficacy of therapy. They can be done at home, but there is some controversy over the reliability of the results.[47]

OSA can be suspected based on a constellation of clinical symptoms. Clinical indicators such as habitual snoring, interrupted nocturnal breathing during sleep (as reported by others), excessive daytime sleepiness and arterial hypertension are frequently seen in patients with OSA, as well as nocturnal choking, waking unrefreshed, morning headaches, excessive daytime sleepiness, and poor sleep quality. However, clinical indicators (with the exception of observed sleep apnea) alone fall short of being sensitive or specific enough to predict OSA.[48,49] However, when observed sleep apnea is combined with other factors such as age $\geqslant$ 38 years, fasting insulin level $\geqslant$ 28 mol/l, glycosylated hemoglobin A_{Ic} level $\geqslant$ 6%, and neck circumference $\geqslant$ 43 cm the patients scored from 1 to 6; a score $\geqslant$3 of the five predictors had a sensitivity of 80% and specificity of 91% for apnea hypopnea index (AHI) $\geqslant$ 15 (moderate OSA), and 86% and 84%, respectively, for AHI $\geqslant$ 30 (severe OSA). Unfortunately, most patients coming for elective surgery do not have readily available insulin and glycosylated hemoglobin levels, but if it is desired to look for some screening testing to do, using a screening system can be less cumbersome than sleep studies.

The treatment of OSA can be categorized as *conservative* (weight loss, lateral sleeping position, treat nasal congestion, and avoidance of alcohol and sedative medications prior to sleep),[50] *medical – first line* (continuous positive airway pressure, CPAP or bi-level positive airway pressure, BiPAP)[51] *medical – second line* (appliances that advance the tongue and/or mandible), or *surgical* (tonsillectomy, uvulo-palato-pharyngoplasty, laser-assisted uvulo-palatoplasty, partial resection or ablation of the tongue, major reconstruction of the mandible or maxillae, and tracheostomy).[52] The first two are only sometimes effective, use of CPAP or BiPAP is very effective and widespread, and surgical methods are reserved for severe cases that are not responsive to CPAP/BiPAP. While there is no question that CPAP/BiPAP therapy is effective in improving quality of life in patients with OSA,[53] there is no objective evidence that pre-operative diagnosis of OSA with sleep studies and subsequent therapy with CPAP/BiPAP. While CPAP/BiPAP via a nasal or a face mask may be difficult to tolerate and learn how to use if first encountered in the immediate post-operative period, patients can be taught to use CPAP/BiPAP pre-operatively and that can be done on clinical suspicion only and does not require pre-operative sleep studies.

The implications for administration of anesthesia in patients with OSA are multiple. If patients have concomitant cardiac dysfunction from the OSA, then fluid management may be problematic during and after the procedure. In addition, because of the incidence of RVH and pulmonary hypertension, if invasive monitoring is used, the threshold for pulmonary artery

catheterization may be lower, since central venous pressure monitoring will be less accurate. Airway management may be a problem (this will be discussed below). Patients with OSA are much more sensitive to narcotics and sedatives than other patients. While many anesthesiologists are concerned about the induction of general anesthesia and intubation in these patients, many times the truly most unpredictable times are after extubation and in the post-operative period. It may be very difficult to balance pain control and apneas, and patients who are given more narcotic intra-operatively have a higher incidence of post-extubation complications.[54] Patients commonly have lower oxygen saturations than other patients, and the most common therapy for this, oxygen administration, does not help because patients will have longer apneas, since their breathing is triggered not by carbon dioxide (CO_2) tension, but by oxygen saturation. Regional or central neuraxial techniques may be helpful in decreasing narcotic dose, but may be technically difficult in the morbidly obese.

Patients with OSA who are already on CPAP/BiPAP can receive their therapy post-operatively. It is very helpful during the pre-operative evaluation to obtain the patient's type of therapy (CPAP vs. BiPAP). CPAP gives patients a continuous airway pressure, while BiPAP gives usually a lower baseline airway pressure and a higher inspiratory pressure. BiPAP may sometimes be better tolerated in patients who do not tolerate CPAP, but some sleep specialists start out with BiPAP on all their patients, so the mere fact that a patient is on BiPAP does not mean that they will not tolerate CPAP. It is usually a good idea to have the patient obtain their settings from their sleep specialist so that, if CPAP therapy is needed post-operatively, it can be started at the same pressure known to be effective in a given patient. Also, since mask fit can have a big part to play in patient adherence to CPAP/BiPAP and thus its efficacy,[55] and different masks fit patients different ways, it is sometimes helpful to have patients bring their own mask and headgear to the hospital to allow better fit and compliance with in-hospital CPAP/BiPAP.

Post-operative use of CPAP/BiPAP can allow patients to receive slightly higher dosage of analgesics and in general tolerate the post-operative period with a larger safety margin. It can be sometimes unsettling to nurses and doctors in the post-operative period to see patients routinely desaturate to the 70–80% range, and patients with moderate sleep apnea will do that during sleep, even with supplemental oxygen. It can sometimes lead to patients being kept in post-anesthesia care units far longer than they need to, delaying mobilization and discharge unnecessarily. Use of CPAP/BiPAP can be difficult to impossible with the presence of a naso-gastric tube, but otherwise, if a patient is somnolent post-operatively, and certainly for patients with diagnosed OSA being admitted to the hospital, they should get their CPAP/BiPAP if at all possible.

2.4.4 Obesity hypoventilation syndrome

Similar to but distinct from OSA is OHS. OHS (also known as Pickwickian syndrome) was originally described as a combination of morbid obesity, hypersomnolence, plethora, and edema.[56] While in OSA the patient breathes normally while awake, in OHS the patient is hypercapneic at rest while awake as well. The cause of OHS in unknown, but it likely involves a combination of a disorder in the brain's control over breathing and the effects of obesity on the chest wall. With the excess weight of massive obesity, the muscles of the chest wall can have difficulty expanding the chest enough to exchange air efficiently. This results in a decreased ability to oxygenate the blood, and the retention of CO_2. Affected individuals suffer from chronic fatigue due to sleep loss, poor sleep quality, and chronic hypoxia. Morbid obesity is the main risk factor. While patients may have concomitant OSA, it may or not be present, and some sleep experts contend that patients with OSA should not be considered to also have OHS.[57] OHS can be treated by CPAP/BiPAP,[58] but there is a subset of patients who do not respond to non-invasive ventilation (known in the past as having *central sleep apnea*). Patients with OHS may seem to have obesity-related cardiac disorders more often than patients with OSA but this may be due to the sheer number of mild and moderate OSA patients that are seen.[59] While routine placement of arterial lines and planned post-operative mechanical ventilation has not been shown to offer any benefit for morbidly obese patients,[60] for patients with OHS it seems prudent to at least have a baseline arterial blood gas to know how severe the hypoxia is at rest. The author has seen pre-operative PaO_2 as low as 35 mmHg in an asymptomatic patient. Pre-operative hypercapnea can also be hinted at by a higher than normal CO_2 reading on routine pre-operative chemistry testing. A simple protocol is to get a room air saturation on all morbidly obese patients presenting for surgery, and getting arterial blood gases and/or placing arterial lines in patients with an SpO_2 lower than or a HCO_3 greater than some pre-set point (for example, $SpO_2 < 95\%$ or $HCO_3 > 29$ mmol/l), but it is important to realize that there is no objective data that this conveys a benefit.

2.5 Pre-operative considerations: airway evaluation and management

Morbid obesity is commonly thought to be associated with a difficulty in visualizing the larynx during laryngoscopy (see also Chapter 21). While this may be a widespread belief, it is only partially substantiated in the literature. Whether it is truly more difficult to visualize the larynx and to intubate obese patients is difficult to determine for the simple reason that in the various studies difficulty with laryngoscopy and intubation are classified in a number of ways, and the studies use different end points for obesity. It has been said that the incidence of difficult intubation is as high as 13[61]–24%[62] in morbidly obese patients, but that is much higher than seen in a later study.[63] In studies looking at obesity and its association with difficult intubation and laryngoscopy, some studies show it as being associated with difficulty,[64–67] and others show that it is not.[62,68–70]

While it may be uncertain whether or not patients with morbid obesity are indeed more difficult to intubate and laryngoscope than patients who are not obese, it is clear from many people's experience that the airway examination of patients who are morbidly obese many times indicates potential difficulty with intubation. This is due to the fact that obesity results in the deposition of adipose tissue into the pharyngeal tissues, and the uvula, the tonsils, the tonsillar pillars, the tongue, aryepiglottic folds, and the lateral pharyngeal walls all can be larger than normal.[71] This clearly can make the examination to indicate a more difficult laryngoscopy. While some measurements not usually done during a routine airway examination, such as neck circumference[68] or ultrasonic measurement of pre-tracheal fat pad[72] may be a better indicator of difficulty with intubation than the usual airway examination, it is clearly more difficult to predict a difficult airway in the morbidly obese patient. The sheer volume of patients with morbid obesity presenting for surgery, coupled with the number of patients who appear to be difficult intubations but are in fact not, in many cases precludes treating each and every patient with morbid obesity and a difficult airway by examination as a known difficult airway. Also, the availability of the laryngeal mask airway takes away a lot of concern about difficulty mask ventilating patients with morbid obesity. Ultimately, the decision to perform an awake intubation on a patient with morbid obesity and a difficult airway by examination comes down to the skill and experience of the anesthesiologist.

If an awake intubation is performed, it must be done with the following in mind. First, the deposition of fat around the airway tends to make using such instruments as fiberoptic bronchoscopes more difficult, since the soft tissues tend to collapse on the scope, making visualization difficult. In addition, the prevalence of OSA in these patients makes the effective sedation of these patients difficult, as there is a smaller margin between being sedated for the procedure and being apneic. Ketamine is well known to cause sedation with little respiratory depression, but its resulting increase in airway secretions makes its use in awake intubation less than optimal. Use of a sedative such as dexmedetomidine, which also causes little or no respiratory depression and tends to dry secretions, may prove especially beneficial in this instance.[73] More careful topical anesthesia and nerve block anesthesia must also be done to decrease reliance on sedation. Care must also be taken to provide a steady stream of oxygen to the patient, because of the patient's decreased FRC and the usual rapid desaturation in morbidly obese patients.

If asleep intubation is performed, then it is essential to have all the equipment available in case the airway turns out to be difficult, such as laryngeal mask airways, fiberoptic laryngoscopes, etc.; a difficult intubation cart is preferable. Extra care must be paid to patient positioning. It can be very difficult to place a morbidly obese patient in the proper sniffing position if they are supine because the fat pad in the back of the neck prevents this motion. Frequently, a pad or ramp must be placed under the shoulders to raise the back up and get the fat pad at the back of the neck off the operating room (OR) table, giving the neck room to then move anteriorly into more of a sniffing position. Frequently, attaining proper mask seal during positive pressure ventilation can be a problem, and sometimes a two-person, two-handed technique must be used. Proper pre-oxygenation is essential, as these patients with their decreased FRC will desaturate very rapidly.

2.6 Intra-operative considerations: drug dosing

The pharmacological management of the morbidly obese patient is the subject of conflicting information. It is more complex than can be reviewed here[74] (see also Chapter 15). Very briefly, there seems to be no difference in absorption or bioavailability of medications between obese and lean patients. The story for drug disposition is quite different. On the one hand, patients obviously have a larger mass of fatty tissue, and it would seem logical that drugs that are highly lipophilic would have higher volumes of distribution

(V_{dss}) and would be subject to dosing changes and longer durations of action. Thiopental and diazepam show significant increases in V_{dss} for obese individuals relative to normal weight individuals. This is not true for all lipophilic substances, as digoxin and procainamide have relatively consistent V_{dss} in the two groups. Polar compounds, on the other hand, can have lower V_{dss} than one would expect from body weight. Such is the case for atracurium.[75] When calculated on a total body weight (TBW) basis, equivalent dosing of atracurium

Table 2.2 Dosing parenteral medications in the morbidly obese

Medication	Findings	Recommendation
Opioid analgesics		
Morphine	Morphine dosing lower in morbidly obese but wide interpatient variability.	Interpatient analgesic variability precludes use of a single calculation for estimating dosing requirements – dosing should be titrated to effect.
Remifentanil	Remifentanil peripheral V_{dss}, inter-departmental clearance lower in morbidly obese patients than for patients than patients with normal weight.	Remifentanil should be dosed using IBW.
Sedatives		
Benzodiazepines		
Diazepam	V_{dss} higher than expected even when corrected for TBW. Clearance greater but not when corrected for TBW. Terminal elimination half-life increased.	Suggestion of using TBW for single i.v. doses and IBW for maintenance doses, based on pharmacological data, but also the suggestion that it may be more clinically prudent to titrate to effect.
Midazolam	V_{dss} higher than expected even when corrected for TBW. Clearance unchanged unless corrected for TBW. Terminal elimination half-life increased.	
Propofol	Similar pharmacokinetics found in obese and normal weight individuals when corrected for TBW, but potentially severe hemodynamic consequences of large doses noted.	Conservative approach to dose based on IBW then use "mini-doses" to achieve desired clinical effect.
Neuromuscular blocking agents		
Rocuronium, Vecuronium	Onset time shorter and V_{dss} and clearance slightly (but not significantly) smaller in the obese.	Dose based on IBW.
Atracurium	V_{dss} and clearance not different when corrected for IBW, but some evidence that higher serum concentrations were needed for same effect.	Loading dose based on ABW is suggested, with maintenance doses based on clinical correlation (nerve stimulation, etc.).
Cardiac agents		
Amiodarone	Amiodarone very lipophilic but has wide interpatient variability in effect.	Use commonly recommended dosing regimens.
Digoxin	Absolute V_{dss} similar for morbidly obese and lean individuals, but no correlation with IBW found, so digoxin was felt to distribute into IBW.	Dosing should be based on IBW.
Lidocaine	V_{dss} not different when corrected for TBW.	Dose based on TBW.
Procainamide	V_{dss} different when corrected for TBW, but not when corrected for IBW.	Dose based on IBW.
Propranolol; labetalol	Does not distribute into adipose tissue, despite lipophilic nature. V_{dss} not different when corrected for IBW.	Dose based on IBW.
Verapamil	V_{dss} proportional to TBW, but clearance decreased, higher serum concentrations needed for same effect.	Loading dose may be higher, but not quite based on TBW; a loading dose based on ABW is suggested. Maintenance doses should be the same as normal weight individuals.

From: Ref [83].

yielded higher blood atracurium levels in obese patients than in normal weight individuals, but the duration and intensity of effect were similar, leading the authors to suggest a decreased sensitivity to the drug.

Plasma protein binding is also important in pharmacokinetics, and the two major blood proteins that bind drug behave differently in obese patients. Drugs primarily bound by albumin (such as thiopental and phenytoin) show no significant changes with obesity,[74] while drugs bound to alpha$_1$-acid glycoprotein (AAG), which binds primarily basic drugs, show decreases in serum concentrations. This may be due to increased AAG concentrations in the morbidly obese,[76,77] or it may be due to changes in the affinity of the binding protein.[78] Clearance of drugs can also be affected by obesity, but this may be related more to changes in V_{dss} than to changes in half-life. The effects of obesity on drug metabolism are unclear. It is well established that obese patients develop hepatic steatosis.[79] It was previously thought that hepatic oxidative metabolism is not different from normal weight individuals,[80] but cytochrome P450 activity was shown to be increased in another study,[81] so the effect is far from clear. Other processes, such as glucuronidation and sulfonation have been shown to increase in obese individuals. This has important implications because benzodiazepines, commonly used in anesthesia, are cleared by glucuronidation, and the clearance of oxazepam and lorazepam has been shown to be significantly increased by obesity.[82] It seems that glucuronidation is enhanced a lot more than sulfonation.

All these lead to the confusion over drug dosing. A main concern is what weight to use when calculating dosing – some have proposed using ideal body weight (IBW), some actual body weight (ABW), some an adjusted body weight of IBW plus 40% of the difference between ABW and IBW. Some have even used body surface area. A comprehensive review of dosing parenteral medications in the morbidly obese goes into much more detail than is possible here.[83] The summary of the findings of the review is presented in table format (Table 2.2). What is clear is that drug pharmacology is changed in morbidly obese individuals, and dosing and administration must be more carefully titrated.

2.7 Intra-operative considerations: anesthetic techniques

The decision on choice of anesthetic technique has to take into account the pharmacological principals discussed above. Use of short-acting, more easily titratable medications over longer-acting ones may overcome the pharmacological differences between morbidly obese patients and leaner ones, and may minimize the increased risks of aspiration pneumonitis, hemodynamic instability, and delay in recovery (see also Chapter 23).[84] With patients having increased risk of OSA, the use of remifentanil allows deep enough anesthesia to blunt intra-operative catecholamine response but ensures that there will be no residual effect of narcotics post-operatively (see Chapter 16). Among inhalational anesthetics, the rapid elimination and analgesic qualities of nitrous oxide make it an ideal adjunct to intravenous (i.v.) medications in the morbidly obese patient, but the increased inspired oxygen concentration usually required in these patients and its low potency limit its ability to be used.

The choice of volatile anesthetic involves multiple factors (see Chapter 22). Isoflurane clearly has a cost advantage over the desflurane and sevoflurane, but it has a longer washout period and produces slower awakening than the other two.[85–87] Desflurane has partition coefficients that allow for faster washout and elimination than sevoflurane, and it is apparent that even with use of bispectral index (BIS)-guided administration desflurane produces a faster awakening. Sevoflurane may, however, be preferred because it causes less tachycardia than desflurane and this may be critical in taking care of a patient with co-existing cardiac disease.[88] Ultimately, the choice of inhalational anesthetic agent comes down to the importance of having an easier way to awaken patient (for a patient with OSA or a difficult airway) or better heart rate control (for the patient with cardiac disease).

2.8 Intra-operative considerations: positioning and padding

Positioning morbidly obese patients on operating tables can be problematic (see Chapter 20). Patients frequently are much wider than the table, and, positioning an arm at the side may be difficult. When patients are supine, their shoulders frequently are far enough above the table and arm boards to that the arms may not lay on the arm boards without discomfort; fastening them to the arm board under tension may place the brachial plexus under tension as well.[89] To prevent this, extra padding may need to be placed on top of the arm boards. Patients with BMI $\geqslant$ 38 kg/m^2 have a much higher incidence of ulnar neuropathy than other patients.[90] OR tables, both powered and manual, have weight limits, and those limits need to be known because overloading a table can lead to breakage. If

patients > 150 kg are common it would be advantageous to have a powered table that is specially made for patients as heavy as 400 kg. Operations on the super-obese (300+ kg) may require two tables placed side by side. Standard straps may not reach around a patient, and since these patients may be more prone to falling or sliding off the OR table, care must be taken to make sure that the straps are long enough and strong enough to secure the patient to the table.

Obese patients are more at risk for pressure-related injuries in the OR than other patients. Proper padding of the buttocks and back is necessary to prevent the potentially fatal complication of a gluteal compartment syndrome leading to rhabdomyolysis and renal failure.[91] Patients on the table for longer than 4 h are at risk for developing this syndrome, and it appears that use of additional padding for these cases, as well as using mannitol diuresis and aggressive hydration for patients whose creatinine phosphokinase (CPK) levels raise above 5000 mg/dl may be helpful in improving patient outcome.

2.9 Intra-operative considerations: laparoscopy and pneumoperitoneum

Abdominal operative procedures are increasingly being done via the laparoscopic approach in all patients, including morbidly obese patients (see Chapter 7). While laparoscopic procedures are associated with reduced morbidity and hospital stay, both the pneumoperitoneum that is induced during the procedure, the systemic absorption of CO_2 and positioning during the laparoscopy all can have negative sequelae. Morbidly obese patients have decreased static respiratory system compliance, and increased respiratory resistance at baseline and have larger deviation from baseline with pneumoperitoneum than patients with normal body weight.[92] Body position, however, whether it was Trendelenberg or reverse Trendelenberg, did not have a large effect on the same measurements. Oxygenation was adversely affected only by increased body weight, and not by the pneumoperitoneum or the positional changes. A later study confirming these changes, also pointed out that the oxygenation was not improved by increasing tidal volume or respiratory rate, two common changes made to increase oxygenation during laparoscopy.[93] These two studies point out that commonly performed maneuvers to improve oxygenation during laparoscopy may not be effective, although the authors did not test the effects of increasing positive end-expiratory pressure (PEEP). In lean individuals, however, an alveolar recruitment strategy of ventilating the patient to an airway pressure of 40 cmH_2O for 10 breaths over 1 min, followed by mechanical ventilation with standardized settings plus 5 cmH_2O PEEP increased PaO_2 in the post-insufflation period.

The hemodynamic effects of pneumoperitoneum well described[94] – insufflation causes a decrease in cardiac index and an increase in systemic vascular resistance (SVR) and mean arterial blood pressure, but, over the next few minutes there is a partial improvement in cardiac index and SVR but no change in blood pressure and heart rate. This is caused by an interaction between raised intra-abdominal pressure, absorbed CO_2, and neurohumoral responses. The changes are short lived and may be totally back to baseline 10 min after insufflation.[95] In laparoscopic gastric bypass, the changes may have little clinical significance.[96] The recent development of gasless techniques to obtain visualization of the abdominal viscera results in no difference in hemodynamic parameters.[97] While the acute hemodynamic effects need to be guarded against, they may not have the significance usually thought.

2.10 Post-operative considerations: pain management

Pain management in the post-operative period for morbidly obese patients is of major concern to anesthesiologists (see Chapters 25 and 29). The concern starts in the pre-operative period, where planning for surgery includes, in a large part, planning for post-operative analgesia. The major reason for the concern is mainly the association of obesity and sleep apnea, as set forth above, and the concern that narcotic analgesics in doses sufficient to provide the necessary amount of analgesia will also cause significant respiratory depression, intermittent airway obstruction and desaturations. For that reason, regional analgesic techniques are frequently employed because they are felt to cause less respiratory depression and cause less post-operative ileus.[98] But for gastric bypass, there may be technical difficulties in placing catheters or needles for central neuraxial analgesia, plus morbidly obese patients may not tolerate even the slightest amount of motor blockade, which may not allow them to move out of bed and walk around. In patients undergoing open gastric bypass, i.v. PCA compared to epidural analgesia had similar quality of pain control, the time to ambulation, frequency of nausea, incidence of pruritus, duration of post-operative ileus, and length of hospital stay.[99] In fact, patients receiving epidural analgesia had a greater risk of wound infection than

subjects with PCA. In view of these studies, central neuraxial analgesia loses most of the advantages it may have held over parenteral narcotic techniques. The shift towards laparoscopy gastric bypass also makes central neuraxial analgesia less attractive, since it is less painful and more easily managed with infiltration of the wounds with local anesthetic and parenteral opioid narcotics.

2.11 Practical considerations dealing with the morbidly obese: equipment

We have already discussed the special tables that may be required for the patient in the OR. There are other pieces of equipment that are helpful as well. The OR table is not the only thing that needs to have a higher weight limit. Post-operatively, the bed also may need to have a higher weight limit, or the bed may not change position and the head of the bed may not go into a position that is the best are for pulmonary toilette. Many specialty beds are designed for morbidly obese patients, with capacities of 850 lb and more. These specialty beds, such as those manufactured by KCI (Kinetic Concepts, Inc., San Antonio, TX, USA) offer the additional advantages of being able to go from a flat position to a chair position to allow the patient to be able to walk right out of the bed without having to swing the legs over the side, ideal for a patient with an abdominal incision. Some models of the bed have weight limits up to 1000 lb, and others have built-in percussors for chest physiotherapy, and others have special mattresses to lessen the chance of development of pressure ulcers. Use of these beds is essential for the bed-bound morbidly obese.

There are other, less expensive but no less important items that are needed. Blood pressure cuffs may be very difficult to fit properly. Usual sized cuffs are too small, larger cuffs ("thigh" cuffs) are usually too wide and extend down past the antecubial fossa on most patients. Also, morbidly obese patients many times have conical-shaped upper arms that are difficult to keep a blood pressure cuff in place on. A blood pressure cuff in the shape of a half moon is available that will overcome this conical shape to the upper arm. Alternatively, a regular sized cuff can be reversed and placed between the wrist and the elbow, and will be much more accurate than an improperly fitting upper arm cuff.

Another vital set of equipment to have is that needed to perform laryngoscopy. The decreased neck extension these patients have because of the posterior cervical fat pad and adipose tissue on the chest wall (and breast tissue in female patients) can make the simple placing of a laryngoscope into the mouth difficult. Two types of aids for this exist: *short laryngoscope handles*, half the size of normal ones, can help; the other item is *laryngoscope blades* that are angled at the flange so that they can fit into the mouth yet still be used normally.

2.12 Conclusion

The anesthetic care of the morbidly obese patient can be challenging, but with the proper knowledge of the considerations of their care, along with proper planning and preparation, these patients can be safely taken care of in the peri-operative period.

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INFORMED CONSENT IN BARIATRIC SURGERY AND ANESTHESIA

3

G.S.M. Cowan Jr.

3.1 Abstract

Informed consent is mistakenly regarded by some as merely the witnessed signature of a patient that gives his/her consent for a given procedure(s). It means far more than that. This chapter will address informed consent in detail, particularly as regards bariatric surgery and associated anesthesia.

3.2 Introduction

Informed consent is a process mandated by law and ethics whereby the patient has the right to direct his/her health care and the physician has the duty to educate the patient concerning this care. It starts when the potential surgical patient first learns about bariatric surgery and extends through the time of the surgery. The key part of this process is the patient's learning enough about the proposed procedure(s) to make an informed decision of whether to undergo the surgery or not. Additionally, the patient's relationship with the surgeon and staff needs to be sufficiently open that they may successfully complete the necessary elements of the informed consent process. Signing the informed consent document is only a step that indicates that the informed consent process has occurred.

Decades ago when paternalism was dominant in the American practice of medicine, informed consent was ignored as neither appropriate for academic discussion nor a matter of practical concern.[1] There are cultures elsewhere in the world that are currently in a similar transition.[2–4]

Today's increasingly complex and litiginous medical practice has dramatically changed that state of affairs in the Western world. Informed consent requirements challenge the surgeon, including the bariatric

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surgeon, to be a competent communicator of relevant, correct, and useful information conveyed in easily comprehensible layperson's terms.[5]

3.3 The process

The process of obtaining informed consent is not standardized; no two surgeons' process is necessarily identical. However, the process that surgeons and their staff employ must meet the elemental requirements of informed consent.[6]

They are that the patient:

- **a** receives adequate, relevant information, including recommended surgical choice(s), via the surgeon and his/her support staff;
- **b** understands this information;
- **c** provides consent, usually by means of a document;
- **d** is competent;
- **e** has a chance to ask questions and receive answers acceptable to him/her;
- **f** actively, autonomously and knowledgeably participates in the decision-making process.

This process requires a considerable investment of time spent in patient education. The educational format may include one-on-one interview with the surgeon, seminar/lecture presentation by surgeon and/or staff, augmented with various mixtures of videotape(s), audiotape(s), books, pamphlets, brochures and other written material. To demonstrate the value of ancillary materials, a study of physician discussions plus or minus videotape presentations showed that addition of videotape produced more correct answers to content questions than discussion alone.[7]

The surgeon may also delegate portions of the educational tasks to hospital or office staff who assist with patient education and answering patients' questions as well as certain approved ancillary materials.[8,9]

3.3.1 Adequate relevant information

The medical center's role in the consent process is limited to credentialing and verifying that the physician has obtained the patient's informed consent before the physician performs the procedure.

The disclosure of adequate, relevant and significant information to patients begins with surgical and support personnel who have a good, working knowledge of bariatric surgery in all of its related areas, past and present. This professional team is expected to be involved in active bariatric surgical practice, regularly read journals, maintain membership or liaison with accepted bariatric surgery organizations and attend their meetings. Thus informed, they are obligated to disclose their knowledge and experience to their patients. This involves information that a reasonable person with the patient's morbid obesity and co-morbidities would regard as significant when deciding to accept or decline bariatric surgery.

Based upon the team's training, experience and knowledge, they provide quality patient education. Patients have different comprehension abilities but all will benefit from clear-minded presentations, couched in lay language that clearly present the necessary information to them. This will include education concerning the options, risks, benefits, possible complications and implications of their proposed bariatric, and any other, surgery.

Options

Most patients have worked with, and failed, many voluntary weight loss modalities. Their weight loss history requires review, documentation and consideration as to why they may or may not be continued with or without surgery. Many primary bariatric surgical options also exist as alternatives and they need to be reviewed with patients. Ancillary procedures may also be fully described and concurrently offered such as ventral herniorrhapy, cholecystectomy, wedge liver biopsy, gastrostomy, jejunostomy, hiatal herniorrhaphy, vagotomy, tubal ligation and other possibilities. It is wise to have the patient consent to performance of "any other procedure(s) as may be necessary in the surgeon's judgment" since unforeseen findings may, understandably, cause the surgeon to alter the original plan(s).

Risks

Patients need to learn the same information that any reasonable layperson would consider necessary in order to decide whether or not to proceed with the bariatric surgery. This relies on judgment not to alarm the patient unnecessarily while still providing full and honest risk disclosure. Many surgeons use the literature to disclose all but the rarest of possibilities. This includes gastric leak, pulmonary embolus, or hemorrhage, each with a "worst case scenario". If the worst possible outcome, such as emergency re-operation, ventilator in an intensive care unit (ICU) for days or death, is disclosed to the patient, he/she cannot later successfully claim that he/she would not have proceeded with the surgery when faced with some lesser problem.

Additionally, patients are wisely informed that the risk of death ranges from less than 0.5% to well over 1% depending upon the patient's body mass index

(BMI), age, medical status and other variables including proposed procedure(s), surgeon's experience in this and other procedures, numbers of procedures performed per year, the hospital, as well as other variables, some indefinable.

The three most common causes of death, in order of usual frequency, include pulmonary embolism, leak and hemorrhage. Wherever reasonable, local experience is a risk component that may be constructively presented to the patient.

Additionally, the risks of not having bariatric surgery may be substantial and, where such exists, as is the case with many morbidly obese persons, are important to be addressed. It is important to remember that solely reciting risk statistics may have little relevance to patients. For example, risks can be stated more clearly in terms of "one person in 200" than the more arcane 0.5% statistic.

Complications

A good general rule of thumb is to inform the patient of common complications even ones that are not serious and of very serious complications even when they are not common. The chance of complications occurring generally ranges from $<5\%$ to $>20\%$. They number over 100 and range from the relatively small to those of a highly serious, or material, nature. However, while it is impractical to educate the patient in all of these, the material complications, even infrequent ones, are important to the patient. This is particularly the case with sufficiently severe complications that may cause the patient to reject the surgery; they ordinarily need to be made known to him/her. They are covered elsewhere in this book. Those possible complications that are unknown at the time of patient education, such as may arise years hence, are immaterial and it is not reasonable to expect the surgeon to be aware of them.

Benefits

Many patients meet realistic weight-loss goals that result in the "cure" or amelioration of their morbid obesity co-morbidities. The statistics of the benefits derived through bariatric surgery are impressive and usually present a very strong risk-to-benefit ratio. However, there is no guarantee, express or implied, that this will be the case or that the patient may realistically lose even a single pound or derive any medical, physical, economic or psychosocial benefit from bariatric surgery. It is wise to stress this possibility to the patient and avoid counseling with terms such as "everyone does well" or "my patients all do well". These latter claims do not comport with general experience.

Implications

Some patients approach the surgery as "magic" and they need to be disabused of this fantasy. Otherwise, they may not properly anticipate or understand the post-operative realities when they occur. These include the likelihood of post-operative pain, nausea, vomiting, diarrhea, catheters and other tubes, and taste changes. Also, they must learn that the need to eat small food portions, chewed well and eaten slowly, are well-known, expected, limitations or consequences that may arise from bariatric surgery itself. They are not necessarily complications at all but, rather, implications of most bariatric procedures.

For instance, we teach patients about "feedback", which occurs when their "feed goes down" and then their "feed comes back". This usually means that they are eating too much, too fast, not chewing adequately, not waiting sufficient time between mouthfuls, ingesting the "wrong" food that does not agree with them or mixing liquids with solids. Their take-home lesson from "feedback" is that *they* are likely doing something wrong to cause their problem, not the surgery. In fact, the surgery is designed to produce certain consequences of their non-compliance such as feedback in order to help induce the massive weight loss that usually follows the surgery. It is also wise to address some of the fundamental psychosocial changes that may occur due to the increased energy and cosmetic effects that are often associated with massive weight loss.

3.3.2 Patient understanding

This is a difficult area. Even well-educated patients may claim that they did not understand the material as presented. Therefore, we have developed certain time-tested (>15 years use without material change or successful legal challenge) written true–false bariatric surgical examinations that we present in the appendix of this chapter so that the patient, in his/her own hand, demonstrates understanding of material issues.

3.3.3 Patient consent

Most patient informed consent sheet(s) vary in content between hospitals, even within the same geographic area. They usually constitute technical, impersonal, paragraphs of medical information that are not completely comprehensible to the average layperson. There is usually a place for entering the operative procedure(s), surgeon(s) and any limitation(s) that the patient wishes to stipulate. Somewhere, usually at the bottom, is a place for the patient's (or surrogate's) and a witness's signatures, dated and timed.

In addition to the surgical consent forms, patients often have to sign special consent forms upon entering the hospital relative to its environment and personnel, receiving blood, having certain studies performed, accepting or denying advance directives, etc.; these seem to be in ever-increasing number and inevitable bureaucratic product.

However, *we are aware of certain hospitals whose medical staff by-laws and directives do not require any written informed consent between surgeon and patient. While, in a sense, this appears to be a relief, it potentially places the surgeon and staff at risk for claims of inadequate, or absent, informed consent. This is particularly true when the surgeon, understandably, lacks independent recall of the informed consent process in the face of litigation years later*.

At the time of completion of the "informed consent" process, we strongly recommend that the surgeon write something into the progress notes, or on the informed consent form, similar to this text: "We have thoroughly reviewed the procedures, options, possible complications, risks, benefits and implications of the proposed surgery. The patient completely accepts all of same without any reservation(s) and has had opportunity to ask questions and receive answers". This provides additional documentation so that, should a complication later develop, wherein no record of receiving the surgeon's informed consent exists, the surgeon lacks independent recall, and the patient denies receiving or understanding it, a record indeed exists that this counseling did, in fact, take place.

Also, patient reading of the "fact sheets" and completion of the applicable patient examination(s) in the appendix will provide additional evidence that the patient was not only instructed concerning primary and re-operative bariatric surgery but that this information was sufficiently understood by that individual to enable a perfect score (at least on the second re-examination if needed) to be achieved.[10]

The examination also goes a long way to fulfill the so-called "layman's standard". This standard, a legal requirement in many states, requires that the surgeon must disclose what any reasonable person would have been expected to disclose. It derives from the 1972 case, *Canterbury vs. Spence*.[11]

Given the evolving nature of informed consent law, it seems wise to also incorporate the earlier professional standard of disclosure. It requires the physician to disclose information that other physicians disclose as standard in the individual's community or an equivalent location.

Legal precedent or legislation exists in most American states that determine the necessary standard for informed consent. The question then comes down to just how much information is enough. We must simultaneously meet both our professional obligation to provide the best care and also respect the patient who has legal control over his/her own final health care decisions. However, in order to provide sufficient information, the surgeon or staff may cause undue patient anxiety or result in possibly "bad" choices on the patient's part. Therefore, the question reduces to whether we inflict significant harm on patients by stressing them with detailed surgery and anesthesia risk information.

The term "therapeutic privilege" arises from concerns addressing this question. It is a concept which has been used to limit discussion with patients concerning the details of the risks they may take with surgery and anesthesia. However, research of patient anxiety in response to receipt of detailed vs. non-detailed risk information has not shown significant differences in anxiety levels between groups. Therefore, it is reasonable to provide detailed, even-handed, fully-informed, discussion of patient risks with bariatric surgery and anesthesia.

3.3.4 Patient competency

Most bariatric surgery candidates are unequivocally competent.[12]

However, we have found that about 15% are not acceptable as candidates from a psychological standpoint. Hence, careful pre-operative psychological screening of potential bariatric surgery patients is wise.

Another concern is the effect of medication on patients' ability to provide valid informed consent to bariatric surgery or anesthesia. That is, when patients receive pre-operative sedative "shots," and are then seen by anesthesia and the surgeon prior to surgery, are they sufficiently affected by the medication to invalidate their ability to provide informed consent? This is a common occurrence and, therefore, it is also common to withhold these medications pre-operatively in anticipation of the need to obtain consent free of these medications. However, the premedication is often valuable in relieving bariatric surgery patient anxiety and stress. The relief from such emotional distress may, in fact, improve the patient's decision-making ability and allow her/him to more clearly focus on the choices necessary to complete the informed consent process. In fact, the withholding of premedication solely for consent purposes may be considered, itself, as a coercive act. However, if the patient cannot listen, understand or focus on his/her situation together

with the options, risks, benefits, and possible complications of surgery and anesthesia, then the patient is, for this brief period of time, incompetent to complete the process. *Therefore, where sedative premedication is employed, the presence or absence of this state is wisely documented by the anesthesia person(s) and surgeon. It essentially provides proof that the patient's ability to provide informed consent has not been significantly affected by the premedication(s) as demonstrated by the patient having the capacity to understand the surgical and anesthesia options, risks, possible complications and implications and can clearly relate his/her choice to proceed. It also demonstrates that the patient has not been coerced into consenting to surgery and anesthesia but, rather, has exercised his/her patient autonomy.*

3.3.5 Patient questions

Patients must be provided an opportunity to ask questions and time to receive answers that are acceptable to them. With today's Internet-educated patients, this sometimes may appear somewhat redundant but patients must be accommodated in order to fulfill this informed consent element. It is also wise to encourage questions and remind the patient of the old adage "the only stupid question is the one you did not ask". Thereby, the patient understands that none of his/her questions will be regarded as foolish or stupid and that the surgeon and staff accept any limited ability on the part of the patient to articulate questions.

While a non-physician may have the patient review and sign the informed consent document, this act does not absolve the surgeon and anesthesia person from direct, personal interaction with the patient.

The surgeon and anesthesia person must make her/himself available, at some time prior to surgery or anesthesia, to fulfill any lacking informed consent elements including answering patient questions concerning medical information.

Nurses or technicians can answer questions such as "How long does surgery usually last?" It is not their responsibility to answer questions such as "Will I need to be on a breathing machine after my surgery?" or "Are you also going to take out my gallbladder?" A signed "informed consent form" cannot explain why these may or may not occur. *Therefore, it is important that the surgeon and anesthesia person have face-to-face time with the patient at some time prior to surgery to allay these concerns.*

This is not meant to imply that videotapes, audiotapes, brochures, pamphlets or books written or approved by the surgeon or anesthesia person cannot be provided to the patient in advance. If well done, these enduring materials can often answer all of the patient's questions, and then some. However, each patient must be given the opportunity to ask, and time to receive, acceptable answers to his/her questions and concerns from the surgeon and the anesthesia person.

3.3.6 Patient autonomy

Some patients may feel powerless. To encourage voluntariness, the surgeon and anesthesia person can make clear to the patient that she/he is participating in a decision and not merely signing a form. In effect, they are encouraging and inviting her/him to participate in her/his health care decisions. In doing so, the surgeon and anesthesia person wisely inform the patient that they are obligated to provide a recommendation and share his/her reasoning process with the patient.

Patients' decisions concerning these recommendations must be completely voluntary on their part. Coercion or undue influence by others, including those responsible for their medical/surgical care, is, therefore, unacceptable as is manipulation which is ethically questionable. Persuasion, however, involves the delivery of a set of rational possibilities, together with the logical basis for each choice. As long as the patient is provided a clear, unimpeded, choice from among these possibilities, persuasion is acceptable. In fact, in many instances, it may be desirable since the patient's surgeon and anesthesia person are employing their expertise in presenting a fair, respectful and forthright presentation of options from which the patient has the right, and expectation, to choose.[13]

In contradistinction, some patients may try to avoid making decisions. They may utter words like, "You decide the procedure for me, you're the doctor" or "I don't want to know all about the gory stuff; I'm willing to take my chances". The surgeon and staff must insist on the patient not relinquishing autonomy. It is important that the patient be involved in the entire corpus of material information required for informed consent, particularly where he/she will have to live with the consequences of bariatric surgery.

In fact, the chronicity of morbid obesity, the electiveness of the surgery, the average patient age in the mid- to upper-30s, and rare incidence of patient incompetence, allow the potential for as near to ideal circumstances for patients to satisfactorily complete the informed consent process prior to bariatric surgery and anesthesia with the requisite autonomy.

The importance of education in obtaining properly informed consent contrasts strongly with obtaining a lower level basic consent. Basic consent involves informing the patient what you would like to do and then

asking them their permission to do so. This is acceptable when, for example, blood is to be drawn. These types of decisions have a lesser educational mandate since the patient's local and national community has a consensus, and basic knowledge, that such activity is understood and generally acceptable.

3.4 Anesthesia informed consent issues

Anesthesia persons are no more equipped to discuss operative risk with patients than surgeons are able to discuss anesthesia risks and related information leading to informed consent. Therefore, throughout this Chapter, we have consistently mentioned the surgeon and the anesthesia person individually. The informed consent process requires that patients receive the best available information about procedures, options, risks and other informed consent information and, obviously, this arises from each of these respective specialists.

Most informed consent documents contain a phrase, or mention, consent for anesthesia care, such as:

> "I hereby consent to the anesthesia service checked above and authorize it to be administered by _____ or his/her associates, all of whom have proper credentials for anesthesia services at this health facility. I also consent to an alternative type of anesthesia, if necessary, as may be deemed appropriate by them. I expressly request that the following considerations be observed (or write "none") _____.

However, the informed consent process requires that the anesthesia person conduct separate discussion of anesthesia risks with the patient.

Informed consent for anesthesia has been studied in many settings. Generalizing them, it has been found that some patients, particularly the elderly, requested a lesser preference for education about possible complications or similar unpleasanties. Many studies in anesthesia have also documented the extent of how poorly informed patients are about medical procedures and how little they recall they have of the educational information provided to them. All studies reported that patients gave the highest priority to actually meeting with the anesthesia person prior to surgery together with high-priority concerns about post-operative eating and drinking.[14,15]

In contrast to the informed consent process for bariatric surgery, informed consent for anesthesia is often obtained just minutes before surgery during which time the anesthesiologist and patient have their very first meeting.

A separate anesthesia informed consent form is standard in most institutions. However, a collection of what appears to be some useful key wording concepts commonly appear, not in any particular or specific order, viz.:

> The anesthesia person(s) _____ has/have reviewed the proposed anesthetic with me and answered my questions in this regard.
>
> I understand that anesthesia involves additional risks and hazards but I request the use of anesthetics for the relief and protection from pain during the planned and any possible additional procedure(s).
>
> I realize the anesthesia may have to be changed possibly without explanation to me.
>
> I understand that certain complications may result from the use of any anesthesia technique.
>
> I consent to the administration of anesthesia and to the use of such anesthetics as may be deemed advisable by my physician/anesthesiologist. In addition, the alternatives, risks, and benefits and possible complications of the planned anesthesia including breathing problems, paralysis, brain or other nerve damage, drug reaction, or even death have been explained to me. Other risks and possible complications that may result from the use of general anesthesia range from minor discomfort to injury to my teeth, vocal cords, or eyes.
>
> I understand that I may have nausea and vomiting after surgery as these are among the known side effects of anesthesia for 24–48 h following general anesthesia and surgery.
>
> Following anesthesia for obesity surgery, I may have a sore throat for a few days.
>
> Rarely, dental injuries may occur while putting the breathing tube in place or while I am waking up due to my biting down on a tooth that is fragile, causing it crack or break. This is not necessarily related to anything that the anesthesia person has done.
>
> Patients with apparently similar medical conditions to mine may have varying responses to certain anesthetics or procedures.
>
> General anesthesia involves some risks and no guarantees or promises can be made concerning the results of my procedure or treatment. Possible specific risks include, but are not limited to, allergic or drug reactions. These include infection, pneumonia, inflammation of the veins, blood clots, a blood clot going to my lungs, nerve injury or paralysis leading to loss of sensation or limb function, stroke, damage to or failure of the heart (including heart attack), liver, kidneys and/or brain and death. These more severe complications are highly unlikely but can occur in some cases, regardless of the experience, care and skill of the anesthesia provider.
>
> Previous drug or alcohol abuse may damage my vital organs such as the heart, liver, or kidneys. This could have an effect on my ability to tolerate the anesthesia. Therefore, withholding medical information, including such fact(s) that could lead to complications or problems

that may have been prevented if that information were known prior to my surgery, may cause harm to me.

Bariatric surgical anesthesia is a team effort that includes the surgeon(s) and an anesthesia person(s), a physician anesthesiologist or certified registered nurse anesthetist (CRNA) who administer the general, and possibly other, anesthesia.

Somewhere on the anesthesia informed consent form, the following warning may appear:

DO NOT SIGN THIS FORM WITHOUT READING AND UNDERSTANDING ITS CONTENTS.

3.5 The anesthesia person's informed consent evaluation duties

The anesthesia person's name must be provided to the patient. She/he evaluates the patient and the medical record prior to surgery. This includes examination, at the very least, of the patient's heart, lungs, neck size and consideration for possible airway problems. Patient medications and allergies are also evaluated to eliminate any possible conflict between the proposed anesthetic or other medications to be used. This process is usually facilitated by the surgeon's prior history and physical examination plus radiological, psychological, laboratory and other possible work-up, including specialist consultation.

The anesthesia person also must confirm that the patient has been fully informed of the intended operative and anesthesia procedures and personally indicates that she/he understands the risks and possible complications that are associated with the administration of anesthesia. Since many patients' main concern is the operative procedure, they are likely unaware that the anesthesia person's work as part of this team extends into their peri-operative care. Therefore, the anesthesia person is wise to inform them of his/her role and responsibility in this regards as well as address issues and questions that relate to pain and discomfort after surgery and sedation. It is also wise to document, time, date and sign that each of the above took place and when.

3.6 Some risk management consent issues

Teaching institutions usually insist that the patient consent to any personnel allowed to observe or otherwise act by the surgeon, including students and business personnel who may be under the direct supervision, responsibility and control of the surgeon. This is necessary since there have been lawsuits for involvement of students or other personnel in surgery of whom the patient was not aware and the patient did not give prior general permission for them to be present at, or active in, his/her surgery.

Another institutional concern is confidentiality which has been considerably heightened since implementation of Health Insurance Portability and Accountability Act (HIPPAA) regulations. Essentially, the surgeon, anesthesia person, hospital and others are responsible to assure that the medical records, and events that may occur, are kept completely confidential and not provided to others than are officially permitted access by hospital regulation or law which may include licensing, accrediting, and/or regulatory agencies. Outside of this group of individuals, any information that is disclosed, such as statistics, must be only in non-individually identifiable form. The issues are too detailed to discuss further in this chapter, and are readily available elsewhere.

Informed consent is necessary since the patient involved does not give up the right to control what is done with his/her body, particularly during the time he/she is most vulnerable and unaware, namely under anesthesia or medication. The physician, therefore, has both an ethical and a legal duty to obtain the patient's informed consent, or that of the patient's legal representative, to bariatric surgery, anesthesia and any other relevant medical/surgical treatment or procedure(s). Failure to obtain the patient's consent in accordance with the applicable legal standards in the institution's legal jurisdiction, may result in a charge of negligence, battery, or unprofessional conduct.

Ethical conduct in human research in anesthesia includes approval by an institutional review board (IRB) or ethics committee and informed consent. Smaller, or rural institutions, or those located in third world countries, may not have established, or obtained familiarity with these requirements to have implemented them. Evidence of these is even sometimes lacking in journal publications. Suggestions have been made that clearer guidelines (and author adherence) for all types of publication are needed, both as a protection for research subjects and to maintain public trust in the process.[16]

Studies repeatedly have shown that clinical research subjects have trouble appreciating the implications for their clinical care while they are participating in a clinical trial. When this failure is based on a lack of appreciation of the impact on individualized clinical care of elements of the research design, it has been called the "therapeutic misconception". Failure to distinguish the consequences of research participation from receiving ordinary treatment may seriously undermine the informed consent of research subjects.

The results of this research suggest that subjects often sign consents to participate in clinical trials with only the most modest appreciation of the risks and disadvantages of participation.[17]

3.7 Re-operative obesity surgery informed consent

Re-operative obesity surgery can be extremely complex, relatively straightforward and sometimes surprising. The surgery is required due to complications having occurred as a result of problems with the surgery or poor patient compliance.

We recommend that the anesthesia person, surgeon and team follow the same basic informed consent process as has been described in this Chapter for primary bariatric surgery. This includes having the patient take the 20 Question True–False Examination in the type of bariatric surgery that the surgeon plans to produce with his/her re-operation. For example, where re-operative conversion of vertical banded to gastric bypass was planned, the patient would take the examination in Appendix A as well as the supplemental re-operative bariatric surgery examination in Appendix F after being given sufficient time to read and sign the re-operative bariatric surgery fact sheet. It is not necessary for the patient to read the fact sheet for primary bariatric surgery since the two are very similar and cover much of the same information.

As what we consider an important strategy of the informed consent counseling, we ask each patient whether at least a 50% improvement of their problems would be satisfactory. They almost invariably agree with this realistic goal which is usually surpassable. As a result, the re-operative surgeon is not held by the patient to a 100% "cure" or all of their problems and complaints which is not realistic in many instances.

3.8 The patient informed consent examinations

The Appendices at the end of this chapter contain two fact sheets and four examinations. Appendices B, C and D cover the currently performed primary bariatric surgery procedures while Appendix F provides a re-operative examination.

Each patient is first requested to read a review of previously taught information prior to taking the informed consent examination. Patients having a primary bariatric surgical procedure will be given the fact sheet in Appendix A; re-operative bariatric surgery patients will be given the fact sheet in Appendix E. A nurse ordinarily witnesses and signs the examination document, checks for any incorrect answers, and reviews these with the patient. Following this, the patient re-answers the incorrect answers, initialing each corrected answer. The nurse, or other team member, then records the results of the examinations in the patient's chart.

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Appendices

Appendix A: Fact sheet–record of receiving facts about obesity surgery

Obesity surgery is done for carefully defined reasons on morbidly obese individuals. Many operative procedures are available for morbidly obese individuals including stomach stapling (gastroplasty), placing a band around the upper stomach (inflatable and non-inflatable gastric band), stomach bypass (gastric bypass Roux-en-Y), etc. Other options include not having bariatric surgery but, instead, continuing to try to lose weight by dieting and other non-surgical method(s).

While many patients have done quite well, no guarantee of any benefit deriving from this surgery exists. For each anticipated benefit, including "cured" diabetes mellitus, hypertension, or low back pain, failures have occurred.

Regardless of the bariatric surgeon's reputation and expertise, each patient is at risk for complication(s). No guarantees exist that a significant complication will not occur in any patient.

Usually the massive weight loss till 1 year following surgery will amount to approximately one-half or more of the patient's excess weight. While this happens with many patients, some patients do not lose much weight and other patients gain their weight back again. There is no guarantee that weight regain will not occur.

In order to obtain the benefits of a considerably lowered weight, the patient must change his/her lifestyle as the dietitian suggests by taking small meals regularly for life, do not eat snacks, have mostly diet drinks for daily liquid requirements, eat slowly and make positive eating and drinking habit changes.

Sooner or later, every surgeon will experience complications associated with bariatric surgery. This places all patients at risk for at least one complication. There are no guarantees that a significantly serious medical problem will not occur. Examples of these complications include the following:

Wound infection the body cavity or lungs (e.g. pneumonia) can occur.

Infection or inflammation of various organs may occur: stomach (gastritis, stomach ulcer), pancreas (pancreatitis), esophagus (with chest pain, retrosternal pain, etc.), liver (hepatitis), gallbladder (cholecystitis, gallstones), kidney (pyelonephritis, kidney failure), kidneys (kidney failure, nephritis, and pyelonephritis), bladder (cystitis), and duodenum (duodenal ulcer, duodenitis).

Spleen injury may occur and need to be removed. This can significantly increase infection risks throughout the body.

Heart, kidney, liver, lung and other organ failure has occurred following obesity surgery.

Blood clots can form in large veins the pelvis as well as in the legs or elsewhere. These clots can, at any time, break away and travel to the lungs. These may cause breathing difficulties, swelling, or death. The clots can also even cause permanent or transient ulceration or swelling of the organization.

Stomach or intestinal fluids may leak into the body cavity, other organs or the skin. They may continue to drain into a bag for a considerable period of time.

Food and taste preferences often change. Some patients have difficulties eating red meats, bread and rice for at least 6 months after their surgery. Certain cravings for some foods, such as sweets, may occur.

Liquids, purees, or food may not be able to pass through the stomach pouch, lower stomach or intestines, which may need stretching (dilating) by instruments or endoscopies (which have their own risk). Tubes for nourishment fluids may need to be placed into the veins, stomach, or intestines if the patient is unable to drink or eat enough by mouth. Re-operation may be necessary.

Diarrhea or vomiting can often occur after bariatric surgery and may make it a problem to eat certain types or amounts of food. This can be thought of, in a sense, as a benefit of this surgery since it prevents drinking or eating of certain food(s) for fear of vomiting or diarrhea.

Complications of anesthesia, psychiatric problems, such as depression requiring psychiatric care and possibly admission to a psychiatric facility, and even death, are all possible as a result of surgery. Across the US, approximately one in 200 patients dies after obesity surgery although this varies widely.

Persistent nausea, vomiting, heartburn, swelling of the abdomen, etc. may occur and can make the patient think seriously of having the operation undone in certain instances.

The stomach pouch or its outlet may get bigger or the staple-lines burst or give-way so that, in time, the patient can eat more at a mealtime and even gain back to the original, or greater, weight.

No patient should have obesity surgery performed who is not ready to accept the need for re-operation should it be needed. Breakdown of the surgical stitches, hernia, bleeding from the stomach or elsewhere may make it necessary to re-operate for these or other reasons. For example, about 2 to 3 per cent of patients will develop "locked bowels" or leakage which requires emergency surgery.

Admission to an intensive care unit may be needed to closely observe the patient or treat any problems that can result from surgery.

During the months and years following this surgery, any type of nutritional problem or infection may occur, including lack of vitamin(s), calories, minerals, protein, etc. Signs of this can include weakness, confusion, paralysis, rashes, low blood, hair loss, bone and joint problems, poor wound healing, tongue soreness, numbness, swollen legs, night blindness, etc. for life. The obesity surgery patient may need to have vitamin injections every month or so for life. Food may also stick in the stomach pouch and need to be taken out with a special tube or scope.

Following obesity surgery, it is necessary for life to take extra vitamins, protein and minerals and also to be followed by the obesity surgeon, or a physician well experienced in this area faithfully at least every year and sometimes more often.

The patient may lose more weight than desired, too little weight, or actually gain weight, at any time following surgery.

Following massive weight loss, the skin on the face, neck, arms, abdomen and elsewhere may become wrinkled, sag, droop, or hang in large folds. It may become quite annoying, embarrassing, or develop rashes or infections and odors. As a result, the patient may feel a need for further surgery. If this happens, the surgeon or colleague will be available to discuss this and any other matter.

As soon as any problem arises, medical help must be obtained quickly – the patient has the duty to call for help quickly, without delay, and not neglect him/herself.

Most of the types of obesity surgeries performed at present are still relatively new. Therefore, the long-term results of such surgery, including weight loss or possible complications, are not fully known at this time.

I have read the above, which has been described to me by my surgeon. I understand this material, the risks, benefits, possible complication, other choices and implications of obesity surgery, as well as the operation that my surgeon recommends for my case and why.

By signing this statement, I am showing that I have read and accept all of the above and that I understand it. I have been encouraged to ask any and all questions that I want; they have been well answered to my satisfaction and I understand the answers.

_____ _____

Signed (patient) Signed (person present)

Date: _____ Time: _____

Appendix B: Obesity surgery patient examination (gastroplasty and gastric band)

You are taking this examination to show your obesity surgeon that you understand the information that he/she and the other team members have discussed with you. Any incorrect answer(s) that you may make will lead her/him to review this area with you and re-test you until she/he is satisfied that you understand the material and concepts involved. Where you re-take the examination using this same sheet, please date and initial your change in each answer.

All questions are true/false. Please tick each answer that you choose as "True"/"False".

	True	False
1. There are other morbid obesity operations that I can have other than gastric banding or stomach stapling.	❒	❒
2. The stomach can *never* leak or result in infection or communication between the stomach and the skin after this surgery.	❒	❒
3. Sometimes obesity surgery patients get clots in the veins of their legs or pelvis. The clots can sometimes loosen and travel to the lungs, causing breathlessness and chest pain.	❒	❒
4. After obesity surgery, for life, the patient is able to drink or eat *anything* that he or she wants in any amount.	❒	❒
5. It is *guaranteed* that, following obesity surgery, the patient will permanently lose large amounts of weight and keep it off forever.	❒	❒
6. Knee and back pain, diabetes, high blood pressure and similar problems *always* get better after obesity surgery.	❒	❒
7. I could possibly need intensive care, long or short term, in hospital after obesity surgery.	❒	❒
8. Sometimes re-operation is needed due to bleeding, a hernia, blockage of the stomach or intestines and for other reasons.	❒	❒
9. I will need to make at least yearly physician visits, will have to follow strict eating rules and run the risk of re-operation for the rest of my life.	❒	❒
10. I will also need to take vitamin–mineral supplements and have nutritional examinations and laboratories drawn at least yearly for the rest of my life.	❒	❒
11. I will never again be able to swallow whole (uncrushed or unchewed) pills or tablets after this surgery.	❒	❒
12. Obesity surgery is *not* very serious or risky.	❒	❒
13. Obesity surgery patients can sometimes vomit a lot.	❒	❒
14. After I go home following surgery, I should *not* call my surgeon for at least 2 or 3 days after a problem starts.	❒	❒
15. No patient ever gets very dangerously depressed after obesity surgery.	❒	❒
16. For the first 24 h after obesity surgery patients are usually quite miserable or uncomfortable.	❒	❒
17. I am guaranteed to lose weight after this surgery.	❒	❒
18. It is absolutely necessary that I take prescribed vitamins for life following my surgery.	❒	❒
19. No one ever dies as a result of obesity surgery.	❒	❒
20. After this surgery, I will need to eat small bites, chew very well and eat and drink slowly.	❒	❒

This is to certify that I took this test myself without any help in the actual answers to questions during the examination.

Signature of the Person Examined: _____

Examiner's Signature: _____

Appendix C: Obesity surgery patient examination (gastric bypass)

You are taking this examination to show your obesity surgeon that you understand the information that he/she and the other team members have discussed with you. Any incorrect answer(s) that you may make will lead her/him to review this area with you and re-test you until she/he is satisfied that you understand the material and concepts involved. Where you re-take the examination using this same sheet, please date and initial your change in each answer.

All questions are true/false. Please tick each answer that you choose as "True"/"False".

	True	False
1. There are other morbid obesity operations that I can have other than gastric bypass.	❒	❒
2. My staple lines can *never* leak or result in infection or communication between the stomach or intestines and the skin after this surgery.	❒	❒
3. Sometimes obesity surgery patients get clots in the veins of their legs or pelvis. The clots can sometimes loosen and travel to the lungs, causing breathlessness and chest pain.	❒	❒
4. After obesity surgery, for life, the patient is able to drink or eat *anything* that he or she wants in any amount.	❒	❒
5. It is *guaranteed* that, following obesity surgery, the patient will permanently lose large amounts of weight and keep it off forever.	❒	❒
6. Knee and back pain, diabetes, high blood pressure and similar problems *always* get better after obesity surgery.	❒	❒
7. I could possibly need intensive care, long or short term, in hospital after obesity surgery.	❒	❒
8. Sometimes re-operation is needed due to bleeding, a hernia, blockage of the stomach or intestines and for other reasons.	❒	❒
9. I will need to make at least yearly physician visits, will have to follow strict eating rules and run the risk of re-operation for the rest of my life.	❒	❒
10. I will also need to take vitamin–mineral supplements and have nutritional examinations and laboratories drawn at least yearly for the rest of my life.	❒	❒
11. After my gastric bypass, I will probably have diarrhea or "dumping" especially after eating too fast, too much or after the wrong kind(s) of food.	❒	❒
12. Obesity surgery is *not* very serious or risky.	❒	❒
13. Obesity surgery patients can sometimes vomit a lot.	❒	❒
14. After I go home following surgery, I should *not* call my surgeon for at least 2 or 3 days after a problem starts.	❒	❒
15. No patient ever gets very dangerously depressed after obesity surgery.	❒	❒
16. For the first 24 h after obesity surgery patients are usually quite miserable or uncomfortable.	❒	❒
17. I am guaranteed to lose weight after gastric bypass surgery.	❒	❒
18. Significant protein, vitamin, salt, iron or body fluids may become abnormal in some patients soon, or a long time following, obesity surgery.	❒	❒
19. No one ever dies as a result of obesity surgery.	❒	❒
20. After this surgery, I will need to eat small bites, chew very well and eat and drink slowly.	❒	❒

This is to certify that I took this test myself without any help in the actual answers to questions during the examination.

Signature of the Person Examined: _____

Examiner's Signature: _____

Appendix D: Obesity surgery patient examination (duodenal switch or bilio-pancreatic diversion Scopinaro's procedure)

You are taking this examination to show your obesity surgeon that you understand the information that he/she and the other team members have discussed with you. Any incorrect answer(s) that you may make will lead her/him to review this area with you and re-test you until she/he is satisfied that you understand the material and concepts involved. Where you re-take the examination using this same sheet, please date and initial your change in each answer.

All questions are true/false. Please tick each answer that you choose as "True"/"False".

	True	False
1. It is important for me to eat high protein foods such as eggs, cheese, fish and chicken after my surgery or risk becoming malnourished.	❒	❒
2. There are no other operations for morbid obesity available than the duodenal switch or bilio-pancreatic bypass.	❒	❒
3. Sometimes obesity surgery patients get clots in the veins of their legs or pelvis. The clots can sometimes loosen and travel to the lungs, causing breathlessness and chest pain.	❒	❒
4. Staple or suture lines *never* leak and result in infection or communication between the stomach or the intestines and the skin.	❒	❒
5. Patients with bilio-pancreatic bypass or duodenal switch can often experience more frequent, soft, strongly smelling bowel movements and gas.	❒	❒
6. Knee and back pain, diabetes, high blood pressure and similar problems *always* get better after obesity surgery.	❒	❒
7. I could possibly need intensive care, long or short term, in hospital after obesity surgery.	❒	❒
8. Sometimes re-operation is needed due to bleeding, a hernia, blockage of the stomach or intestines and for other reasons.	❒	❒
9. I will need to make at least yearly physician visits, will have to follow strict eating rules and run the risk of re-operation for the rest of my life.	❒	❒
10. I will also need to take vitamin–mineral supplements and have nutritional examinations and laboratories drawn at least yearly for the rest of my life.	❒	❒
11. I will never again be able to swallow whole (uncrushed or unchewed) pills or tablets after this surgery.	❒	❒
12. Obesity surgery is *not* very serious or risky.	❒	❒
13. Patients do not vomit at all following obesity surgery.	❒	❒
14. After I go home following surgery, I should *not* call my surgeon for at least 2 or 3 days after a problem starts.	❒	❒
15. No patient ever gets very dangerously depressed after obesity surgery.	❒	❒
16. For the first 24 h after obesity surgery patients are usually quite miserable or uncomfortable.	❒	❒
17. I am guaranteed to lose weight after this surgery.	❒	❒
18. This surgery will result in a large portion of my stomach being surgically removed from my body.	❒	❒
19. No one ever dies as a result of obesity surgery.	❒	❒
20. Significant protein, vitamin, salt, iron or body fluids may become abnormal in some patients soon, or a long time following obesity surgery.	❒	❒

This is to certify that I took this test myself without any help in the actual answers to questions during the examination.

Signature of the Person Examined: _____ Date: _____

Examiner's Signature: _____

Appendix E: Re-operative obesity surgery fact sheet

Re-operative obesity surgery is done for a variety of different reasons. Since there are no formal, broadly accepted agreements among experienced obesity surgeons concerning re-operative obesity surgery, these reasons largely depend on your surgeon's judgment relative to your problems with the results of the earlier obesity surgery. Therefore, your surgeon reserves the right to accept or reject patients for re-operative surgery based upon his clinical judgment.

There are many operations available to modify, change, correct, or alter previous obesity surgery. Your surgeon will tell you the most likely plan but you must understand that what the surgeon finds at surgery may change this plan considerably. For example, heavy amounts of scar tissue or unexpected findings can cause the surgeon to change plans from something relatively simple to a very complex procedure or vice versa.

While re-operative obesity surgery usually produces benefits, it is not anything "magic" or guaranteed. To increase your chances for success for life, you must co-operate and make changes in your lifestyle, eating and drinking habits. The surgeon may also require that you be involved in certain behavioral training and exercise programs, usually together with a diet program.

Almost every surgeon who has performed re-operative obesity surgery has complications some time or another. Every patient has a real risk for one or more complications, There are no guarantees that a serious complication will not occur in any case. The more frequent or serious complications that can occur are as follows.

Infection or the wound, body cavity (abdomen or chest especially), lungs (pneumonia, for example) can occur. A lesser problem is collapse of small parts of lung tissue called atelectasis: it is most often due to difficulties taking deep breaths after surgery. It is a frequent cause of increased body temperature and is treated by breathing treatments or exercises.

Inflammation or infection of these organs can occur: pancreas (pancreatitis), stomach (gastritis, stomach ulcer), esophagus (esophagitis with chest pain, burning, etc) liver (hepatitis), gallbladder (cholecystitis, gallstones), kidney (pyelonephritis, kidney failure, and nephritis), bladder (cystitis), duodenum (duodenitis, duodenal ulcer).

The spleen may be injured during surgery and need to be removed. This can seriously increase the risks of infection in the patient's body.

Organ failure such as of the heart, kidney, liver and lungs has occurred after re-operative obesity surgery.

Clots in the lower limbs, pelvis or elsewhere in the body can form and travel to lungs, causing difficulties with breathing or even death. These clots can also result in temporary or permanent swelling or ulceration, especially in the legs.

Fluids from the stomach or intestines can leak into the body cavity, other organs or through the skin. They may continue to drain into a bag for a long time.

Changes in taste and food preferences often occur. Many patients have difficulties eating certain foods such as red meats, which they may have liked, before surgery. Sometimes after surgery, certain cravings for some foods may occur in some patients.

Food or liquids may not be able to pass through the pouch, lower stomach or intestines, which may need stretching (dilating) by instruments or endoscopes (which have their own risks). Tubes for nourishing fluids may have to be placed into stomach, intestines, or veins, if the patient is unable to eat or drink enough by mouth. Operation may be necessary.

Vomiting or diarrhea can frequently occur after this type of surgery and may make it a problem to eat certain types or quantities of food. This can be, in one sense, a benefit of this surgery, because it prevents eating or drinking of certain food(s) for fear of diarrhea or vomiting.

Bleeding from the stomach, a hernia forming due to the breakdown of the surgical stitches, may make your surgeon need to re-operate for these or other reasons. Complications of anesthesia, psychiatric problems such as depression, requiring care and admission to a psychiatric ward, and even resulting in death, are all possible as result of surgery. Approximately one in 200 (1/2%), of all morbidly obese patients die after open (not laparoscopic "keyhole") gallbladder surgery; the risk is about the same for morbidly obese patients following obesity surgery, with or without the gallbladder being removed. Depending on the extent of the re-operation you need, you may have an even greater risk of dying as a result of this surgery.

Persistent vomiting, nausea, swelling of the abdomen, heartburn, etc., can occur and may make the patient think seriously of having the operation undone in certain instances.

The stomach pouch or its outlet may get bigger or the staple lines open up, so that the patient can eat more at a mealtime or even gain back to the original or greater weight. If you have a gastric band, it may become displaced or you may have other problems that cause it to need to be re-positioned, replaced or a new type of obesity surgery performed.

Re-operation may be necessary again, and no patient should have re-operative obesity surgery performed that is not prepared to accept the need for further re-operation if it should become necessary. When this occurs, the risk of surgery is usually somewhat more than the original surgery but it varies with the type of original and re-operative surgery involved. Risk of injury to spleen, bleeding and need for blood transfusion also increase. Many experienced obesity surgeons order blood transfusion approximately 50% of the time following re-operative obesity surgery.

Admission to an intensive care unit may be necessary to observe you closely or to treat any of the problems that can arise from your surgery.

Over the months and years, any type of nutrition problem or infection may occur, including lack of vitamin(s), protein, calories, mineral(s), etc. Signs of this can include weakness, paralysis, confusion, rashes, anemia, hair loss, bone or joint problems, wounds that heal poorly, tongue soreness, night blindness, numbness, etc. After obesity surgery of any kind, taking vitamins and minerals and being followed by the obesity surgeon or a physician well experienced in this area, is necessary for life. It is the patient's responsibility to make sure that such appointments are regularly made and kept whether he/she "feels well" or not. The patient may need to have vitamin B12 injections every month for life. Food may get stuck in the stomach pouch and may need to be taken out with a special tube or a scope.

The patient's weight loss goal, no weight loss or even further gain of weight may occur after re-operative obesity surgery.

With weight loss, the skin on the arms, legs, neck, abdomen, face and elsewhere may become wrinkled, sag, droop, or hang as large folds and develop rashes or infections or odors. It may become quite annoying or embarrassing. As a result, you may feel a need for further surgery.

As soon as any problem arises, proper medical help must be obtained soon – you have the duty to call for help quickly and without delay.

All of the currently performed types of re-operative surgery for obesity are still relatively new. Therefore, the extremely long-term results of such surgery, including weight loss or possible complications, are unknown at this time.

I have read the above, which has been described to me by my surgeon. I understand this material, the risks, possible complications, other choices and the possible benefits of obesity surgery, as well as the operation, which my surgeon recommends, for my case.

By signing this statement, I am showing that I have read and accept the above and that I understand it. I have been encouraged to ask all the questions I want; they have been answered well, and I understand the answers.

Patient Signature: _____ Witness: _____

Date: _____ Time: _____

Appendix F: Obesity surgery patient's examination (re-operative obesity surgery) "To be taken with either Appendix A, B or C examination that covers primary obesity surgery"

You are taking this examination to show your obesity surgeon that you understand the information about re-operative obesity surgery that she/he and the other team members have discussed with you. Any incorrect answer(s) that you may make will lead her/him to review this area with you and re-test you until she/he is satisfied that you understand the material and concepts involved. Where you re-take the examination using this same sheet, please date and initial your change in each answer.

All questions are true/false. Please tick each answer that you choose as "True"/"False".

	True	False
1. In re-operative surgery patients, the spleen, which may have adhesions to the stomach from previous surgery, has no greater chance of having to be removed than first time obesity surgery.	❒	❒
2. Re-operative obesity surgery patients have a higher chance of needing to receive blood than first-time obesity surgery patients.	❒	❒
3. It is occasionally necessary to not perform part or all of the surgery planned due to unexpected events or findings.	❒	❒
4. Re-operative obesity surgery absolutely guarantees that additional surgery will not be necessary.	❒	❒
5. It is definitely guaranteed that all of the problems for which re-operative obesity surgery is performed will be cured.	❒	❒
6. It is *not* important to take nutritional supplements recommended to me by my surgeon and staff, especially proteins, vitamins and minerals for life.	❒	❒
7. Diarrhea, nausea, vomiting, or constipation *never* follow re-operative obesity surgery.	❒	❒
8. Re-operative obesity surgery has all of the possible problems which can occur with the first-time surgery plus some additional ones.	❒	❒

Signature of the Person Examined: _____ Date: _____

Examiner's Signature: _____

PATHOPHYSIOLOGY

SECTION 2

LUNG PHYSIOLOGY 4

M.A. Campos & A. Wanner

4.1 Introduction

Clinicians taking care of morbidly obese patients need to be aware of the significant physiologic changes that obesity is associated with. There are several unique changes in pulmonary function that lead to reduced lung volumes, increase work of breathing, and alterations in control of breathing and gas exchange. However, it has to be emphasized that most of the obesity-associated changes in pulmonary function have great variability and may not necessarily correlate with weight or body mass index (BMI).[1] Dyspnea and exercise intolerance are common complains among obese patients, as well as the prevalence of certain disorders such as asthma, obstructive sleep apnea and the obesity-hypoventilation syndrome. In addition, obese individuals are at increased risk of developing certain complications such as atelectasis, aspiration, ventilatory failure and pulmonary embolism in the post-operative state.[2,3] This chapter will describe the important physiologic changes in the respiratory system associated with obesity and describe briefly the pathologic consequences that can derive from them. A summary of these changes is shown in Table 4.1.

4.2 Alterations in pulmonary function

4.2.1 Alteration in lung mechanisms

Compared to non-obese individuals, morbid obesity is associated with an increase in the total work of breathing of about 70% and a 4-fold increase in the energy or oxygen cost of breathing.[2] There are several physiologic changes that account for this increased work of breathing, but the two most important mechanical factors are a decrease in total respiratory system compliance (C_{rs}) and an increase in airway resistance associated with the obese state.[4,5]

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Table 4.1 Summary of changes in pulmonary physiology associated with obesity

Parameter	Change in morbid obesity
Forced vital capacity (FVC)	Decreased
Forced expiratory volume at 1s (FEV_1)	Decreased
FEV_1/FVC	Normal
Total lung capacity (TLC)	Decreased
Expiratory reserve volume (ERV)	Decreased
Functional residual capacity (FRC)	Decreased
Inspiratory capacity (IC)	Increased
Residual volume (RV)	Normal or increased
Lung compliance (C_L)	Decreased
Chest wall compliance (C_{CW})	Decreased
Airway resistance	Increased
Maximal voluntary ventilation	Decreased
Partial pressure of O_2	Decreased
Alveolar–arterial oxygen gradient	Increased
Partial pressure CO_2	Increased or normal
Respiratory drive	Increased
Minute ventilation ($\dot{V}e$)	Increased
Respiratory rate	Increased
Tidal volume (V_t)	Decreased or normal
Oxygen consumption (rest)	Increased
Oxygen consumption (exertion)	Increased
Diffusing capacity of CO (DL_{CO})	Normal or increased

Compliance is defined as the deformation of the lung or chest wall per unit of force applied. Typically, deformation is expressed as change in lung volume and force as change in distending pressure. So, compliance is expressed as $\Delta V/\Delta P$, where ΔV is change in lung volume and ΔP is the concomitant change in distending pressure. Compliance can be determined under static and dynamic conditions. Static compliance (C_{st}) is more relevant in obesity and is measured either between portions of breathhold or, for practical reasons, during a slow expiratory or inspiratory manuever (quasi-static compliance). The compliance of the lung (C_L) is defined as $\Delta V/\Delta P_{tp}$, where P_{tp} is the transpulmonary pressure (measured between the airway opening and the pleural space). The compliances of the lung and the chest wall are in series; therefore, $1/C_{rs} = 1/C_L + 1/C_{CW}$, where C_{CW} is the compliance of the chest bellows (chest wall).

Here, C_{rs} is the compliance of the total respiratory system which is defined as $\Delta V/\Delta P_{tt}$, where P_{tt} is measured between the airway opening and the atmosphere. Although the C_L itself is somewhat decreased in the obese state, the decrease in total lung compliance occurs primarily from a decrease in the C_{CW} caused by the increased weight of the chest and abdominal walls.[5,6] The contribution of the abdominal wall can be demonstrated by the addition of weight to the lower thorax and abdomen of normal individuals, which produces a pressure–volume relationship similar to that observed in obese individuals.[7] The excess weight on the chest wall exerts mainly an effect in increasing the inspiratory threshold load (the load that the inspiratory muscles must overcome before inspiratory flow can begin) since when this is taken into account, the measured chest wall compliance in simple obesity is relatively normal.[6] The decrease in C_L is probably secondary to the decreased lung volumes and narrowing of dependent airways seen in obesity (see below), but as mentioned before, its contribution to the decrement in the C_{rs} is of lesser magnitude.[7,8] There are dynamic changes in lung mechanics when obese individuals undergo surgery. During general anesthesia, it has been shown that the C_{rs} and C_L decrease further whereas the already decreased C_{CW} is only minimally affected.[9] When the abdominal wall component is eliminated during laparotomy, obese individuals show a partial but significant increase in C_L and C_{rs} 1 h after the peritoneum is opened, which returns to original values after the peritoneum is closed.[10] When obese subjects under general anesthesia are placed on the prone position, the C_{CW} decreases further, while the resistance of the total respiratory system, lung, and chest wall does not change.[11]

Airway resistance is defined as the force which must be overcome by the respiratory muscles because of the frictional resistance to gas flow. Obesity is associated with an increase in airway resistance, probably secondary to a reduction in elastic tension of the lung (and increase in elastic tension of the chest wall) at lower lung volumes, which leads to a reduction in the caliber of the smaller airways.[12,13] So, obese subjects have increased respiratory resistance as a result of the reduction in lung volumes related to being overweight. Both total respiratory system resistance and airway resistance increase as the level of obesity increases.[14] The difference between the total respiratory system resistance and airway resistance does not widen significantly with higher degrees of obesity, suggesting that the chest wall resistance is not the factor that increases respiratory system resistance. There is no intrinsic airway pathology associated with obesity, so the increase in airway resistance is associated with a normal airway conductance.[12,13] Air trapping can be demonstrated in obese individuals by obtaining higher values of total lung capacity (TLC) when measured by

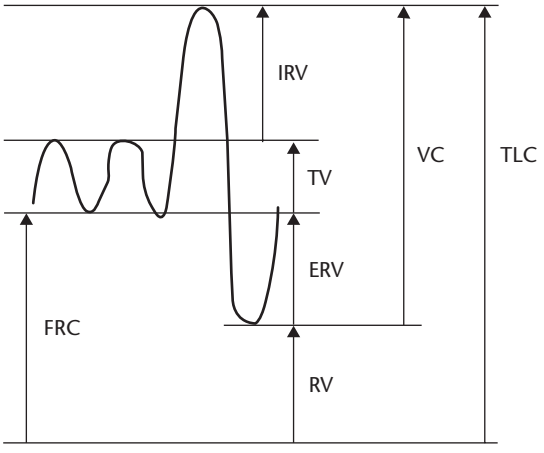

Figure 4.1 Lung volumes and capacities in relation to normal tidal breathing. IRV, inspiratory reserve volume; for other abbreviations refer to text.

plethysmography as compared with the value of TLC measured by the helium dilution technique.[12]

TLC can be subdivided into several volumes (smallest divisions) and capacities (sum of two or more volumes) (Figure 4.1).

The functional residual capacity (FRC) is the volume remaining in the lungs at the end of a normal expiration. This volume can be divided into two: the expiratory reserve volume (ERV, the volume expired by active expiration after passive expiration) and the residual volume (RV, the volume left in the lungs after maximal expiratory effort). The closing volume (CV) is the lung volume above RV at which airway collapse occurs during expiration, mainly in lower lung zones due to gravitational forces. The relation between the CV and the FRC is determined by the balance between the inward elastic recoil of lung and the outward pull of thoracic cage. If the CV exceeds the ERV, as occurs in severe obesity due to a decrease in ERV, some airways will be closed during the tidal breathing cycle, and this can result in arterial hypoxemia (Figure 4.3). This situation worsens during anesthesia and the postoperative period because the FRC decreases even more. It can also worsen when sighs are absent (for example inhibited by surgical pain and opioids), since sighs help re-expand closed airways (and should normally occur at approximately 1 min intervals). It has been noted that airway closure and airflow obstruction become more pronounced when obese individuals assume the supine position, since the increased weight of the chest wall and abdomen acts further on the lungs as the CV is reached, impairing further exhalation.[15] In normal adults the closing capacity (CV + RV) rises above the FRC in the supine position at about the age of 45 years and above the FRC in the erect position at about 65 years; these changes occur earlier in life in obese subjects.

4.2.2 Obesity and upper airway resistance

Many obese individuals have a narrowing of the upper airway craniofacial and soft tissue structures that affect the flow of air. The final caliber of the upper airway is determined not only by the basal pharyngeal area but by several other factors such as collapsibility of the airway, the luminal pressure (negative during inspiration), the pressure on the outer side of the pharyngeal walls (usually positive in obese people due to excess adipose tissue), and the pressure exerted by the pharyngeal dilating muscles.[2] Efforts to identify a particular site(s) of obstruction by measuring pressure–flow relationships at various upper airway levels revealed that obstruction often, but not always, occurs at the retropalatal level.[16] Other anatomical factors can significantly contribute to the upper airway narrowing in these individuals are presence of paranasal sinus disease, tonsil and adenoid hypertrophy, hypertrophy and morphologic abnormalities of the soft palate and palatine uvula, low-set soft palate, micrognathia, macroglossia and tongue root depression.[17] Also, the shape of the upper airway changes from having a longer transverse axis to a longer anteroposterior axis, which leads to a less effective work by the pharyngeal dilating muscles.[18] It has been shown that the lower lung volumes of obesity results in a decrease in the baseline area of the pharynx, an increase in its collapsibility and a loss of caudal traction on the trachea.[19,20] It is not uncommon for obese individuals to experience airway collapse during expiration as well, resulting from the anatomic changes described above.[21] If the increased upper airway resistance produces symptoms, such as disruption of sleep due to increased ventilatory efforts in response to the upper-airway closure and daytime sleepiness and the alterations are considered a pathologic state and known as the obstructive sleep apnea syndrome (OSA). It has been shown that individuals who suffer from this disorder have an increase in the soft tissue volume of the upper airway (mainly in the retropalatal and retroglossal lateral pharyngeal walls, soft palate, tongue, and genioglossus muscles) and less ability to dilate the pharynx during inspiration.[22,23]

OSA encompasses the syndromes of sleep apnea, sleep hypopnea, and upper-airway resistance syndrome.[24] Apnea is the complete cessation of airflow for at least 10 s. Hypopnea is a 30–50% reduction of airflow for the same amount of time. Although obstructive apnea may be associated with greater oxyhemoglobin desaturation, distinguishing the two has little effect

treatment, and therefore the combined number of apnea and hypopnea episodes per hour of sleep are expressed as the apnea–hypopnea index or respiratory-disturbance index. The upper-airway resistance syndrome is characterized by arousal in response to increased upper-airway resistance without an elevated apnea or hypopnea index. Patients with the upper-airway resistance syndrome are usually heavy snorers. More than 70% of patients who suffer this condition are obese.[25,26] Upper body obesity seems to be more important than total obesity as a factor to develop OSA.[27] Due to reasons explained above, obese subjects with OSA also can also have lower airway obstruction that add to the already high obesity-associated breathing load.[28,29] These derangements of pulmonary mechanics as well as the level of oxygenation when awakening (generally attributable to obesity and diffuse airway obstruction) are of major importance in establishing the severity of nocturnal hypoxemia in obese patients with OSA.[30] These patients usually suffer from daytime sleepiness and altered cardiopulmonary function.

4.2.3 Obesity and alterations in respiratory muscle function

Obesity is associated with alterations in respiratory muscle function, induced by both the increased load, which the muscles are required to overcome, and by some reduction in their capacity.[31] Among the most significant changes are a decrease in maximum voluntary ventilation (MVV)[32,33] and low maximum inspiratory pressures.[34] Probably these abnormalities are related to alterations in diaphragmatic function because the diaphragm is displaced higher in the thoracic cavity (overstretched), creating a mechanical disadvantage by placing the diaphragmatic fibers at a suboptimal length. This condition worsens when obese individuals are placed in the supine position.[35] Analysis of the diaphragmatic electromyogram reveals a persistence of activity into early expiration in proportion to the degree of obesity.[36] These finding suggests that the diaphragm's volume-generating function in the obese is reduced. During carbon dioxide (CO_2) stimulation, obese individuals also show an enhanced electromyographic diaphragmatic signal that is three to four times the signal observed in lean subjects, indicating greater than normal diaphragmatic activity as a probable response to the higher workload.[37]

Both muscle biopsy specimens and measurements of CT density show fatty infiltration of non-respiratory skeletal muscle in obese individuals, but the extent to which this affects muscle strength is unclear.[38,39] Interestingly, the phenotype of diaphragmatic muscle fibers can also change in the obese state. In animal studies, diaphragmatic fibers of obese rats change by decreasing the number of type II and increasing the number of type I myosin heavy chain isoforms, which indicates a fast-to-slow shift, when compared to fibers from lean animals.[40] An increase in oxidative capacity occurs as well. This diaphragmatic phenotype can be reversed when leptin is replaced in obese leptin-deficient mice.[41] In humans, the enhanced diaphragmatic electromyographic activity decrease after weight loss[2] and it has been shown that 6 months after bariatric surgery the MVV and respiratory muscle endurance increase in relation to the decrease in BMI.[42]

4.2.4 Obesity and alterations in gas exchange

Arterial blood gas analyses of eucapnic obese individuals not uncommonly show hypoxemia and an elevated alveolar-to-arterial oxygen difference. As mentioned before, this results in part from the closure of some airways during tidal breathing as the CV exceeds the ERV in severe obesity. It has been shown that obesity is associated with clinically significant alterations in ventilation : perfusion ($\dot{V}/\dot{Q}$) matching, since there is preferential ventilation in the upper lung zones while still having perfusion favor the bases.[43] The $\dot{V}/\dot{Q}$ mismatch is worse in the supine position, but improves during exercise because of the enhanced ventilation at the bases of the lung.[44] Surgery can worsen hypoxemia by altering the $\dot{V}/\dot{Q}$ relationship further. Sedation and paralysis causes a reduction in lung volumes and an excessive unopposed intra-abdominal pressure.[45] It has been noted that hypoxemia can improve when obese patients under anesthesia are turned to the prone position.[11] During thoracic surgery, obese individuals show more hypoxemia than non-obese subjects during one lung ventilation, likely from the same reasons.[46]

4.2.5 Obesity and alterations in respiratory drive

Eucapnic obese individuals show an increased respiratory drive in response to CO_2 stimulation, as measured by minute ventilation ($\dot{V}e$) or resting inspiratory neuromuscular drive (mouth occlusion pressure or inspiratory pressure at 100 ms, $P_{0.1}$).[47–50] The mouth occlusion pressure is believed to reflect the neurogenic drive to the respiratory muscles and is independent on respiratory muscle function or lung mechanics. In simple obesity, the $P_{0.1}$ is increased about two times.[51,52] The increased $\dot{V}e$ is associated with a significant decrease in the expiratory time per breath, so the alteration in the inspiratory-to-expiratory time ratio may indicate an alteration in central breath

timing.[52] When a 45 kg load is applied to the chest of normal subjects, the $P_{0.1}$ and the inspiratory transfer index (defined as $P_{0.1}$/mean inspiratory flow) increases, reflecting a strategy of maintaining similar ventilation by increasing inspiratory force against the load.[53] It has been postulated that this increased drive is what produces an increase in the sensation of dyspnea among obese individuals.[4] In general, eucapnic obese subjects also have an increased ventilatory responsiveness to hypoxia.[52] A subgroup of obese people develops clinically significant hypercapnia due to a blunted CO_2 responsiveness of the respiratory center, that may be as low as half of what is found in normal subjects or individuals with simple obesity.[54] The fact that voluntary hyperventilation can normalize the partial pressure of CO_2 in these individuals, adds evidence of impaired ventilatory control.[55] These condition has been coined as the obesity-hypoventilation syndrome (OHS), also known as the "Pickwickian syndrome", after the fat boy Joe, in Charles Dickens' Pickwick Papers.[56] When compared with individuals with simple obesity, obese individuals with OHS have even lower lung volumes, lower total C_{rs} and weaker inspiratory muscles.[7,8,57] They also have severe gas exchange impairment and pulmonary hypertension is quite frequent.[58] The daytime hypoxemia and raised alveolar–arterial oxygen gradient suggests a combination of $V/\dot{Q}$ inequality and alveolar hypoventilation.[59] It is still unclear why some morbidly obese individuals develop this waking alveolar hypoventilation while others with similar obesity do not. Diurnal hypercapnia in the morbidly obese is frequently associated with ventilatory restriction and sleep related respiratory disturbances such as obstructive sleep apnea even without other concomitant disorders such as chronic obstructive pulmonary disease.[58,60,61] Some evidence suggests that obese individuals with OHS may have a measurable pre-morbid impairment of ventilatory chemoresponsiveness.[62] Since no familiar pattern for these derangements has been detected, it has been suggested that it might be an acquired and reversible consequence of severe OSA or other sleep-breathing disorders other than OSA that are prevalent in this population.[63] The pathophysiology of obesity-related breathing disorders is still unclear, and has been related to be from mechanical factors such as the obesity-associated increase in respiratory work to relative deficiencies in leptin or leptin resistance.[64]

4.2.6 Obesity and alterations in breathing pattern

To overcome the decreased C_{rs}, obese individuals adopt a rapid and shallow breathing pattern. In eucapnic morbidly obese individuals, the respiratory rate is about 40% higher than normal at rest, while the tidal volume (V_t) and the fraction of inspiration time over total breathing time are normal.[51,65,66] However, when normalized to body weight, the V_t is smaller, especially when measured during exertion.[59,67] Obese individuals partition their V_t preferentially to their rib cage compartment, choosing to leave the abdominal compartment relatively immobile.[36] The rapid and shallow breathing pattern, while an appropriate adaptation to the decreased C_{rs} nonetheless, leads to an increased work of breathing and oxygen consumption by the respiratory muscles.[68]

4.2.7 Obesity and alterations in exercise capacity

At rest, obese individuals consume approximately 25% more oxygen than lean individuals.[69,70] The basal metabolic rate and consequently the rate total body oxygen consumption ($\dot{V}O_2$) increases as weight increases. However, since adipose tissue has a lower metabolic rate than other tissues, the increase in $\dot{V}O_2$ is proportionally less than the increase in weight. Consequently, if $\dot{V}O_2$ is expressed by kilogram body weight, the values obtained in obese individuals are lower than normal values.[71] It has been suggested by early studies that only a small proportion (around 3%) of the oxygen consumed is due to the work of the respiratory muscles.[31] However, this has been called into question by the observation that when obese patients undergoing bariatric surgery (average BMI 53.4 kg/m^2) are switched from spontaneous to mechanical ventilation, the $\dot{V}O_2$ decreases 16% while healthy controls decrease by less than 1%.[72] During exertion, obese individuals have also greater $\dot{V}O_2$ for any degree of external work.[69,70] The increase in $\dot{V}O_2$ has been calculated to be around 5.8 ml/min for each incremental kilogram of body weight.[73,74] Most of the work is spent in moving the lower extremities.

Overall, young people with simple obesity have nearly normal exercise capacity. They have a maximal exercise oxygen consumption and a maximal exercise $\dot{V}e$ that is around 90% of normal.[69,70] When expressed in terms of absolute weight, this is still lower than values from normal individuals and inversely proportional to the degree of total body fat.[75]

4.3 Pulmonary function tests in obesity

Obesity produces a typical pattern in pulmonary function as shown in Table 4.1.

It has to be emphasized that although obesity is a separate risk factor for postoperative pulmonary

complications[76] and can produce some "classic" alterations in pulmonary function testing, so far no prospective study has shown a positive correlation between pulmonary function abnormalities and the development of pulmonary complications.[77] It is possible that this is because so far no large-scale studies have been conducted with sufficient power to detect a difference. As mentioned before, pulmonary function abnormalities do not occur in all individuals with a similar degree of obesity.[1] In overweight children, increased BMI has been noted to have a positive impact on lung function in girls, but this is not a uniform finding in boys, perhaps because of distinct sex-dependent patterns of fat distribution in children.[78] Given this lack of direct correlation between obesity and the development of pulmonary abnormalities, it is important to separate the changes related to an increased BMI from those that may be due to other processes. Most subjects fall within the generally accepted 95% confidence limits for the predicted values of spirometric and lung volume values.[57] An abnormal spirometric value should be considered as caused by intrinsic lung disease and not by obesity, except in those with extreme obesity. With the current data and tools available, this distinction has to be based primarily with careful history, physical examination and clinical judgment.

4.3.1 Spirometry

Mild degrees of obesity affect spirometric values only minimally. The first abnormality that can be noted as weight increases is a reduction in the MVV,[1,33,79] although some authors have not demonstrated this.[43,57,80] Interestingly in one study, individuals with a low MVV (<80% of predicted) had also decreases in forced vital capacity (FVC), forced expiratory volume at 1 s (FEV_1), forced expiratory flow at 50% of vital capacity, VC ($\dot{V}_{50}$) and lower maximum inspiratory flow rate (MIFR), despite having only a slightly increased BMI.[33] These individuals with low MVV, had reduced lung volumes, and reduced maximal inspiratory pressures as well. The authors pointed out that peripheral airway abnormalities may be in part responsible for these observations.[33] The MVV can decrease because of the alterations in lung mechanics mentioned before, because of a greater limitation to expiratory flow from the higher ventilation, and because higher flows that might be needed to perform the maneuver.[79] In addition, since the respiratory muscles must generate an increased force with each breath, they may not be able to perform optimally like those of normal subjects. Finally, some obese individuals may have higher upper-airway resistance that can limit inspiratory flow and affect the MVV. Since a low MVV can be associated with several other abnormalities in pulmonary function, it raises the possibility of its use as a screening tool to detect individuals at risk for pulmonary complications of obesity.

As the degree of obesity increases, other spirometric abnormalities can occur besides a decrease in MVV. FVC and FEV_1 decrease with physical inactivity and with increase in fat stores.[81,82] In both men and women, the change of these spirometric variables are not significantly associated with body mass or BMI, as they are with the percentage of body fat (negative correlation) and the fat-free mass (positive correlation).[83] Gross obesity has been reported as being associated with decreased FVC in 43 grossly obese non-smoking subjects, but the measure of obesity was weight/height rather than BMI.[57] It has been suggested that both FVC and FEV_1 are negatively associated with sub-scapular skin-fold thickness in young obese men (ages between 30 and 59 years) and with the abdominal girth to hip breadth ratio in men between 50 and 59 years.[84] In a prospective 6-year follow-up population study, weight gain was associated with a decrease in both FVC and FEV_1. This variables were highest in the group that gained <1.0 kg, lowest in the group that gained ⩾4.0 kg, and intermediate in the group that gained 1.0–3.9 kg in both men and women, but the effect of weight gain on pulmonary function was greater in men than in women.[85] The authors concluded that each kilogram of weight gain was associated with an excess loss of 26 ml in FVC and 23 ml in FEV_1 in men, and 14 ml and 9 ml, respectively in women. The decreases in FVC and FEV_1 are more pronounced in morbidly obese patients (average BMI 47 in men and 45 in women), when compared with age-matched controls.[12] It is common for these patients to manifest other markers of increased airway resistance such as reductions in mid- and end-expiratory flow rates. It is important to emphasize that the most obese patients usually need a longer time to complete an adequate spirometric maneuver, so its not rare to observe suboptimal values.[86]

Although the influence of obesity on pulmonary function tests has been examined, the role of body fat distribution has received limited attention. Deposition of excess body fat in obese subjects is often described in two distinct patterns: a central (or upper body) pattern typically seen in obese men, and a peripheral (or lower body) pattern more typical of obese premenopausal women. These patterns appear to be important in determining the consequences of obesity. Pulmonary studies of male patients with upper body fat distribution (waist-to-hip ratio >0.95) suggest they have more severely compromised lung volumes than

obese patients with lower body obesity.[87] As mentioned before in the case of children, in adults, differences in body fat distribution appears to be the reason for the gender differences observed in obesity-associated alterations on pulmonary function.[78] In general, body fat distribution has independent effects on lung function that are more prominent in men than in women. In a large cross-sectional study it was noted that the waist-to-hip ratio inversely correlates with FEV_1 in men but not in women, after accounting for BMI and other variables and that larger values were associated with greater reductions of FVC in men compared to women.[88] In another study, adjusted FVC was negatively associated with waist circumference and waist-to-hip ratio in men but not in women.[83]

4.3.2 Flow-volume loop

Since the cross-sectional area of the upper airway is dependent on the lung volume, so it is not surprising to find flow-volume loop (FVL) abnormalities in severely obese patients.[89,90] The FVL does not help to distinguish individuals with OSA, but sometimes this can be suggested when it shows a "sawtooth" pattern[91,92] (Figure 4.2).

The sawtooth sign was first described in obstructive sleep apnea but is not unique to this disorder as it can also occur in normal individuals, patients with extrathoracic airway obstruction, excess airway secretions, burn victims at risk for airway obstruction, and in patients with Parkinson's disease.[90,93] It consists of reproducible oscillations occurring at constant interval on the forced expiratory and/or inspiratory part of the FVL, caused by fluttering tissue in the upper airways. In sleep apnea patients, the presence of the saw-tooth sign is associated with a higher apnea index and lower nocturnal minimum oxygen saturation than those without the sawtooth sign.[94] It has to be emphasized that the characteristics of the FLV do not always predict sleep apnea in obese patients when confounding factors are accounted for.[95] From the FVL, the ratio of the forced expiratory flow at 50% of the VC ($FEF_{50\%}$) to the forced inspiratory flow at 50% of the VC ($FIF_{50\%}$) can be estimated. A ratio greater than 1 is a non-specific sign that has been described in snorers and patients with upper airway abnormalities such as extrathoracic airway obstruction and sleep apnea.[96] The ratio has a sensitivity and specificity less than the sawtooth sign in predicting obstructive sleep apnea among obese people.[97] Finally, plateauing of the inspiratory flow rate in the FVL has also been associated with obesity and sleep apnea.[98]

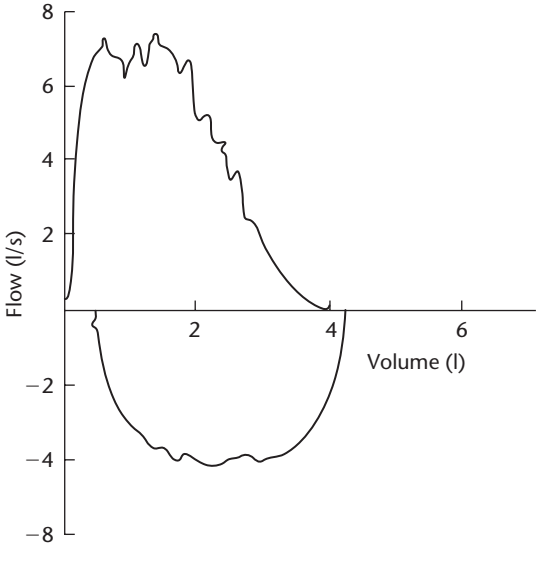

Figure 4.2 Saw-tooth pattern seen in the FVL of a morbidly obese individual.

4.3.3 Lung volumes

The most predictable changes in pulmonary function in obese individuals occur in lung volumes (Figure 4.3).

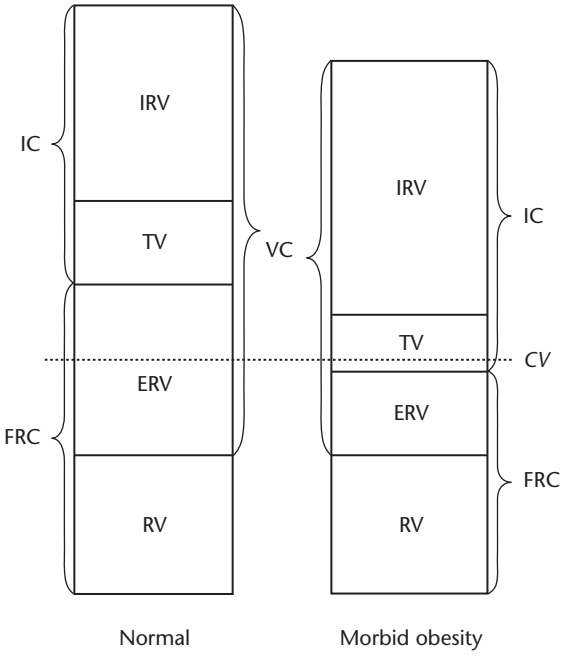

Figure 4.3 Comparison of lung volumes between lean and obese subjects. IRV, inspiratory reserve volume; for other abbreviations refer to text. In severe obesity, sometimes the CV can be above the reduced ERV, which leads to closure of some airways during the tidal breathing cycle resulting in arterial hypoxemia.

The added weight and decreased compliance of the chest wall usually produces the first abnormalities: a reduction in ERV and FRC.[1,12,32,33] There is a correlation between the reduction in these volumes and increasing weight, and reductions are noted even in mild obesity.[87,99] The ERV and FRC became significantly reduced when the weight (kg) to height (cm) ratio is about 0.7.[57] Some authors have found a correlation between the reduction in ERV and symptoms of OSA.[100] It has been noted that during exercise, in contrast to leaner individuals, moderately obese women fail to decrease their end-expiratory lung volumes.[101] In mild obesity, VC and TLC are well preserved because there is a compensatory increase in inspiratory capacity (IC).[57] In more obese individuals, reductions in VC and TLC can be seen, especially as the weight-to-height ratio becomes greater than 1. Others have noted that the biceps skin-fold thickness is the anthropometric measurement that has the strongest inverse relationship with TLC.[87] When the VC decreases in severe obesity, is mainly due to reductions in ERV, as the IC remains well preserved.[57] The RV becomes slightly low when the weight-to-height ratio is mildly increased (from 0.5 to 0.8), but then increases as the ratio gets bigger.[57] Due to air trapping (see above), with weight-to-height ratios greater than one, the RV and the RV-to-TLC ratio becomes significantly elevated.[12] The decrease in TLC therefore is not as dramatic as the reduction seen in VC.

4.3.4 Diffusion capacity and arterial blood gases

The diffusing capacity of carbon monoxide (DL_{CO}) is well preserved in obesity and no abnormalities in this test can be attributed to that condition, so it is a useful test that can be used to separate other pathology from obesity alone.[4] Theoretically, the presence of an increased RV and an increased RV-to-TLC ratio associated with obesity can lead to an actual increase in DL_{CO} when corrected for alveolar volume (DL_{CO}/VA).[57] However, this has not been a consistent finding.[32,102] The fact that DL_{CO} is preserved in obese individuals adds to the evidence that the lung parenchyma is normal and that the changes in pulmonary function are due to abnormal chest wall mechanics and lower lung volumes.

As mentioned above, a greater ventilation to the upper lobes with perfusion preferentially favoring the bases, results in $\dot{V}/\dot{Q}$ mismatching that can be manifested as hypoxia and an increase in the alveolar–arterial oxygen gradient on arterial blood gas analysis.[103] The magnitude of hypoxemia correlates with weight gain and is detectable even in mild obesity.[99] Hypoxemia may also occur because of hypoventilation.

4.4 Dyspnea and obesity

Breathlessness is very common among obese subjects. In a large epidemiologic study, 80% of obese middle age subjects reported shortness of breath after climbing two flights of stairs compared with only 16% of matched non-obese controls, even when smoking was less frequent among the obese.[104] Obese subjects with dyspnea have a significantly reduced forced expiratory flow at 75%VC, MVV, and maximum static expiratory mouth pressure when compared with obese subjects without dyspnea,[105] but most subjects with dyspnea do not have objective airflow obstruction.[106] Large airway function (FVC, FEV_1, and FEV_1-to-FVC ratio), lung volumes, and gas exchange parameters are usually unchanged. Some have suggested that the dyspnea noted by obese subjects is probably related to their increased respiratory drive.[4]

4.5 Obesity, airway hyperresponsiveness and asthma

It has been reported that obese subjects are more likely to report wheezing and other asthma-like symptoms.[107–109] In adults, the prevalence of self-reported asthma increases with increasing BMI after controlling for several confounders. In one study, the odds ratios of having asthma was 1.84 when comparing women with BMI $\geqslant 30$ with those with BMI < 25.[107] The association between obesity and asthma appears to be stronger in women. Such an association has also been described in children.[110,111] Although obesity has been associated with an exercise-induced fall in FEV_1,[111] the self-report of wheezing or asthma does not appear to be accompanied by non-specific airway hyper-responsiveness or prevalence of atopy.[112] Despite a higher prevalence of self-reported asthma and bronchodilator use among the most obese individuals, many do not have objective evidence for airflow obstruction.[106] It is not clear if obesity predisposes to asthma or asthma leads to obesity, possibly due to inactivity or the use of glucorticosteroids. Severe obesity may also cause changes in the upper airway and wheeze may result from extrathoracic obstruction caused by fat deposition. In addition, obstructive sleep apnea, prevalent with severe obesity, can lead to nocturnal awakening with shortness of breath or choking that may be misinterpreted as asthma. Alternatively, there are mechanisms by which obesity could predispose to either respiratory symptoms or changes in the airways that may cause wheezing and/or asthma. As described before, obesity may have a direct effect on the mechanical properties of the respiratory system by altering lung volume, airway caliber, or respiratory

muscle strength. In asthma, airway obstruction causes early airway closure during expiration. This feature is accentuated in the obese state, especially when patients are lying down. Obese individuals have a decrease of FRC to a volume close to 500 ml. In normal subjects, changes in lung volume of this magnitude (induced by voluntarily breathing below FRC) can increase airway responsiveness, suggesting that changes in lung volume act to alter the forces of interdependence between airways and parenchyma that oppose airway smooth muscle contraction.[113] Several studies have shown that asthma and airway obstruction improves with weight loss (see below). Collectively, these studies suggest that airway obstruction detected by pulmonary function testing can occur in overweight subjects.

4.6 Effects of weight loss on respiratory function

Loss of weight in the morbidly obese is associated with improved lung function. Weight loss induced by gastric surgery has been associated with significant increases in FVC, FEV_1, FRC, RV, TLC and ERV, even when the preoperative values were within normal limits before the surgery, and improvements in respiratory muscle endurance.[42,114] Resting arterial blood gas tensions improved as well, with a rise in arterial oxygen tension and a fall in arterial CO_2 tension. Some have reported that an initial worsening in respiratory function (decrease FVC and hypoxia) occurs, that later improves as fat tissue is lost.[115] There is no correlation between the magnitude of weight loss and the magnitude of change in blood gas tensions or lung volumes. In general, a decrease of BMI from 50 to 37 kg/m^2, correlates with an increase in ERV of approximately 75%, an increase in RV and FRC of 25% and an increase in MVV of about 10%.[66,114,116,117] Improvements in lung volumes and oxygenation has also been noted with a 15 kg weight loss induced by personalized diet and psychologic support in people with BMI $> 35\,kg/m^2$.[118] In a small study were moderate weight loss was induced by behavioral management (BMI from 45 to 39 kg/m^2), ERV and FRC improved significantly but no benefits in oxygenation was noted.[117] It has also been reported that weight loss reduces the oxygen cost of breathing to almost normal values (up to a 9-fold reduction) and improves the diaphragmatic response to inhaled CO_2 more than 10-fold.[2]

Weight reduction in obese patients with asthma improves lung function, symptoms, morbidity, and health status. Improvements in FVC and FEV_1 have been noted among obese asthmatics undergoing weight-reducing programs.[119] Weight reduction reduces the closing capacity, so dependent airways close later in expiration, which tends to increase the FEV_1 and the FVC. The improvement of airflow limitation is more marked with truncal fat mass loss.[120,121] It has been demonstrated also that weight loss reduces airway obstruction as well as peak expiratory flow variability in obese patients with asthma.[122] The mechanisms by which weight loss can alleviate asthma may include alleviation of airway collapse, stimulation of adrenal activity, and reduction in possible allergens, bronchoconstrictors, or salt content in the diet.[119] Weight reduction also reduces the exercise load, which may alleviate asthma symptoms during exercise. Gastrointestinal reflux may worsen asthma symptoms, and reduction of fat around the abdomen may reduce reflux and decrease symptoms. The psychologic benefit of having lost weight may also alleviate symptoms. Finally, numerous studies have indicated that OSA and other obesity-related sleep disorders improve with weight loss.[123–127] In summary, all points that obese patients benefit from weight loss by improving pulmonary mechanics and a better control of airway obstruction.

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CARDIAC MORPHOLOGY AND VENTRICULAR FUNCTION

5

M.A. Alpert

5.1 Introduction

Obesity produces a variety of hemodynamic alterations that affect cardiac morphology and ventricular function.[1–14] These alterations occur in persons with mild-to-moderate obesity, but are most pronounced in those with morbid obesity.[1,4,8,10,13] This chapter discusses the hemodynamic changes that occur with mild, moderate and morbid obesity, reviews their impact of cardiac morphology and ventricular function, describes the clinical syndrome of obesity cardiomyopathy and discusses the effects of weight loss on these alterations. These changes in cardiac structure and function may have important implications for anesthesiologists concerning the choice of anesthesia and peri-operative care of the surgical patient.

5.2 Classification of obesity

The World Health Organization classifies obesity in terms of body mass index (BMI). The classifications are as follows: lean or normal range (18.5–24.9 kg/m^2); pre-obese or overweight (25.0–29.9 kg/m^2); mild or class I obesity (30.0–34.9 kg/m^2); moderate or class II obesity (35.0–39.9 kg/m^2); and morbid or class III obesity ($\geq$40.0 kg/m^2). Many of the studies cited in this review used this classification system. However, some of the studies used different criteria for obesity and morbid obesity. Obesity was defined by some as $\geq$20% over ideal body weight or relative weight $\geq$120%. Morbid obesity was defined by some as $\geq$twice ideal body weight or relative weight $\geq$200%.

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5.3 Hemodynamic alterations associated with obesity

Excessive fat accumulation is associated with an increase in total and circulating blood volume, oxygen consumption and arteriovenous oxygen difference.[1–6] The increase in circulating blood volume in association with a decrease in systemic vascular resistance results in augmentation of cardiac output.[1–6] Cardiac output increases primarily due to increased stroke volume as heart rate rises little if at all with fat accumulation.[1–6] This hemodynamic sequence was originally attributed to the high metabolic demand of adipose tissue.[1–14] However, recent studies have demonstrated that the metabolic activity of fat does not account fully for all of the increase in cardiac output observed in obese subjects.[1,4] There is also an increase in lean body mass, which contributes to the aforementioned hemodynamic alterations.[1,4,7] Cardiac output rises in proportion to the increase in fat mass.[1–3,5,7] The augmentation of cardiac output produces an increase in left ventricular (LV) volume (preload). LV wall stress increases in accordance with the law of Laplace.[1–6] The resultant increase in afterload is hypothesized to predispose to secondary or eccentric LV hypertrophy (LVH) and subsequently to LV diastolic dysfunction.[1–3,6] LV systolic dysfunction in obese subjects has been attributed to persistent elevation of LV systolic wall stress and inadequate LVH.[1–3] The evidence supporting this hypothesis is reviewed in the sections that follow.

5.4 Cardiac morphology in obesity

5.4.1 Fatty infiltration of the heart

From ancient times through the Victorian era it was presumed that cardiac dysfunction associated with obesity resulted from fatty infiltration of the heart, hence the term "cor adiposum."[15] This misconception was fostered by the frequent presence of excessive epicardial fat which was readily observed during autopsies of obese patients. In 1933, Smith and Willius reported excessive epicardial fat at necropsy in 95% of 135 obese patients.[16] Right ventricular (RV) penetration by cords of epicardial fat was frequently identified, but LV penetration was not.[16] Microscopic analysis showed that fatty metamorphosis and excessive intracellular fat content were absent.[16] During the same year Saphir and Corrigan, published a post-mortem study of 58 patients with fatty infiltration of myocardium.[17] Obesity was present in 18 and emaciation was present in nine of these patients.[17] They considered fatty infiltration to be an incidental finding in all but two cases. In a subsequent autopsy study of 52 obese and 52 lean patients Carpenter described two distinct patterns of fatty infiltration.[18] One was characterized by cords of fat that emanated from epicardial fat and intermingles with atrophic muscle bundles.[18] This form of fatty infiltration occurred as commonly in lean as in obese patients.[18] The second form consisted of areas of fat in myocardium surrounded by fibrosis that was not attached to epicardial fat.[18] It occurred mainly in patients with coronary artery disease.[18] These studies suggest that fatty infiltration of myocardium does not cause ventricular dysfunction in most obese persons.

5.4.2 Post-mortem studies of cardiac morphology

Smith and Willius reported cardiac morphologic findings based on post-mortem examination in 135 obese patients.[16] Their weights ranged from 102 to 150 kg.[16] In this study heart weight increased in proportion to body weight up to 105 kg and to a lesser extent thereafter.[16] Heart weights for both women and men were higher than predicted and heart-to-body weight ratios were lower than predicted for healthier subjects.[16] The increase in heart weight was attributed in part to excessive epicardial fat, but LVH was also a common and consistent finding.[16]

Several autopsy studies built on Smith's and Willius' observations.[19–22] In 1968, Amad *et al.* reported necropsy finding in 12 morbidly obese subjects.[20] Most were hypertensive during life and three died of congestive heart failure (CHF).[20] Heart weight increased linearly with body weight and was higher than predicted for healthy persons.[20] Increased LV wall thickness was present in nine patients and increased RV wall thickness was noted in two.[20] Interstitial and perivascular fibrosis were sporadic and excess epicardial fat was identified in only two patients.[20] In an autopsy study of nine hypertensive morbidly obese patients who had died of heart failure, Alexander and Pettigrove reported that LVH was present in all subjects and RV hypertrophy (RVH) was detected in one.[21] Warnes and Roberts reported post-mortem cardiac findings on 12 patients whose body weights ranged from 312 to more than 500 pounds.[22] Heart weights were increased and heart-to-body weight ratios were decreased in all patients.[22] The LV cavity was dilated in 11 and the RV cavity was dilated in all 12 patients.[22] Gross and microscopic symmetric LVH was present in all patients.[22] The left atrial wall was thickened in six and RVH was identified in four patients.[22] Significant coronary atherosclerosis was rarely observed.[22] Excessive epicardial fat was present

in nine and RV fatty infiltration was detected in three patients.[22]

The results of these studies suggest that LV dilation and hypertrophy are the most common cardiac morphologic abnormalities noted in symptomatic morbidly obese subjects. Left atrial hypertrophy and RVH occur less commonly in such patients.

5.4.3 Endomyocardial biopsy

Kasper and co-workers reported the results of an endomyocardial biopsy study of 43 obese and 409 lean patients with CHF.[23] A specific cause of CHF was identified in 65% of lean and only 23% of obese subjects.[23] LVH was the most common morphologic alteration present in obese subjects.[23] These findings, when considered in light of the aforementioned post-mortem findings, lend credence to the concept of an obesity cardiomyopathy that is characterized primarily by eccentric LVH.[23]

5.4.4 Echocardiographic studies of cardiac morphology

Post-mortem studies have tended to focus on a limited number of only the most symptomatic of morbidly obese patients. The advent of echocardiography has provided the opportunity to study cardiac morphology in asymptomatic morbidly obese subjects as well as in less severely obese individuals.

Early studies of such patients demonstrated that LV dilation occurred in 8–40%, left atrial enlargement occurred in 39% and RV enlargement occurred in 40%.[24–26] Increased LV wall thickness or LV mass occurred in 8–87%.[24–26] The higher frequencies occurred in the more severely obese patients. LVH is almost always present in symptomatic morbidly obese subjects and has been reported in approximately two-thirds of asymptomatic morbidly obese patients.[1,24]

Multiple studies have compared LV morphology in obese and lean subjects.[27–32] Degrees of obesity ranged from mild to severe.[27–32] LV diastolic chamber size was significantly larger in obese than in lean subjects in all studies.[27–32] LV wall thickness, mass and mass index or mass/height index were significantly greater in obese than in lean patients in more than 80% of studies.[27–32] The LV radius-to-thickness ratio was higher in obese than in lean subjects in one of two studies.[27–32] These findings support the hypothesis that LVH in obesity, even mild-to-moderate obesity, is eccentric in nature.

Several studies have examined the relation between LV mass or chamber size and severity of obesity.[33–36] The largest of these is derived from the Framingham Study database.[33,34] Lauer studied 3927 mildly-to-moderately obese subjects and reported a significant positive correlation between BMI and LV mass.[33,34] In a smaller study of 50 morbidly obese subjects Alpert *et al.* reported a significant positive correlation between the percent overweight and LV mass/height index.[35] de la Maza and colleagues reported a positive correlation between LV mass and BMI in both hypertensive and normotensive moderately obese patients.[36] Rasooly and co-workers noted a similar relation between both waist circumference and waist-to-hip ratio and LV mass.[37] Thus, increasing degrees of obesity, particularly central obesity, are associated with commensurate increases in LV mass.

There are multiple factors that contribute to the development of LVH. Alpert *et al.* reported significant positive correlations between LV mass/height index and the echocardiographic LV internal dimension in diastole (a preload surrogate) and both systolic blood pressure and LV end-systolic wall stress (markers of afterload) in 50 asymptomatic, normotensive morbidly obese patients.[35] In a subsequent study comparing this group with 24 normotensive morbidly obese patients with CHF, Alpert and colleagues found that LV diastolic chamber size, LV mass/height index, left atrial dimension and RV chamber size were greater in those with CHF than in those without heart failure.[38] Alpert and co-workers showed that duration of morbid obesity correlated significantly with both LV mass/height index and loading conditions for both asymptomatic morbidly obese subjects and morbidly obese subjects with CHF.[38,39] In less severely obese patients, Nakajima *et al.* reported that those who were obese $\geqslant$15 years were more likely to experience LV dilation than those who were obese $<$15 years.[30]

Several studies have demonstrated that obesity in children may produce similar effects on LV chamber size, thickness and mass.[40–44] However, an increase in lean body mass is thought to play a more important role in effecting these changes in children than increasing fat mass.[44]

Sasson and co-workers reported echocardiographic left atrial enlargement in 37% of obese patients and in 6% of lean patients.[45] Left atrial enlargement was closely associated with the presence of LVH.[45]

In summary, post-mortem studies have shown that eccentric LVH is the most common alteration of cardiac morphology in morbidly obese patients. The echocardiographic studies cited support this observation in morbidly obese subjects. These studies also demonstrate that the process begins with less

severe degrees of obesity, is driven by adverse cardiac loading conditions (even in normotensive patients), is related to duration of obesity and may occur in obese children.

5.5 Ventricular function in obesity

5.5.1 Left ventricular diastolic function

The presence of eccentric LVH in morbid obesity is associated with reduced LV compliance.[46] This, in association with high circulating blood volume and high cardiac output, causes elevation of LV filling pressure in many morbidly obese persons.[1,4,8,46] An additional increase in cardiac output with exercise markedly increases LV filling pressure, often exceeding the threshold for pulmonary edema.[8] Little information exists concerning LV filling pressure in mildly-to-moderately obese subjects. DeDivitiis *et al.* demonstrated that mean LV filling pressure at rest exceeded the normal range in 10 moderately-to-severely obese patients.[11] LV filling pressure correlated positively and significantly with BMI.[11] The extent to which LV filling pressure is elevated in mild-to-moderate obesity is uncertain.

Indices derived from cardiac Doppler evaluation or radionuclide angiography have been used to assess the relation of obesity and LV diastolic filling.[46] These techniques have been employed not only in morbidly obese subjects, but also in those with lesser degrees of obesity.

Studies comparing LV diastolic filling in mildly, moderately and severely obese patients, and lean subjects have shown remarkably consistent findings.[46–54] In each study the non-invasive measure of LV diastolic filling was significantly more impaired in obese than in lean patients.[46–54]

Alpert and co-workers reported increasing impairment of diastolic filling as the percent overweight increased in 25 morbidly obese subjects.[55] Grossman and colleagues reported similar findings in less severely obese patients.[47] Grossman also noted increasing impairment LV of diastolic filling with increasing LV mass index.[47] Alpert's study also showed that LV diastolic filling became progressively more impaired as LV mass/height index, the LV internal dimension in diastole, systolic blood pressure and LV end-systolic wall stress increased.[55] In one study of variably obese subjects, impaired LV diastolic filling occurred in the absence of LVH.[49] Whether impairment of LV diastolic filling in obese persons is due entirely to LVH, to adverse loading conditions or both is uncertain. Longer duration of morbid obesity was found by Alpert and co-workers to correlate with greater impairment LV diastolic filling.[39] Alpert *et al.* also showed that morbidly obese patients with CHF have greater impairment of LV diastolic filling than those without CHF.[38]

The results of these studies show that LV diastolic filling is frequently impaired in morbidly obese and less severely obese patients, even in the absence of hypertension. LV diastolic dysfunction is associated with LVH, adverse cardiac loading conditions and duration of obesity in such patients.

5.5.2 Left ventricular and right ventricular systolic function

Echocardiography, systolic time intervals and radionuclide left ventriculography have been used to assess LV systolic function in obese subjects.[56] Indices of LV systolic function derived from these techniques include LV ejection fraction, LV fractional shortening, mean velocity of circumferential fiber shortening (V_{cf}) and the pre-ejection period to LV ejection time (systolic time interval) ratio.[56]

Multiple studies have compared LV systolic function in obese and lean subjects.[28,48,50,57–59] Four studies have reported significantly lower values for indices of LV systolic function in predominantly moderately obese patients than in lean controls.[49,50,57,58] In contrast, three other studies (including one in children) showed no significant difference in mean indices of LV systolic function between moderately-to-severely obese subjects and lean controls.[28,41,58]

Alpert and co-workers reported a significant negative correlation between LV fractional shortening and percent overweight in 39 morbidly obese patients.[60] Previously, Stoddard *et al.* reported a significant negative correlation between percent overweight and the systolic time interval ratio in moderately obese patients.[50]

Alpert and colleagues reported a significant negative correlation between LV fractional shortening and markers of preload and afterload (LV internal dimension in diastole, systolic blood pressure and LV end-systolic wall stress) in 39 morbidly obese patients.[60] Previously Alexander *et al.* had reported a negative correlation between LV fractional shortening and LV end-systolic wall stress in such patients.[4] Duration of morbid obesity correlated negatively and significantly with LV fractional shortening in morbidly obese subjects.[39] This was not observed by Nakajama in less severely obese patients.[30] Alpert *et al.* and others demonstrated that exercise produces the expected

improvement in LV systolic function in morbidly obese subjects with normal LV mass, but produces no change in LV systolic function in those with LVH.[61,62] Alpert *et al.* reported that mean LV fractional shortening was significantly lower in 24 patients with CHF than in 50 patients without heart failure.[38]

The results of these studies suggest that in morbidly obese subjects, systolic function decreases with increasing adipose weight, with progressively adverse LV loading conditions and with increasing duration of obesity. These relationships are less consistently apparent in patients with mild-to-moderate obesity. It is important to emphasize that even in studies where LV ejection fraction, LV fractional shortening or mean V_{cf} were lower in obese than in lean subjects, LV systolic function remained within the normal range in most, but not all patients.

Little information exists concerning RV systolic function in obesity. Alpert and co-workers reported that RV systolic function increased with exercise when the RV internal dimension was normal ($\leqslant$2.3 cm), but did not change when the RV internal dimension was high ($>$2.3 cm).[63]

5.6 Effect of systemic hypertension on cardiac morphology and ventricular function

Obesity is a volume overload state that produces LV dilation and secondary or eccentric hypertrophy.[1–3,64,65] Systemic hypertension is a pressure overload state that predisposes to concentric LVH.[64,65] When these two conditions co-exist, they produce a hybrid form of LVH.[1–3,64,65] In such patients LV chamber size increases less than with obesity alone and LV wall thickness increases less than with systemic hypertension alone.[64,65] LV mass is typically higher and diastolic filling is more impaired than with either obesity or hypertension alone.[64,65] LV systolic function remains normal in most cases.[64,65] However, patients with this hybrid form of LVH are more prone to CHF than with either obesity or systemic hypertension alone.[64,65]

5.7 Obesity cardiomyopathy

Obesity cardiomyopathy is the clinical syndrome of CHF that occurs due to obesity and its sequelae.[1–3,66] Although hemodynamic and structural cardiac alterations may be observed in patients with mild-to-moderate obesity, the clinical syndrome of obesity cardiomyopathy is seen primarily in those with morbid obesity.[1–3,66]

5.7.1 Pathogenesis

The increase in circulating blood volume and decrease in systemic vascular resistance produce an increase in cardiac output, due primarily to augmentation of stroke volume.[1–14,66] This causes LV dilation, which is turn leads to an increase in LV wall stress in accordance with the law of Laplace.[1–6,66] This increase in afterload stimulates secondary or eccentric LVH in an attempt to normalize wall stress.[1–6,66] The presence of LVH is associated with a decrease in LV compliance, which in turn impairs LV diastolic filling.[1–6,66] The co-existence of LVH, impaired diastolic filling and a high cardiac output states leads to elevation of LV filling pressure and diastolic LV failure.[1–14,66] If LV wall stress remains high (thought to be due to inadequate LVH), LV systolic dysfunction may ensue resulting in LV failure with elements of diastolic and systolic dysfunction.[1–3] The presence of LV failure produces pulmonary venous hypertension and eventually pulmonary arterial hypertension.[66,67] This, in association with pulmonary hypertension related to sleep apnea (which occurs in 50–90% of morbidly obese sessions) and severe alveolar hypoventilation (which occurs in 5–10% of morbidly obese persons) leads to RVH.[66,67] The hypercirculatory state contributes to RV dilation which in association with RVH predisposes to RV failure.[66,67] Obesity cardiomyopathy is always characterized by LV $\pm$ RV failure.[1–3,66,67] Isolated RV failure due to pulmonary complications does not occur in morbidly obese patients.[3]

5.7.2 Clinical manifestations

The clinical manifestations of obesity include standard symptoms and signs of CHF, such as lassitude, nocturia, paroxysmal nocturnal dyspnea, orthopnea, dyspnea on exertion or at rest, swollen legs, Cheyne–Stokes respiration, a fourth (and occasionally a third) heart sound, pulmonary crackles, jugular venous distension, hepatomegaly, ascites and lower extremity brawny edema.[1–3,66,68–75] Atrial fibrillation may occur in some patients.[1–3] Pulmonary and systemic congestion may wax and wane for several years with gain and loss of weight.[1–3,66,68–75] Eventually however, symptoms and signs of CHF become persistent. There are several features related primarily to alveolar hypoventilation that occur in advanced cases of obesity cardiomyopathy that set this syndrome apart from other forms of CHF.[1–3,66,68–75] These include somnolence, conjunctival suffusion, retinal venous

congestion and papilledema.[1–3,66,68–75] In advanced cases, coma may ensue.[1–3,66,68–75]

5.7.3 Management: treatment of active congestive heart failure

Episodes of CHF should be treated with supplementary low flow oxygen, dietary sodium restriction (two grams per day), low-dose unfractionated heparin (5000 units subcutaneously three times per day or 7500 units subcutaneously twice per day) and a loop diuretic.[1–3,76,77] Digitalis may be considered in patients with LV systolic dysfunction who remain symptomatic despite the aforementioned measures or in those with atrial fibrillation and a rapid ventricular reponse.[1–3,76–78] An angiotensin converting enzyme inhibitor should be employed when LV systolic dysfunction is present.[76,77] An angiotensin II receptor blocker may be used as an alternative in patients who are intolerant of angiotensin converting enzyme inhibitors. The role of beta-blockers, aldosterone antagonists and natriuretic peptides has not been elucidated in patients with obesity cardiomyopathy. Similarly, no single antihypertensive agent has proven to be more effective than others in patients with obesity cardiomyopathy and normal systolic function. Techniques such a continuous positive airway pressure (C-PAP) or bi-level positive airway pressure (Bi-PAP) may reduce sleep apneas.

5.8 Effects of weight loss

5.8.1 Effects of weight loss on cardiac performance and morphology in obesity

While the medical measures cited in the previous section may ameliorate many of the clinical manifestations of obesity cardiomyopathy, substantial weight loss offers the best long-term hope for improvement.[77,79,80] This section reviews the effects of weight reduction on central hemodynamics, cardiac morphology and ventricular function in mild, moderate and morbid obesity.

Many of the resting hemodynamic changes cited previously are reversible with weight loss. In moderately-to-severely and morbidly obese subjects substantial weight loss decreases circulating blood volume, oxygen consumption, arteriovenous oxygen difference, cardiac output and stroke volume.[77,79,80] Systemic vascular resistance usually, but not invariably increases with weight reduction.[77,79,80] The response of blood pressure is similarly variable.[79–84] LV filling pressure does not consistently fall during weight loss in such individuals, perhaps due to permanent interstitial changes associated with LVH.[76,77,79,80] The response of right heart pressures to weight loss is similarly variable.[77,78,80,81] After weight loss, cardiac output during exercise is higher than before weight loss.[79]

Alpert and colleagues have demonstrated that substantial weight loss following bariatric surgery in morbidly obese patients significantly decreases LV chamber size and LV mass/height index in those with eccentric LVH prior to weight loss, but not in those without LVH.[85] The decrease in LV mass/height index was accompanied by a decline in the LV dimension in diastole, systolic blood pressure and LV end-systolic wall stress.[85] Thus, improvement in cardiac loading conditions produces regression of LVH in morbidly obese patients with eccentric LVH.[85]

Weight reduction may also produce favorable alterations of LV morphology in mildly-to-moderately obese persons.[86–90] Multiple studies of such individuals reported variable decreases in LV chamber size, LV wall thickness or LV mass following weight loss.[86–90]

Alpert and co-workers demonstrated that substantial weight loss significantly improved LV diastolic filling in 25 morbidly obese patients.[55] The improvement was accompanied by a commensurate decline in mean LV mass/height index and by reduction of the mean LV internal dimension in diastole, mean systolic blood pressure and mean LV end systolic wall stress.[55] In a study of 41 moderately-to-severely obese patients Karason *et al.* reported similar improvements in LV diastolic filling in normotensive patients, but no improvement in hypertensive subjects.[58] The response of LV diastolic filling indices to weight loss was more variable in DasGupta's study of 11 normotensive mildly-to-moderately obese subjects.[91] Reid *et al.* reported no improvement in LV diastolic filling with weight loss in a small group of mildly obese persons.[92]

In their study of 39 normotensive morbidly obese subjects, Alpert and colleagues reported significant improvement in mean LV fractional shortening in patients with impaired LV systolic function prior to weight loss, but no change in LV fractional shortening in those with normal pre-weight loss LV systolic function.[60] This improvement was accompanied by significant decreases in mean systolic blood pressure and mean LV end-systolic wall stress, but not by a decrease in the mean LV internal dimension in diastole.[60] This suggests that increased afterload may play a more important role than increased preload in producing LV systolic dysfunction in morbidly obese patients. Mean LV ejection fraction rose significantly with substantial weight loss in 41 moderate-to-severely obese subjects reported by Karason *et al.*[58] Similar findings were reported by Wirth and Kroger in moderately obese subjects.[89] In contrast, DasGupta *et al.*

reported no change in LV systolic function following weight loss in mildly obese patients.[91] Both DasGupta and colleagues[91] and Alaud-din and co-workers[10] reported a significant increase in mean exercise LV ejection fraction following weight loss. Prior to weight loss, exercise had produced no significant change in LV systolic function.[10] The results of these studies suggest that substantial weight loss can produce improvement in resting LV systolic function in moderately-to-severely obese subjects with impaired LV systolic function prior to weight loss. This is due at least in part to a reduction in afterload (even in normotensive patients). The blunting of exercise LV ejection fraction in patients with morbid obesity improves with weight loss.

5.8.2 Effect of weight loss on congestive heart failure in patients with obesity cardiomyopathy

Little information exists concerning the effect of weight loss on CHF in morbidly obese patients with obesity cardiomyopathy. Estes reported the effects of weight loss on a variety of clinical variables in six morbidly obese subjects with the "Pickwickian" syndrome.[72] Substantial weight loss reversed all clinical and electrocardiographic abnormalities in five patients including all three with CHF.[72] Alpert and co-workers studied 14 normotensive morbidly obese patients with CHF and obesity cardiomyopathy.[38] New York Heart Association functional class improved in 10 patients; from class II to class I in five, from class III to class I in three, and from class III to class II in two.[38] There was no change in functional class in two patients.[38]

5.9 Summary

Obesity, particularly morbid obesity is a high cardiac output state that predisposes to eccentric LVH, LV diastolic dysfunction and, in some, LV systolic dysfunction. These alterations are due in part to adverse LV loading conditions and occur more commonly in those with a longer duration of morbid obesity. Although the hemodynamic factors that underly the morphologic changes occur in those with mild-to-moderate obesity, the more severe alterations of cardiac morphology and ventricular function, including CHF due to obesity cardiomyopathy, are seen predominantly in morbidly obese patients. Acute exacerbations of CHF respond to many of the standard measures used to treat this syndrome. However, weight reduction is the most effective long-term countermeasure. Substantial weight reduction is capable of reversing most of the hemodynamic alterations associated with morbid obesity. It is also capable of causing regression of LVH. In addition, weight reduction produces improvement in both LV diastolic filling and LV systolic function when these variables are impaired prior to weight loss. Finally, limited data suggest that weight loss improves functional capacity in patients with CHF due to obesity cardiomyopathy.

5.10 Implications for anesthesiologists

Patients with morbid obesity, including those who are normotensive and asymptomatic, have a high prevalence of eccentric LVH. Impaired LV diastolic filling is present in many of these individuals and LV systolic dysfunction occurs in some. Because of these alterations in cardiac morphology and ventricular function, morbidly obese persons are more sensitive to acute changes in preload and afterload than lean individuals. Thus, it is essential to evaluate for the presence of abnormal cardiac structure, impaired ventricular function and CHF in morbidly obese patients receiving general or spinal anesthesia and undergoing high or intermediate risk surgery. An electrocardiogram and chest X-ray should be performed on all such patients, as part of their pre-operative evaluation. Consideration should be given to performing a transthoracic echocardiogram prior to anesthesia and surgery. Critical echocardiographic information concerning cardiac morphology and ventricular function can be obtained in approximately 70% of morbidly obese patients.[93] In patients without adequate echocardiographic windows, radionuclide ventriculography may be used to assess LV and RV morphology and function. Unfortunately, studies concerning the effect of such an evaluation on outcome are lacking. However, the information derived from non-invasive cardiac evaluation may assist the anesthesiologist in choosing an anesthetic/analgesic regimen that does not increase the risk for development of hemodynamic distress during the peri-operative period.

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PATHOPHYSIOLOGY OF CARDIOVASCULAR CO-MORBIDITIES

6

T.J.J. Blanck, I. Muntyan & H. Zayed-Moustafa

6.1 Introduction

The peri-operative care of a morbidly obese patient requires a knowledge of the pathophysiology of morbid obesity that might contribute to a problematic outcome. The concerns, like those for most patients exposed to anesthesia are: airway, respiratory, gastrointestinal, endocrine, and cardiovascular. The assessment of each of these areas is essential for the safe care of the patient. This chapter is devoted to a consideration of the cardiovascular physiology and pathology of the morbidly obese patient.

The prevalence of obesity is increasing worldwide. Over 65% of the adult population in the US is reported to be overweight (body mass index, BMI $> 25\,kg/m^2$) and 31% are characterized as obese (BMI $> 30\,kg/m^2$). The incidence of type 2 diabetes, a disease closely linked to obesity, has increased 10-fold between 1982 and 1994.[1]

The Framingham Heart Study examined the development of cardiovascular complications over a 44-year follow-up as a function of (BMI, weight in kilograms divided by the square of height in meters). The study population was divided into three groups: normal (BMI 18.5–24.9), overweight (BMI 25.0–29.9), and obese (BMI $\geqslant 30$) individuals. 5209 subjects were enrolled in the Framingham Study between 1948–1951, they ranged in age at the time of enrollment from 30 to 62 years. The investigators used pooled repeated measures which allowed the contribution of multiple person examinations to the data set as they met the inclusion criteria at the beginning of each observation interval.[2] If a patient had a BMI $\geqslant 18.5$ and was free of cardiovascular disease they were eligible for the next period of observation. Participants were examined every 2 years from the time of enrollment into the study. Table 6.1[2] describes the patient characteristics according to their BMI status. Notably, over the period studied, the incidence of smoking in the normal weight group was remarkably high, and, although not evaluated, might be related to the ability of the normal group to maintain a "normal" weight. This high incidence probably reflects the prevalence of smoking in the 1940s and 1950s. The incidence of risk factors and the occurrence of events per BMI category is demonstrated in Table 6.2.[2] The appearance of hypertension as well as diabetes mellitus is markedly increased in both men and women in the overweight and obese groups. In essentially every event category other than cardiovascular death and total death the occurrence of cardiovascular events was markedly increased in both the overweight and obese categories relative to individuals with a normal BMI.

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Table 6.1 Characteristics of participants*

	BMI category (kg/m^2)		
Characteristic	**18.5–24.9**	**25.0–29.9**	**⩾30.0**
Age distribution (years)			
35–45	23/24	20/14	19/12
46–55	30/30	31/28	30/27
56–65	29/28	31/34	32/36
66–75	18/19	18/25	19/26
Prevalent conditions			
Diabetes mellitus	7/9	9/10	13/13
Hypertension	15/17	23/29	36/45
Elevated cholesterol	32/45	38/53	40/51
Cigarette smoker	58/43	43/28	43/23
Number of persons-years of observation	15,484/30,888	23,026/21,806	5950/9366

*Data are percentage of participants (men/women) unless otherwise specified.
Adapted from Wilson 2002.

Table 6.2 Incidence of risk factors and events*

	BMI category (kg/m^2)		
	18.5–24.9	**25.0–29.9**	**⩾30.0**
Risk factor			
Hypertension	4.0/4.0	5.8/7.4	8.5/11.2
Hypercholesterolemia	10.2/13.0	11.0/15.9	10.2/13.6
Diabetes mellitus	1.1/1.3	1.5/1.4	2.4/2.0
Any one of above	14.7/16.5	17.1/23.1	23.1/23.6
Event			
Angina pectoris	1.1/0.7	1.6/1.2	2.1/1.6
Myocardial infarction	1.3/0.4	1.7/0.4	1.6/0.7
Hard CHD	1.4/0.4	1.9/0.5	2.1/0.8
Total CHD	2.3/1.1	3.3/1.7	4.0/2.4
CVD	0.5/0.4	0.7/0.6	1.0/0.6
Total CVD	3.8/2.1	4.7/2.9	5.7/4.1
CVD death	0.7/0.4	0.7/0.3	0.7/0.7
Total mortality	2.4/1.2	1.6/1.2	2.2/1.6

*Data are incidence (per 1000 person-years) of participants (men/women). CHD, coronary heart disease; CVD, cardiovascular disease. Adapted from Wilson 2002.

The above study determined that the relative risk for hypertension and diabetes mellitus in obese men was 2.23 and 1.85, respectively, while in obese women the relative risk for these disorders was 2.63 and 1.36, respectively. The authors concluded in the 44-year follow-up study that one could attribute 26% of the incidence of hypertension in obese men to obesity, and 21% of the incidence of diabetes mellitus to obesity. In obese women their analysis attributed 28% of hypertension to obesity but only 3% of diabetes mellitus.

Obesity results in a complex syndrome leading to abnormalities in the neuroendocrine activation, renal sodium retention, and oxidative stress all contributing to pathologic modifications of the cardiovascular system (Figure 6.1).[3,4]

A recent report emphasized the overwhelming association of oxidative stress with obesity.[5] 2828 subjects from the Framingham Heart Study were examined and creatinine-indexed levels of 8-Epi-PGF$_{2\alpha}$, an oxidation product of arachidonic acid, were measured

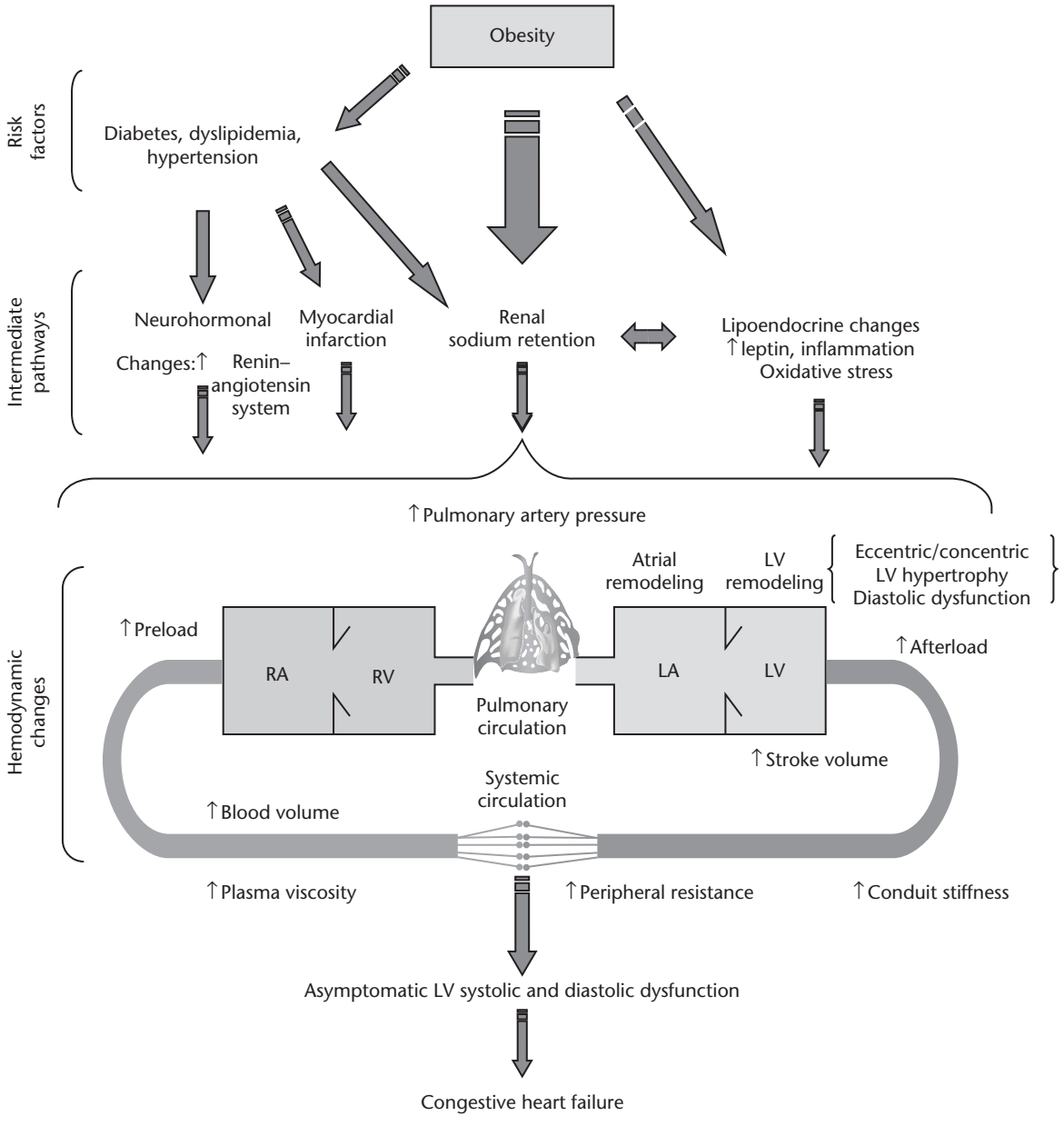

Figure 6.1 Interacting factors leading to cardiovascular changes in the obese patient. Adapted from Ref. [4]. RA, right atrium; RV, right ventricle; LA, left atrium; LV, left ventricle.

in the urine. The investigators found that for each $5\,kg/m^2$ of BMI there was a 9.9% increase in urinary creatinine-indexed 8-epi-$PGF_{2\alpha}$ levels. The strong association ($P < 0.0001$) was found not only for BMI but also for waist-to-hip ratio. Previous studies had suggested this type of link but they were all performed on smaller samples.[6] The idea that obesity is a state of heightened oxidative stress is consistent with the known development of insulin resistance in obese patients as well as the increased incidence of hypertension and coronary artery disease (CAD).

6.2 Hemodynamics in the morbidly obese

The obese individual exists with hemodynamic overload. The expanded metabolic demand of adipose

Table 6.3 Echocardiographic findings in obese individuals

Echocardiographic data	Hypotensive	Non-hypotensive	*P* value
ED LV wall thickness (cm)	1.5 ± 0.3	1.1 ± 0.2	<0.001
LV mass (g/m^2)	182	141	<0.001

Adapted from Ref. [11].

tissue and the increase in fat-free mass to support the excess adipose tissue leads to a hyperdynamic circulation with increased blood volume.[5] In 1962 Alexander *et al.*[7] reported data from 40 obese subjects, they observed a linear correlation between the degree of overweight and the blood volume and cardiac output. Although these 40 obese subjects did not have elevated heart rates compared to lean individuals, their stroke volume (SV), stroke work, and cardiac work were all increased in proportion to the degree of overweight.[8] Their maximal oxygen consumption was elevated, but the arteriovenous difference was normal. Alexander has compared them with constantly exercising individuals, always having an elevated oxygen consumption. De Divitiis *et al.* studied 10 obese volunteers who had a mean age of 36.5 ± 10.3 years and weighed 123.6 ± 28.7 kg and had no known co-morbidities.[9] Right and left heart catheterizations were performed. They found elevated oxygen demand, arteriovenous oxygen difference, cardiac output, SV, right ventricular end-diastolic pressure, mean pulmonary artery pressure, mean pulmonary capillary wedge, and pulmonary vascular resistance relative to lean subjects. Furthermore the left ventricular (LV) function curve showed impaired ventricular function, both V_{max} and the ratio of stroke work index to LV end-diastolic pressure were reduced indicating that depressed LV function was already present in relatively young obese individuals. However, LV hypertrophy (LVH) and chamber stiffness might contribute to their assessment of LV function although load independent contractility might be normal.[10]

Madu studied 23 obese patients who were referred for evaluation of suspected CAD. The patients were suspected of having CAD and were offered a transesophageal echo-dobutamine stress study because they were unable to adequately exercise or had had suboptimal evaluations by more standard techniques due to their morbid obesity. The study consisted of 19 men and four women of 48 ± 7 years of age and a mean weight of 164 ± 8 kg. Interestingly nine patients had significant wall motion abnormalities and 10 of the 23 patients developed hypotension during the dobutamine transesophageal echo stress test.[11] There were no statistically significant differences between the hypotensive and non-hypotensive patients with respect to LV volumes, ejection fractions, and LV outflow velocity. The author attributed the hypotensive episodes to LVH, the hypotensive patients had increased LV wall thickness and LV mass (Table 6.3).

6.3 Effect of the duration of obesity

While there are clear associations of obesity with hypertension, LVH, congestive heart failure (CHF), and CAD, most studies have focused on the occurrence and severity of these abnormalities rather than on their development. An echocardiographic study of 35 patients aged 16–60 years whose weight ranged from 57 to 118 kg was performed to determine the effect of duration of obesity on cardiac function.[12] The patients exceeded ideal body weight by 122–195%. The study was divided into two groups according to the duration of obesity: group 1 consisted of patients that had been obese for <15 years and group 2 consisted of patients that had been obese for more than 15 years. These groups were compared to 30 age-matched non-obese patients. They found that obesity markedly increased end-diastolic radius/wall thickness (R/Th), end-systolic wall stress, SV, stroke index (SI), and cardiac output. In comparing group 1 to group 2, R/Th, SI, and diastolic dimension index (DdI) were statistically significantly higher in those patients who had been obese for >15 years. Furthermore, plotting the data for each individual as a function of years of obesity demonstrated a significantly positive correlation between those parameters and the years of obesity (Figure 6.2).

Alpert *et al.* also examined the relationship between the duration of obesity and the development of LVH and diastolic dysfunction[13] (see also Chapter 5). They demonstrated an impressive positive linear relationship between systolic pressure and duration of obesity. Relationships were also found between *E/A* ratio (decreasing), the E-wave deceleration time (increasing), the percent LV-fractional shortening (decreasing) and the duration of obesity, respectively (Figure 6.3).

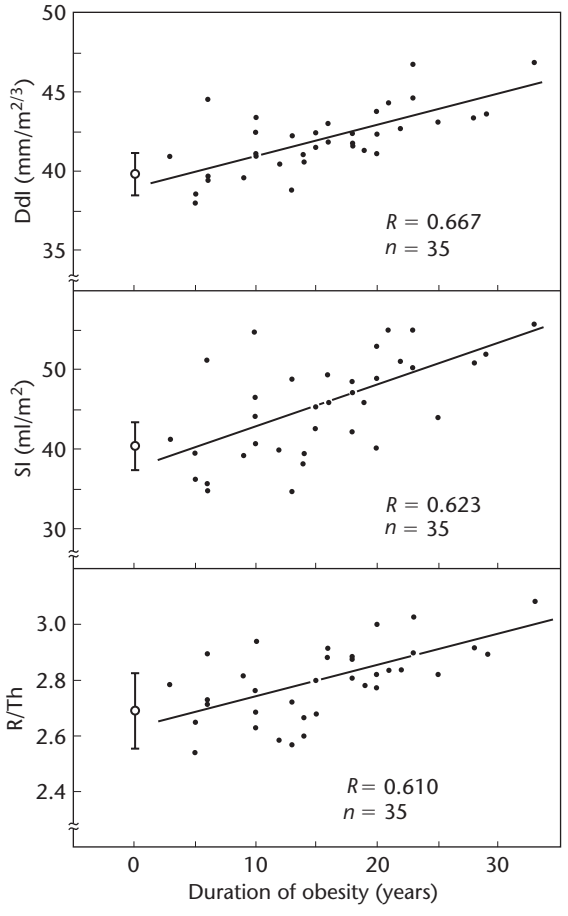

Figure 6.2 Effect of years of obesity on end-diastolic R/Th, SI, and DdI. All parameters increased with the duration of obesity. ♀ : Non-obese controls (mean ± SD). Adapted from Ref. [12].

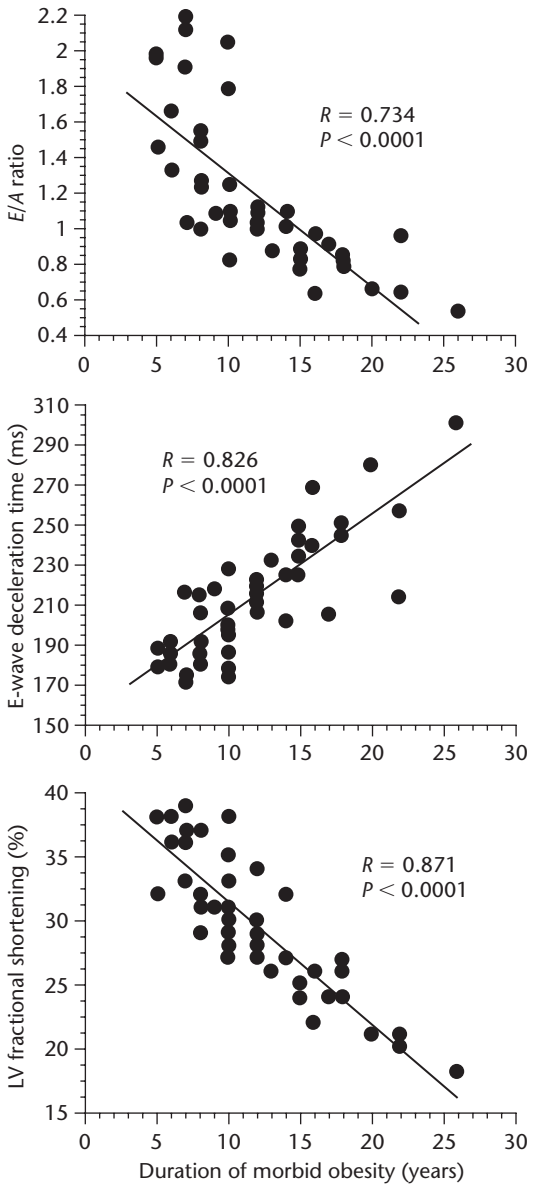

Figure 6.3 The decrease in *E/A* ratio as a function of the years of obesity; the increase in E-wave deceleration time as a function of the years of obesity; and the decrease in the percent LV fractional shortening as a function of duration of obesity. Adapted from Ref. [13].

The negative relationship between the percent LV fractional shortening and duration of obesity was particularly impressive with an correlation coefficient of 0.871. It is apparent that duration of obesity increases the likelihood of LVH and it also has a significant effect on diastolic function of the heart. The duration of obesity also strongly contributes to the likelihood of CHF (Table 6.4 and Figure 6.4).

6.4 Cardiac dysfunction

Echocardiographic analysis of 50 obese subjects (40 female and 10 male) revealed a progressive decline in the *E/A* ratio as a function of the duration of obesity. *E* represents the early diastolic mitral inflow velocity, while *A* represents late diastolic mitral inflow velocity. A declining *E/A* ratio suggests progressive diastolic dysfunction. In summary these investigators demonstrated the importance of duration of obesity as an increased risk factor for cardiac systolic and diastolic dysfunction.

In a recent study Pascual *et al*. evaluated LV systolic and diastolic function in 48 obese women with isolated obesity and no other pathologic conditions and

Table 6.4 Factors associated with CHF in morbidly obese patients

Factor	*P* value
Duration of morbid obesity	<0.00000002
LV interval dimension in diastolic	<0.00003
LV end-systolic wall stress	<0.00004
E-wave deceleration time	<0.0000002
E/A ratio	<0.00008
Left atrial dimension	<0.000001
Right ventricular internal dimension	<0.00004

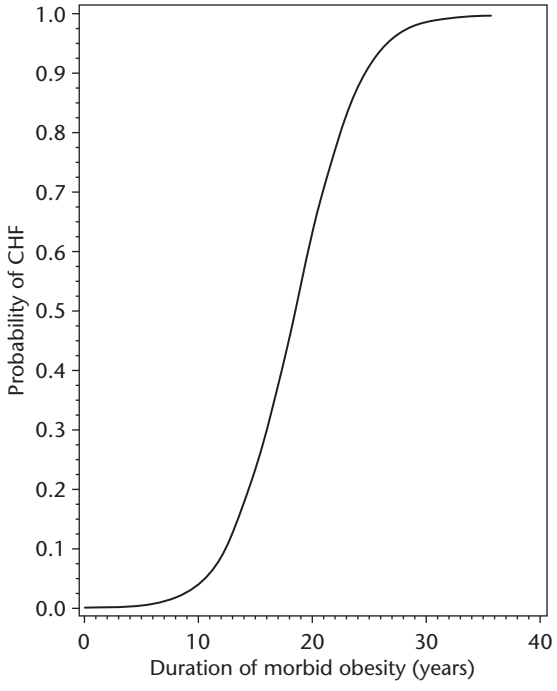

Figure 6.4 The relationship between the probability of CHF and the duration of obesity. Adapted from Alpert.

compared them with 25 normal weight women.[14] The 48 subjects were divided into three categories: slightly obese ($n = 17$; BMI 25–29.9 kg/m^2), moderately obese ($n = 20$; BMI 30–34.9 kg/m^2), and severely obese ($n = 11$; BMI $\geq$ 35 kg/m^2). Echocardiographic indices of systolic and diastolic function were obtained; dysfunction was assumed when at least two values were $\geq$2 standard deviations from the normal controls. Ejection fraction, fractional shortening, and mean velocity of circumferential shortening were statistically significantly increased in the slight and moderately obese groups. LV dimensions were increased but wall thickness was not. It was concluded that none of the obese patients fulfilled criteria for systolic dysfunction. However, it was found that the mitral valve pressure half-time, and the left atrial diameter were increased and the deceleration slope decreased. Subclinical diastolic dysfunction was more prevalent in the severely obese group (45%), but was apparent in two (12%) of the slightly obese, and seven (35%) of the moderately obese subjects. The diastolic dysfunction correlates with BMI, and it appears early in obesity that systolic function is initially enhanced. While this study importantly examined isolated obesity and concluded that diastolic dysfunction appears to occur early in obesity, Vasan was concerned that the interpretation of the data might have been overstated.[4] He pointed out that an increase in mitral valve pressure half-time with increased BMI might be explained by the increase in LV end diastolic volume and might not be related to intrinsic changes in myocardial relaxation. Furthermore other investigators studying obese patients have reported increased, decreased, and unchanged transmitral E-wave velocities. Vasan suggests that one can infer that diastolic filling patterns are modified in the obese patient but further examination of LV diastolic filling including exercise protocols are necessary in order to make a definitive conclusion that diastolic dysfunction exists.

A European study has examined the prevalence of diastolic dysfunction in an age-stratified population. They examined 1274 subjects, 25–75 years of age. Echocardiograms were obtained from left parasternal and apical windows yielding M-mode echocardiograms, and Doppler recordings were performed. They determined early (E) and late (A) diastolic velocities, as well as isovolumic relaxation time (IVRT). The European Study Group on Diastolic Heart Failure defined the following parameters as abnormal: $E/A_{<50\ \text{years}}$ was <1, or $E/A_{>50\ \text{years}}$ was 0.5, or $\text{IVRT}_{<30\ \text{years}}$ was >92 ms, or $\text{IVRT}_{30–50\ \text{years}}$ was 100 ms, or $\text{IVRT}_{>50\ \text{years}}$ was 105 ms in the presence of an ejection fraction $\geq$0.5. Diastolic dysfunction was defined as echocardiographically determined diastolic abnormalities in the presence of current diuretic therapy and/or left atrial enlargement. Obesity was found to be an independent risk factor for diastolic dysfunction (relative risk = 1.6). Two other strong risk factors for diastolic dysfunction were arterial hypertension (relative risk = 2.8) and LVH (relative risk = 7.6). Since obese individuals often suffer from hypertension and LVH, the prevalence of diastolic abnormalities and diastolic dysfunction probably approach 16% and 7%, respectively.[15]

Despite this high prevalence of diastolic abnormalities and dysfunction, systolic function appears well

preserved in the obese individual. In an echocardiographic examination measuring mid-wall shortening in normotensive and hypertensive normal and obese subjects the presence of overweight or frank obesity did not worsen LV myocardial efficiency in hypertensive individuals. They found that mid-wall LV systolic performance in asymptomatic overweight or frankly obese individuals was comparable to that in normal-weight individuals in both the presence and absence of arterial hypertension. However, maintenance of normal LV performance in obese individuals occurs in the presence of LV chamber enlargement suggesting that preload reserve has been recruited moving the LV function curve further to the right. This finding potentially explains the lack of increase in SV that is observed in exercising obese individuals; obese individuals have already optimized their LV filling in the resting state and have no ability to further dilate the LV.[10] The occurrence of CHF in obese individuals appears to be the result of long-term obesity.[3,16] At this time data is not available to determine whether one can really distinguish between systolic failure and diastolic failure in the obese patient.

6.5 Arrhythmias

The heart and coronary vasculature of obese individuals are subjects to a variety of coronary risk factors and hemodynamic changes, which increase the risk of coronary pathology. Ultimately, myocardial ischemia, cardiac arrhythmias, or both may develop, increasing the risk of sudden death.[17,18]

Cardiac arrhythmias and conduction deficits are common in obese patients (see also Chapter 17) Several factors predispose these individuals to arrhythmias. Presence of ectopic beats and ventricular tachyarrhythmias may be a result of a concentric pattern of LVH.[9] Sleep apnea syndrome can itself lead to sinus bradycardia and heart block during apneic episodes. Obesity is also a significant risk factor for atrial fibrillation. Fatty infiltration of pacemaker pathways can lead to a disruption or improper conduction of electric impulses.[17] Arrhythmias may also be precipitated by hypercapnia, hypoxia, increased catecholamine concentrations and electrolyte disturbances secondary to diuretic therapy. Morbid obesity can produce a variety of electrocardiographic (EKG) alterations including but not limited to low QRS voltage, leftward shift of the P, QRS, and T axes and multiple EKG criteria for LVH and left atrial enlargement. Alpert *et al*. concluded that substantial weight loss is capable of reversing many of the EKG alterations associated with morbid obesity.[19] Weight loss significantly shifted the mean P-wave, QRS, T-wave axis rightward.

6.6 Hypertension

Hypertension in combination with severe obesity burdens the heart due to increased preload and afterload.[20] It has been reported that approximately 60% of obese individuals have hypertension [21,22], and that the prevalence is two times higher in overweight subjects compared with individuals of normal weight.

The association between obesity and arterial hypertension has been established in a great number of studies. The Framingham Heart Study documented that a weight gain of 5% increases the risk of hypertension by 30% in a 4-year period[23] (Figure 6.5).

Specifically, stimulated sympathetic outflow and activated renin–angiotensin system have been identified as characteristic features in obese hypertensive patients.[24] Obese patients have hyperdynamic circulation that may further increase blood pressure levels.[25] Likewise, blood visosity which is elevated due to an increased hematocrit level, adds to a pressure load on the heart.[26]

Obesity is associated with volumetric arterial hypertension and with early increase in heart rate and decreased heart rate variability. Sorof *et al*. found that increased heart rate and blood pressure variability in obese children with isolated systolic hypertension suggest that sympathetic nervous system hyperactivity may contribute to its pathogenesis.[27] It has been demonstrated that obesity related hypertension causes marked changes in gene expression in right atrium as well as in the LV that may contribute to early functional changes and to long-term structural changes such as LVH and remodeling.[28] Weight reduction induced by gastric operations for severe obesity is

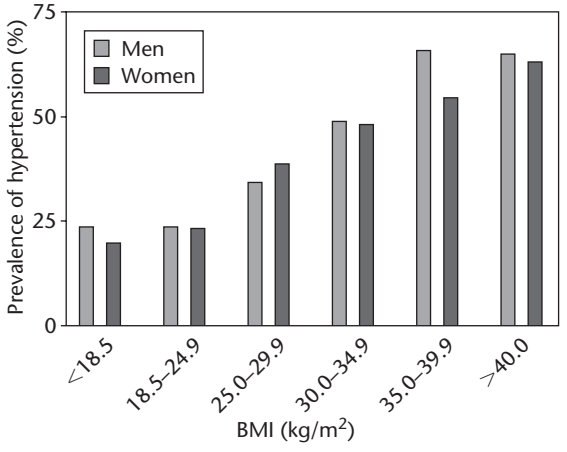

Figure 6.5 The prevalence of hypertension in men and women as a function of BMI. Adapted from Ref. [23].

associated with resolution of hypertension as well as improved systolic function of the heart.[20]

6.7 Coronary artery disease and insulin resistance

Obesity is an independent risk factor for development of CAD. Obese individuals also have an increased risk for CAD through its association with insulin resistance, hyperlipidemia, and hypertension (Figure 6.6).

The insulin resistant state, even in the absence of clinical diabetes mellitus, is a major risk factor for the development of the CAD.[29–31] Both obese[32,33] and non-obese[34,35] non-diabetic subjects with body fat accumulation at the abdominal level are characterized by alterations in plasma glucose–insulin homeostasis similar to those observed in type 2 diabetes. Abdominal fat distribution pattern has been correlated with alterations in lipid–lipoprotein metabolism predictive of an increased risk of CAD.[36,37] These results have been confirmed by studies that have examined the effect of visceral obesity on lipid disturbances in obese populations[38–40] as well as in non-obese populations.[41,42] Increased generalized obesity *per se* has also been associated with deterioration in lipid–lipoprotein levels.[43] Many long-term studies suggested presence of strong relationship between central obesity and coronary heart disease.[44–49] Several investigations identified the presence of a high waste-to-hip ratio as an independent risk factor for coronary artery heart disease, where as peripheral obesity has not been shown to be a risk factor for CAD.[41,49–52] The Framingham Study[44] and Normative Aging Study[53] demonstrated that age at onset of obesity is an important factor in the development of CAD. In these studies, there was in inverse correlation between the age of onset of obesity and the probability of developing coronary heart disease. Han *et al*. showed an increased prevalence of adverse risk factors, such as low high-density lipoprotein (HDL) levels, hypercholesterolemia, and hypertension as a function of waist circumference[54] (Figure 6.7).

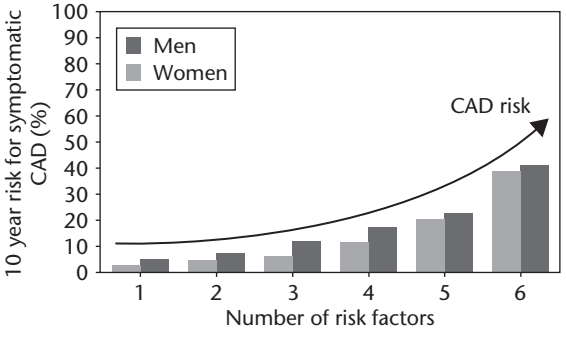

Figure 6.6 The 10-year cumulative risk of CAD as a function of the number of risk factors, including low HDL, hypercholesterolemia, smoking, diabetes, and LVH. Adapted from Shunkert (2002).

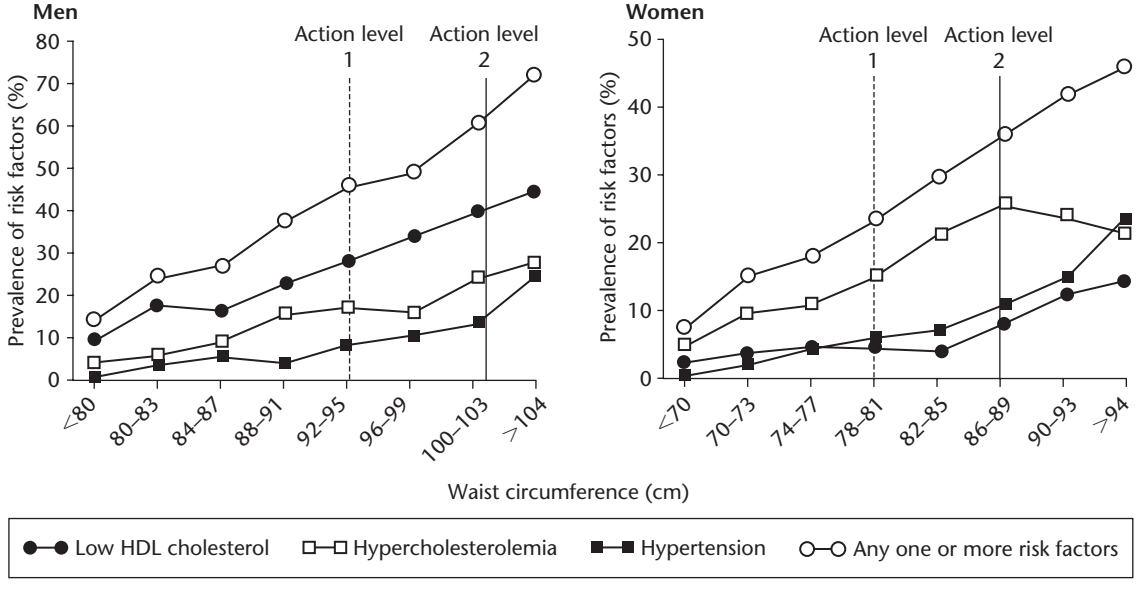

Figure 6.7 The increased prevalence of adverse risk factors as a function of waist circumference in cm. Adapted from Ref. [54].

In patients with established CAD there was an association between BMI and the risk of recurrent coronary events.[55] Weight reduction may favorably alter CAD risk factors associated with obesity. Dietary weight reduction results in a lesser degree of dislipidemia in obese subjects, with lowering of total cholesterol, LDL, triglycerides and VLDL and increase in HDL levels. When hyperinsulinimia with or without diabetes is present, substantial weight loss is accompanied by improvement in obese individuals, with enhanced glucose oxidation and increased insulin sensitivity[56,57] both with total fat mass reduction[56–58] and predominant reduction in abdominal visceral fat.[59,60]

6.8 Anesthetic considerations related to the cardiovascular system

The cardiovascular concerns will be clarified by a thorough history and examination and if necessary consultants' responses particularly the cardiologist. The points that need clarification are:

1. Degree of obesity, what is the BMI and how is the weight distributed, that is, the waist-to-hip ratio?
2. How old is the patient and how long have they been obese?
3. Are they hypertensive?
4. Are they diabetic?
5. What is their exercise tolerance?
6. Are there signs and symptoms of CHF?
7. Is there a history or evidence of arrhythmias?
8. What medications are they taking?

Why do we want to have answers to these questions? It is because the development of obesity cardiomyopathy is an inevitable consequence of obesity and is related to duration of obesity and concommitant problems such as hypertension and diabetes. The development of hypertension and diabetes suggests, but does not prove, that the patient has been obese for several years.

We know that the obese individual has a hyperdynamic circulation, manifest by increased intravascular volume, increased cardiac output, and increased SV. We also know that a consequence of the hyperdyanamic circulation is a dilated heart, that over time also hypertrophies. Early on in the obese patient's obesity the compensation for increased oxygen demand of the adipose tissue is an increased blood volume that leads to dilated LV. It has been said that obesity is similar to exercise, but it is a constant state of "exercise". Since the ventricle is already dilated there is a decreased possibility that increased demand can be met by an increasing preload, rather increased demand will require an increased heart rate. However, if the patient has been obese for many years it is likely that his/her LV mass has also increased resulting in a stiff, thick chamber that has some compromise of both its relaxing properties and its perfusion properties. There is currently a distinction between systolic heart failure ($EF \leqslant 0.5$) and diastolic heart failure ($EF \geqslant 0.5$).[3] If heart failure exists and the EF is below 0.5 it is characterized as diastolic failure, with the progression of obesity and hypertension it is likely that heart failure will most likely be due to diastolic dysfunction, eventually, however, systolic dysfunction might also come into play. One should be concerned about ischemia resulting from an elevated heart rate and consideration should be given to perioperative β adrenergic blockade (see also Chapter 11).

One therefore needs to maintain the volume status of the patient in order to maintain cardiac output and consider β blockade. If the patient has been NPO for 8–12 h early fluid replacement should be initiated. Of course one needs to be aware of any signs or symptoms of CHF or whether the patient has been on chronic diuretic therapy prior to initiating fluid therapy. In summary the cardiovascular status of a morbidly obese patient should be considered abnormal and the duration of their obesity should be ascertained in evaluating the degree of cardiovascular dysfunction that exists (see also Chapter 9).

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PHYSIOLOGICAL CHANGES DURING LAPAROSCOPY

7

M. Fried

7.1 Introduction

Bariatric surgery represents a true challenge, however significant accomplishments have been achieved in this field in the past decades. Complexity of surgery for morbid obesity lies mainly in the specialized care and knowledge required for successful pre-, intra- and post-operative outcome as well as for minimizing long-term complications and achieving substantial and lasting weight loss results (see Chapter 1).

Throughout surgical history, one of the main objectives has been to minimize operative trauma and improve peri-operative and post-operative outcome. There have been many different attempts to reach this goal. However until surgery has been invaded and overwhelmed by laparoscopy such attempts have been just of moderate success. Laparoscopic methods offered so far the least invasive approach with lower morbidity and mortality in comparison with majority of "classic" laparotomy procedures (Figures 7.1 and 7.2).

Furthermore, the laparoscopic approach offers early mobilization and rehabilitation, especially advantageous in bariatric surgery. Today, the advantages of laparoscopy have extended the technique to include a wide range of physical condition and ages.[1]

Despite of advantages resulting in less post-operative pain, fewer pulmonary complications, faster post-operative recovery and often shorter hospital stay, laparoscopic surgery is associated with more pronounced intra-operative respiratory and cardiovascular changes than "open" surgery. As laparoscopy has moved from the young healthy patient undergoing mostly gynecological laparoscopies performed even under local or regional anesthesia in the 1970s and 1980s to a more diverse and obese population, presence of chronic medical conditions and co-morbidities has increased among the potential surgical candidates.

Obese patients have with no doubt increased prevalence of serious co-morbidities which associate obesity with increased risk of complications. This might be especially pronounced in bariatric surgery where as a

Figure 7.1 Laparoscopic bariatric surgery is less invasive in comparison with laparotomy procedures.

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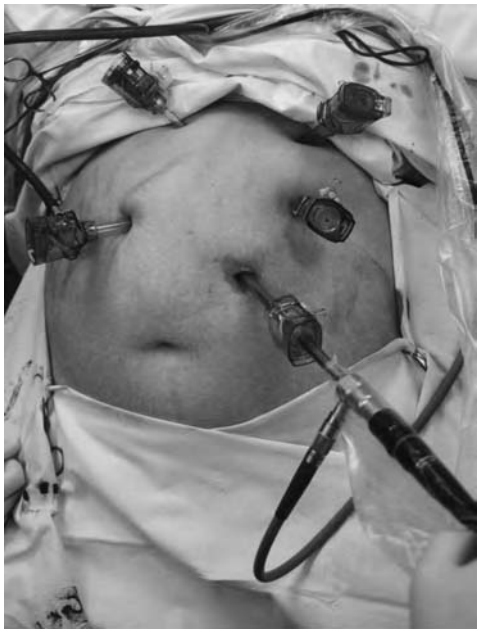

Figure 7.2 Laparoscopic bariatric surgery is less invasive in comparison with laparotomy procedures.

result of this fear to operate on morbidly obese patients might be quite a common case.[2–4] Some anesthetists are reluctant to anesthetize such a patient because surgical intervention and namely laparoscopy as well as general anesthesia with endotracheal intubation itself remain in their view potentially problematic procedure.

However many studies on obesity and anesthesia reveal that from a cardio-pulmonary point of view carbon dioxide (CO_2) abdominal insufflation is surprisingly well tolerated in morbidly obese and in fact capnoperitoneum (CP) does not cause any dramatic changes in cardiac output (CO) as well as in respiratory functions however there are differences in hemodynamic consequences of peritoneal insufflation in obese and non-obese patients. Moreover hemodynamic and respiratory differences could be detected even at baseline (BL) (rest) examination comparing non-obese and obese individuals (see also Chapters 4 and 5).

There is no doubt that surgical approach to the morbidly obese patient remains a challenge for the surgeon and for the anesthesiologist.

The obese have an increased prevalence of some systemic disease usually associated with obesity, such as type II diabetes, hypertension, hyperlipidemia, hypercholesterolemia and many others which generally speaking impair their level of health.

Systemic hypertension is common among obese individuals and there is positive correlation between obesity and systemic hypertension.

Starting from moderate obesity patients are susceptible to hypoventilation associated with increase in ventilation–perfusion inequalities at rest as well as during exercise. Other factors that play role in ventilation pathologies found in morbidly obese are increased respiratory muscle work load and decreased in breathing efficiency. In hypercapneic obese patients the work for lung inflation increases by 100% and for the chest wall movements even higher, to 200% in comparison with non-obese individuals.

Therefore great care should be taken of all pre-, intra- as well as post-operative steps and investigations in order to avoid to maximum possible level any foreseeable complication.

Pre-operatively it is essential to include detailed patient history with focus on possible presence of ischemia, hypertension, left or right heart failure and/or peripheral vascular disease.[5–9] (see also Chapter 9)

In our opinion in obese patients undergoing bariatric procedure general anesthesia with endotracheal intubation to adequately protect airway and mechanically control ventilation without gastric distention is adequate justification for this technique.[10]

Regardless of the anesthetic technique finally used, vigilance is of enormous importance. Laparoscopic technique uses smaller incisions and is with no doubt less invasive to the patient, there are still important factors and physiological effects that need to be taken into account.

In the post-operative period closer monitoring of obese patients is essential and important (see Chapter 25). This feature will allow to react immediately if needed as especially in morbidly obese some warning signs and symptoms might be hidden for quite a long period before becoming evident.

7.2 Physiology of laparoscopy

Laparoscopy from its basic technical design usually possesses three main physiological functions: respiratory, hemodynamics and cardiovascular.

7.2.1 Respiratory functions

In all laparoscopic procedures effect of CP and its consequences must be taken into account. This fact can contribute to pulmonary atelectasis and decrease in the functional residual capacity (FRC) of the lungs as well as to high peak airway pressure.

Metabolic activities in obese patients and raised VO_2 and VCO_2 necessitate higher alveolar ventilation. Mass loading of the body wall reduces respiratory compliance for more than one-third lower than would be expected in non-obese individuals.

Generally speaking, $PaCO_2$ increases with CP and must be compensated for by increased ventilation. On the other hand, abdominal distention and patient position impairs ventilation. Moreover CO_2 is absorbed from the abdominal cavity and diaphragm elevation during laparoscopy results in mismatch of ventilation and pulmonary perfusion. Increased in the arterio-alveolar CO_2 difference is associated with increased physiological dead space.[11]

Complications associated with intra-abdominal CO_2 insufflation might result in subcutaneous emphysema, pneumothorax and/or pneumomediastinum. Clinical findings of crepitance into the chest, shoulders and neck may be the first sign which might later on develop into respiratory distress and pneumothorax. Signs of tension pneumothorax should be of major concern. The most common cause of such a complication is related to improper insufflation (Veress) needle placement and/or use of high insufflation intra-abdominal CO_2 pressure.[12]

7.2.2 Hemodynamic and cardiovascular functions

Generally, obesity has an adverse effect on the cardiovascular system. Increase might be found in CO, stroke volume (SV), cardiac index, left ventricular (LV) and right ventricular (RV) stroke and mean pulmonary artery pressure as a result of usually increased metabolic need of obese patient. Blood and extracellular volumes may increase as well despite the fact that blood volume–body weight proportion is relatively small affecting LV changes including increase of LV load. Increased activity of renin–angiotensin–aldosterone system contributes to even further intravascular volume expansion as well as to usually increased mean arterial pressure and mean pulmonary artery pressure. On the other hand, slight decrease of systemic vascular resistance (SVR) might be noted.[9,13–16]

Increased body mass index (BMI) is responsible for increase in CO which is associated with increased SV and cardiac work.

RV changes are mostly affected by excess weight resulting in higher RV filling pressure.

The CP might result in changes in CO, increased blood pressure and increased SVR and peripheral vascular resistance (PVR). Effect of intra-abdominal pressure however enormously depends on its level. Highly elevated intra-abdominal pressure might be responsible for reduced venous return – decreased preload, and an increase in afterload, finally leading to reduced CO. However little information is available on cardiac contractility variations during laparoscopy.[17,18] Various humoral factors probably stand behind increased SVR because they outlast the CP. CO depends not only on the above mentioned, however it should be noted that CO is influenced by dynamic summary of current interactions of heart rate (HR), SV (which depend mainly on preload, contractility, afterload and in some conditions on possibly affected heart wall motion capability and/or possible valvular dysfunction).[13–15]

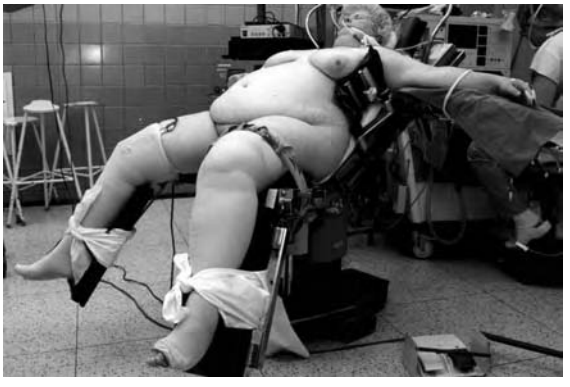

Figure 7.3 Patient position for bariatric procedure – gastric banding.

If the intra-abdominal pressure is higher than 20 mmHg, renal blood flow falls. Glomerular filtration lowers to even less than one-quarter of normal (see Chapter 14). Such a high intra-abdominal pressure might also affect substantially blood flow to the intestines.

Effect of laparoscopy on cardiovascular system depends as well on patient's position (see Chapter 20). In the head-up position CO decreases in proportion to the steepness of tilt. Together with effect of CP on blood pooling and venous stasis in the legs, and length of the procedure, this can contribute to increased risk of venous thrombosis and pulmonary embolism (Figure 7.3).

On contrary, steep head-down patient position necessary in some laparoscopic procedures might cause reduced FRC, total lung volume and pulmonary compliance. It might contribute to the development of atelectasis as well. This position often results in increased central venous pressure which may affect cerebral circulation and cause increased intra-ocular venous pressure.

Various cardiac arrhythmias may result from the reflex increase in vagal tone caused among other reasons by

peritoneal stretching and/or manipulation with the viscera.

Hypercarbia if it occurs, have cardiovascular implications (increase in cardiac rate and affecting contractility) conducted by its sympathetic effect. Increase in tidal volume which might be required in order to compensate increased CO_2 from the abdominal cavity may produce increase in the mean pulmonary artery pressure. This may result in decrease of SV and CO.[19]

If cardiovascular collapse occurs in the intra-operative or immediate post-operative period the eventuality of gas (CO_2) embolism should be considered. This event might be associated with or present as non-cardiogenic pulmonary edema and/or neurologic affection from anoxia or cerebral embolization.

Venous gas embolism can occur if the CO_2 intra-abdominal pressure is higher than the central venous pressure. Small amounts of venous gas embolism usually do not cause any major physiologic changes. However larger amounts can cause hypoxemia due to low ventilation/perfusion rates, pulmonary hypertension associated with this event and/or mechanical obstruction of the right heart ventricle might result in rapid cardiogenic shock and life-threatening condition from RV failure.[20] Massive bleeding caused by trocar injury to intra-abdominal vessel might be another cause of rapid cardiovascular collapse.

7.3 Own data and experience

Being focused for almost two decades on laparoscopic and bariatric surgery it is natural that one of our main interests has been in evaluating impact of laparoscopy on cardiac functions both on non-obese as well as on obese individuals undergoing general laparoscopic surgical procedures and/or laparoscopic bariatric operations.[21]

Monitoring of cardiac functions during laparoscopic surgery has been performed by many authors with different approaches and methods. However reviewing published literature data, only limited information on safety or potential danger of laparoscopic procedures in morbidly obese patients with or even without cardiovascular disease is available. Moreover many of the so far published data vary according to anesthesiological and surgical protocol, measurement techniques and reproducibility of patient status.[13]

In a view of the fact that so far published data differ substantially even in basic observations due to the effect of laparoscopy on cardiovascular and respiratory functions in obese individuals, it was impossible to present a consistent didactic overview. Therefore we feel that it is more appropriate to present some own data and experience in this field rather than trying to accomplish impossible consensus.

For purposes of our evaluation we selected transesophageal echocardiography (TEE) – with HP Sonos 5500 with transthoracal S4 probe and omniplanar transesophageal probe – in order to measure at the same time the systolic and diastolic LV performance and to be able to monitor CO (Figure 7.4).

Moreover TEE is feasible to perform during anesthesia and it does not represent any additional substantial risk to the patient. For comparison purposes group of 10 non-obese patients undergoing laparoscopic surgery for benign diagnoses (three lap-cholecystectomy, two lap-inguinal hernia repair, five lap-Nisssen fundoplication) underwent the same examination as the group of 10 obese patients scheduled for laparoscopic bariatric procedure (nine of them Swedish adjustable gastric band (SAGB) and one gastric bypass (GP)). Usually, all such additional investigations are approved by the Local Ethics Committee. Data obtained were analyzed statistically using ANOVA method; for independent subgroups comparison *t*-test has been applied as well as Friedman's test for repeated measurements.

Patients were examined pre-operatively by transthoracal probe, and transesophageally again after introduction of general anesthesia and endotracheal intubation. As effect of laparoscopy on respiratory, hemodynamics and cardiovascular functions usually depends on CO_2 insufflation and patient position during the procedure, three sets of data were evaluated:

- **a** pre-operative BL values obtained well in advance of the planned operation,
- **b** values following surgical intra-abdominal CO_2 insufflation (CP),
- **c** values measured after positioning (SP) patient for respective surgical procedures.

In order to obtain as much as possible objective data all the measurements were repeated three times and averaged. LV outflow tract diameter *(D)* was measured at the beginning of the procedure. LV outflow tract pulsed wave Doppler velocity recordings were performed as well and velocity–time integral (VTI) was measured in all sets of data.

For HR monitoring simultaneous ECG was used and CO was calculated as:

$$\mathrm{CO} \times \frac{\pi \times \mathrm{D} \times 2}{4 \times \mathrm{VTI} \times \mathrm{HR}}\ (\mathrm{ml/min}).$$

Total PVR was calculated as :

$$\mathrm{PVR} = (\text{mean arterial blood pressure} \times 80)/\mathrm{CO}.$$

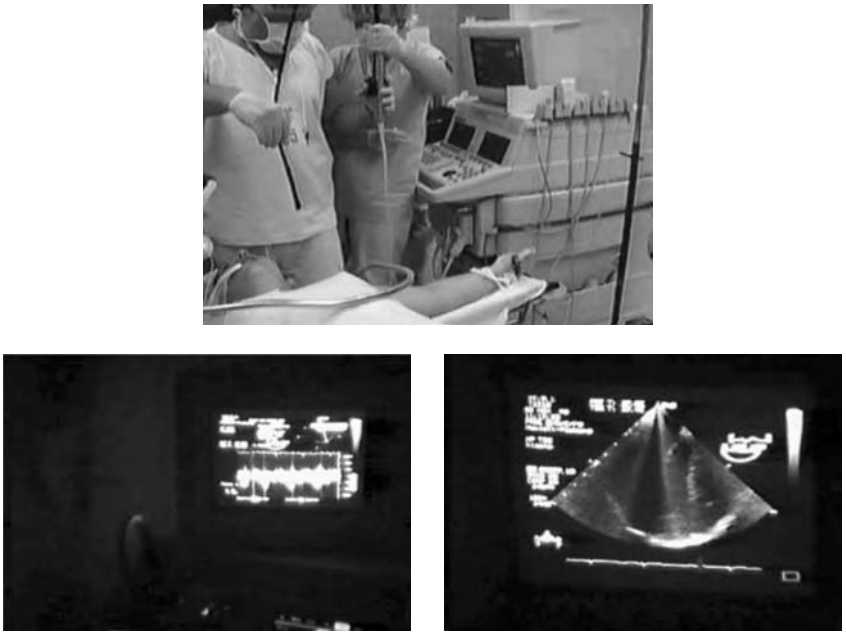

Figure 7.4 TEE performed during our study on obese and non-obese patients undergoing various laparoscopic procedures.

Ejection fraction (EF) was evaluated using Simpson's formula from the view allowing best LV cavity visualization. The same view was used throughout the entire procedure. Transmitral flow was monitored by measuring the velocities of peaks E and A, and calculating their ratio.

For blood pressure (BP) measurement, standard oscillometric device was used with cuff size appropriate to patient's arm circumference.

Pressure–rate product was calculated as BP × HR values (Table 7.1).

7.3.1 Effect of laparoscopy on heart rate

As it has been anticipated, at BL the pressure–rate product was higher in obese individuals and significant increase ($P < 0.01$) in HR after CP introduction in all laparoscopic procedures in obese and non-obese patients has been observed in comparison with the BL values. The increase copied the already higher BL levels in obese patients, compared to non-obese individuals and BL values and absolute increase in CO were significantly ($P < 0.05$) greater in obese patients.

The HR did not change significantly after positioning the patients (there was no statistical difference between CP and SP) however there has been more pronounced HR increase in conjunction with SP in obese individuals. The measured differences did not reach statistical difference. Therefore it could be speculated that the increase in HR is probably accompanied by increase of myocardial contractility caused among other reasons by increase in sympathetic tones which stabilizes within the first 15–20 min after CP introduction. An increase in the endogenous catecholamine level is usually observed with hypercapnia during SP.[7]

7.3.2 Effect of laparoscopy on cardiac output

The BL and absolute increase in CO was significantly lower ($P < 0.05$) in non-obese patients. After CP introduction there was increase in BP and pressure–rate product levels noted in obese patients. However even at BL, the pressure–rate product was higher in obese individuals and the increase copied the already higher BL levels. The increase in CO was due to tachycardia and occurred despite a significant increase in arterial pressure. This has had no significant effect on LV EF and no significant decrease in EF was noted.

Similarly as in HR levels there were no significant changes between CP and SP observed in CO.

7.3.3 Effect on peripheral vascular resistance

The PVR values have been the same both among non-obese individuals compared to obese patients. During repeated measurements PVR did not change

Table 7.1 Hemodynamic parameters in the overall study population and in subgroups of non-obese and obese patients

	Overall (n = 20)			Non-obese (n = 10)			Obese (n = 10)		
	BL	CP	SP	BL	CP	SP	BL	CP	SP
Heart rate (bpm)	75 ± 6	84 ± 11	83 ± 8	74 ± 6	78 ± 9	79 ± 9	76 ± 6	87 ± 11	88 ± 4
CO (l/min)	5.7 ± 6.5	6.6 ± 2.6*	6.7 ± 2.7*	4.1 ± 1.2	4.6 ± 1.3*	5.3 ± 1.6*	7.5 ± 1.8$^{\#}$	8.4 ± 2.1*$^{\#}$	8.2 ± 2.6*$^{\#}$
CI (l/min/m^2)	2.54 ± 0.65	2.82 ± 0.72*	2.81 ± 0.90*	2.27 ± 0.46	2.51 ± 0.55	2.56 ± 0.63	2.80 ± 0.74	3.13 ± 0.79	3.05 ± 1.12
MAP (mmHg)	95 ± 11	103 ± 11	108 ± 12*	89 ± 12	94 ± 12	98 ± 7	98 ± 5	110 ± 10	118 ± 7*
PVR (dyn s/cm^5)	1508 ± 546	1511 ± 609	1618 ± 533	1821 ± 592	1822 ± 635	1818 ± 325	1195 ± 282	1205 ± 440	1415 ± 655
Pressure–rate product	9234 ± 1225	11,718 ± 3219*	12,047 ± 2762*	8842 ± 1623	9653 ± 1939	9785 ± 1365	9625 ± 603	13,790 ± 2986*	14,312 ± 1584*
EF (%)	65 ± 9	64 ± 5	63 ± 4	66 ± 8	63 ± 7	64 ± 6	67 ± 7	62 ± 5	62 ± 2
E/A	1.9 ± 1.8	1.9 ± 0.8	1.8 ± 0.7	2.0 ± 0.8	1.8 ± 0.7	1.9 ± 0.7	1.8 ± 0.9	1.9 ± 0.9	1.8 ± 1.8

BL, baseline; CP, capnoperitoneum; SP, surgery position; CI, cardiac index; MAP, mean arterial blood pressure; PVR, peripheral vascular resistance; EF, ejection fraction; E/A, peak E to A wave velocity ratio of transmitral filling flow. Data are mean ± SD. *$P < 0.05$ vs. BL data.
$^{\#}P < 0.05$ vs. non-obese subgroup.

significantly in neither of the groups. The only observed change was in decrease of EF, which was however not significant and in fact negligible.

In our experience there are no dramatic changes associated with obese patient positioning for surgery. Semi-sitting position used for majority of bariatric procedures seems to be safe and has no significant hemodynamic impact despite the fact that decrease in pre-load in this position could be expected. As obese patients have a higher intra-abdominal pressure in supine position than non-obese individuals, head-up position with caudal shift of viscera decreases significantly pressure on the diaphragm in obese. As a result of this, obese might have better abdominal compliance to CP than non-obese and that could probably help to further minimize the hemodynamic effects of CP.

Some authors describe negative hemodynamic effect of Trendelenburg position which in their experience leads to important increase in venous return and filling pressure; however in our experience this fact has no major impact on hemodynamic status as well, although there are not enough data available yet on this issue to allow us to draw statistically reproducible conclusion. Moreover in some studies even if patients were placed in a 20° head-down Trendelenburg position, their hemodynamic profile was comparable to the non-obese patient during laparoscopic procedures.[22]

It can be only hypothesized that sympathetic stimulation which might be higher in obese individuals plays predominant role in the circulatory response to CP leading to increased HR and BP with CP being the major stimulus of the hemodynamic load during minimally invasive surgery.

Changes in venous return related both to CP insufflation and SP are not even in obese patients not probably intense enough in our hands (providing that the above mentioned during operation CP criteria are respected) to produce any significant modification of evaluated parameters.

In comparison of both groups (obese vs. morbidly obese), obese individuals had a more pronounced increase in HR and CO. However the difference in CO was not significant after adjustment made to body size. Nevertheless there has been noted greater absolute increase in CO in obese individuals who represent a supplementary load to their cardiovascular system and may present certain higher risk in comparison with non-obese patients. This conclusion corresponds with observation of a significantly more pronounced increase in pressure–rate product in obese patients compared to non-obese group.

Our experience confirm that minimally invasive approach in obese patients without concomitant cardiovascular disease is accompanied with an increase in CO without any significant decrease in LV systolic performance. This hemodynamic response has been observed not only in non-obese but also in morbidly obese patients.

Such data are of particular clinical interest. On one hand, the increase in HR and CO and PVR may be interpreted as a potentially dangerous load which may lead to possible cardiac complications in certain patients. On the other hand the increase in CO in the overall population investigated for the study purposes did not exceed 10%. Such an increase should be well tolerated even by subjects with cardiovascular involvement.

7.4 Conclusion

In conclusion we might assume that from circulatory and respiratory point of view laparoscopic bariatric procedures are safe for morbidly obese patients especially having on mind that even less post-operative anesthetic problems are usually observed after minimally invasive procedure than following open surgery for obesity.

Nowadays bariatric surgery is a well established and worldwide accepted approach to morbid obesity treatment. In fact it is the only currently available treatment with acceptable long-term results offering substantial weight losses as well as weight reduction maintainance and low morbidity and mortality procedure-related complication rates. On top of that laparoscopic bariatric procedures have firmly anchored in surgical armory for obesity treatment as the least invasive approach with many advantages (Figure 7.5).

Figure 7.5 Laparoscopic bariatric surgery is prevailing in surgical obesity treatment.

Of course new technical approaches to morbidly obese patient with substantial co-morbidities have been accompanied with new challenging problems. It is encouraging that as each new problem is identified, in majority of cases it is solved in turn by joint effort from different medical specialties.

All these have resulted in remarkable improvement in results of bariatric surgery in last few decades and despite the fact that morbidly obese patient is at risk of higher intra- and post-operative morbidity and mortality, meticulous attention during the entire treatment period should reduce this risk to equivalent risk seen in general non-obese population. We are lucky enough to already witness this period in bariatric surgery (see Chapter 30).

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DIGESTIVE PHYSIOLOGY AND GASTRIC ASPIRATION

8

P. Marko, A. Gabrielli, L.J. Caruso & A.J. Layon

8.1 Physiology of gastric acid production

8.1.1 Introduction

The stomach secretes hydrochloric acid, intrinsic factor, bicarbonate, and mucus into its lumen. Functionally the stomach is divided into two parts: proximal and distal. The proximal part comprises the anatomic corpus and fundus. The distal portion is the antrum or pyloric gland region.

The cells responsible for gastric secretions are mucosal cells that line the surface of the gastric wall. The major secretory cells in the proximal part of stomach are parietal (oxyntic) cells, which secrete acid and intrinsic factor, and the chief (or peptic) cells, which secrete group I pepsinogen. In the distal portion of the stomach, pyloric glands secrete the hormones gastrin and somatostatin. Throughout the stomach, mucus neck cells secrete mucus and group II pepsinogen, and surface epithelial cells secrete bicarbonate, mucus, and group II pepsinogen.

Gastric acid secretion varies according to the time of the day, the time and types of food intake, psychological states, and other metabolic activities of the body. The *cephalic phase* of gastric secretion regulation is activated by thoughts of food, by sight, smell, and taste of food, and by the acts of chewing and swallowing. The vagus nerve is the major stimulatory pathway via M1 muscarinic cholinergic receptors. Distention of the

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stomach and the presence of protein and certain other food substances in the gastric lumen stimulates gastrin secretion by pyloric glands in the *gastric phase*. Acidification of the gastric contents leads to feedback inhibition of gastric secretion by inhibiting the release of gastrin. After food leaves stomach and undergoes intestinal absorption, additional pathways in the *intestinal phase* are activated that can either stimulate or inhibit gastric secretion.

Parietal cell activity is regulated via nerves, hormones, and locally secreted substances. Adjacent regulatory cells are the enterochromaffin-like (ECL) cells and the D (somatostatin releasing) cells. ECL cells secrete histamine, which activates parietal cell secretion via H_2 receptors. The D cells release somatostatin, which inhibits histamine release by ECL cells via type 2 somatostatin receptor. Other inhibitory hormones are cholecystokinin and secretin, which have a role in the intestinal phase of regulation of gastric secretion.[1]

Gastric fluid volume and pH of the gastric fluid are functions of:

- continuous gastric secretion, which is about 50 ml/h in an average size adult;
- swallowing of saliva, which contributes about 1 ml/kg/h;
- ingestion of solid foods and liquids;
- the rate of gastric emptying.

Gastric emptying of clear liquids is rapid. Estimated half time is about 12 min, thus 95% of ingested clear liquids are emptied in 1 h. Solids are emptied from the stomach only when they are changed to a liquefied form, which requires an unpredictable period of time – up to 12 h. It is estimated that nearly 50% of solid food would remain in the stomach 2 h after ingestion. It is important to remember that trauma, pain, and certain drugs, especially opioids, may slow the rate of gastric emptying.[2]

8.1.2 Specifics in morbid obesity

Morbidly obese (MO) patients are found to have increased prevalence of hiatal hernias. Intra-abdominal pressure increases linearly with increasing weight. Furthermore in about 90% of fasting MO patients scheduled for elective surgery gastric fluid volumes will be >25 cc, and gastric fluid pH <2.5 at the time of induction of anesthesia.[3] This volume and pH are traditionally considered to be high risk for developing clinically apparent pulmonary damage if gastric aspiration occurs although it is unlikely that all gastric contents will be aspirated.[4]

Other risk factors that were traditionally attributed to MO patients – delayed gastric emptying and an increased incidence of gastro-esophageal reflux (GER) – were recently challenged. It was shown[5] that obese patients without symptoms of GER have a resistance gradient between the stomach and the gastro-esophageal junction similar to that in non-obese subjects in both sitting and lying positions. Although obese individuals have a 75% greater gastric volume than normal individuals, gastric emptying is actually faster in the obese, but as a result of the larger gastric volume, the residual volume is larger in obese individuals.[6] Both the faster gastric emptying and the larger gastric volume can be partially reversed by weight loss.[7] Despite such conflicting evidence it is still recommended to take precautions against acid aspiration.

8.1.3 Specifics after gastric reduction surgery

With the growing percentage of obese population in western countries, improving surgical techniques for the treatment of MO patients, and the current availability and acceptance of the surgical approach to this problem, one might expect to see more patients who have undergone some type of gastric reduction surgery. These patients present for surgery and their aspiration risk is not very well understood by anesthesiologists caring for them.

Studies performed to understand the mechanisms of how the surgical approach to MO works showed that gastric emptying of solid food is delayed in patients having undergone gastric partitioning procedures as compared to their pre-operative values. Emptying of the liquid meals does not seem to be affected as much.[8]

If sufficient time has elapsed since the performance of the bariatric surgery, these patients will have lost some weight and might not be easily recognized as being at risk for aspiration as a result of their delayed gastric emptying. To further complicate the picture, different bariatric procedures may have differential effects on gastric pouch emptying and the gastric emptying pattern might change over time.

Radionuclide labeled gastric emptying of fluid in patients after gastroplasty was found to be delayed 3 months after the procedure, but 12 months post-operatively their gastric emptying was found to be faster then the pre-surgical baseline.[9] In addition, some types of bariatric surgeries (especially those involving truncal vagotomy) result in a long-term post-operative decrease of gastric acid secretion and in this way their risk of pneumonitis as a consequence of gastric aspiration may be lower.[10] At the same time, there is an increased risk for gastric bacterial overgrowth and decreased gastric emptying resulting from decreased

hydrochloric acid secretion, and changed motility and anatomy of the stomach pouch.

In conclusion, it can be said that gastric reduction surgeries result in long-term effects on gastric physiology. Of those effects, post-operative gastric emptying and gastric acid secretion have been investigated in detail, but the precise risk for aspiration in this patient population is not well understood. Anesthesiologists should therefore consider that patients after bariatric surgeries may still pose higher risks of aspiration despite the fact that they are no longer MO.

8.2 Pathophysiology of gastric acid aspiration

8.2.1 History: evolution of the concept

In 1946 Mendelson, in his classical paper,[11] reported 66 pregnant patients at term who were thought to have aspirated gastric contents during either labor or the induction of anesthesia. He is considered to be the first to bring to general awareness the concept of gastric acid causing extensive lung injury in aspiration pneumonitis. In the same paper he reports results on a series of his experiments in rabbits designed to investigate the cause of aspiration lung injury. He found that instillation of large volumes of either hydrochloric acid or the unneutralized vomitus into the lungs of rabbits caused severe hemorrhagic pneumonitis and pulmonary edema. Installation of normal saline or neutralized vomitus caused only minimal changes. His conclusion was that aspiration of gastric acid is responsible for the clinical findings observed in his patients. He described what is now known as "Mendelson's syndrome" – signs of acute respiratory insufficiency, cyanosis, tachypnea, and tachycardia due to the aspiration of acid gastric contents.

Later, a critical pH level of <2.5 was found necessary to cause lung damage in most animal species. Maximal lung injury was found to occur at pH of 1.5 and below. The required volume of acid aspirated was found to be at least 2–4 ml/kg of body weight to result in significant injury in experimental animals.[12] Traditionally, gastric fluid volume >25 ml is considered a risk factor for identifying patients at risk for developing aspiration pneumonitis, should aspiration occur. This has been challenged recently[2] and a volume 20 times greater suggested. Data suggest that existing gastric volume does not increase the risk of pulmonary aspiration in patients undergoing elective surgeries.[4] Later an animal model of aspiration pneumonitis was developed. This model incorporates injection of large volumes of a highly concentrated solution of hydrochloric acid into one or both lungs of experimental animals.[12] Much of our present knowledge of aspiration comes from this animal model.

8.2.2 Acid aspiration

Pathologic and microscopic findings

After injection of hydrochloric acid into the lung of experimental animals rapid distribution occurs throughout the lungs, reaching periphery of the lungs within 12–18 s. Zones of atelectasis appear on the lung surface within minutes. Surprisingly, microscopic findings of the lungs of the animals killed within 1 h after aspiration showed only mild abnormalities.[12]

In the next 4 h after aspiration, the pathologic findings become more severe. Complete desquamation of the bronchial epithelium is observed, and polymorphonuclear leukocytes (PMNL) infiltrate the submucosa. The airways fill with desquamated epithelial and inflammatory cells. Lung injury is patchy and nonuniform, reflecting the unequal distribution of the acid throughout lung. Large numbers of PMNL infiltrate the bronchial lumen walls and the peribronchial alveoli, thus creating the microscopic picture of bronchiolitis. The alveolar space is filled with a large amount of edema fluid, red blood cells, and PMNL. Degeneration of both type 1 and type 2 alveolar cells and separation of the cells from the basement membrane is also observed.[12]

In the next 24–36 h alveolar consolidation develops. Forty-eight hours after aspiration, hyaline membranes can be noted, and by 72 h signs of lung organization and resolution may already be noted. A decrease in acute inflammatory changes, degeneration of bronchial epithelium, and proliferation of fibroblasts may be seen at this stage. Three weeks after aspiration, the lungs of experimental animals are usually normal or slightly increased in weight and microscopically characteristic signs of bronchiolitis obliterans can be seen.[12]

Clinical findings

Very soon after acid enters the lung, profound hypoxemia develops. Gas exchange abnormalities occurring in the first hour after aspiration far exceed the severity of the noted microscopic findings. This early hypoxemia is thought to be caused by reflex airway closure and atelectasis, as alveolar edema is seldom seen so early in the course of aspiration.

Later, microscopic and physiologic pictures are more closely correlated. The increased alveolar capillary permeability leads to plasma exudation, causing a large increase in extravascular lung water, which reduces

Table 8.1 Traditional risk factors for aspiration

Risk factor	Proposed mechanism
Increased age	Total swallowing duration is prolonged in older patients.[19] Physiologic insults to older patients are more likely to result in a swallowing abnormality and aspiration.
Decreased consciousness • Anesthesia, sedation • Drugs	Co-ordination between swallowing and breathing is reduced in the unconscious patient. Using a radioactive tracer as a marker, a pharyngeal aspiration rate of 45% was observed in normal subjects during sleep. This increased to 70% in patients with a pre-existing depressed level of consciousness.[40]
Neurologic dysfunction • Cerebrovascular accident • Dysphagia • Progressive neurologic disorders • Seizure	Impairment of the sensory or motor function of the oral or pharyngeal stages of swallowing.
Gastroesophageal reflux (GER)	GER is the initial event in the aspiration of gastric contents. Patients with GER have a slower onset of pharyngeal peristalsis and other pharyngeal abnormalities compared with normal controls.[82]
Gastroparesis and gastric distention	Gastric distention results in relaxation of the lower esophageal sphincter (LES). Increased relaxations of the LES results in more frequent episodes of GER and potentially aspiration.[83] Gastric decompression can decrease the incidence of aspiration pneumonia post-operatively.[21]
Tracheal intubation	Tracheal intubation decreases a patient's ability to maintain normal laryngeal function. It interferes with closure of the glottis and increases oral secretions. The cuffed ETT does not offer absolute protection against aspiration.[84] "Micro-aspirations" can occur.[85] Alterations in swallowing reflex can develop after extubation.[86]
Presence of nasal or oral feeding tubes	Impairment of the upper and lower esophageal sphincters. Presence of tubes in the pharynx increases transient lower esophageal relaxation, which predisposes patients to GER.[87]
Body position	Increase in aspiration events in the supine (horizontal) position. Reduction in aspiration with patients in the semirecumbent position.[88,89]

lung compliance and increases intrapulmonary shunt. These results, and the concomitant decrease in intravascular volume, lead to hemoconcentration, decreased cardiac output, and hypotension. The pulmonary artery pressure rises initially and then falls together with cardiac output. Pulmonary resistance remains elevated. The increased pulmonary vascular resistance is most likely caused by hypoxic vasoconstriction, but there is some evidence of *in situ* pulmonary artery thrombosis. If left untreated, the mortality of laboratory animals injured in this way approaches 100%.[12]

8.2.3 Particulate

Aspiration of materials such as barium or tube feeds may result in reflex bronchoconstriction. Patients may develop sudden wheezing, chest pain, and respiratory failure. Immediate airway suctioning and pulmonary lavage are required. Bacterial lung infection may develop if this obstruction is not cleared in 1–2 days. Aspiration of much larger volumes of neutral fluid or particulate matter can also cause pulmonary dysfunction caused by obstruction of airways. The contribution of other components of gastric aspiration (for example, bile salts and sucralfate) have not been studied.[13]

8.2.4 Risk factors

Numerous factors are believed to increase aspiration risk, and patients frequently tend to have multiple risk factors. Attributing an aspiration event to one particular risk factor is difficult. The commonly mentioned risk factors that are believed to increase the risk of pulmonary aspiration and their proposed mechanisms are summarized in Table 8.1. The importance of individual factors is still a topic of ongoing discussions. Risk factors, as classified by North American Summit on aspiration,[14] are summarized (Table 8.2).

Table 8.2 Risk factors for aspiration[14]

Major risk factors	Additional risk factors
• Documented previous episode of aspiration • Decreased level of consciousness (sedation, increased intracranial pressure) • Neuromuscular disease and structural abnormalities of the digestive tract • Endotracheal intubation • Vomiting • Persistently high gastric residual • Need for prolonged supine position	• Presence of a nasoenteric tube • Non-continuous or intermittent feeding • Abdominal/thoracic surgery or trauma • Delayed gastric emptying (diabetes, hyperglycemia independent of diabetes, electrolyte abnormalities, drugs known to reduce gastric emptying) • Poor oral care • Age • Inadequate nursing staff • Large size or diameter of feeding tube • Malpositioned feeding tube • Transport

Peri-operatively the greatest risk of pulmonary aspiration was found to be associated with increasing American Society of Anesthesiologists (ASA) status and emergency surgery.[15] The majority of perioperative aspirations occur during laryngoscopy and during tracheal extubation. Aspiration occurs despite the use of cricoid pressure in patients who were identified as having predisposing conditions.[10]

Predisposing factors identified in patients who suffered pulmonary aspiration included inadequate skeletal muscle relaxation (gagging) or difficult laryngoscopy.[15,16] GER, considered a traditional risk factor for pulmonary aspiration, was found to be rare in the perioperative period and is associated with predictable factors such as awakening and the reaction to the presence of an endotracheal tube.[17] This suggests that the risk of aspiration is more a function of how the anesthetic is conducted than is the presence of traditional risk factors.[2]

Aspiration outside the operating room is closely associated with impairment of swallowing and most aspiration events occur in patients with a swallowing impairment or abnormality.

Swallowing occurs in three stages: oral, pharyngeal, and esophageal.[18]

- The oral phase involves preparation and movement of food from the oral cavity to the pharynx.
- Once in the pharynx, the tongue rises to the hard palate to push materials into the oropharynx. The soft palate rises to close off the nasal cavities. Respiration is temporarily inhibited. The vocal cords adduct to protect the upper airway. The epiglottis tilts over the larynx and shields it from materials from the pharynx. The pharynx contracts and creates a pressure gradient into the esophagus.
- The upper esophageal sphincter relaxes and the materials within the pharynx are passed into the esophagus.

This is a very complex series of events, which requires precise muscular co-ordination. Any disease process or artificial device that inhibits this swallowing event can lead to aspiration.

Although increased age was frequently cited as a risk factor for aspiration, it is currently not believed that swallowing function decreases with age. There is an age-related increase in total swallowing duration that is consistent with an overall slowing of the central nervous system (CNS).[19] While physiologic insults to older patients are more likely to result in a swallowing abnormality and aspiration as compared with younger patients, there is no difference in aspiration between younger and older healthy adults.[20]

The CNS is critical in co-ordinating the swallowing function and in protecting the upper airways against aspiration. The co-ordination between swallowing and breathing is reduced with decreasing level of consciousness. For example, 45% of a normal healthy population was observed to aspirate during sleep. The aspiration rate increases significantly in patients with a pre-existing depressed level of consciousness.[12] Commonly used drugs during anesthesia and in the intensive care unit, ICU (anesthetics, sedatives, analgesics, neuromuscular blocking agents) can impair or completely abolish protective airway and pharyngeal reflexes against aspiration.

The GER or vomiting are the initial events in the aspiration of gastric contents. Patients with GER have a slower onset of pharyngeal peristalsis and other pharyngeal abnormalities compared with normal controls and therefore may be more predisposed to aspiration.[1]

MO patients have a higher incidence of GER. Patients with GER and altered mental status are believed to be at very high risk for gastric aspiration. This is especially true for those patients who have large volume gastric contents.

Gastric distention results in relaxation of the lower esophageal sphincter (LES). Hyperglycemia influences esophageal motility by reducing LES pressure and decreasing the velocity of esophageal peristalsis, while increasing the duration of peristaltic contractions and the number of transient LES relaxations.[14] Drugs used during induction of anesthesia can have additive effects on decreasing the tone of the LES. Increased relaxations of the LES result in more frequent episodes of GER and potentially aspiration. In elective post-thoracotomy patients with normal swallowing pre-operatively, pre-emptive gastric decompression during the first 24 h post-operatively reduces aspiration and respiratory failure overall.[21]

Patients with endotracheal tubes have a significant risk for aspiration. The literature reports aspiration events in the 50–75% range for patients with endotracheal tubes.[22,23] Although the presence of a properly placed endotracheal tube prevents massive pulmonary aspiration, the endotracheal tube cuff does not create a complete or absolute seal. It would be necessary to inflate the cuff to pressures higher than mucosal capillary perfusion pressure to achieve complete mechanical seal of the airway. Prolonged swallowing dysfunction after intubation may lead to aspiration after tracheal decannulation.

Pulmonary *aspiration associated with enteral feeding* is a well-known complication with a varied prevalence. An aspiration rate of 0–40% is reported in the literature.[24] There is also much controversy regarding aspiration associated *with gastric vs. small bowel feedings*. There are some early studies demonstrating a reduction in aspiration events with small bowel feedings in patients who had a prior, witnessed tube feeding aspiration event with gastric feedings.[25] Subsequent studies of intensive care patients have not shown a difference in aspiration events between gastric vs. small bowel feedings.[24,26–28] One of the explanatory reasons might be that the incidence of clinically significant gastric dysfunction in this patient population is small. Further speculation is that the aspiration events associated with jejunal feedings may be more related to gastric content aspiration, rather than tube feeding aspiration from the small intestine. It has been suggested that jejunal feeding may increase GER.[29]

The recent conclusion, based on radioisotope studies, of the North American Summit on aspiration[14] suggests that small bowel feeding significantly reduces the incidence of GER and possibly the incidence of aspiration compared with gastric feeding. Small bowel feeding increases delivery of enteral nutrients compared with gastric feeds. Although current studies in the literature evaluating the impact of enteral feeding on aspiration pneumonia are small and underpowered; aggregating the data through meta-analysis shows a significant treatment effect in which small bowel feeds reduce risk of aspiration pneumonia compared with gastric feeds. Positioning the tip of the feeding tube beyond the ligament of Treitz may be more effective in reducing risk of aspiration than simple post-pyloric placement.[14]

8.2.5 Epidemiology

Massive pulmonary aspiration in MO patients is fortunately a rare event in current anesthesia practice. But the occurrence of less obvious, unwitnessed "micro-aspirations" in the post-operative period is difficult to assess because of the diagnostic problems.

The incidence of difficult intubation among MO patients has been quoted at around 13%.[30] There is association between difficult airway management for tracheal intubation and pulmonary aspiration.[16] Gastric insufflation during ineffective mask ventilation will further increase the risk of regurgitation and aspiration of stomach contents. In the general population, aspiration is an uncommon event in modern anesthetic practice, quoted as occurring in between 1 : 10,000 and 5 : 10,000 general anesthetics.[31] This rare event would require a large study group of MO patients to detect true occurrence of peri-operative aspiration.

A multicenter, prospective study of nearly 200,000 operative interventions from 1978 to 1982 found the overall incidence of clinically apparent aspiration to be 1.4 per 10,000 anesthetics. More than 50% of these aspiration events were noted to occur post-operatively.[32] A review of computer-based records of approximately 185,000 adult anesthetics administered between 1967–1970 and 1975–1983 noted an incidence of 4.7 aspirations per 10,000 anesthetics.[33] Recognized clinical aspiration occurred in 67 of 172,334 consecutive adults who underwent 215,488 general anesthetics from June 1985 to June 1991 with overall incidence 3.1 per 10,000. Of those 67 patients, 66 patients survived their surgery, the one death being attributed to a non-aspiration related cause. Of these 66 survivors who aspirated, 64% did not develop a cough or wheeze, a decrease in arterial hemoglobin oxygen (O_2) saturation, or abnormalities on chest radiograph within 2 h of aspiration. Particulate matter was observed in eight patients. These eight patients underwent immediate fiberoptic bronchoscopy, but this intervention was

effective in finding and removing additional particulate material in only three of these eight patients. Thirty-six percent of those who aspirated developed clinically apparent aspiration. From these patients, over 50% required mechanical ventilation for >6 h, and about a quarter of those who developed clinically apparent aspiration required mechanical ventilation for more than 24 h. Three patients of the 67 who aspirated (5%) died from respiratory failure with overall mortality from aspiration 0.12 per 10,000 anesthetics. In relatively healthy patients (ASA physical status I and II), clinically apparent aspiration was observed in 1 : 8000 patients and none of these aspirations resulted in serious complications. This study makes an interesting conclusion that patients with clinically apparent aspiration who do not develop symptoms within 2 h are unlikely to develop significant respiratory complications.[34] Contrary to these data suggesting relatively low incidence and good outcome of aspiration during anesthesia, data from hospitalized patients and patients requiring intensive care suggest more serious outcomes.

Aspiration pneumonia is the second most common cause of nosocomial infection in hospitalized patients.[35] It is the most common cause of death in patients with dysphagia secondary to neurologic disorders.[36] Aspiration pneumonia accounts for 13–48% of all infections in nursing home residents.[37,38] With the presumption that the majority of the pneumonias were from aspiration, a nosocomial infection rate of 22% was reported after a mean of 8 days in 264 consecutive patients admitted to the ICU. However, there was no attempt to delineate which infections were aspiration associated.[39] Aspiration rates of up to 70% have been described in patients with a depressed level of consciousness[40] and 50–75% in patients with endotracheal tubes.[14]

Most *mortality* rates reported for aspiration pneumonia come from very ill, hospitalized patients. Aspiration associated mortality for this group would be expected to be much higher than in a group of relatively healthy MO patients undergoing elective bariatric surgeries. Unfortunately, this distinction is not clearly described in the literature. In 47 patients who had a witnessed aspiration event, the reported overall mortality rate was 62%.[41] If only one lobe of the lung was involved, the mortality was approximately 40%. If two or more lobes of the lung were involved, the mortality rate was about 90%. The right lower lobe was the most frequent site of aspiration. Mortality depended on the presumed volume of the aspirate.

Other authors have reported similar aspiration rates. In a group of 104 patients with witnessed gastric aspiration, the overall mortality was found to be 70%.[42] Reported mortality in a group of 20 patients with diagnosed aspiration pneumonia was 55%.[43] These data imply that significant gastric aspiration in a vulnerable patient can be devastating. An otherwise healthy MO patient most likely does not fall into the group termed "vulnerable".

8.3 Diagnosis

For diagnostic purposes the North American Summit on Aspiration[14] defines the following diagnostic categories:

- *Aspiration.* Witnessed regurgitation/aspiration event at the bedside, accompanied by coughing, choking, expectoration of material; visualization in the larynx below the true vocal cords of endogenous (oropharyngeal secretions or gastric contents) or exogenous (feeding) material by laryngoscopy, barium by videofluoroscopy, or radioisotope by scintigraphy; or by the presence in tracheal secretions of bile, gastric juice, food or formula, oropharyngeal secretions, or an exogenous marker (radioisotope labeling).
- *Possible pneumonia.* Development of acute symptoms (fever, leukocytosis, leukopenia, left shift, change in sputum production, or hypoxemia), a new or worsening infiltrate on chest X-ray (CXR), and a clinical course consistent with pneumonia (a positive pathogen on endotracheal aspirate or expectorated sputum and clinical improvement in response to appropriate antibiotic therapy) in a patient who, for whatever reason, does not undergo bronchoscopy to obtain quantitative cultures.
- *Probable bacterial pneumonia.* Development of acute signs and symptoms (fever, leukocytosis, leukopenia, left shift, change in sputum production, or hypoxemia) and a new or worsening infiltrate on CXR, confirmed by positive bronchoscopic specimens and quantitative cultures by bronchoalveolar lavage (BAL) or protected specimen brush (PSB) growing at least one organism in significant concentration as follows:
  - BAL $> 10^4$ CFU/ml;
  - PSB $> 10^3$ CFU/ml.
- *Definitive bacterial pneumonia* Development of acute symptoms (fever, leukocytosis, leukopenia with a left shift, change in sputum production, or hypoxemia) and a new or worsening infiltrate on CXR, confirmed by histology or pleural fluid analysis based on fulfillment of at least one of the following criteria:
  - positive result of pleural fluid culture;
  - rapid cavitation of the lung infiltrate as determined by computed tomography (CT) scan;
  - histopathologic demonstration of pneumonia (presence of consolidation with intense PMNL

accumulation in bronchioles and adjacent alveoli involving several adjacent low-power microscopic fields, with or without tissue necrosis) during biopsy or autopsy.

- *Pneumonia definitively ruled out*. Fulfillment of at least one of the following criteria:
  - full recovery with complete resolution of fever and pulmonary infiltrate without antimicrobial therapy (or without modification of prior antimicrobial therapy initiated more than 3 days before the appearance of the new pulmonary infiltrates);
  - no signs of bacterial pneumonia at autopsy in patients who had not received new antibiotics in the interim.

8.3.1 Diagnosis of aspiration pneumonia

When aspiration episodes are of small volume, they may be both difficult to diagnose and clinically insignificant. Even after massive aspiration, if the event is missed, the exact cause of the pneumonia may be missed. Respiratory failure may occur without confirmation of aspiration.[44] There is no good, accepted, and clinically useful way to diagnose unwitnessed aspiration. Traditional methods and monitors of aspiration during tube feeding, such as measuring glucose concentration in tracheal secretion or blue food coloring, are no longer recommended, although we still use the blue food coloring technique on occasion.[14]

Regardless of whether the glucose concentration in tracheal secretions is assessed by laboratory assay or glucose oxidase reagent strips, the specificity of the glucose oxidase method for detecting aspiration of glucose-containing formula is quite low. Positive glucose values (>20 mg/dl) are more closely associated with serum glucose concentrations than with aspiration. Any blood in the tracheal secretions conceivably can cause a false-positive reading for aspiration of glucose-containing formula. Use of blue food coloring is poorly standardized and has been shown to have low sensitivity for detecting aspiration. Cases of absorption of blue dye from endotracheal tube feeds (ETF) in critically ill patients with reports of death have raised concern about safety of the dye material itself, suggesting a toxic effect on mitochondria.

Clinical impression remains a poor "gold standard" for the diagnosis of aspiration in enterally fed patients.[45] While the clinical diagnosis of pneumonia is not accurate – with up to 30% error – in ICU patients, the diagnosis of pneumonia is based on evaluation of the following criteria[13] (see Table 8.3):

1. positive blood or pleural cultures – for the same micro-organism recovered in the tracheal aspirate;
2. new or progressive pulmonary infiltrate;
3. fever (>38°C);
4. leukocytosis (>10,000/mm^3);
5. gram stained sputum samples with >10 polymorphonuclear cells per high power field;
6. no other source of infection but the lungs.

To assist in therapeutic decisions, clinical diagnosis of pneumonia is classified as *definite* or *probable*. Pneumonia is considered *definite* when criteria 1 and 2 or criteria 2 through 6 are met; it is considered *probable* when criteria 2 through 5 or criteria 2 and 6, with the addition of at least one of the following 3, 4, or 5 are met.

The clinical course of *aspiration-induced* "*chemical*" *pneumonitis* occurs in two phases.[13] The first is generally self-limited and characterized by bronchospasm associated with irritative exudation of fluid, which neutralizes the acidic pH within minutes of the aspiration event. The second phase occurring 4–6 h after the insult, is in some patients, quite intense.

Table 8.3 Diagnosis of aspiration pneumonia

Diagnostic criteria	Degree of certainty of the diagnosis	Presence of diagnostic criteria
1 Positive blood or pleural cultures for the same micro-organism recovered in the tracheal aspirate **2** New or progressive pulmonary infiltrate **3** Fever (>38°C) **4** Leukocytosis (>10,000/mm^3) **5** Gram stained sputum samples with >10 polymorphonuclear cells per high power field **6** No other source of infection but the lungs	Definitive diagnosis Probable diagnosis	1 & 2/2 & 3 & 4 & 5 & 6 2 & 3 & 4 & 5/2 & 6 and at least one of 3 or 4 or 5

Aspiration has long been recognized to be a risk factor for acute respiratory distress syndrome (ARDS).[46]

Physical examination of lungs in MO patient is frequently of limited diagnostic value. The clinical diagnosis of aspiration is further complicated by technical difficulties in obtaining diagnostic CXR arising from patient size. Portable CXRs obtained in ICU settings are often non-diagnostic, either from penetration difficulties or from the presence of multiple artifacts, such as superimposed skin folds or soft tissue (Figures 8.1–8.3).

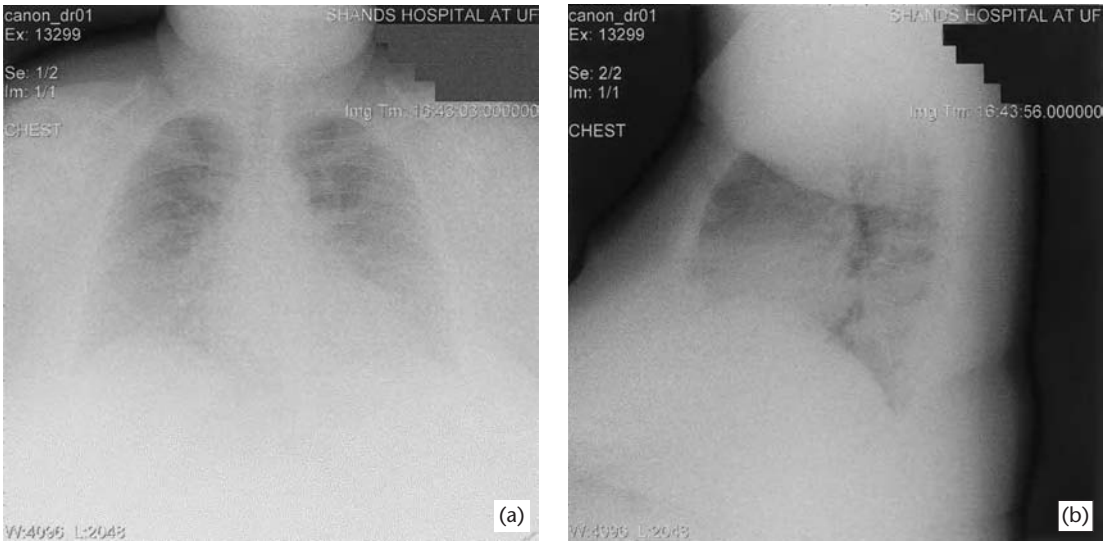

Figure 8.1 Postero-anterior and lateral film of a MO woman. Note the small lung volumes, the density of the overlying tissue, and the difficulty in trying to read the subtleties of the film. This is a pre-operative film November 12, 2002.

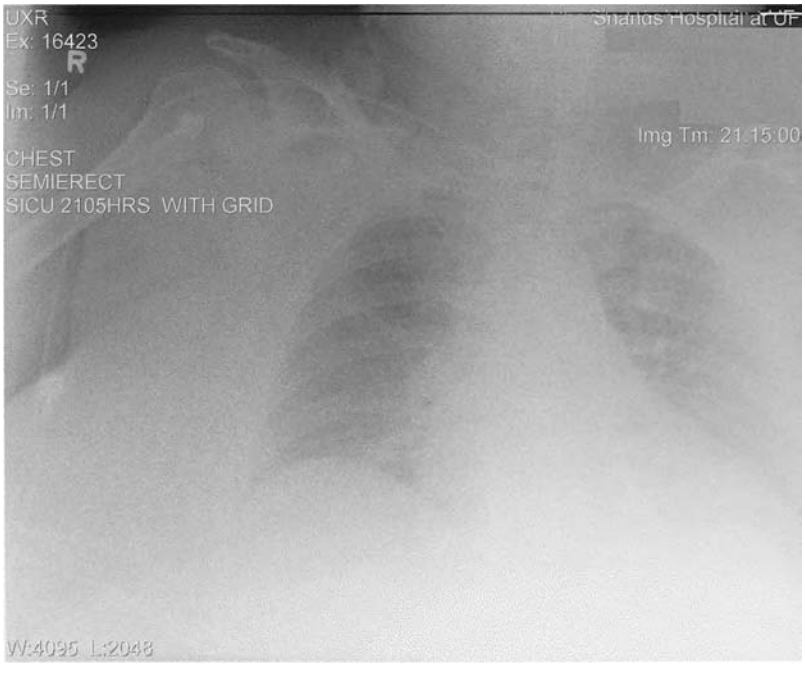

Figure 8.2 On the first post-operative day after a gastric bypass, note that the patient's trachea is cannulated. There is also retrocardiac collapse and a hint of increased pulmonary vasculature.

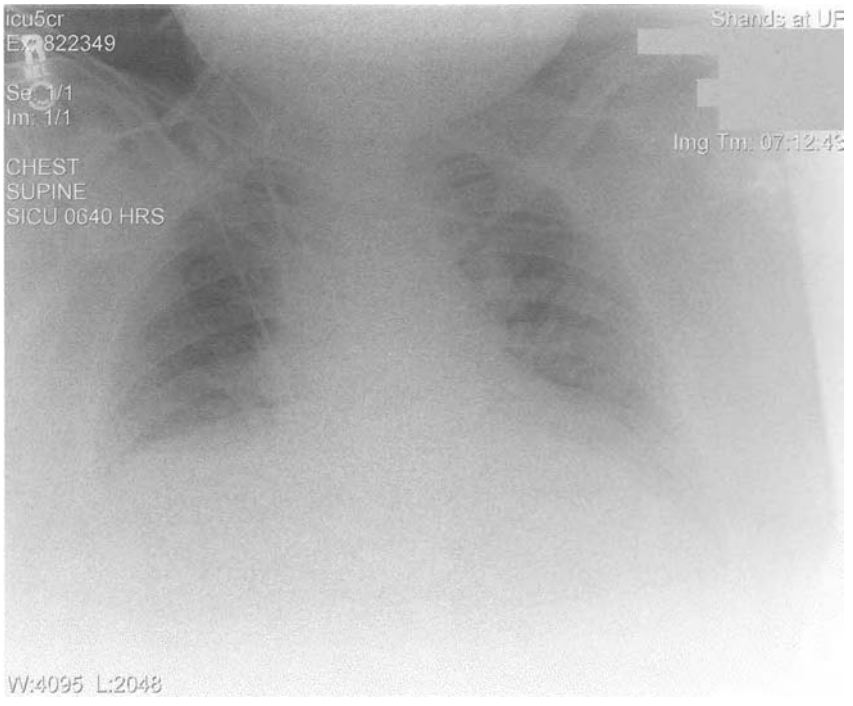

Figure 8.3 On March 3, 2003, the patient is still in the hospital. Note that her trachea is cannulated, she has an infiltrate in the right lower lobe that may be located with some difficulty. Her retrocardiac collapse is mostly resolved. Again, note the difficulty in attempting to read the subtleties of this film caused by the patient's morbid obesity.

One study showed that 40% of MO patients did show radiological evidence of basal pulmonary infiltrates (attributed to atelectasis) on the initial post-operative CXR, although no episode of gastric acid aspiration syndrome occurred.[47] Additionally the most frequent post-operative complication after bariatric surgery is deep vein thrombosis of the lower extremities, with the incidence reported to be between 2.4% and 4.5%.[48]

In MO patients undergoing bariatric surgery, there is an unexpectedly high rate of clinically silent pulmonary emboli, contributing to morbidity and mortality. From patients who died in the post-operative period only 20% were suspected to have pulmonary emboli yet, at autopsy, 80% indeed had such emboli.[49] Small pulmonary emboli, which might not cause significant hemodynamic changes, can have very similar initial respiratory presentation as pulmonary aspiration. Not infrequently even CT (chest CT or spiral CT pulmonary angiogram) will not resolve the diagnostic dilemma, because the MO patient might not fit into the regular CT machine. Anecdotally, veterinary CT facilities have been used in situations in which the MO patient does not fit into the regular CT scanner.

8.4 Prevention

Most studies about the prophylaxis of aspiration focus on chemoprophylactic agents, such as antacids, H_2 antagonists, gastrokinetics, and proton pump inhibitors, in patients undergoing general anesthesia. One large retrospective study[15] found that aspiration developed approximately equally in the group that received chemoprophylaxis and in those patients who did not. Given the very low incidence of aspiration and infrequent serious consequences of aspiration in modern anesthesia practice, routine chemoprophylaxis is no longer recommended in the general population.[2]

The MO patients are traditionally considered at increased risk for aspiration and the majority of literature still recommends preventive measures, although no supportive data exists. In a national survey study, aspiration prophylaxis was deemed important in MO patients and histamine type 2 receptor antagonists, metoclopramide and cricoid pressure were used commonly for that purpose among New Zealand anesthetists.[50] Single-dose oral famotidine has been found to be equally effective for preventing acid aspiration syndrome in MO patients as double-dose oral

ranitidine with resulting gastric volume <25 ml and pH > 2.5.[51]

One can argue that, given the minimal side effects of H_2 antagonists, such as ranitidine and famotidine, when used pre-operatively, and the perceived increased risk for aspiration, MO patients should receive pre-operative prophylaxis. Similar argument can be made for non-particulate antacids, such as sodium citrate and sodium bicarbonate. Use of agents increasing gastric pH (H_2 antagonists, antacids, and proton pump inhibitors) for ulcer and aspiration prophylaxis in the intensive care settings carries the risk of gastric colonization by pathogenic bacteria and their subsequent pulmonary aspiration. There are presently no data to recommend the use of medications such as metoclopramide, proton pump inhibitors, antiemetics, or anticholinergics for pre-operative chemoprophylaxis of aspiration in MO patients.

Cricoid pressure – also known as the Sellick maneuver – has been traditionally recommended to prevent regurgitation and subsequent aspiration during intubation of MO patients. Recently, the efficacy and safety of cricoid pressure in the general population has been questioned.[52,53] Application of cricoid pressure in animals was found to decrease the tone of LES and to hence increase the risk of regurgitation. There have been no studies proving that cricoid pressure is beneficial, yet there is evidence that it is often ineffective and that it may increase the risk of failed intubation and regurgitation.[52] The situation becomes even more complex in the settings of potentially difficult airway management in MO patients with the potential of the cricoid pressure to worsen the laryngoscopic view. None-the-less, our practice is to prophylactically administer a non-particulate antacid and either H_2 blockers or proton pump inhibitors to MO patients before anesthesia. Further, we use, as a matter of course, cricoid pressure during laryngoscopy; for more details see chapter on airway management.

8.5 Complications of gastric acid aspiration

The clinical manifestations and severity of witnessed or suspected aspiration depends upon several factors.

- Type of aspirated material, whether it be sterile gastric juice, particulate matter, or oropharyngeal secretions.
- The amount of aspirated material or frequency of repeated aspirations (that is, micro-aspirations vs. macro-aspirations).
- The integrity of the patient's systemic and local defense mechanisms and the patient's response to the aspirated material. Response is influenced by the patient's level of consciousness, quality of oropharyngeal hygiene, and changes in oropharyngeal flora.

Interaction of these factors will determine the type and severity of resulting aspiration syndrome. Two main syndromes are aspiration pneumonitis and aspiration pneumonia although it is understood that overlap exists between these two clinical entities. *Aspiration pneumonitis* (Mendelson's syndrome) is a chemical pneumonitis caused by aspiration of acid gastric contents. *Aspiration pneumonia* is an infectious process caused by aspiration of oropharyngeal secretions colonized by pathogenic bacteria (see Table 8.4).

Although aspiration is the mechanism of *ventilator-associated pneumonia* in the vast majority of cases, for the purpose of this review it will not be discussed separately from aspiration pneumonia. With the exception that the colonization and aspiration of oropharyngeal secretions probably have greater pathogenic significance than the colonization and aspiration of gastric contents, the conclusions made for aspiration pneumonia apply to ventilator-associated pneumonia as well.

8.5.1 Aspiration pneumonia

Aspiration of contaminated oropharyngeal secretions, a common event in healthy individuals, is usually of little consequence because the host response is capable of eliminating the low number of organisms present. Indeed, 45% of a normal healthy population was observed to aspirate during sleep.[40]

Hospitalized patients and especially patients admitted to ICUs have many other factors that can increase the risk of aspiration: depressed level of consciousness, forced supine position, and the presence of nasogastric or endotracheal tubes.[54–56] Some of these risk factors can be controlled (see Table 8.5).

Aspiration pneumonia is thought to proceed through the following stages:

- airway contamination,
- colonization of the airways,
- bronchiolitis,
- focal pneumonia,
- confluent pneumonia.

The critically ill patients and patients with prolonged ICU stays are more likely to proceed to the stage of confluent pneumonia.[13] Whether confluent pneumonia develops from aspiration depends on three factors (see Table 8.6):

1. number of bacteria in the aspirate,
2. the virulence of the contaminating organism,
3. the host's ability to mount an immune response.

Table 8.4 Comparison of aspiration pneumonia and aspiration pneumonitis

	Aspiration pneumonitis	Aspiration pneumonia
Mechanism	Aspiration of sterile acid gastric contents	Aspiration of colonized oropharyngeal secretions
Pathophysiology	ALI due to acidic and particulate gastric material	Acute infectious process due to bacteria and bacterial products
Major risk factors	Decreased level of consciousness	Dysphagia, gastric dysmotility
Age group	Any age, usually young	Usually elderly
Time frame	Usually peri-operative: during intubation and/or extubation	Usually post-operative: during mechanical ventilation in ICU and after long-term intubation
Witnessed	Maybe witnessed	Usually not witnessed
Typical presentation	Relatively rapid development of respiratory symptoms and pulmonary infiltrate	Symptoms of pneumonia and pulmonary infiltrate develop day(s) after aspiration; dysphagia
Clinical features	Vary from asymptomatic, through non-productive cough, to bronchospasm and respiratory insufficiency 2–5 h after aspiration	Tachypnea, cough and clinical signs of pneumonia

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Table 8.5 Modifiable risk factors for aspiration[14]

Modifiable risk factors
- Reassess need, level, and choice of agents used for sedation
- Re-evaluate need for opioid analgesia and minimize use of narcotics
- Keep head of bed elevated to >30–45° (provided the patient is positioned so that the bend of the bed is at the patient's lower back). If not possible, position patient in reverse Trendelenberg at 30–45°
- Change infusion from bolus/intermittent to continuous
- Optimize oral health
- Consider moving high-risk patient to a monitored unit with increased staffing
- Tight glycemic control

Additional considerations
- Prokinetic agents
- Metoclopramide
- Erythromycin (could this contribute to bacterial resistance?)
- Continuous aspiration of subglottic secretions
- Kinetic beds

Measures not recommended to be employed solely to reduce risk
- Switching to a smaller diameter nasoenteric tube – the decision to reduce the diameter of the tube should be based on patient discomfort
- Converting an nasogastric (NG) tube to percutaneous endoscopic gastrostomy (PEG) – there is insufficient data in the critical care setting to support the concept that converting an NG tube to a PEG tube reduces risk of aspiration and some procedural-related morbidity occurs with PEG placement. Both factors mitigate against the practice of PEG placement solely to reduce risk of aspiration. The decision for PEG placement should be based on anticipated longevity of ETF (>4 weeks)
- Switching to total parenteral nutrition (TPN)
- Adding acid to formula
- Selective decontamination of the gut

Table 8.6 Factors responsible for development of aspiration pneumonia

Factor	Etiologic mechanism
Number of bacteria in the aspirate	Gastroparesis and duodenogastric reflux Advancing the rate of enteral tube feeding
The virulence of the contaminating organism	Oropharynx and stomach become more heavily colonized with virulent organisms over the first week in ICU Shift from more normal oral flora including *S. pneumoniae, H. influenzae,* and *S. aureus* to hospital-acquired antibiotic resistant Gram-negative organisms, including *Pseudomonas aeruginosa, Acinetobacter species, Enterobacter species,* and methicillin-resistant *S. aureus* (MRSA)[90]
The host's ability to mount an immune response	Progressive failure of the patient's innate immune response Stress-induced acute protein malnutrition Red blood cell transfusions Compensatory anti-inflammatory response syndrome (CARS)

8.5.2 Acute lung injury and the acute respiratory distress syndrome

Aspiration is a recognized risk factor for the development of ARDS.[46] ARDS is a clinical syndrome of increased alveolar-capillary membrane permeability associated with a constellation of clinical, radiologic, and physiologic findings that are not the result of left atrial or pulmonary capillary hypertension.

In certain patients, aspiration can serve as a "second hit" in patients with an ongoing systemic inflammatory response syndrome (SIRS).[57] After a variety of "first hit insults" such as shock, sepsis, regional ischemia/reperfusion, patients may be resuscitated into a state of systemic hyperinflammation, referred to as SIRS. The host inflammatory response is "primed", such that a second, otherwise innocuous, insult "activates" the non-specific inflammatory response, resulting in lung ventilation/perfusion mismatch. This may progress to acute lung injury (ALI) or further evolve into ARDS, diagnosed depending upon the severity of the gas exchange abnormality, respectively, a PaO_2/FiO_2 ratio of $<$300 and 200. Unlike other ARDS scenarios where an extrapulmonary problem is driving the SIRS response to cause multiple organ failure, aspiration is a localized "second hit", and patients tend to develop relatively isolated ALI/ARDS.

Regardless of the specific etiology, clinical and histopathologic abnormalities of ARDS generally progress through four defined phases:[13]

1 The initial injury phase is characterized clinically by mild symptoms of respiratory distress and pathologically by PMNL sequestration in pulmonary capillaries.
2 Next, hypoxemia and fluffy radiographic infiltrates develop. Histologically PMNLs can be identified in the interstitium.
3 Further progression leads to increased work of breathing and worsened hypoxemia, which frequently mandates mechanical ventilatory support. Histologically, this corresponds with alveolar inflammatory exudates.
4 Unless death or prompt resolution occurs, the fourth phase of late ARDS ensues. Clinically, oxygenation worsens and is unresponsive to positive end-expiratory pressure (PEEP)/continuous positive airway pressure (CPAP). Elimination of carbon dioxide (CO_2) is impaired because of high dead space ventilation. Pulmonary compliance decreases, and ventilator pressures become alarmingly high. The histopathologic progressive fibroproliferation is found. This reflects an attempt to repair injured pulmonary endothelial and epithelial cells.

At the time of this writing, treatment of patients with ARDS is primarily supportive, including ventilatory, circulatory, and nutritional support. Lower tidal volumes[58] (based on ideal body weight in MO patients) and "proper" level of PEEP/CPAP to minimize ventilator-induced lung injury resultant from "sheer" forces due to repetitive opening–closing of unstable alveoli are recommended and increasingly accepted in management of patients with ARDS.

Recently, there has been a renewed interest in the late use of corticosteroids in patients with refractory ARDS.[59] Pathologic changes in the late fibroproliferative phase of ARDS should be more responsive to corticosteroid therapy. Studies have shown that high-dose methylprednisolone does not affect polymorphonuclear (PMN) migration, the predominant

mechanism of injury in early ARDS, but does down-regulate macrophage collagenase activity and promotes type II pneumocyte proliferation. Thus, corticosteroids may be effective in alleviating the fibroproliferation that characterizes late ARDS. There will be an occasional patient with aspiration-induced refractory ARDS who will benefit from this therapy.[13] Of course, the clinician must ensure, to the extent possible, that a subclinical or occult infectious process is not ongoing prior to the initiation of steroid therapy.

8.6 Treatment

The treatment of aspiration involves confirming the diagnosis, providing supportive care, monitoring for clinical consequences, and instituting secondary prevention. Patients with a witnessed aspiration should initially be positioned with their head turned to the side to facilitate suctioning of the oropharynx and trachea to clear residual aspirated material and to ascertain the presence of particulate material. Next, determination must be made as regards intubation. Although the anesthesiology literature suggests that routine endotracheal intubation improves outcome, definitive data to support this recommendation in ICU patients are lacking.[13] None-the-less, in the presence of hypoxia, utilization of invasive positive pressure ventilation – that is, with endotracheal intubation – may be life saving.

The benefits include securing the airway, better suctioning, delivery of positive pressure, and facilitation of bronchoscopy. The risks include intubation mishaps, depressed local defenses, and contamination of the airway. A decision may be made to intubate patients with presumed large volume aspiration in significant respiratory distress and those with particulate matter to facilitate bronchoscopy with saline lavage. Saline lavage will not be of much benefit in liquid gastric aspiration because the acidic pH is neutralized within minutes of the aspiration event. All patients should then receive aggressive pulmonary care to enhance lung volume and clear secretions.

Patients who do not require intubation should be positioned in a semirecumbent position or be up out of bed in a chair as much as tolerated, as this maneuver may increase functional residual capacity (FRC). Incentive spirometry needs to be instituted aggressively. Our practice is to have the patient use the incentive spirometer with respiratory therapist or nurse supervision, 10 times every hour while awake. Humidified O_2 can be used to symptomatically treat mild hypoxia; bronchodilators should be used to treat bronchospasm. Non-invasive positive pressure ventilation (NIPPV) should be considered. Intermittent positive pressure breathing treatments should be reserved for patients who cannot generate adequate volumes by incentive spirometry. Non-invasive bi-level positive airway pressure (BiPAP) can be used to avoid intubation in selected patients. Patients should be instructed to cough deeply, and nasotracheal suctioning can be used in those patients who cannot adequately clear secretions. Chest physiotherapy, which includes patient positioning, chest wall percussion/vibration, and enhanced coughing, should be considered. Intubated patients should be suctioned through the endotracheal tube immediately after intubation and then receive positive pressure ventilation. For patients who are developing ALI, protective lung strategy should be used with a tidal volume based more on an ideal body weight than actual weight. Sufficient PEEP/CPAP should be applied to prevent the development of shear forces.

Simultaneously with the initial treatment, patients should undergo clinical assessment, which includes physical examination, monitoring of oxygenation, and serial CXRs and arterial blood gas analysis. Signs of worsening ALI with progression to ARDS should be the major early concern and patients who worsen despite aggressive, non-invasive pulmonary care should be endotracheally intubated and mechanical ventilation initiated. Early corticosteroids and prophylactic antibiotics are not indicated.[13] Concurrent with these therapeutic interventions, one must ensure that appropriate prophylactic measures are being employed to avoid recurrent aspiration.

8.6.1 Non-invasive positive pressure ventilation

The role of NIPPV remains a topic of ongoing debate and controversy in the post-operative care of the MO patients. This modality has not been universally accepted for patients following upper gastro-intestinal surgery because of concerns that pressurized air will inflate the stomach and proximal intestine, resulting in an anastomotic disruption. Significant numbers of MO patients use some form of NIPPV (CPAP or BiPAP) chronically before the surgery, especially during the night for the treatment of obstructive sleep apnea (OSA). Up to 5% of MO patients carry the diagnosis of OSA.[60] Post-operatively, especially in the immediate post-operative period, MO patients are at a risk for prolonged anesthetic and sedative effects of various anesthetics and analgesics used in the perioperative period due to their altered pharmacokinetics. This situation creates conditions for the development of airway obstruction not only in those MO patients who were diagnosed and treated for OSA

pre-operatively, but also in a significant number of previously undiagnosed patients. Clinical experience suggests that MO patients are, in general, at risk for the development of airway obstruction post-operatively.[61,62]

Episodes of OSA are most frequent during rapid eye movement sleep, the extent of which is relatively low in the initial post-operative period, but significant on the third to fifth post-operative nights. The hazards of OSA may, therefore, be at their worst some days after surgery; this has obvious implications for the duration of post-operative oximetry and O_2 therapy.[63]

While some practices use NIPPV routinely in the post-operative care of MO patients after bariatric surgeries and frequently resume NIPPV immediately after extubation, others are reluctant because of the fear of anastomotic disruption. There is limited literature upon which to base a decision related to the efficacy and safety of NIPPV in MO patients after bariatric surgery.

A recent prospective study of 1067 patients undergoing gastric bypass were evaluated for the risk of developing anastomotic leaks and pulmonary complications after the Roux-en-Y gastric bypass (RYGB) procedure. Of the 1067 patients (837 women [78%] and 230 men [22%]) undergoing a gastrojejunostomy as part of a RYGB procedure, 420 had OSA and 159 were dependent on CPAP. There were 15 major anastomotic leaks, two of which occurred in CPAP-treated patients. Contingency table analysis demonstrated that there was no correlation between CPAP utilization and the incidence of major anastomotic leakage ($P = 0.6$). Notably, no episodes of pneumonia were diagnosed in either group. Despite the theoretical risk of anastomotic injury from pressurized air delivered by CPAP, no anastomotic leaks occurred that were attributable to CPAP. Authors concluded that CPAP is a useful modality for treating hypoventilation after RYGB without increasing the risk of developing post-operative anastomotic leaks.[64]

In another study, investigators evaluated the effects of BiPAP on pulmonary function in MO patients following open gastric bypass surgery. Patients with a body mass index (BMI) of at least 40 kg/m^2 who were undergoing elective gastric bypass were eligible to be randomized to receive either BiPAP during the first 24 h post-operatively or conventional post-operative care. The FVC and FEV1.0 were significantly higher on each of the three consecutive post-operative days in the patients who received BiPAP therapy. The SpO_2 was significantly increased in the study group over the same time period.[65]

Prophylactic BiPAP during the first 12–24 h post-operatively resulted in significantly improved measures of pulmonary function in severely obese patients having undergone elective gastric bypass surgery. These improved measures of pulmonary function, however, did not translate into fewer hospital days or a lower complication rate in the study population of otherwise healthy obese patients.[65]

When BiPAP is used prophylactically, during the first 24 h post-operatively, it significantly reduces pulmonary dysfunction after gastroplasty in MO patients and accelerates re-establishment of pre-operative pulmonary function.[66] In addition, it is known that early identification and treatment of OSA allows safer use of sedative, analgesic, and anesthetic drugs without major complications in the peri-operative period for patients undergoing various types of surgical procedures.[67]

The peri-operative administration of supplemental O_2 was found to reduce the incidence of surgical-wound infections.[68] This is in agreement with known facts about the positive role of O_2 in wound healing and the accelerating role of hyperbaric O_2 therapy on wound healing.[69] Although there are currently no data to suggest that NIPPV can positively affect wound healing in MO patients after bariatric surgery, this possible benefit should not be ignored. Unfortunately studies with a large number of patients would be needed to detect eventual decrease in anastomotic leaks. Based upon all of these data and the accumulated clinical experience, NIPPV may be considered in the post-operative care of MO patients having undergone bariatric surgery. Clinicians caring for these patients should consider its use when indicated. Our practice, however, after years of extensive discussions with surgical colleagues at the University of Florida, is to significantly limit the use of non-invasive ventilation after bariatric surgery.

8.6.2 Invasive positive pressure ventilation

After endotracheal intubation, the MO patient will be placed on a ventilator. MO patients have an increased work of breathing, and this is further increased by the imposed work of breathing caused by the resistance of the endotracheal tube. The laryngeal size of the MO patient often does not allow use of an endotracheal tube with a sufficiently large diameter to compensate for resistance in the setting of increased minute ventilation. When initiating mechanical ventilation, one must consider specifics in the respiratory mechanics of MO patients. Morbid obesity is associated with reductions in FRC, expiratory reserve volume (ERV) and total lung capacity. FRC declines exponentially

with increasing BMI.[70] These changes have been attributed to mass loading and splinting of diaphragm. FRC may be reduced even in the awake, upright patient to the extent that it falls within the range of alveolar closing capacity with all the negative consequences. Sedation, anesthesia, and supine position will further reduce FRC up to 50% compared to 20% in non-obese subjects.[71] Clinical results are small airway closure, ventilation/perfusion mismatch, and impaired gas exchange with resulting hypoxemia.

Oxygen consumption and CO_2 production are increased in the MO patient as a result of the metabolic activity of the excess fat and the increased workload on supportive tissues.[72] Normocapnia is maintained by increased minute ventilation. Total compliance of the respiratory system in the obese (lungs and chest wall together) declines exponentially with increasing BMI down to as little as 30% of predicted normal.[73] These alterations in pulmonary function are important when considering mechanical ventilation in the obese patient. A tidal volume based on the patient's actual body weight is likely to produce alveolar over distention and high airway pressure, increasing the risk of barotrauma. An initial tidal volume based on ideal body weight should be used, which can then be adjusted according to airway pressures and arterial blood gas analysis.[74] There are data suggesting that lung protective strategy with smaller tidal volumes and adequate PEEP/CPAP can improve patient survival.[58] It is our impression that many clinicians are uncomfortable with the use of PEEP/CPAP greater than about 20 cmH_2O; we have no aversion to the use of expiratory airway pressures higher than this. Maintaining the patient's spontaneous respiratory effort and supporting it with the pressure support ventilation mode can further decrease mean airway pressure and improve ventilator-patient synchrony.

Use of PEEP/CPAP in MO patients may help to prevent airway closure[75] but may result in a decreased cardiac output; fluid loading will correct this. Weaning from mechanical ventilation may be difficult because of high O_2 requirements, increased work of breathing, reduced lung volumes, and V–Q mismatch.

8.6.3 Role of bronchoscopy

The literature does not provide clear indications for bronchoscopy after witnessed or suspected aspiration. There are possibly three areas in which bronchoscopy can be helpful in managing patients with aspiration: confirmation of aspiration, removal of particulate material from airways, and obtaining the semi-quantitative cultures in suspected aspiration pneumonia.

Visualization of endogenous (oropharyngeal secretions, gastric contents, or bile) or exogenous (feeding) material in the airways can confirm that aspiration has occurred. If the presence of particulate matter in the aspirate is suspected or cannot be excluded, one should consider bronchoscopic removal. One large study[15] of 215,488 anesthetics identified recognized aspiration in 67 patients. Particulate matter was observed in eight of these patients. These eight patients underwent immediate fiberoptic bronchoscopy, but the intervention was effective in finding and removing additional particulate material in only three of them. Rigid bronchoscopy is indicated for removal of an aspirated foreign body.

Invasive diagnostic techniques (such as BAL) should be used when the diagnosis of aspiration pneumonia is not certain (see Table 8.3). In patients with definite clinical criteria for aspiration pneumonia, routine endotracheal tube aspirate (ETA) cultures accurately reflect the responsible pathogens.[76] But patients that have been intubated for more than 1–3 days frequently are colonized, and therefore the routine ETA culture will be positive, possibly reflecting only colonized oropharyngeal organisms and not a true pathogen. Finally, therapeutic bronchoscopy with secretion aspiration or intrabronchial O_2 insufflation may occasionally be needed in patients with refractory lobar collapse[77] secondary to aspiration pneumonia. Intrabronchial O_2 insufflation is a procedure described by Haenel and colleagues[77] using a 3-way stop-cock. The "male" end of a 2.5 mm endotracheal tube adapter is inserted into the "female" portion of the stop-cock. Thereafter, the "male" end of this complex is inserted into the operating channel of the bronchoscope and positive pressure breaths to a maximum of 39 cmH_2O are given. The success rate of this technique in critical hypoxia (mean $PaO_2/F_iO_2 = 76 \pm 9$ mmHg) unresponsive to conventional therapy was 82%; apparently, no patient required recurrent treatment after initial success.

8.6.4 Role of antibiotics

Another adverse outcome after aspiration for which patients are monitored is secondary pneumonia. Most agree that early presumptive (that is, "prophylactic") antibiotics for aspiration are not indicated and will likely result in selecting out more resistant organisms. Surprisingly, however, in a survey study[78] in cases of suspected and confirmed aspiration, 52% and 78% of respondents, respectively, would prescribe an antimicrobial agent in the absence of a definitive infectious process, with administration of dual antimicrobial therapy increasing from 29% to 46% in suspected vs. confirmed cases of aspiration.

On the other hand, these patients are at high risk and should be closely followed. If pulmonary infiltrates on CXR do not clear or worsen, early empiric antibiotics can be started. For patients with "witnessed" aspiration, it has been common practice to cover anerobes. However, two recent studies using PSB sampling followed by quantitative and anerobic culturing in patients with acute aspiration syndrome showed that no anerobic organisms were isolated.[79,80]

Patients that have been intubated for more than 24 h are frequently colonized, and therefore the routine semiquantitative ETA culture will be positive.[13] In patients with definite clinical criteria (see Table 8.3) for pneumonia, routine ETA cultures may accurately reflect the responsible pathogens.[81] However, when the clinical diagnosis is only "probable", the ETA culture may reflect colonized oropharyngeal organisms. The clinician is thus faced with a dilemma. They can overtreat with empiric therapy, which will increase expense and promote the emergence of resistant stains, or they can intentionally undertreat and wait for definite signs. In high-risk ICU patients, delay in treatment will increase mortality. Therefore, high-risk ICU patients are usually treated empirically, and invasive diagnostic techniques are employed to enhance early diagnosis and direct early antibiotic therapy. Currently, PSB and BAL are viable alternatives.

There is no ideal antibiotic regimen for aspiration pneumonia. Treatment decisions are based on three factors:

1 clinical diagnostic certainty (definite vs. probable);
2 time of onset after intubation early (<5 days) *vs.* late (>5 days);
3 host factors (high risk vs. low risk based on whether the patient can tolerate a mistake).

Unit-specific resistance patterns and known frequency of specific pathogens are quite helpful in developing guidelines for empiric treatment. For patients with a definite clinical diagnosis, one should obtain a routine sputum sample for semiquantitative culture and Gram stain. Based upon Gram stain results and suspected pathogens, empiric antibiotics should be started (Table 8.7). If the onset is early (<5 days), a single agent should be chosen to cover suspected pathogens. *Streptococcus pneumoniae* and *Haemophilus influenzae* are adequately covered by a third-generation cephalosporin such as ceftriaxone, and *Staphylococcus aureus* can be treated with nafcillin. If the onset is late (>5 days), double antibiotic coverage should be initiated to cover Gram-negative organisms. We would use a fourth-generation cephalosporin (cefepime) combined with an aminoglycoside (tobramycin). For patients at perceived risk of renal failure, we would use the same fourth-generation cephalosporin (cefepime) combined with a fluoroquinolone (levofloxacin). Gram-positive coverage should be added if Gram stain shows mixed flora or if the patient is quite ill and cannot afford delay in treatment. Vancomycin should be used in ICUs that have a high incidence of methicillin-resistant *Staphylococcus aureus.*

Most ICU patients fall into the category of probable aspiration pneumonia (see Table 8.3). In this category, initial bronchoscopy is recommended for quantitative culture and Gram stain. The presence of intracellular organisms on Gram stain is considered diagnostic for pneumonia and should direct empiric therapy.[26] Otherwise, the general condition of the patient will

Table 8.7 Treatment of aspiration pneumonia[13]

Definitive diagnosis		
Early onset <5 days	Single agent regimen for suspected pathogen	Third generation cephalosporin (ceftriaxone) for *S. pneumoniae* and *H. influenzae;* Nafcillin for *S. aureus*
Late onset >5 days	Double agent regimen	To cover Gram negatives fourth generation cephalosporin (cefepime) combined with an aminoglycoside (tobramycin or gentamycin)
	Risk of renal failure	Fourth generation cephalosporin (cefepime) combined with a fluoroquinolone (levofloxacin)
	Mixed flora on Gram stain or high risk patient	To cover Gram positives vancomycin in ICU with high incidence of MRSA
Probable diagnosis		
High risk patient	Empirical treatment as for definitive diagnosis	
Low risk patients	Antibiotics can be withheld until culture results	

dictate whether empiric antibiotics are started before culture results becoming available.

High-risk patients are those who cannot afford delay in treatment, usually immunodepressed with low physiologic reserve. Most ICU patients fit this category and will have empiric therapy started with the same decision algorithm as described above for patients with a "definite" diagnosis. Low-risk patients are those with only low probability of having pneumonia or those patients who are immunocompetent with good reserve. In these patients, antibiotics are withheld until quantitative culture results are known.

Controversies

Although the cut-point for a positive BAL culture is controversial, $>10^4$ CFU/ml is generally accepted as a positive result that requires treatment. Once culture and sensitivity results become known, empiric therapy should be narrowed to treat the identified pathogens with the best available agents. Although some authorities promote stopping empiric antibiotics with a negative BAL culture, this is not always easy to enforce, given the fact that a BAL culture is only 85% sensitive. For example, it is difficult to stop antibiotics in patients who have exhibited a definite clinical response to empiric therapy, but have a BAL culture with $<10^4$ CFU/ml.

Duration of antibiotic therapy

While the standard has been to treat aspiration pneumonia for 10–14 days, a recent trend has been to reduce duration. The following recommendations[13] have been made:

1. three days for patients with negative BAL culture results;
2. seven days for an "early" pneumonia showing good response to treatment;
3. ten days for a "late" pneumonia with hospital-acquired Gram-negative pathogen;
4. fourteen days for late pneumonia with antibiotic-resistant pathogen;
5. twenty-one days in an immunocompromised patient.

These recommendations most closely follow our clinical practice.

8.6.5 Other issues

While there are data supporting the use of prostaglandin E_1 (PGE_1, 20–80 μg/h, nebulized. Of generated particles 84% were in the 0.5–10 μm range) and prostacyclin (PGI_2, 12–35 ng/kg body weight i.v.) to improve pulmonary artery pressures (PGE_1 and PGI_2) and oxygenation (PGE_1)[91,92]; this is not the case for the use of systemic steroids, either experimentally[93] or in patients.[94,95] Inhaled nitric oxide, while not impacting outcome, may improve ventilation/perfusion mismatch and decrease pulmonary artery pressure.[96,97]

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SECTION 3

PRE-OPERATIVE MANAGEMENT

PRE-OPERATIVE EVALUATION OF THE PATIENT FOR BARIATRIC SURGERY

9

R.A. Beers & M.F. Roizen

9.1 Overview

No randomized controlled trials give irrefutable evidence that pre-operative evaluation of the obese patient, even before bariatric surgery, makes a significant difference to patient mortality. But much evidence indicates that such evaluations, like for other patients, makes the peri-operative period more efficient, reduces provider and patient anxiety, sets appropriate expectations that lead to increased patient satisfaction with pain therapy and with the entire peri-operative experience. We believe such an assessment can also spot important variations in airway, pulmonary, cardiovascular, metabolic and nervous system physiology that lead to improved provider preparedness and patient outcome, and the feeling of both about the quality of the peri-operative care. Such may be an important part of surgery in the obese and especially bariatric surgery (see Chapter 1). And motivating and ensuring prophylaxis for deep vein thrombosis can be an important determinant for acute outcome, as pulmonary emboli are the greatest cause of adverse peri-operative 30 day mortality. Importantly, any contribution the anesthesiologist can make toward evaluating psychologic attitude and preparation of the patient (for example, "the patient stopped exercising 3 weeks ago") is usually most welcomed and important to the surgeon. For it is the psychologic readiness of each patient and that patient's commitment to outcome after this operation that appears to determine its long-term worth for that patient.

9.2 Introduction

Obesity in society and in an individual may not be of recent origin, but the rapid increase in treatments involving successful surgery without huge morbidity for obesity is. Recently, the rate and numbers of obese in all societies is increasing with epidemic speed. In fact, obesity may be increasing even faster than surgery for it. For example, in the US, more than 50% of adults weigh more than 20% above what is considered the optimum body weight for their height – a recent increase from 30%.[1] And that increase occurred in just 18 years. One measure of obesity is body mass index (BMI), for which a value above 31 represents morbid obesity and its risks, and a value above 27 for women

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Table 9.1 BMI (kg/m^2)

	BMI value													
Height (in)	19	20	21	22	23	24	25	26	27	28	29	30	35	40
58	91	96	100	105	110	115	119	124	129	134	138	143	167	191
59	94	99	104	109	114	119	124	128	133	138	143	148	173	198
60	97	102	107	112	118	123	128	133	138	143	148	153	179	204
61	100	106	111	116	122	127	132	137	143	148	153	158	183	211
62	104	109	115	120	126	131	136	142	147	153	158	164	191	218
63	107	113	118	124	130	135	141	146	152	158	163	169	197	225
64	110	116	122	128	134	140	145	151	157	163	169	174	204	232
65	114	120	126	132	138	144	150	156	162	168	174	180	210	240
66	118	124	130	136	142	148	153	161	167	173	179	186	216	247
67	121	127	134	140	146	153	159	166	172	178	185	191	223	255
68	125	131	138	144	151	158	164	171	177	184	190	197	230	262
69	128	135	142	149	153	162	169	176	182	189	196	203	236	270
70	132	139	146	153	160	167	174	181	188	195	202	207	243	278
71	136	143	150	157	165	172	179	186	193	200	208	215	250	286
72	140	147	154	162	169	177	184	191	199	206	213	221	258	294
73	144	151	159	166	174	182	189	197	204	212	219	227	265	302
74	148	155	163	171	179	186	194	202	210	218	225	233	272	311
75	152	160	168	176	184	192	200	208	216	224	232	240	279	319
76	156	164	172	180	189	197	205	213	221	230	238	246	287	328

*Each entry gives the body weight in pounds (lb) for the person of a given height and BMI. Pounds have been rounded off. To use the table, find the appropriate height in the left-hand column. Move across the row to a given weight. The number at the top of the column is the BMI for the height and weight. overweight; obese range; above 40. Are in the morbid obesity range.

and 28 for men corresponds to weight 25% above ideal (Table 9.1)[2] (Appendix A). The pathophysiologic consequences of obesity involve every major organ system.[2–4]

Despite obesity as the condition that is increasing most both in percentage and numerical terms, few studies examine the non-surgical peri-operative factors that make a difference to morbidity after bariatric operations. In fact, surgery is almost always reserved for patients with medical complications of obesity, rather than just obesity *per se*. This stance is controversial as many patients consider obesity without overt medical complications as a major cause of adverse quality of life. But in terms of outcome, it is obesity's complications that cause most of its aging effects.[2–4]

While many of the complications of obesity that make peri-operative care more hazardous, such as difficult airway and joint problems are evident on simple observation of the walking patient, many such as sleep apnea, hypertension (both systemic and pulmonary) and diabetes require careful history, physical examination and review of laboratory assessment to evaluate. And it is these latter that seem to make the most difference to the obese patient chronically and in the peri-operative period (Tables 9.2 and 9.3).

Table 9.2 The effect of side effects of obesity

RealAge[2,3] effect of side effects is relatively large at calendar age 55
RealAge effect of a *BMI* of 33 is 3.3–3.6 years older
RealAge effect of *hypertension* is up to 25 years older
RealAge effect of *arthritis* is up to 6 years older
RealAge effect of *diabetes* is 0.5 years older each year of average control
RealAge effect of *sleep apnea* is 3–9 years older
RealAge effect of *inactivity* is 3–9 years older
RealAge effect of *altered body image* is up to 32 years older

Many of the metabolic, hormonal, and physiologic changes associated with obesity (for example, insulin resistance, decreased number of insulin receptors, and subsequent diabetes mellitus) can be induced by overfeeding normal subjects and can be reversed by weight reduction.[4] Obesity itself, its complications, and its treatment have significance for the anesthesiologist. A person who is 30% overweight has a 40%

Table 9.3 The Real Age effect of obesity

Calendar age	Real age								
	BMI								
	18.5	18.6–21.9	22–24.1	24.2–26.4	26.5–28.7	28.8–31.0	31.1–33.3	33.4–35.7	>35.7
Men									
35	35.2	34.7	35	35.4	35.8	36.1	36.1	36.2	36.3
55	55.3	54.3	55	56.0	57.0	58.2	58.2	58.5	58.6
70	70.5	69.0	70	71.4	72.8	74.7	74.7	75.3	75.4
Women									
35	34.9	34.6	35	35.5	36	36.6	37.1	37.5	37.6
55	54.9	54.4	55	55.8	56.6	57.6	58.6	59.6	60.0
70	69.9	69.2	70	71.0	72.1	73.4	75.0	76.1	76.7

increased chance of dying from heart disease and a 50% *increased* chance of dying from a stroke. Obesity is also associated with higher resource utilization (more peri-operative days in the hospital) and greater peri-operative morbidity and mortality.[5,6]

Although many conditions associated with obesity (diabetes, hyperlipidemia, cholelithiasis, gastrointestinal reflux disease, cirrhosis, degenerative joint and disc disease, venous stasis and thrombotic/ embolic disease, sleep disorders, and emotional and altered body image disorders) contribute to chronic morbidity in the obese, the main concerns for the anesthesiologist have been the same for over three decades – derangements of the cardiopulmonary system[7,8] (see Chapters 4–6 and 11).

9.3 Airway and pulmonary evaluation and optimization

Airway and pulmonary related factors that increase peri-operative risks in the morbidly obese are airway anatomy, loss of functional residual capacity (FRC) and ensuing rapid desaturation when anesthesia is induced, propensity for desaturation in the recumbent (as opposed to the upright position) and the potential need to induce and recover such patients in the upright position, propensity for and presence of sleep apnea, chronic respiratory insufficiency, pulmonary hypertension, predisposition to deep vein thrombosis and its consequences, and the need for active participation to overcome uncomfortableness and to motivate ambulation in the post-operative period.

Morbid obesity (BMI $> 30\,kg/m^2$) is the most common and a major risk factor for obstructive sleep apnea syndrome (OSA).[9] An increase in BMI by about two units (for example, from 27 to 29) increases the likelihood of co-existing OSA by a factor of four.[10] OSA in the obese generally improves following weight reduction.[11] Whereas the prevalence of OSA in the general US population is 2% in women and 4% in men,[9] it is 3–25% and 40–78% in morbidly obese women and men, respectively.[11–14] Sleep apnea in obese patients is usually obstructive and a consequence of both airway narrowing from abundant peripharyngeal adipose tissue and an abnormal decrease of upper airway muscle tone during rapid-eye-movement (REM) sleep.[9]

The presence and severity of OSA in obese patients cannot be reliably predicted by BMI, neck circumference, pulmonary function tests (PFTs), daytime room air arterial blood gases (ABGs), and/or questionnaires aimed to detect and quantify sleep-related complaints.[15–19] In the USA, 80–90% of sleep apnea sufferers are undiagnosed.[10,20] Consequently, pre-operative patients with this condition frequently present with suggestive symptoms, but without prior evaluation. (Bariatric surgery may be a nice option compared to chronic tracheostomy in patients with OSA, and need for tracheostomy is listed frequently as an indication for such bariatric surgery.)

The definitive diagnostic test for OSA is polysomnography. The presence of sleep apnea is defined as five or more apneic events (cessation of airflow lasting 10 s or longer despite continued respiratory effort) per hour or 15 or more hypopneic events (decrease in airflow of more than 50% lasting 10 s or longer) per hour during a 7 h sleep study.[21] The apneic/hypopneic index (AHI) is the total number of apneic and/or hypopneic events per hour during sleep;

the severity of OSA is directly related to the magnitude of the AHI.[9] Hypopneic and apneic events are associated with arousal from REM sleep and oxyhemoglobin desaturation. Daytime somnolence is a frequent complaint because sleep is fragmented such that the patient cannot sustain adequate intervals of REM sleep. Concomitant with apneic/hypopneic events, sympathetic nervous system activation occurs in response to hypoxemia. This finding may explain the strong association between OSA and systemic hypertension.[22]

The detection of OSA among obese patients presenting for bariatric surgery may be important for two reasons. First, patients with OSA are more sensitive to the consequences of the depressant effects of hypnotics and opioids on airway muscle tone and respiration.[23] Post-operative parenteral or neuraxial opioid administration to obese patients with OSA carries the potential for fatal or near fatal respiratory misadventure.[24,25] More intense post-operative nursing care and monitoring may be indicated when symptoms or signs of sleep apnea exist and either systemic or neuraxial opioids are necessary for post-operative pain control. Second, OSA is associated with difficulty with laryngoscopy[26,27] and difficult mask ventilation.[25,28] In addition, obese patients have reduced oxygen stores because of their diminished expiratory reserve volume (ERV).[29,30] The combination of these factors sets the stage for airway catastrophe. As a large percentage of obese patients have sleep apnea, identification those who do likely *not* have the condition may be more appropriate; in fact, some experts recommend presuming that *all* morbidly obese patients presenting for bariatric surgery have OSA. Thus, they recommend all pre-operative patients scheduled for bariatric surgery be trained for continuous positive airway pressure (CPAP) or bi-level positive airway pressure (BiPAP) usage.[31]

In the absence of prior polysomnographic testing, the presence and severity of OSA in the pre-operative bariatric surgical patient is most conveniently assessed by history. Useful information can often be elicited from the patient's roommate or sleeping partner. Historical information presumptive of sleep apnea includes habitual snoring, interrupted breathing during sleep (apneic spells followed by short gasps, grunts, or resuscitative snorting), impaired daytime performance, morning headache, and irritability.[9] Systemic hypertension and increased neck circumference (>40–42 cm at the cricoid cartilage) are consistent with the presumptive diagnosis of OSA.[20–22,32] Other abnormalities detected by physical examination associated with OSA are somnolence and physical signs of difficult mask airway and/or difficult intubation (for example, Mallampati class III or IV, hypognathia, decreased thyromental distance).[23,25,27]

Polysomnographic testing might be indicated in morbidly obese pre-operative patients who habitually snore and report daytime somnolence and/or have observed periods of interrupted breathing during sleep.[9] However, morbid obesity and symptoms of OSA are not *per se* indications for pre-operative pulmonary function testing and room air blood gas analyses. In the absence of uncharacterized symptoms or signs of pulmonary disease, these tests have neither predictive value nor utility in optimizing post-operative management or outcome of bariatric surgery patients.[24,33–35]

Obesity *per se* is not a common cause for chronic respiratory insufficiency.[36] Clinically significant impairment of gas exchange and pulmonary function are more common when chronic obstructive pulmonary disease (COPD) and obesity co-exist. The two conditions together cause greater impairment of gas exchange than expected from simple summation of the impairment caused by each pathophysiologic process.[37] As in all patients, the presence of concomitant pulmonary system disease may be detected by smoking history and symptoms or signs such as cough, wheezing, or dyspnea on exertion.

In obese patients, chronic daytime hypoxemia is a better predictor of pulmonary hypertension and cor pulmonale than the presence and severity of OSA.[38–40] Room air pulse oximetry may be a useful, non-invasive means to screen patients for daytime hypoxemia, particularly if measured and compared in both the upright and supine positions. A *supine* room air SpO_2 of less than 96% may merit further investigation (for example, PFTs, room air ABGs, chest radiographs, and echocardiography). An elevated hematocrit may also be a clue of chronic hypoxemia.

A sub-group of obese patients develop a syndrome characterized by chronic daytime hypoventilation, dubbed the obesity–hypoventilation syndrome (OHS).[36] OHS is also associated with chronic daytime hypoxemia ($PO_2 < 65$ mmHg), conveniently detected during the pre-operative visit by routine measurement of room air pulse oximetry. Sustained hypercapnia ($PCO_2 > 45$ mmHg) in the obese patient without significant obstructive pulmonary disease is diagnostic for this syndrome. These patients typically are extremely obese (BMI $> 40\,kg/m^2$), and the likelihood of OHS increases strongly as BMI increases.[41] The precise underlying pathophysiology of OHS is unclear and likely multifactorial; however, chronic alveolar hypoventilation may be attributed to the compressive effect of extreme adiposity on the thoracic

cage and diaphragm.[19,36] The majority of obese patients with OHS also have OSA; nevertheless, obese patients with OSA do not commonly have OHS.[19,36] Patients on the "severe" end of the OHS spectrum who have signs and symptoms of cor pulmonale are termed "Pickwickian".[19] In one study of obese patients with OSA but without airflow obstruction, 56 of 58 patients with chronic daytime hypoxemia proved by testing to have OHS.[40]

The reason to be wary of, and to try to diagnose if obesity co-exists with either OHS *or* COPD is that such combination often causes chronic daytime hypoxemia. And chronic daytime hypoxemia leads to pulmonary hypertension, right ventricular hypertrophy, and/or right ventricular failure. These conditions (Pickwickian) have an increased peri-operative morbidity and mortality, and assessment of these patients may require extensive testing to guide pre-operative medical optimization and post-operative management.[19,22,23,42]

Prevalent electrocardiographic (EKG) findings in obese patients are low QRS voltage, left ventricular hypertrophy or strain, left atrial abnormality, and T-wave flattening in the inferior and lateral leads.[43] EKG evidence in the obese of right ventricular hypertrophy or strain, right axis deviation, right bundle branch block, and/or P pulmonale is not common in the absence of pulmonary hypertension and cor pulmonale.

Morbidly obesity with minimal or no co-existing pulmonary conditions (for example, no OHS, nor COPD) will be referred to as "simple" obesity. In simple obesity, the pathophysiology of mild alterations in daytime gas exchange and pulmonary function also may result from compression and restriction of the chest wall and diaphragm by excess adipose tissue.[44] Typically, in the obese ERV and FRC are most affected and reduced to 60% and 80% of normal, respectively. If ERV decreases below the closing volume, then airway closure occurs during normal tidal breathing, and dependent alveoli are relatively or completely under-ventilated. Daytime hypoxemia results if shunt and ventilation–perfusion mismatch is of sufficient magnitude. Following massive weight loss, morbidly obese patients demonstrate marked improvement in PaO_2 and the alveolar–arterial oxygen gradient; variables reflecting oxygenation improve to an extent directly proportional to the increase in the ERV.[45,46]

Whereas vital capacity in simple obesity is reduced to 90% of control, it is reduced to 60% of normal in OHS.[47] The addition reduction in lung volume seen in OHS may be sufficient to cause marked increases in distal airway resistance. Airway resistance, increased by 133% in simple obesity, is increased by 650% in OHS.[47] In comparison with simple obesity, the forced expiratory volume in one second (FEV_1) and maximum expiratory flow rate and maximum voluntary ventilation (MVV) are reduced by 40%[47] in OHS. Accompanying these physiologic changes are the mechanical disadvantages of an overstretched diaphragm. In combination, these factors may lead to chronic respiratory muscle fatigue and the chronic hypoventilation characteristic of OHS.[19] In addition, the reduced lung volume associated with OHS may further impair ventilation–perfusion matching, causing decreases in PaO_2 and increases in the A–a gradient greater than those of simple obesity. However, most of the reduction of PaO_2 in OHS patients is postulated as due to alveolar hypoxia from hypercarbia.[19]

Table 9.4 The dyspnea index

Grade*	Description
0	No dyspnea while walking on the level at a normal pace.
1	"I am able to walk as far as I like provided I take my time."
2	Specific (street) block limitations: "I have to stop for a while after two blocks."
3	Dyspnea on mild exertion: "I have to stop and rest while going from the living room to the bathroom."
4	Dyspnea at rest.

* Grade of dyspnea caused by respiratory problems (assessed in terms of walking on the level at a normal pace).

Especially in patients with OHS, the supine position further reduces lung volume and increases distal airway resistance.[28,44] Ferretti *et al.*[11] found that orthopnea in obese patients may be attributable to these physiologic causes.

During the pre-operative assessment, the extent of dyspnea the patient experiences in the supine position may yield useful information (Tables 9.4 and 9.5).

In the peri-operative setting, reduction of chest wall and diaphragmatic muscle tone following induction of general anesthesia and skeletal muscle relaxation further impairs oxygenation. In simple obesity, the net effect may reduce ERV and FRC to less than 50% of pre-induction values, excluding even more alveoli from effective gas exchange.[44] In addition, reduction of ERV and FRC predisposes to atelectasis and limits effective clearance of secretions in the post-operative period.

ERV is the primary source of oxygen reserve during apnea. Therefore, in the obese patient, pre-oxygenation

Table 9.5 Estimated energy requirements for various activities[a]

METs[b]	Activity
1	• Can you take care of yourself? • Can you eat, dress, and use the toilet? • Can you walk indoors around the house? • Can you walk a block or two on level ground at 2–3 mph (3.2–4.8 km/h)?
4	• Can you climb a flight of stairs or walk up a hill? • Can you walk on level ground at 4 mph (6.4 km/h)? • Can you run a short distance? • Can you do heavy work around the house such as scrubbing floors or moving heavy furniture? • Can you participate in moderate recreational activities such as golfing, bowling, dancing, doubles tennis, or throwing a baseball or football?
10	• Can you participate in strenuous sports such as swimming, singles tennis, football, basketball, or skiing?

[a] Adapted from the Duke Activity Status Index and the American Heart Association Exercise Standards.

[b] METs: Metabolic equivalents.

is less effective and, following apnea, the time to hemoglobin desaturation below 90% is reduced.[48,49] In the obese, anesthetized, relaxed patient, the combination of a reduced "apneic oxygenation reserve" and the likelihood of difficultly with positive pressure mask ventilation amplifies the potential for a hypoxemic misadventure.[27] Elective awake tracheal intubation may be safest approach if a patient scheduled for bariatric surgery has signs indicating the potential of difficult intubation, such as poor visualization of the posterior pharyngeal wall.[50] Positioning the patient with a roll under the scapulae, an occipital rest, and asking the patient to extend fully at the atlanto-occipital joint prior to induction may facilitate awake or conventional laryngoscopy and intubation.

Some investigators found that obesity (BMI $>$ 30 kg/m^2) is associated with an increased risk of difficult laryngoscopy (inadequate exposure of the glottis) compared with subjects of normal BMI.[51] Others found no correlation between problematic intubation and BMI, but found an association between difficulty of intubation and either a large neck circumference ($>$40–42 cm) or a Mallampati score of III or IV.[52] This difference may be explained by the observation that obese patients are more likely to have both a large neck circumference and a higher Mallampati classification.[31] Furthermore, obese patients have increased volume and acidity of gastric juices pre-operatively, perhaps indicating the wisdom of premedicating such patients with cimetidine, ranitidine, bicitra or metoclopramide. (The simplest, least expensive scientifically tested regimen appears to be administration of cimetidine the night and morning before surgery.) Others would conclude that awake intubation is indicated, but preference for this technique must be balanced by the realization that most episodes of gastroesophageal reflux and the greatest potential for pulmonary aspiration occur from and during "bucking" on an endotracheal tube[53,54] (see Chapter 8).

Following major open abdominal surgery and without post-operative oxygen supplementation, even normal patients experience hypoxemia ($SpO_2 < 90\%$) that persists several days and is most prevalent and severe on the night of the second post-operative day.[55] On the first post-operative day following open bariatric surgery, 75% of obese patients had a $PaO_2 <$ 60 mmHg; PaO_2 averaged 14 mmHg less than pre-operative baseline measurements.[56] Although some improvement was seen, oxygenation remained significantly less than baseline during subsequent post-operative days. These facts emphasize the importance of obtaining a pre-operative assessment of baseline oxygenation via pulse oximetry, and preparing for specific treatments should pre-operative values minus 14 mmHg be hazardous.

More extensive PFTs and pre-operative treatment of any treatable abnormality (for example, infectious and bronchospastic components of pulmonary disease) may be indicated for the obese patient who smokes or has pulmonary symptoms (for example, chronic cough, sputum production, wheezing, shortness of breath at rest or on minor exertion). This evaluation may be indicated even for laparoscopic bariatric surgery. While laparoscopic bariatric surgery may have fewer adverse effects on post-operative pulmonary gas exchange and require less post-operative analgesia, there is always the potential that the surgeon will need to convert to an "open" procedure. But if an open procedure is likely and obesity is severe, ABGs might also be analyzed to quantitate the degree of hypoventilation and to aid in assessing the most appropriate time to extubate the trachea.

Post-operative continuous oxygen supplementation and maintenance of the semi-recumbent or upright

posture[57] might be prudent strategy for all bariatric surgery patients. However, oxygen therapy alone may not be adequate, as determined by co-existing OSA, COPD, or OHS, post-operative opioid analgesic needs, and pre-existing hypoxemia or orthopnea. If the need for opioid analgesics is anticipated in obese patients with OSA, OHS, COPD, baseline SpO_2 is less than 96%, or a history of orthopnea is elicited, then post-operative CPAP or BiPAP therapy might be useful.

Nasal CPAP, a treatment for OSA since 1981, acts by "splinting" the airway during inspiration.[58] Given a patient compliance rate of 50–80%, it may be prudent to question if the patient will accept this nocturnal therapy.[58] In normal weight patients undergoing major abdominal surgery, nasal CPAP and supplemental oxygen was not shown to decrease hypoxemic events in the first post-operative night.[59] However, in surgical patients with OSA, post-operative nasal CPAP therapy has been shown to prevent blood pressure fluctuation associated episodic apneic events.[60]

BiPAP, a more recent refinement respiratory therapy, combines CPAP with additional inspiratory pressure support. Prophylactic BiPAP (12 cmH_2O inspiratory pressure, 4 cmH_2O expiratory pressure) during the first 24–48 h after bariatric surgery significantly improved forced vital capacity, FEV_1, and oxygenation as reflected by continuous SpO_2 monitoring.[61,62] Improvement in lung volume persisted several days and lead to quicker recovery to baseline spirometric volumes; however, the complication rate and length of post-operative stay were not shown to be altered by this therapy.

It is unclear if it is appropriate to delay bariatric surgery for aggressive optimization of airway status and oxygenation with CPAP or BiPAP therapy. Rennotte observed no major post-operative respiratory complications in 14 patients treated with nasal CPAP for up to 3 weeks prior to surgery,[63] but without a prospective control group indicating such would not have occurred without such preparation. Two to three weeks may be necessary not only to maximize medical benefits, but to allow sufficient time for patients unfamiliar with CPAP or BiPAP therapy to acclimate to the nocturnal use of the device. Three weeks of nightly CPAP treatment prior to bariatric surgery improved left ventricular ejection fraction and afterload in obese patients with co-existing heart failure.[64] Eight weeks of pre-operative nasal CPAP therapy may be required to treat hypertension secondary to OSA.[65] After surgery, treatment should be applied as early as possible after extubation.[42]

9.4 Cardiopulmonary evaluation

9.4.1 Venous stasis and thromboembolism evaluation and prevention

While evaluation of venous status might seem strange as the first priority on cardiovascular evaluation, it is importance and prominence becomes obvious when one looks at the mortality data (see Chapter 12). Venous emboli that go to the pulmonary circulation are the major source of pulmonary dysfunction that lead to the 1–2% 30 day mortality rate. Most mortality in the 30 day peri-operative period following bariatric surgery is due to pulmonary embolism (this cause of mortality is three or more times greater than anastomic leak with subsequent sepsis). Various drug regimes to decrease thrombotic tendency have been tried, but there is no agreement. Use of low molecular weight heparin might limit post-operative pain therapy options, and pre-operative aspirin and subsequent coumadin to an international normalized ratio (INR) of 2.3 might be the current treatment of choice. The use of coumadin, a vitamin K antagonist, can be problematic post-operatively, as most patients post Roux-En Y Gastrojejunosity (RNYG) malabsorb fat and fat soluble substances, including vitamin K. This malabsorbtion makes the dose of coumadin difficult to control, and often will require daily adjustment for at least a few weeks. Nevertheless pre-operative evaluation for venous stasis is difficult; many surgeons insist on pre-operative exercise for at least an hour of walking or bicycle exercise 3 days a week for 6 weeks and the absence of leg symptoms (pain, soreness, or redness). Other surgeons or groups require 30 min each day of walking (see below for psychologic factors that determine success). Factors that decrease this risk in multiple patients include pre-operative exercise and anti-thrombotic drug and perhaps stocking prophylaxis, non-polycythemic hematocrit, increased cardiac output, and early ambulation. Thus evaluation of exercise status, drug therapy, absence of signs or symptoms of, and ensuring no pre-existing venous disease, optimal hydration and peri-operative drug therapy all aimed at early ambulation might be the goals of this area of evaluation and prophylaxis. But whatever is done, it should be remembered this area is the major determinant of peri-operative survival.

9.4.2 Cardiovascular evaluation

Cardiac output increases approximately 0.01/min to perfuse each kilogram of adipose tissue. As a result, obese patients often have hypertension, which can cause cardiomegaly and left ventricular failure. Care

should be taken to use a blood pressure cuff of correct size when quantitating the degree of hypertension present. But this may not be easy. Obesity poses difficulties not only for intravenous access, but also for non-invasive blood pressure monitoring. Blood pressure cuff size may be difficult to ascertain, and may require measurement at a site other than the upper arm (for example, the forearm) when the patient has a "cone-shaped" upper arm anatomy. Depending on the extent of cardiopulmonary reserve, direct monitoring of the arterial blood pressure may be necessary to accurately and continuously monitor blood pressure and to enable frequent arterial blood sampling.

The obese may have limited cardiac reserve and a poor tolerance for stress induced by hypotension, hypertension, tachycardia, or fluid overload associated with the pre-operative period. As noted above, massively obese patients with carbon dioxide retention are called Pickwickian, alveolar hypoventilation being the hallmark of this condition. Other components of the Pickwickian syndrome are somnolence, hypoxemia, failure of the right side of the heart, and secondary polycythemia. Many of these patients have right ventricular failure. Thus usual pre-operative assessment in our hands includes not only history taking and physical examination accentuating drug therapy and cardiopulmonary problems but also an ECG examination (looking specifically for left or right ventricular hypertrophy, ischemia, and conduction defects) (see Chapter 17). In cases where biventricular failure is severe and not compensated for by a pre-operative exercise regimen that lasts two or more months, or if large blood loss is anticipated due to individual surgical or clotting status factors, then evaluation of central vascular volume may be indicated for bariatric surgery. Physical examination of peripheral venous access may enable the clinician to plan the need for central venous access. Some prefer transesophageal echocardiography for this assessment of central volume status if a central venous pressure (CVP) is not needed for access.

9.5 Metabolic evaluation

9.5.1 Diabetes

While many of the metabolic changes associated with obesity (for example, insulin resistance, decreased number of insulin receptors, and subsequent diabetes mellitus) can be induced by overfeeding normal subjects and can be reversed by weight reduction[2–4], most obese patients even if walking 30 min a day regularly and especially those presenting for bariatric surgery, still have overt diabetes (see Chapter 10).

Non-insulin-dependent (type II) diabetics constitute more than 90% of the more than 19 million diabetics in the US.[67] While a genetic disease, it is phenotypic expression is increasing exponentially following the increase in weight in the US population. Type II diabetics tend to be relatively resistant to ketoacidosis and susceptible to the development of a hyperglycemic–hyperosmolar non-ketotic state. Plasma insulin levels are normal or elevated but are relatively low for the level of blood glucose. This hyperinsulinemia by itself is postulated to cause accelerated cardiovascular disease.[66–67]

Insulin is first synthesized as proinsulin, converted to insulin by proteolytic cleavage, and then packaged into granules within the β-cells. A large quantity of insulin, normally about 200 units, is stored in the pancreas; continued synthesis is stimulated by glucose. There is a basal, steady-state release of insulin that is crucial to the inhibition of catabolism and ketoacidosis. Glucose and fructose are the primary regulators of insulin release.

While type I diabetes is associated with a 15% prevalence of other autoimmune diseases, including Grave's disease, Hashimoto's thyroiditis, Addison's disease, and myasthenia gravis, no such associations have been reported for the diabetes associated with obesity.

Currently, therapy for type II diabetes usually begins with exercise and dietary management. A 5–10 kg weight loss over 8 weeks, associated with a 20% reduction in calories and an increase in daily physical activity to 30 min, is often associated with normalization of fasting blood glucose,[68] even anecdotally reported in those waiting for bariatric surgery. However, this is a difficult task for many patients, who then progress to the use of oral hypoglycemic medications that act by stimulating release of insulin by pancreatic β-cells and by improving the tissue responsiveness to insulin by reversing the post-binding abnormality. The common orally administered drugs are tolazamide (Tolinase), tolbutamine (Orinase), and the sulfonylureas glyburide (Micronase) and glipizide (Glucotrol). These last drugs have a longer blood glucose-lowering effect, which persists for 24 h or more, and fewer drug–drug interactions. Oral hypoglycemic drugs may produce hypoglycemia for as long as 50 h after intake (chlorpropamide [Diabinese] has the longest half-life). Other drugs include metformin, which decreases hepatic glucose output and may increase peripheral responsiveness to glucose; acarbose, which decreases glucose absorption; and troglitazone, which increases peripheral responsiveness to insulin.[69] Progressively, physicians advocating tight control of blood sugar levels give insulin twice a day, or even more frequently.[70,71]

Absorption of insulin is highly variable and is dependent on the type and species of insulin, the site of administration, and subcutaneous blood flow. Nevertheless, the steady state is dependent on periodic administration of the preparations received by the patient. Thus it seems logical to continue peri-operatively the combinations of preparations the patient has been receiving chronically, after examining the patient's blood glucose monitoring logbook for the degree of control. (In my clinical experience, erratic control can foreshadow peri-operative hypoglycemia in patients receiving insulin prior to bariatric surgery.)

Diabetic patients are also subject to a series of long-term complications, including cataracts, neuropathies, retinopathy, and angiopathy involving peripheral and myocardial vessels, that lead to considerable morbidity and premature mortality. The evidence that hyperglycemia itself accelerates these complications or that tight control of blood sugar levels decreases the rapidity of the progression of microangiopathic disease is becoming more definitive.[72,73]

Glucose itself may be toxic because high levels can promote non-enzymatic glycosylation reactions, leading to the formation of abnormal proteins that may decrease elastance and wound-healing tensile strength. The decrease in elastance is responsible for the stiff joint syndrome and for fixation of the atlanto-occipital joint that makes intubation difficult.[74–76] Glycemia also disrupts autoregulation. Glucose-induced vasodilation prevents target organs from protecting against increases in systemic blood pressure. A glycosylated hemoglobin level of 8.1% is the threshold at which the risk of microalbuminuria increases logarithmically. A person with type I diabetes who has microalbuminuria of more than 29 mg/day has an 80% chance of experiencing renal insufficiency. The threshold for glycemic toxicity differs for various vascular beds. For example, the threshold for retinopathy is a glycosylated hemoglobin value of 8.5–9.0% (12.5 mmol/l or 225 mg/dl); and, for cardiovascular disease, an average blood glucose value of 5.4 mmol/l (96 mg/dl). Thus different degrees of hyperglycemia may be required before different vascular beds are damaged, or certain degrees of glycemia are associated with other risk factors for vascular disease. Diabetes is associated with microangiopathy (in retinal and renal vessels), peripheral neuropathies, autonomic dysfunction, and infection. Diabetics are often treated with angiotensin-converting enzyme inhibitors even in the absence of gross hypertension, in an effort to prevent the effects of disordered autoregulation, including renal failure.

Accumulating data, much from the Diabetes Control and Complications Trials for Type I diabetes, and from the UK Prospective Diabetes Study, clearly indicate that tight control of blood glucose levels reduces the risk of chronic complications in type I and II diabetics.[72,73]

Peri-operative management of the diabetic patient may affect surgical outcome. Physicians advocating tight control of blood glucose levels point to the evidence of increased wound-healing tensile strength and decreased wound infections in animal models of diabetes (type I) under tight control, and now in patients requiring more than 48 h in an intensive care unit after surgery.[77–80]

Infections including those caused by anastomotic account for two-thirds of post-operative complications and about 20% of peri-operative deaths in patients undergoing bariatric surgery, and next to emboli are the greatest risks for such patients. Experimental data suggest many factors that can make the patient with glucose intolerance vulnerable to infection. Many alterations in leukocyte function have been demonstrated in hyperglycemic diabetics, including decreased chemotaxis and impaired phagocytic activity of granulocytes, as well as reduced intracellular killing of pneumococci and staphylococci.[81,82] When diabetic patients are treated aggressively and blood glucose levels are kept below 250 mg/dl, the phagocytic function of granulocytes is improved and intracellular killing of bacteria is restored to near normal levels.[83]

Such benefit also seems to accrue to those undergoing bariatric operations that need intensive care unit (ICU) care for more than 48 h.[77–80]

The key to managing blood glucose levels in diabetic patients peri-operatively is to set clear goals and then to monitor blood glucose levels frequently enough to adjust therapy to achieve those goals. Three regimens that afford various degrees of peri-operative control of blood glucose levels are discussed below.

Classic "non-tight control" regimen

Aim

To prevent hypoglycemia. To prevent ketoacidosis and hyperosmolar states.

Protocol

1. Day before surgery: Patient should be given nothing by mouth after midnight; a 13-ounce glass of clear orange juice should be at the bedside or in the car for emergency use.
2. At 6 a.m. on day of surgery, institute intravenous fluids using plastic cannulae and a solution containing 5% dextrose, infused at the rate of 125 ml/h/70 kg body weight.

3 After institution of intravenous infusion, give one-half the usual morning insulin dose (and usual type of insulin) subcutaneously.
4 Continue 5% dextrose solutions through operative period, giving at least 125 ml/h/70 kg body weight.
5 In recovery room monitor blood glucose concentrations and treat on a sliding scale.

Such a regimen has been found to meet its goals.[84]

"Tight control" regimen 1

Aim

To keep plasma glucose levels at 79–120 mg/dl; this practice may improve wound-healing and prevent wound infections, improve neurologic outcome after global or focal central nervous system (CNS) ischemic insult, and improve outcome in those requiring ICU therapy.

Protocol

1 Evening before operation, determine preprandial blood glucose level.
2 Through a plastic cannula, begin intravenous infusion of 5% dextrose in water at the rate of 50 ml/h/70 kg body weight.
3 "Piggyback" to the dextrose infusion an infusion of regular insulin (50 units in 250 ml or 0.9% sodium chloride) and an infusion pump. Before attaching this piggyback line to the dextrose infusion, flush the line with 60 ml of infusion mixture and discard the flushing solution. This approach saturates insulin-binding sites of the tubing.[85]
4 Set the infusion rate, using the following equation: Insulin (U/h) = plasma glucose (mg/dl)/150. (*Note:* This denominator should be 100 if patient is taking corticosteroids, for example, 100 mg of prednisolone a day or its equivalent, not to include inhaled steroids.)
5 Repeat measurements of blood glucose levels every 4 h as needed, and adjust insulin appropriately to obtain blood glucose levels of 100–200 mg/dl.
6 The day of surgery, intra-operative fluids and electrolytes are managed by continuing to administer non-dextrose-containing solutions, as described in steps 3 and 4.
7 Determine plasma glucose level at the start of operation and every 1 to 2 h for the rest of the 24 h period. Adjust insulin dosage appropriately.

Although I have not found the need to treat hypoglycemia (that is, blood glucose levels of <50 mg/dl), I have been prepared to do so with 15 ml of 50% dextrose in water. Under such circumstances, the insulin infusion would be terminated. Such a regimen has been found to accomplish its goals, with the exception of such tight goals for blood glucose, even in very "brittle" diabetics (that is, those extremely resistant to treatment) given high doses of steroids.[86]

Table 9.6 Intensive therapy of diabetics that require intensive care decreases complication rates and improves survival

Intensive R_X (80–110) %		Conventional R_X(180–200) %
4.6	Death in ICU	8.0
10.6	Post 5 days in ICU	20.2
1.7	First 5 ICU days	1.8
7.2	All deaths	10.9
11.4	>14 days ICU	15.7
7.5	>14 days ventilation	11.9
4.8	R_X dialysis	8.2
28.7	Polyneuropathy	51.9

Leuven ICU Study: intensive insulin R_X in 1548 post-surgery patients.

"Tight control" regimen 2

Aim

Same as for tight control regimen 1

Protocol

1 Obtain a "feedback mechanical pancreas" and set the controls for the desired plasma glucose regimen.
2 Institute two appropriate intravenous lines.

This last regimen may well supersede all others if the cost of a mechanical pancreas can be reduced and if control of hyperglycemia is shown to make a meaningful difference peri-operatively; it has superseded all others in many intensive care units, and for good reason (Table 9.6).[77–79] For bariatric surgery, we rarely use anything except regimen 1.

9.5.2 Hypocalcemia

Inadequate calcium intake is a cause of both hypertension and obesity; in fact, in some normalization of calcium intake can cure both hypertension and the food cravings that cause obesity.[87,88]

9.5.3 Hyperlipidemias and hypolipidemias

Hyperlipidemia are common in obesity. Hyperlipidemia may cause premature coronary or peripheral vascular disease or pancreatitis. Hypercholesterolemia, a form of hyperlipidemia, appears to be associated with premature atherosclerosis. Most cholesterol is carried in serum by low-density lipoprotein (LDL), whereas approximately 30% of total serum cholesterol

is carried by high-density lipoprotein (HDL). HDL cholesterol is carried in roughly equivalent amounts on two types of HDL: on a less dense HDL_2 subfraction that is negatively associated with coronary artery disease, and on a more dense HDL_3 subfraction that is unrelated to coronary artery disease.

In regard to the production of atherosclerosis, LDL is distinguished from HDL by associating L with "lousy" and H with "healthy." That is, the oxidized form of LDL constitutes a risk factor for atherosclerosis, whereas HDL is believed to carry dangerous cholesterol away from the periphery, to be metabolized by the liver, and is therefore protective. Levels of HDL are 25% higher in women than in men; low levels of HDL in women are associated with premature atherosclerosis. Cigarette smoking lowers HDL levels, whereas regular exercise (particularly, strenuous exercise, but even non-strenuous exercise) and small daily intake of alcohol raise HDL levels. However, alcohol increases HDL_3, the HDL subfraction thought to be inert with respect to coronary artery disease; octogenarians have high levels of HDL.

Data showing that coronary events can be reduced by treating individuals with even normal levels of LDL cholesterol with the "statins" – drugs that raise HDL and lower LDL cholesterol levels – has resulted from a decade of rapid progress in preventing reinfarction in high-risk patients.[92,93] Secondary prevention efforts were successful when these high-risk patients stopped smoking, reduced blood pressure, controlled stress, increased physical activity, and used aspirin, vitamin E, β-blocking drugs, angiotensin inhibitors, diet, and other drugs to reduce their levels of LDL and to increase their levels of HDL.[89,90]

Although controlling diet remains a major treatment modality for all types of hyperlipidemia,[91,101] the drugs clofibrate (Atromid-S) and gemfibrozil, used to treat hypertriglyceridemia, can cause myopathy, especially in patients with hepatic or renal disease; clofibrate is also associated with an increased incidence of gallstones. Cholestyramine binds bile acids, as well as oral anticoagulants, digitalis drugs, and thyroid hormones. Nicotinic acid causes peripheral vasodilation and probably should not be continued through the morning of surgery. Probucol (Lorelco) decreases the synthesis of apoprotein A1; its use is associated on rare occasion with fetid perspiration and/or prolongation of the QT interval, and sudden death in animals.

The West of Scotland Coronary Prevention Study (WOSCOPS) and its congeners produced convincing evidence that drugs in the "statin" class (3-hydroxy-3-methylglutaryl coenzyme A [HMG-CoA] reductase inhibitors) prevent the morbidity and mortality related to arterial aging and vascular disease, as well as their consequences, coronary arterial disease, stroke, and peripheral vascular insufficiency.[92,93] Thus the statins – lovastatin (Mevacor), pravastatin (Pravachol), simvastatin, fluvastatin, and atorvastatin – are mainstays of therapy.

But the report of Downs *et al*. from the Air Force/Texas Coronary Atherosclerosis Prevention Study went farther.[92] It showed a 37% reduction in the risk of first acute major coronary events in patients who had not only no risk factors for coronary artery aging but also normal (average) LDL cholesterol levels. In this study, lovastatin did not alter mortality rates; however, that had been true for many early short-term trials with the statins. Although much of the effect of the statins has been attributed to their lipid-lowering effects, statins have also been shown to modify endothelial function, inflammatory responses, plaque stability, and thrombogenicity.[94] While the report of Downs broadened the use of statins, they remain the mainstays of therapy for the hyperlipidemias. They are drugs that block HMG-CoA reductase, the rate-limiting enzyme of cholesterol synthesis. Their use is occasionally accompanied by liver dysfunction, CNS dysfunction, and severe depression not related to the high cost of each drug and its cogeners.

Hypolipidemic conditions are rare diseases often associated with neuropathies, anemia, and renal failure. Although anesthetic experience with hypolipidemic conditions has been limited, some specific recommendations can be made: continuation of caloric intake and intravenous administration of protein hydrolysates and glucose throughout the peri-operative period.

9.6 Psychologic evaluation and psychiatric considerations

Psychologic evaluation is crucial for patient success. It is not an easy year after the surgery, let alone the week after. The patient must be sapient, engaged, and must be able to have the discipline to keep a food diary. The evaluation of the anesthesiologist can provide valuable clues, "has the patient been walking daily?", for example. The patient needs to be emotionally stable. Choices that the anesthesiologist can uncover that correlate with failure are street drug abuse, unaddressed major psychiatric disorders/illness, compulsive eating disorder, and the diagnosis of fibromyalgia or chronic fatigue syndrome. If such are searched for and found on pre-operative evaluation, communication among all including the surgeon can spare the health care team much frustration and save the patient much distress.

9.7 Musculoskeletal, evaluation for positioning and other issues

Other features of obesity are of prognostic and perioperative importance to the anesthesiologist as well. Because of excessive and extensive subcutaneous fat and large size of the extremities, proper positioning of the patient, placement of monitoring devices, and establishment of intravenous sites are more difficult to accomplish, and blood pressure (and cuff size choice) are less easy to ascertain than for patients of normal weight.

The anesthesiologist should also be aware of conditions caused by remedies to obesity. Drastic dieting can produce acidosis, hypokalemia, and hyperuricemia; protein hydrolysate liquid diets are associated with intractable ventricular arrhythmias. These problems seem to have disappeared as the diets have changed from hydrolyzed collagen fasts to the currently used very-low-calorie diet.

Prior drug treatment for obesity also has implications for the anesthesiologist. Amphetamines (and probably mazindol) given *acutely* increase anesthetic requirements; by contrast, amphetamines administered *chronically* decrease anesthetic requirements (see the section on chronic drug therapy). Amphetamines may interfere with the action of vasoactive drugs given to treat hypotension or hypertension.

Since many obese patients have tried drug therapies, the anesthesiologist should consider asking questions about use of adjuvants. If such drugs have been used, the anesthesiologist might consider auscultation and echocardiography to search for mitral valve regurgitant lesions, as some dietary aids (notably "phen-fen") have been associated with these conditions. Because other dietary herbs are known to cause liver dysfunction, searching for use of these adjuvants may be important. Fenfluramine (a drug that inhibits the serotonergic system) by itself may decrease both anesthetic requirement and blood pressure.

Obese persons may metabolize lipophilic drugs to a greater degree (and for longer periods) than their thin counterparts. More fluorine is produced from enflurane given to obese patients than to thin ones. One would assume that responses to drugs stored in fat (for example, narcotics, barbiturates, volatile anesthetics) would be prolonged in the obese. There is no evidence, however, that the use of the more soluble anesthetics delays recovery time in obese subjects. The dose requirements of pharmacologic agents used for analgesia and airway management are also altered by significant obesity (BMI > 27.5). Obesity increases the volume of distribution of sufentanil and slows its elimination. In one study, the elimination half-life of sufentanil was 208 min for eight obese patients (mean weight, 94 kg) vs. 135 min for eight controls (mean weight, 70 kg).[95] Similarly, muscle relaxants that depend on hepatic blood flow for their elimination (that is, pancuronium, vecuronium, and rocuronium) appear to have dosage requirements that are directly proportional to body surface area, as well as longer twitch recovery times. The 25–75% twitch recovery time for vecuronium was 38.4 min for obese patients (mean weight, 93 kg) vs. 17.6 min for non-obese patients (mean weight, 61 kg).[96]

Obesity poses challenges with regard to intravenous access and non-invasive blood pressure monitoring.[97] Examination of the peripheral venous system may assist the clinician in planning for pre-operative insertion of central venous access. Blood pressure cuff size may be difficult to ascertain, and may require measurement at a site other than the upper arm (for example, the forearm), especially when examination reveals a "cone-shaped" upper arm appearance. Depending on the extent of cardiopulmonary reserve, direct monitoring of the arterial blood pressure may be necessary to accurately and continuously monitor blood pressure and enable frequent arterial blood sampling.

Pre-operative consideration of the positioning of obese patients may eliminate some post-operative problems (see Chapter 20). In a retrospective study, Warner and colleagues found that patients whose BMI was greater than 38 kg/m^2 had a 29% incidence of post-operative ulnar neuropathy as compared to a 1% incidence in controls.[98] Upper brachial plexus root injury may result from extreme rotation of the head and cervical spine to the opposite side.[99] Lower root injury may result from hyper-abduction of the arm on the same side as the injury. Pre-operatively, one may assess of sites vulnerable to pressure injury. Intra-operatively, pressure point checks and repositioning periodically makes good sense.[102,103]

A pre-operative evaluation of the deep venous system of the legs is difficult in the obese. (Even more sponges and instruments are left in the obese.) Routine prophylaxis for deep venous thrombosis is commonly initiated pre-operatively, a prudent practice given that obesity is a major risk factor for sudden post-operative death due to massive pulmonary thromboembolism.[100] Anticoagulant prophylaxis is likely to be ordered by the surgeon, and this must be considered if a central neuraxial catheter is to be inserted and utilized for post-operative analgesia. Furthermore, there is an increased incidence of wound infection, deep vein thrombosis, and pulmonary

embolus; the latter two should probably be guarded against with subcutaneous heparin and early ambulation (see Chapters 12 and 13). Thus a knowledge of and/or discussion with the specific surgeon of preferences for post-operative prophylaxis of deep vein thromboses and their consequences and preparation of the patient for this plan may be an important aspect of the pre-operative meeting of anesthesiologist and patient.

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Appendix A

Body mass index formula

BMI is the ratio of weight to height and is expressed in units of kilograms per meter squared (kg/m^2). If BMI is not on the chart, or if you want to calculate a patient's BMI more precisely, the formula for doing so is relatively easy:

1 Convert a patient's weight in pounds to a patient's weight in kilograms. You do this by dividing a patient's weight in pounds by 2.2.
2 Convert a patient's height in inches to a patient's height in meters. You do this by multiplying a patient's height in inches – not feet – by 0.0254. (If you are 5 feet tall, a patient's height is 60 in, or 1.52 m. If you are 6 feet tall, a patient's height is 72 in, or 1.83 m.)
3 Square a patient's height in meters (that is, multiply a patient's height in meters by itself).
4 Divide a patient's weight in kilograms (the number you obtained in #1) by the number you obtained in #3.

The resulting number, a patient's BMI, should be in the 20s or 30s. A number below 23 is a youth-promoting BMI, and a number 27 or higher is an aging BMI.

PERI-OPERATIVE MANAGEMENT OF CO-MORBIDITIES

SECTION 4

DIABETES MELLITUS 10

F.G. Mihm

10.1 Introduction

The incidence of diabetes continues to increase over the last three decades, and its association with obesity is well established.[1] Diabetes has been reported in 6 of 15 (40%) morbidly obese patients.[2] Another larger study documented an incidence of type 2 diabetes mellitus (DM) of 20% in morbidly obese patients.[3] The peri-operative care of the diabetic patient is important on two levels for the anesthesiologist. First, it is important to avoid major complications, for example hypoglycemia, hyperglycemic hyperosmolar state (HHS), diabetic ketoacidosis (DKA), and second, to also improve surgical outcomes. Tighter blood glucose control has been associated with improved outcome in diabetic patients.[1]

Diabetes has recently undergone new nomenclature in order to eliminate the confusion caused by non-insulin and insulin-dependent diabetes mellitus (NIDDM vs. IDDM). This has had little relevance to the peri-operative management of diabetes, since virtually all patients are best managed with insulin. The new terms type 1 (pancreatic β-cell destruction) and type 2 (defective insulin secretion and, usually, insulin resistance) speak more clearly to the pathology rather than the treatment.[1] The most important clinical distinction of these two types is that type 1 patients are prone to lipolysis, proteolysis, and ketogenesis → DKA. In type 2 patients, some amounts of insulin inhibit these processes, so that DKA usually does not occur unless there is an additional stress (for example sepsis or dehydration). Type 2 patients are still at risk for the severe consequences of very high blood sugar elevations → HHS.

It should be no surprise that the patients who are morbidly obese have a high incidence of DM, where it is usually the type 2 variety. Morbid obesity is associated with insulin resistance, even in non-diabetic patients.[4] One specific defect is impaired insulin-stimulated glucose transport into skeletal muscle, which is reversible after weight loss.[5] In one series of 515 patients, disorders of glucose metabolism was noted in 55%, but after gastric bypass diabetes persisted in only 6%.[6] This is a condition that usually resolves within 4 months after successful gastric bypass procedures.[3] Patients requiring high doses of insulin (200 units/day) have been cured after gastric bypass with its associated weight reduction.[7]

10.2 Pre-operative evaluation

Successful intra-operative management of the diabetic patient begins with a full appreciation of the extent of end-organ disease (cardiovascular, renal, joint-connective tissue, immune, and nervous systems) (see also Chapter 9).

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10.2.1 Cardiac

Hypertension and coronary artery disease (CAD) with left ventricular (LV) dysfunction are common co-morbidities in diabetic patients (see Chapter 11). Even in the thrombolytic era, diabetic patients who suffer an acute myocardial infarction (MI) have up to two times the mortality of non-diabetics.[8] Both the systolic and diastolic functional abnormalities may be responsible for heart failure. Subclinical CAD may be associated with silent ischemia because of cardiac dennervation. Peripheral vascular disease may also exist. Cardiac tamponade has also been associated with this disease.

10.2.2 Renal

Diabetics are prone to small vessel disease with a predilection to affect the kidney (glomerulosclerosis) with associated retinopathy (see Chapter 14). Patients with renal impairment demonstrate decreased insulin requirements because of the kidneys' role in insulin clearance. Dialysis does not remove insulin. Some patients may suffer from nephrotic syndrome with its protein-losing state.

10.2.3 Joint-connective tissue

The diabetic condition is associated with abnormal collagen cross linking. This defect results in poor tissue tensile strength and has been implicated in the poor wound healing observed in diabetics. These patients also have a 10 times increase risk of difficult intubation. While difficult intubation is a significant problem in morbidly obese patients, the same is true in the diabetic population. Diabetic patients having renal/pancreas transplants have 10 times the incidence of difficult intubation compared to non-diabetic patients.[9] Type 1 diabetics are prone to develop "stiff joint syndrome" (SJS) with a reported incidence of 33% in 1500 patients.[10] SJS is associated with rapidly progressive micro-angiopathy, non-familial short stature, tight waxy skin, and limited joint mobility.[9] The proposed mechanism of difficult intubation is limited upper cervical spine (atlanto-occipital joint) range of motion. An association with the "prayer sign" (inability to approximate the palmar surfaces against each other with maximal effort) has been suggested.[11]

Table 10.1 Autonomic neuropathy

Signs	Problem
Resting tachycardia Loss of sinus arrhythmia (<5 beats/min) Postural hypotension (>30 mmHg) Miosis (abnormal response to darkness) Impotence	Overall incidence 10–20%, 50% if with hypertension ↑incidence with ↑duration (especially >10 years) Gastrointestinal: gastroparesis → aspiration Cardiovascular: silent ischemia, ↓heart rate, ↓blood pressure, arrest Pulmonary: dennervation of carotid bodies, chemoreceptors

10.2.4 Immune system

Diabetic patients have abnormal granulocyte function with decreased chemotaxis, phagocytosis, and killing activity. This may explain the high incidence of peri-operative infection (see also Chapter 13). Extra care at placing invasive lines in sterile fashion is necessary.

10.2.5 Nervous system: autonomic neuropathy

Diabetic patients may suffer from a number of different peripheral neuropathies, but the presence or absence of autonomic neuropathy is often overlooked, despite significant anesthetic implications (Table 10.1).

While it is much more common with type 1 DM (up to 40%), it may also occur with type 2 DM (~17%).[1] Diabetic patients with autonomic neuropathy have been reported to be seven times more likely to need vaso-active drugs in the operative period.[12]

10.3 Peri-operative blood glucose management

10.3.1 Oral agents

Many type 2 diabetics are managed as outpatients with oral agents. There are four major categories of oral hypoglycemic agents: sulfonylureas, biguanides, thiazolidinediones, and drugs that modify glucose absorption (Table 10.2).

Table 10.2 Oral hypoglycemic agents

Sulfonylureas first generation	Sulfonylureas second generation	Non-sulfonylureas
Acetohexamide (dymelor)	Glimepiride (amaryl)	Metformin (glucophage)
Chlorpropamide (diabenase)	Glipizide (glucotrol)	Acarbose (precose)
Tolazamide (tolinase)	Glyburide (micronase)	Repaglinide (prandin)
Tolbutamide (orinase)		Troglitazone (rezulin)

Sulfonylureas and repaglinide stimulate secretion of insulin by the pancreas and can cause decreased blood glucose. Metformin decreases production and increases glucose uptake and does not directly cause decreased blood glucose. Acarbose inhibits α-glucosidase which delays absorption of glucose. Troglitazone decreases insulin resistance. Both acarbose and troglitazone can cause hepatic toxicity. Metformin, a biguanide, has a long history of effectiveness but does have a rare potential to cause lactic acidosis, especially in the elderly, renal/hepatic failure, and peri-operatively.[1] It is important to be aware that peri-operative hypoglycemia may occur in patients taking long-acting oral agents who are starved.

10.3.2 Insulin regimens

DM, the most common of endocrine disorders, presents not nearly as many problems as controversies regarding how best to manage peri-operative insulin requirements and what degree of blood glucose control is necessary. Both type 1 and 2 diabetes are both best managed with insulin therapy, and the requirements for both types of diabetes are similar.[13] Regular (short-acting) insulin is recommended in order to respond and adjust to the rapidly changing metabolic environment of anesthesia and surgery. The preferred route is intravenous (i.v.), since patients may experience unpredictable absorption from subcutaneous (s.c.) administration in a cold operating room.

For elective surgery in a well-controlled diabetic, various protocols have been recommended:

1. No glucose or insulin pre- or intra-operatively.
   Note: This may be a reasonable strategy for patients under good control pre-operatively and who are undergoing a short anesthetic. Blood glucose levels should be checked in the recovery room.
2. Glucose intra-operatively (D_5W at 125 ml/h), regular insulin (5–20 units) for BS $>$ 200 mg%.
3. Pre-operative glucose (D_5W at 125 ml/h) with partial NPH dose (1/4–2/3 normal dose) regular insulin (5–20 units) for BS $>$ 200 mg%.
   Note: This plan provides risk of hypoglycemia if peak effect of NPH is not anticipated.
4. Glucose intra-operatively (D_5W at 125 ml/h), regular insulin (5–20 units) for BS $>$ 200–300 mg%.
   Note: This regimen has the potential for larger swings in blood glucose, depending on how frequently glucose levels are monitored and insulin dose.
5. Glucose intra-operatively (D_5W at 125 ml/h), continuous i.v. (1–2 units/h) insulin.

Continuous i.v. infusions of insulin seem to be associated with better peri-operative blood sugar control rather than i.v. boluses.[14] Since insulin adheres to syringes and plastic tubing, initial undertreatment can be mistaken for apparent insulin resistance. Much of this problem can be avoided by using high concentrations of insulin in low volumes from a syringe[1] or running some of the insulin containing fluid through the tubing system in order to saturate the plastic before connecting the administration set to the patient.

The important goals of therapy in these patients should be to prevent hypoglycemia, ketosis, and severe hyperglycemia. Protocols that attempt no control (No. 1) do not prevent ketosis in longer anesthetics, while those attempting "tight" control (BS 80–110 mg%) risk hypoglycemia and mandate close monitoring, especially during a general anesthetic where the patient's hypoglycemic symptoms are masked.[15]

I recommend the following for 2+ h surgery:

1. Schedule as first case of the day.
2. BS/K stat at 6 a.m. for 7:30 a.m. start.
3. No long-acting insulin.
4. D_5W at 125 ml/h during anesthetic.
5. BS/K q 30–60 min.
6. Regular insulin i.v. continuous infusion begin at 1–2 units/h and titrate to BS $>$ 100 mg% and $<$175 mg%.

Recommendations for very tight control (80–110 mg%) in critically ill intensive care unit (ICU) patients are based on the findings of decreased multiple-organ failure and septic shock.[15] Since these are usually not relevant issues in the operating room, and the risks of undetected hypoglycemia are greater under an anesthetic, the goals of glucose control have been tempered somewhat.

10.4 Peri-operative diabetic complications

The most serious diabetic complications are: *DKA*, *HHS*, and *hypoglycemia*. These may be the presenting problems on admission to the hospital or develop in the peri-operative period.

10.4.1 Diabetic ketoacidosis with hyperglycemic hyperosmolar state

Patients with either DKA or HHS may present with acute abdominal pain (secondary to the acidosis or mesenteric ischemia) and be taken to the operating for exploratory laparotomy.[16] Current mortality rates for DKA and HHS are $<$5% and ~15%, respectively, recognizing the older population that pre-dominates in HHS.[17] The association of coma and hypotension are correlated with worse outcomes.

Inadequate amounts of insulin (relative or absolute) stimulate hepatic glucose production resulting in hyperglycemia, osmotic diuresis and dehydration, and eventually, hypovolemic shock. As patients develop progressive hypovolemia, decreased renal perfusion results in decreased glucose clearance, enhancing hyperglycemia. This is the common pathway of both HHS and DKA. In HHS, small amounts of insulin prevent lipolysis. In DKA, absolute insulin deficiency along with increased stress hormones (catecholamines, cortisol and growth hormone) is associated with lipolysis, release of free fatty acids (FFA), and hepatic production of ketone bodies (β-hydroxybutyric acid and aceto-acetic acid) with systemic acidosis. This is the additional metabolic pathway of DKA that distinguishes it from HHS[16] (Figure 10.1).

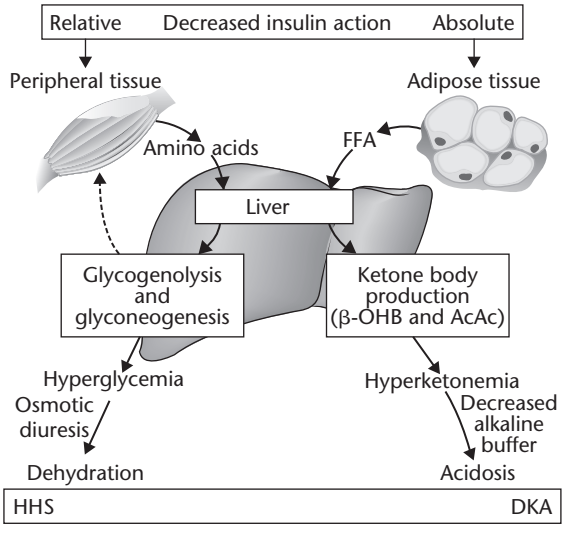

Figure 10.1 Schematic of the pathogenesis of DKA and the HHS. Relative or absolute insulin deficiency stimulates hepatic glucose production, which results in hyperglycemia, osmotic diuresis, and dehydration. In severe insulin deficiency, the liver will augment ketone body production, culminating in hyperketonemia and, eventually, acidosis. β-OHB = β-hydroxybutyric acid; AcAc = aceto-acetic acid [Used with permission from Chiasson JL *et al.* (2003)[16]]

The distinction between DKA and HHS can usually be made based on laboratory data (Table 10.3).

Serum osmolality (mOsm/kgH_2O) is normally markedly elevated in HHS and can be estimated (osmolarity – mOsm/LH_2O) by: $2 \times Na + glucose/18$. A serum osmolality of >320 mOsm/kg defines HHS, a process that typically develops over a number of days, and is associated with very high blood glucose levels. Patients with DKA may also exhibit a hyperosmolar state, but not the extremes observed in HHS. Serum and urine ketones, typically significantly elevated in DKA, may also be slightly elevated in HHS, depending on the length of starvation.

Infection is the most common (20–25%) precipitating factor for DKA or HHS. Other inciting events include, inadequate insulin (especially DKA), cerebrovascular accident, myocardial infarction (especially silent), mesenteric ischemia, pancreatitis, drugs (thiazide diuretics, steroids, calcium channel blockers, phenytoin, propranolol, dobutamine, terbutaline), and anesthesia/surgery.[17] No identifiable cause can be found in some patients.[16] While it is generally appreciated that DKA (few days) develops faster than HHS (days–week), it is possible for DKA to literally develop overnight, given the right circumstances.[18]

While it has been traditionally believed that only type 1 diabetics develop DKA, clinical observations have documented of DKA in the type 2 patients as well, and it has been observed in morbidly obese patients.[19,20]

Table 10.3 Diagnostic criteria for DKA and HHS[17]

	DKA			HHS
	Mild	Moderate	Severe	
Plasma glucose (mg/dl)	>250	>250	>250	>600
Arterial pH	7.25–7.30	7.00–7.24	<7.00	>7.30
Serum bicarbonate (mEq/l)	15–18	10 to <15	<10	>15
Urine ketones*	Positive	Positive	Positive	Small
Serum ketones*	Positive	Positive	Positive	Small
Effective serum osmolality (mOsm/kg)†	Variable	Variable	Variable	>320
Anion gap‡	>10	>12	>12	Variable
Alteration in sensoria or mental obtundation	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

*Nitroprusside reaction method.
†Calculation: 2[measured Na (mEq/l)] + glucose (mg/dl)/18.
‡Calculation: $(Na^+) - (Cl^- + HCO_3^-)$ (mEq/l) [Used with permission from Association AD (2003)[17]].

One study of 141 patients with DKA demonstrated that 55 (39%) had type 2 DM, and over half (51%) of these had body mass index (BMI) > 30.[21]

Metabolic derangements

Acidosis

In both HHS and DKA, acidosis may exist because of hypovolemia with or without septic shock and renal failure. In DKA, acidosis also results from accumulation of β-hydroxybutyric acid and aceto-acetic acid which are strong acids that completely dissociate at physiologic pH. Free hydrogen ion binds bicarbonate and ketone bodies circulate as anions creating the anion "gap". Anion gap can be estimated by: $Na^+ - (Cl^- + HCO_3^-) = 12 \pm 2$. There is a disproportionate increase in β-hydroxybutyric acid, and measurement of ketone bodies (for example nitroprusside test) that do not include this compound may greatly underestimate the role of ketosis in the acidosis observed.[16] In addition, since β-hydroxybutyric acid is the predominant ketone body, and is converted to aceto-acetic acid during recovery, the patient's condition may mistakenly thought to be worsening when, in fact, the ketosis is clearing.[17]

Fluid/electrolyte

Most of the fluid and electrolyte disorders are the result of the osmotic diuresis. Fluid losses average 5–7 l in DKA and 7–12 l in HHS. Sodium (Na) losses may be significant but *pseudohyponatremia* may also exist. Measured serum Na levels must be corrected in the presence of hyperglycemia in order to adjust for the large osmotic shift of fluid from the intracellular space causing Na dilution (1.6 mmol/l Na increase for every 5.6 mmol/l glucose > 5.6 mmol/l).[16] Na concentrations must also be corrected in the presence of hyperlipidemia (1.0 mEq/l Na increase for every 700 mg% triglyceride) (Figure 10.2).

Potassium losses are typically enormous but may be masked by initial measurements that may be normal or even elevated because of acidosis, volume contraction, hypoinsulinemia, and intracellular proteolysis. Phosphate, calcium, and magnesium losses also need to be replaced.[16] Potassium replacement in patients who remain in oliguric renal failure after resuscitation must be accomplished with great care to avoid hyperkalemia.

Therapy

Treatment of DKA and HHS requires aggressive correction of hypovolemia and careful correction of electrolyte abnormalities. Recent recommendations have suggested an algorithm approach, but individualized care is essential[17] (Figures 10.3 and 10.4).

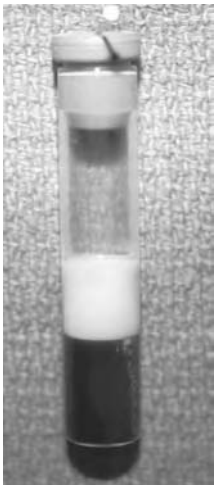

Figure 10.2 Patient blood sample with extreme hyperlipidemia: 28 years old diabetic patient with acute pancreatitis with measured serum Na = 112 mEg/l and triglycerides (TG) = 22,000 mg%. *Na correction*: 1.0 mEq/l for every 700 mg% TG. *To correct Na value*: 22,000/700 = 31. *Corrected Na*: 112 + 31 = 143 mEq/l.

Fluid resuscitation

Aggressive volume expansion is life-saving in patients who are severely hypovolemic or in shock. Hemodynamic monitoring (arterial/central venous catheterization) is important in critically ill patient to avoid complications of fluid overload, especially if the patient is elderly and has cardiac disease. Formula-driven recommendations for fluid therapy must be adapted to individual needs of each patient and can also be guided by physiologic endpoints (blood pressure, urine output, central venous pressure (CVP), cardiac output, central venous saturation). Normal saline is an appropriate initial fluid choice in patients in shock. Since patients in shock may require rapid fluid resuscitation, normal saline will help restore circulation while not dropping serum osmolality too quickly. Patients not in shock can be resuscitated with 0.45% saline or normal saline depending on whether the corrected (for artifactual low values in the presence of high blood sugar or lipids) serum Na is high or low, respectively.[17] This choice will also be affected by how fast serum osmolality is declining. The recommended correction pace is <3 mOsm/kgH_2O/h,[17] which is hoped to avoid cerebral edema – a complication of DKA treatment (rarely seen in HHS), observed in ~1% of children with DKA.[17]

Insulin administration

While there has been little disagreement over how insulin should be administered (i.v. preferred over intramuscular (i.m.) or s.c. routes), there has also been

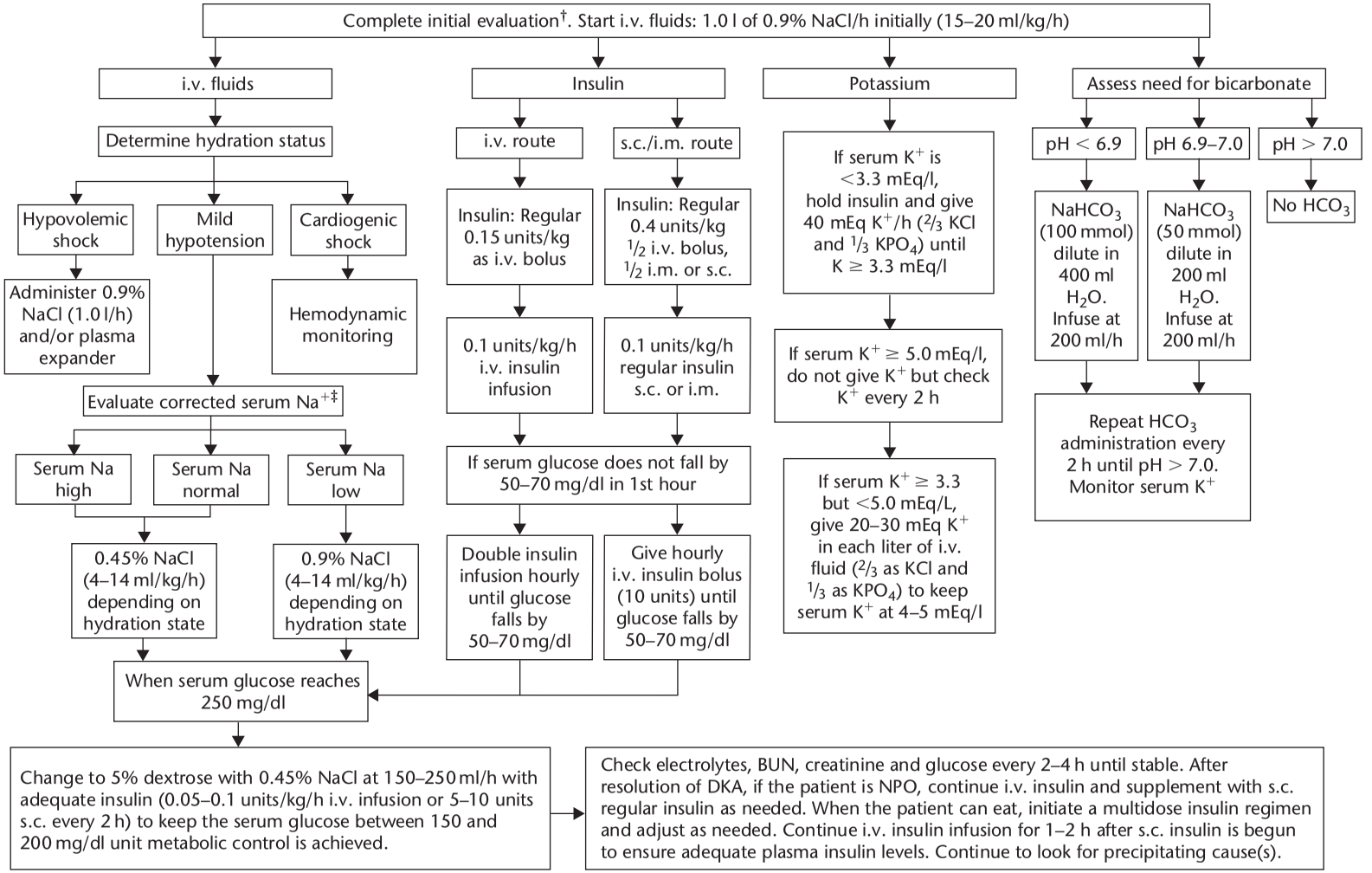

Figure 10.3 Protocol for the management of adult patients with DKA. *DKA diagnostic criteria: blood glucose 250 mg/dl, arterial pH 7.3, bicarbonate 15 mEq/l, and moderate ketonuria or ketonemia. †After history and physical examination, obtain arterial blood gases, complete blood count with differential, urinalysis, blood glucose, blood urea nitrogen (BUN), electrolytes, chemistry profile, and creatinine levels stat as well as an electrocardiogram. Obtain chest X-ray and cultures as needed. ‡Serum Na should be corrected for hyperglycemia (for each 100 mg/dl glucose 100 mg/dl, add 1.6 mEq to Na value for corrected serum Na value). [Used with permission from Association AD (2003)[17]].

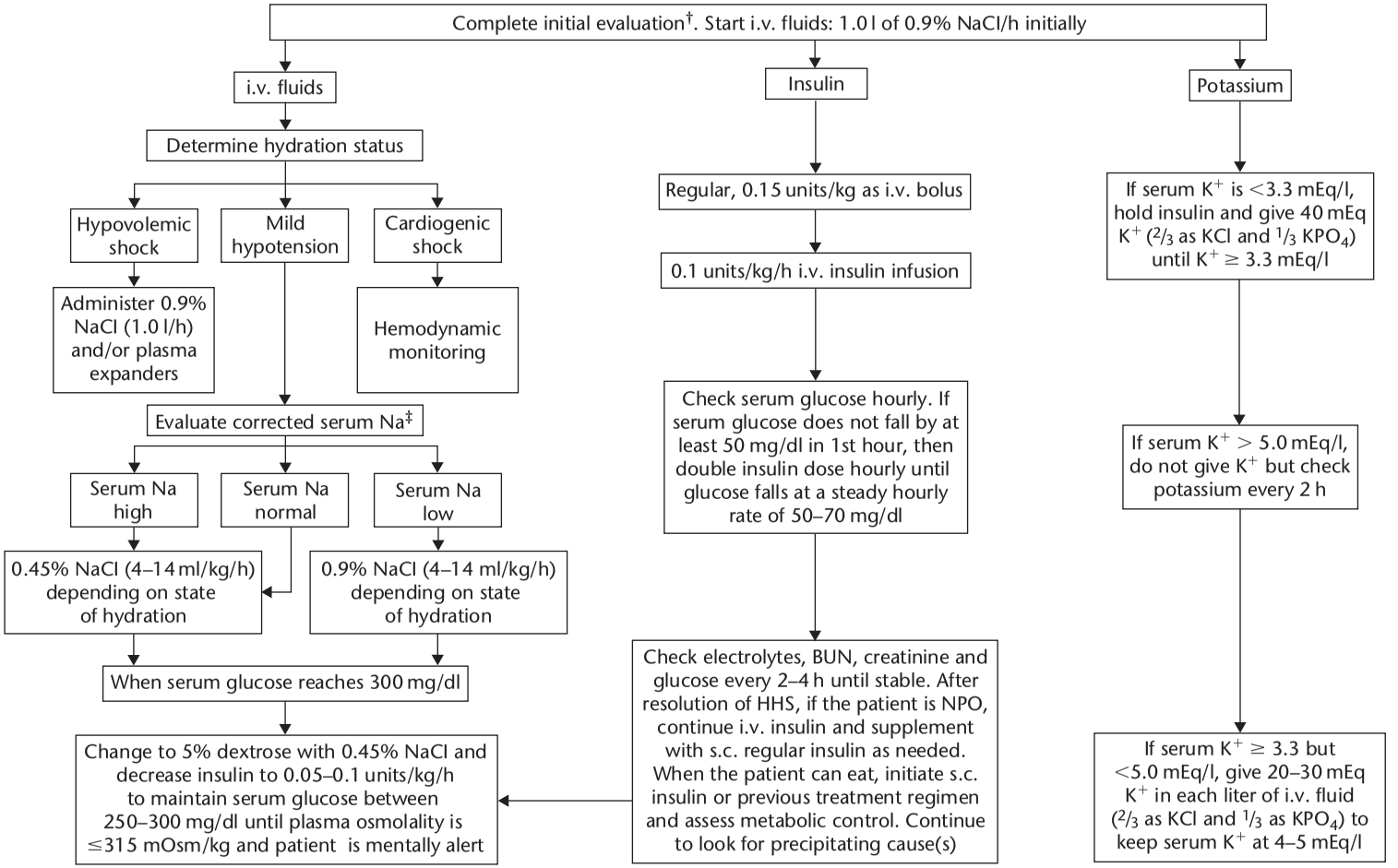

Figure 10.4 Protocol for the management of adult patients with HHS. *Diagnostic criteria: blood glucose 600 mg%, arterial pH 7.3, bicarbonate 15 mEq/l, mild ketonuria or ketonemia, and effective serum osmolality 320 mOsm/kg H_2O. This protocol is for patients admitted with mental status change or severe dehydration who require admission to an ICU. For less severe cases, see text for management guidelines. Effective serum osmolality calculation: 2 [measured Na (mEq/l)] + glucose (mg/dl)/18. †After history and physical examination, obtain arterial blood gases, complete blood count with differential, urinalysis, plasma glucose, blood urea nitrogen (BUN), electrolytes, chemistry profile, and creatinine levels STAT as well as an electrocardiogram. Obtain chest X-ray and cultures as needed. ‡Serum Na should be corrected for hyperglycemia (for each 100 mg% glucose >100 mg%, add 1.6 mEq to Na value for corrected serum value). [Used with permission from Association AD (2003)[17]].

a growing consensus that continuous i.v. insulin infusion (0.1 units/kg/h) is preferable over intermittent i.v. boluses.[22] Insulin should not be started until the potassium level is $\geq$3.3 mEq/l. Low-dose insulin infusions (0.1 units/kg/h) will allow a more gradual, controlled fall in blood glucose levels, as well as osmolality, and less likely to cause dangerous intracellular potassium shifts[16] and hypoglycemia.[22]

The first goal of insulin therapy is to have glucose levels fall 50–70 mg%/h. Patients who present with shock and require immediate large volume fluid resuscitation will experience significant falls in glucose levels without any insulin administration. When levels fall to 215–250 mg%, it is important to add 5% dextrose in administered fluid at 125 ml/h and to continue the insulin infusion at a 50% reduced rate. The second goal of insulin therapy in DKA is to continue it until the ketoacidosis resolves or in HHS, until the mental status changes and hyperosmolality resolves.[16]

When the second goal of continuous insulin therapy has been achieved, as well as normalization of other biochemical variables (glucose $<$ 200 mg%, bicarbonate $\geq$ 18 mEq/l, anion gap $<$ 12 mEq/l), patients who are taking oral fluids can be safely put on an intermittent dose insulin regimen.[23]

Potassium replacement

As soon as it is established that the patient is not in renal failure, it is essential to replace potassium deficits. Even when patients present with hyperkalemia, levels can fall rapidly. The unusual patient who presents with hypokalemia is particularly at risk for life-threatening arrhythmias.[24] Intra-vascular volume expansion, correction of acidosis, and administration of insulin all contribute to rapid changes in K^+ levels.

Administration of potassium should begin early, when the level falls to $<$5 mEq/l. Aggressive K^+ replacement is best done via a central line with infusion rates of 30 mEq/h, assuming patient is not anuric. One bag of on-going i.v. fluids should contain 20–40 mEq/l of potassium (2/3 KCl, 1/3 KPO_4) to maintain desired levels. It is quite acceptable to withhold insulin therapy while correcting potassium deficits that may cause life-threatening arrhythmias or respiratory muscle weakness. Levels should be checked every 1–2 h in the first 6 h of treatment because of the dramatic changes that can occur during initial care of these patients.

Phosphate replacement

Phosphate depletion may be severe, especially in DKA ($\sim$1 mmol/kg), but controversy exists over aggressive replacement which may result in serious hypocalcemia. On the other hand, severe hypophosphatemia ($<$1.0 mg/dl) may be associated with cardiac/skeletal muscle weakness, respiratory failure, anemia, and rhabdomyolisis.[17] Phosphate depletion can be replaced by administering KPO_4 with some of the potassium replacement.

Acidosis

Fluid resuscitation with restoration of circulation and the administration of insulin are the most important steps to resolving the acidosis observed in DKA and HHS. The use of bicarbonate therapy is discouraged unless acidosis is extreme (pH $\leq$ 7.0) and not responding to initial treatment.[17] It should be noted that patients in diabetic crises usually present with dramatic hyperventilation in an attempt to partially compensate for their metabolic acidosis. The pH of arterial blood should be corrected for the patient's hyperventilation since this elevated work of breathing may not be sustained.

Acute correction: $PCO_2\ \Delta 10 \approx$ pH Δ 0.08
Example:
measured blood gases $\rightarrow$ pH 7.10, PCO_2 25
$PCO_2\ \Delta = 40 - 25 = 15$
pH $\Delta = 0.08 \times 15/10 = 0.12$
corrected pH $\rightarrow$ pH 7.10 – 0.12 = 6.98

This patient's pH should be treated with bicarbonate (or some other buffer). Left untreated, life-threatening pH declines may occur if the patient suddenly develops respiratory insufficiency from muscle fatigue, or hypoventilates secondary to central depression from worsening coma.

Complications of DKA and HHS include cerebral edema (more common in children), adult respiratory distress syndrome (rarely in DKA), deep venous thrombosis, hyperchloremic acidosis, and hypoglycemia.[16]

10.4.2 Hypoglycemia

Peri-operative hypoglycemia is a potentially serious event that may even occur in non-diabetic patients and result in permanent neurologic disability.[25] In one recently reported study recommending tight glucose control, treated patients experienced over six times the incidence of severe hypoglycemia (glucose $\leq$ 40 mg%).[15] In the operating room, patients under general anesthesia are at a particular risk because of anesthetic-induced depression of metabolic rate and the inability to elicit symptoms from the patient. In patients with DKA, the risk of hypoglycemia has been associated with fever ($\uparrow$metabolic demand), NPO (starvation), and liver disease ($\downarrow$glycogen stores).[26]

During general anesthesia in diabetic patients, strategies to prevent hypoglycemia include administering glucose containing solution (for example D_5LR at 125 ml/h), low dose continuous insulin infusions,[22] and frequent blood glucose monitoring.[27]

Morbid obesity is often confounded by DM and its associated complications. Attention to pre-operative evaluation and aggressive management of blood glucose levels is necessary in order to avoid diabetic complications. Patients who require an anesthetic in addition to emergent management of DKA or HHS will respond to a carefully thought-out approach.

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CO-EXISTING CARDIAC DISEASE 11

S. Akhtar, V. Kurup & L. Helgeson

11.1 Introduction

Over 150 years ago William Wadd stated "corpulency is not only a disease itself but the harbinger of others".[1] Obesity has been shown to induce multiple risk factors and cluster risk factors which can lead to a variety of co-morbidities including cardiovascular diseases. Obesity is a global problem with the prevalence of obesity continuing to increase. In the US, the age adjusted prevalence of *overweight* individuals with body mass index (BMI $\geqslant$ 25), increased from 55.9% (1988–1994) to 64.5% (1999–2000). Similarly, the prevalence of *obesity* (BMI $\geqslant$ 30), increased from 22.9% to 30.5%, while *extreme obesity* (BMI $\geqslant$ 40) nearly doubled from 2.9% to 4.7%.[2] Cardiovascular diseases are common in obese individuals and manifest as ischemic heart disease (IHD), hypertension, and cardiac failure. The incidence of cardiovascular disease is reported in 37% of the adults with BMI $> 30\,kg/m^2$, 21% with a BMI of 25–30 kg/m^2 and only 10% in those with BMI $< 25\,kg/m^2$. Costs related to cardiovascular disease related to overweight and obesity in the US was estimated to be $31.0 billion in 1996.[3]

The relationship between the increase in blood pressure (BP) and the risk of cardiovascular disease is continuous, consistent, and independent of other risk factors. The chances of myocardial infarction (MI), heart failure, stroke, and kidney disease are all greater with increasing BP.[4] Epidemiological data consistently support a link between obesity and hypertension.[5] Obesity (BMI $\geqslant 30\,kg/m^2$) has been observed to be an independent risk factor for the development of hypertension. BMI has been shown to be significantly associated with increased systolic and diastolic BP, independent of other variables, such as age, alcohol intake, smoking habit, and sodium and potassium excretion. The Framingham Heart Study suggests, that 65% of the risk for hypertension in women and 78% in men can be related to obesity.[6] Populations most severely affected include the poor, the uneducated and certain racial and ethnic groups. Obesity is also well recognized as a risk factor for IHD. Many obese individuals also suffer from "metabolic syndrome" which has a strong association with developing diabetes and cardiovascular disease as well as increased mortality from cardiovascular disorders. Mortality rate was reported to be 3.9 times greater in

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overweight group than the normal weight group who were participating in Framingham Study.[7]

About 40 million inpatient procedures were performed in year 2000.[8] Approximately 25 million of these were performed on individuals who were older than 45 years and are likely to have higher incidence of coronary artery disease (CAD) and obesity.[8] Extrapolating the prevalence of obesity, it is appropriate to assume about approximately 10–12 million individuals who underwent inpatient procedures with anesthetics were obese and likely to suffer from hypertension, IHD and/or cardiac dysfunction. The impact of cardiovascular disease on peri-operative outcomes is well recognized.[9] Morbidly obese individuals presenting for anesthesia should be adequately evaluated for cardiovascular conditions pre-operatively and their intra- and post-operative management must be tailored accordingly.

11.2 Pathophysiology of cardiac disease

Hypertension, IHD, congestive heart failure (CHF) and cardiac arrhythmias are more prevalent in obese patients than in non-obese individuals (see Chapters 5 and 6). It is the complex interaction of hypertension, IHD, and pulmonary hypertension that contributes to the development of global cardiac dysfunction and exacerbates CHF (Figure 11.1).

There is a continuous relationship between BMI and systolic and diastolic BP[10,11] (Figure 11.2).

Though not all obese patients are hypertensive, weight gain increases the probability of becoming hypertensive. Approximately 30% of cases of hypertension may be attributable to obesity. In men under 45 years of age, the incidence may be as high as 60%.[3,12]

BP is normally regulated by a series of feedback loops (baroreceptors) and by the secretion of vasoactive hormones (renin, angiotensin, aldosterone, catecholamines). A derangement in any of these feedback loops can lead to hypertension. In a majority of patients, the cause of hypertension is not known and they are classified as having primary/essential or idiopathic hypertension. In only a small minority of patients with an elevated BP can a specific cause be identified and they are classified as having secondary hypertension (Table 11.1).

The relationship between obesity and hypertension is multifactorial and probably represents a complex interaction of racial, gender, demographic, genetic, neurohumoral, and other factors. Many factors act together to promote vasoconstriction and sodium retention in obesity (Figure 11.3).

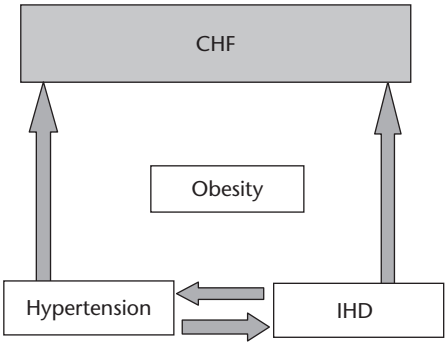

Figure 11.1 Conceptual relationship of obesity with hypertension, IHD and CHF. Hypertension and IHD contribute to heart failure.

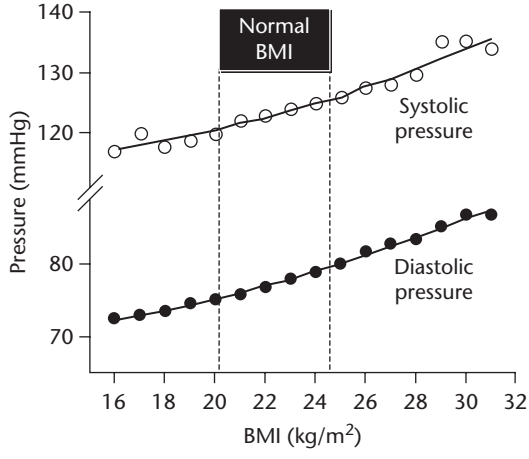

Figure 11.2 Relationship between BP and BMI (reproduced with permission).[13]

Leptin, a hormone which is constitutively secreted by white adipose cells acts on the hypothalamus to increase sympathetic activity. Free fatty acids and insulin interact individually and synergistically with leptin to stimulate sympathetic activity and vasoconstriction.[13] Furthermore, obesity-induced insulin resistance and endothelial dysfunction may act as amplifiers of the vasoconstrictor response. Obstructive sleep apnea, which is also more prevalent in obese patients, leads to periods of apnea and hypoxia, triggering chemoreceptor response which causes sympathetic activation.[13–15]

There are many factors that contribute to abnormal sodium handling and volume overload. Obese patients have elevated glomerular filtration rate and

Table 11.1 Pathophysiological classification of hypertension

Type	Etiology
Essential/primary	Idiopathic (>90%)
Renal	Renovascular stenosis Polycystic renal disease Glomerulonephritis Chronic pyelonephritis
Endocrine	Primary aldosteronism Cushing's syndrome Pheochromocytoma Thyrotoxicosis Myxedema Acromegaly
Neurogenic	Increased intracranial pressure (acute) Spinal cord transaction (acute)
Miscellaneous	Coarctation of aorta Aortic regurgitation Hypercalcemia Fever Drugs: • Estrogen (oral contraceptives) • Steroids (exogenous) • Monoamine oxidase inhibitors • Tri-cyclic anti-depressants • Selective serotonin reuptake inhibitors • Cocaine • Selected herbal supplements

renal blood flow, yet show delayed urinary sodium excretion in response to the saline load.[13] Increased renal sympathetic nerve activity directly promotes tubular reabsorption of sodium at the proximal and distal tubules.[16] The renin–angiotensin–aldosterone system is activated which contributes to sodium retention and increase in extracellular volume, despite elevated BP.[17] Atrial natriuretic peptide levels are low both at basal levels and also in response to salt loading in obese patients.[18] Furthermore, hyperinsulinemia directly promotes tubular absorption of sodium.[19] With prolonged obesity, there may be a gradual loss of nephron function that worsens with time and exacerbates hypertension.[20] Thus hypertension contributes to pressure overload to the heart, while the expansion of extracellular and blood volume contributes to volume overload.

Obesity is a recognized risk factor for IHD.[21,22] The risk is proportional to the duration of obesity and distribution of fat. A constant overweight individual is less likely to be at risk than individuals who continue to gain weight, and individuals with central distribution of fat are more at risk than individuals with peripheral distribution.[14] Furthermore, other risk factors like hypertension, diabetes and hypercholesterolemia, increased levels of low-density lipoprotein (LDL), which are common in obese patients further increase the risk of IHD. Though, one would expect many of these patients to have CAD, >40% of obese patients with angina did not have significant CAD.[14,23] A recent autopsy analysis of 166 morbidly obese patients (BMI > 35) did not show stenosis in any of the main arteries; 42% of left arterial descending artery (LAD) to 62% of left main were not significantly stenosed, while of 48% of LAD to 61% of left main in women were not stenosed; 38% of men and 44% of women had either lesion-free arteries or only the fatty streaks.[24] Occlusive thrombus was noted in only four men and one woman. Cardiomyopathy (hypertrophic non-obstructive or dilated) was the commonest cause of cardiac-related deaths in the study. Many obese patients may present with angina in the absence of significant CAD.[25] Angina is attributable to oxygen supply/demand imbalance due to cardiac hypertrophy.

The morbidly obese patients are at risk for obesity-induced cardiac dysfunction and heart failure. The increase in risk of heart failure is 5% for men and 7% for women for each increase of BMI by 1.[26] Fat infiltration of the heart is uncommon, is limited mostly to the right side of the heart and can contribute to conduction abnormalities and arrhythmias.[27] Increase in epicardial fat is common. There is a linear relationship between body weight and cardiac weight gain. Cardiac weight gain is slower after 105 kg body weight. The cardiac weight gain is attributed to concentric and eccentric hypertrophy, secondary to pressure overload which is due to arterial hypertension and possibly increased blood viscosity. In obese patients, circulating blood volume, plasma volume, and cardiac output increase proportionately with rising weight. At rest, blood flow to fat is 2–3 ml/100 gm tissue. For a patient with a fat mass of 50 kg, blood flow to this fat mass accounts for an extra cardiac output of 1.5–2.0 l/ min which results ventricle enlargement and increase in stroke volume. The hypertrophy that ensues, subsequently contributes to reduced, cardiac compliance and left ventricular (LV) diastolic function,[28] which leads to increased LV end-diastolic pressure and possible pulmonary edema. In long-standing obesity the systolic function is reduced as hypertrophy is unable to keep pace with increasing demand. Decrease in midwall fiber shortening and a decrease in ejection fraction become evident (obesity cardiomyopathy).

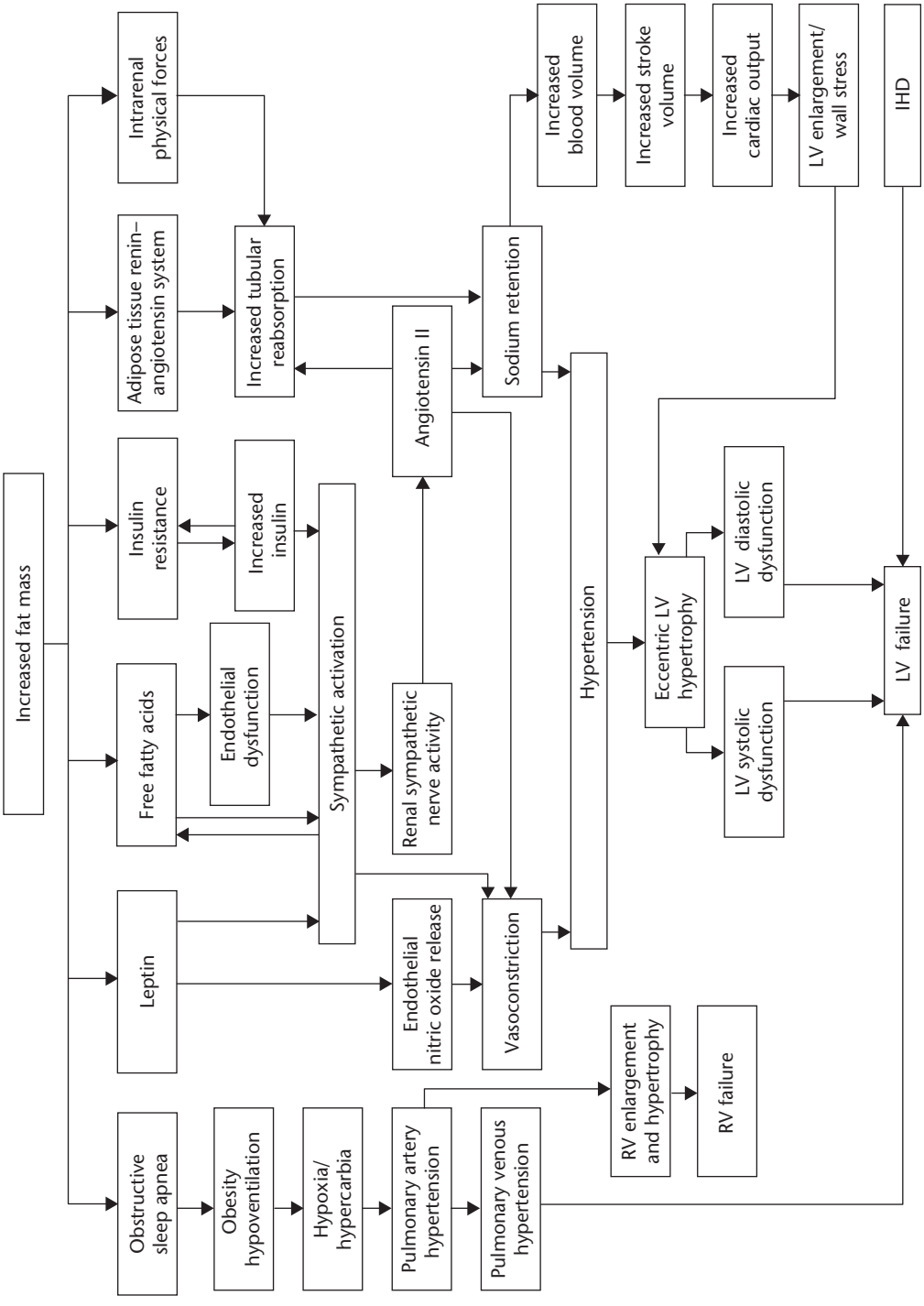

Figure 11.3 Obesity-induced cardiomyopathy and its association with CHF, systemic hypertension, and IHD.

Superimposed hypertension and IHD can compound the problem further (Figure 11.1). Obstructive sleep apnea causes pulmonary hypertension, which leads to progressive right ventricular hypertrophy. Morbidly obese individuals increase cardiac output by increasing heart rate without increasing stroke volume, which can lead to significant increase in filling pressures. Changing from sitting position to supine position can significantly increase cardiac output, pulmonary capillary wedge pressure, and mean pulmonary artery and precipitate acute heart failure.[29] In view of these changes, it is advisable to have a low threshold for performing detailed cardiac investigations in obese patients with demonstrable cardiac disease who are scheduled for non-cardiac surgery.

11.3 Hypertension

11.3.1 Pre-operative assessment and management

A thorough pre-operative evaluation of the obese patient is of paramount importance.

Functional status of various organ systems should be elicited. Particular importance should be given to evaluation of the cardiac system, especially in light of prevalence of associated diseases like hypertension, diabetes, and sleep apnea. Patients should be evaluated and optimized before surgery. The treatment of hypertension in obese patient is guided by the same principles as the treatment in the non-obese patients. Elective surgeries should be deferred until control of the BP has been achieved to reasonable levels. Urgent and emergent surgeries should be evaluated on individual case basis and aggressive control of BP in the peri-operative period is vital.

There is no specific blood pressure which defines increased risk, but increased blood pressure parameters are useful.

Hypertension was traditionally defined as a systolic pressure >140 mmHg or diastolic pressure >90 mmHg. Joint National Committee has added a new category designated as prehypertension[4] (Table 11.2). Patients with BP in the range of 130/80–139/89 who are included in this category are at increased risk for progression to hypertension, and it is recommended that this group be actively monitored and lifestyle modifications advocated. In the past few years the terms "white-coat hypertension" (WCH) and "white-coat effect" (WCE) have been used frequently. WCH refers to a subset of patients who are hypertensive according to their clinic BP but normotensive at other

Table 11.2 Classification and management of BP in adults

BP classification	SBP[a] (mmHg)	DBP[a] (mmHg)	Lifestyle modification	Initial drug therapy	
				Without compelling indication	With compelling indications[c]
Normal	<120	<80	Encourage	No anti-hypertensive drug indicated	Drugs for compelling indications[c]
Prehypertension	120–139	80–89	Yes		
Hypertension					
Stage 1	140–159	90–99	Yes	Thiazide-type diuretics for most. May consider ACE inhibitors, ARB or BB or CCB or combination	Drugs for the compelling indications. Other anti-hypertensive drugs (diuretics, ACE inhibitors, ARB, BB, CCB) as needed
Stage 2	>160	>100	Yes	Two drug combination for most[b] (usually thiazide-type diuretic and ACE inhibitors or BB or CCB	

Reproduced with permission from Montani JP (2002).[13]

DBP, diastolic BP; SBP, systolic BP; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BB, beta-blocker; CCB, calcium channel blocker.

[a] Treatment determined by highest BP category.
[b] Initial combined therapy should be used cautiously in those at risk for aorthostatic hypotension.
[c] Treat patients with chronic kidney disease or diabetes to BP goal of <130/80 mmHg.

times.[30] The WCE is conceived as the increase of BP that occurs at the time of a clinic visit and dissipates soon thereafter. Thus, WCH is a measure of BP level, whereas WCE is a measure of BP change. The significance of this effect has been a subject of debate. So far, the magnitude of the WCE (measured as the clinic–daytime difference) has not been found to correlate with target-organ damage as measured by echocardiography, microalbuminuria or cardiovascular events. An exception to this was reported by Palatini *et al*. who found that the WCE was an independent predictor of LV mass.[15,31]

Practical issues with measurement of BP are the site of measurement of the pressure. Obese individuals tend to have a conical shape of the upper arm (gynoid obesity) and accurate measurement of BP is difficult with conventional cuffs. As an alternative, the cuff can be placed around the forearm for more predictable cuff pressures. The values may also be used to follow the trend if they differ significantly from upper arm measurements. Measurement of BP in the standing position is indicated peri-operatively, especially in those at risk for postural hypotension due to either a disease process or due to the anti-hypertensive medication that they are on. An appropriate-sized cuff (cuff bladder encircling at least 80% of the arm) should be used to ensure accuracy. Increasing arm circumference is associated with miscalculation of BP using standard length cuffs[32] (Table 11.3).

Table 11.3 Miscalculation of BP using standard length cuffs with varying arm circumference

Bladder width (cm)			12.0		15.0	18.0
Ideal arm circumference (cm)			30.0		37.5	45.0
Arm circumference range (cm)			26–33		33–41	>41
Arm circumference (cm)	SBP	DBP	SBP	DBP	SBP	DBP
26	+5	+3	+7	+5	+9	+5
28	+3	+2	+5	+4	+8	+5
30	0	0	+4	+3	+7	+4
32	−2	−1	+3	+2	+6	+4
34	−4	−3	+2	+1	+5	+3
36	−6	−4	0	+1	+5	+3
40	−8	−6	−1	0	+4	+2
38	−10	−7	−2	−1	+3	+1
42	−12	−9	−4	−2	+2	+1
46	−14	−10	−5	−3	1	0
48	−16	−11	−6	−3	0	0
50	−18	−13	−7	−4	−1	−1
40	−21	−14	−9	−5	−1	−1

Reproduced with permission from Graves JW (2003).[180]

An electrocardiogram (EKG) should be obtained to evaluate the heart for LV or RV strain pattern. In patients with associated diabetes, signs of silent MI may be uncovered. An echocardiogram is not routinely obtained, but may be indicated in a specific subset of patients who have evidence of heart failure or LV dysfunction. Specific tests to rule out renovascular hypertension, primary aldosteronism, or pheochromocytoma may be indicated in the following groups of patients:[33]

1. patients <15 years of age with hypertension;
2. patients >65 years of age with recent onset of severe hypertension;
3. individuals with persistent hypertension after triple-drug therapy that includes a diuretic;
4. patients with hypertension and symptoms of headache or unusual patterns of sweating and palpitations.

The ultimate goal of anti-hypertensive therapy is the reduction of cardiovascular and renal morbidity and mortality. In clinical trials, anti-hypertensive therapy has been associated with 35–40% reductions in the incidence of stroke; 20–25% reduction in the incidence of MI and >50% reduction in heart failure.[10,34] It is estimated that in patients with stage 1 hypertension (systolic BP 140–159 mmHg and/or diastolic BP 90–99 mmHg) and additional cardiovascular risk factors, achieving a sustained 12 mmHg reduction in systolic BP over 10 years will prevent one death for every 11 patients treated.[4]

The treatment of hypertension is by a multi-modal approach. Lifestyle modification is especially important in hypertension associated with obesity. Physical activity and dietary modifications have been shown to promote BP control and in obesity-associated hypertension, weight reduction has been demonstrated to decrease BP, enhance drug efficacy and decrease cardiovascular risk.[4] The pharmacological treatment of hypertension involves several classes of drugs, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), beta-blockers, calcium channel blockers, and thiazide-type diuretics. They have all been shown to be effective and reduce the complications of hypertension.

Thiazide-type diuretics have been the basis of anti-hypertensive therapy in most outcome trials.[35] In these trials, including the recently published Anti-hypertensive and Lipid Lowering treatment to prevent Heart Attack Trial (ALLHAT), diuretics have been virtually unsurpassed in preventing the cardiovascular complications of hypertension.[36] The exception is the Second Australian National Blood Pressure

Trial which reported slightly better outcomes in white men with a regimen that began with an ACE inhibitors compared to one starting with a diuretic.[4] Diuretics enhance the anti-hypertensive efficacy of multi-drug regimens and are also quite cost effective. It is usually recommended to start therapy for hypertension with thiazide diuretics, either alone or in combination with one of the other classes of drugs. Most patients will require two or more anti-hypertensive medications to achieve BP control.

Thiazide diuretics are one of the oldest, most widely prescribed and low cost diuretics in the current armamentarium. The side-effects commonly seen with these drugs are hypokalemia, hyperuricemic, glucose intolerance and hypercholesterolemia. However, it is possible to minimize these side-effects by combining thiazide diuretics with drugs from other classes and at the same time preserve their anti-hypertensive effect. Diuretics may also be effective in treating edema and CHF, and they have been shown to work especially well in black and elderly patients.[37]

Loop diuretics do not appear to be as good as thiazide diuretics in lowering BP. It is important to monitor electrolyte levels in patients on diuretics especially if they are also on digoxin or other medications which may be affected by electrolyte abnormalities.

The beta-blockers are also commonly used as anti-hypertensives. Currently, beta-1 selective blockers are frequently chosen to treat hypertension. There is a growing body of literature supporting the cardioprotective effects of beta-blockers in patients with hypertension, similar to their protective effects in patients after MI.[38] Non-selective beta-blockers should be avoided in patients with asthma, chronic obstructive pulmonary disease, Raynaud's phenomenon, severe peripheral vascular disease, and in diabetic patients prone to hypoglycemia (in whom these drugs may mask the symptoms of hypoglycemia).

ACE inhibitors lower BP by decreasing the conversion of angiotensin I to II. They act synergistically especially in black patients, preventing excessive renin release in the setting of hypovolemia, and also reducing side-effects. Obesity is often seen to be associated with sympathetic overactivity, diabetes, impaired glucose tolerance, and hyperinsulinemia.[39] In this regard, the ability of ACE inhibitors to reduce angiotensin II levels and improve insulin sensitivity may be advantageous.[40]

ARB are newer class of agents that antagonize the renin–angiotensin–aldosterone axis. They selectively block binding of angiotensin II to the type 1 angiotensin II receptor, resulting in decreased BP and decreased aldosterone production. ARB may improve vascular remodeling abnormalities associated with hypertension.[41] ARB are contraindicated in pregnant women because of concern of adverse fetal effects.

Long-acting calcium channel blockers are effective anti-hypertensive agents. In addition to their vasodilatory effects, they are also useful in the settings of angina pectoris and CHF related to diastolic dysfunction. Due to their synergistic effect, they must be used with caution in patients taking beta-blockers.

In any pre-operative evaluation, information regarding the type of anti-hypertensive medication that the patient is taking is important because appropriate laboratory work may be indicated. Patients on diuretics may need their electrolyte levels assessed before surgery and may also be more dehydrated than other patients. There is concern about potential hemodynamic instability and hypotension in patients receiving ACE inhibitors in the peri-operative period. Prolonged hypotension has been observed in patients undergoing general anesthesia for minor surgery who continue to receive ACE inhibitors up to the morning of surgery.[42] The hypotension observed has been responsive to crystalloid fluid infusion and/or administration of a sympathomimetic agents, such as ephedrine or phenylephrine.[43] Patients are usually advised to continue taking their anti-hypertensive medications according to schedule until the morning of surgery. Exceptions to this rule are ACE inhibitors, ARB due to concerns discussed above and in patients who are at high risk for dehydration, possibly diuretics.

11.3.2 Intra-operative management

The choice of anesthetic is guided by the same principles as for the non-obese, with attention paid to the presence of co-morbid conditions, the type and duration of surgery. Greater than 90% of body metabolism is thought to occur in lean tissue, thus the dosing of drugs should be based on ideal body weight rather than actual body weight. The effect of body weight on pharmacokinetics suggest that lean body mass is a better guide for drug dosing than total body mass.[34] Large doses of highly lipid soluble agents are avoided due to the propensity of these medications to accumulate in the fat depots and exert their effect for prolonged time in the post-operative period.

Measurement of BP by non-invasive cuff placed on the forearm is seen to be an alternative method in patients with conical-shaped upper arms. It is obvious that trying to place a cylindrical BP cuff on a conical-shaped upper arm is problematic. Additionally, BP readings would be inaccurate due to the amount of fatty tissue

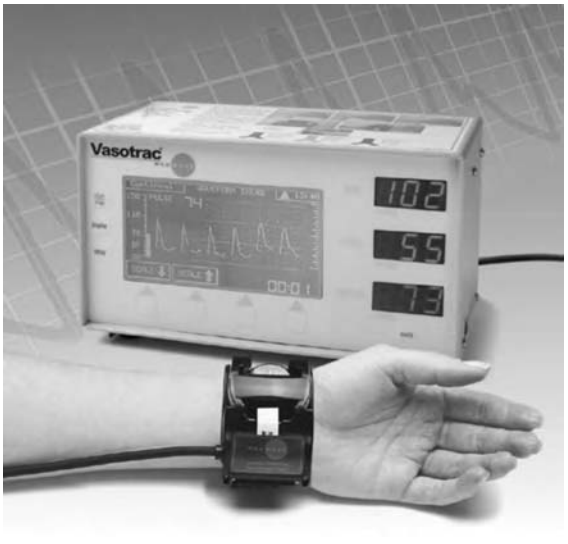

Figure 11.4 "Vasotrac" (Medwave, Arden Hills, MN) that provide BP measurements every 12–15 beats have also seen to be useful in obese patients. *Courtesy:* Medwave Corp. Danvers, MA, USA.

between the brachial artery and oscillometric bladder of the BP cuff. Additional artifact comes from the need to use a larger cuff to encompass the upper arm. The cuff width likewise increases to create a disparity in arm length to cuff width ratio. Newer, non-invasive BP monitors,[44] like the "T-line" (Tensys, San Diego, CA) and the "Vasotrac" (Medwave, Arden Hills, MN) that provide near continuous BP measurements every 12–15 beats have also seen to be useful in obese patients (Figure 11.4).

Most obese patients do not have significant fat distribution at the wrist area and these monitors can be placed with predictable readings. Some patients could thus be spared an invasive procedure with its (radial arterial line) associated difficulties. In patients in whom the above monitors cannot be used arterial line may be the only practical option to monitor BP. The decision to adopt invasive monitoring should also be guided by the co-morbid conditions and the type of surgery to be performed. The time involved and potential difficulty in placing these lines due to obscured landmarks should be taken into consideration. If deemed necessary the invasive monitors may have to be placed the night before surgery.

The goals for BP control should be the same as in the non-obese population and maintained within 20% of baseline pressures. Intra-operative hypertension should be evaluated and treated after addressing other variables, such as light anesthesia, kinking of the

Table 11.4 Causes of hypertension in PACU

1	Technical problems (small cuff, inappropriate transducer level)
2	Hypoxia
3	Hypercarbia
4	Pain
5	Metabolism of pre-operative anti-hypertensive medication
6	Residual effect of vasopressors used intra-operatively
7	Drug interactions (for example, monoamine oxidase inhibitors and meperidine)
8	Hypothermia
9	Raised intracranial pressure
10	Malignant hyperthermia

cable, inappropriate transducer level, etc. Beta-blockers, calcium channel blockers, and direct acting vasodilators can all be used if indicated. Intravenous (i.v.) narcotics as well as non-steroidal analgesics can be given to control pain and minimize hypertension at emergence.

11.3.3 Post-operative management

All pre-operative medications should be continued in the post-operative period unless specifically contraindicated. Regional techniques for post-operative pain control work well, if technically feasible. They limit the amount of i.v. narcotics needed and help respiratory mechanics as well as a smooth emergence from anesthesia. Non-steroidal analgesics are also a good choice for pain control if not surgically contraindicated. If the patient is not allowed to have medications orally, oral antihypertensive medications should be substituted by intravenous formulations. Hypertension in the post-anesthesia care unit (PACU) should be evaluated and treated after making sure that pain is adequately controlled and the patient is not hypoxic or hypercarbic (Table 11.4). Obese patients are more likely to be resistant to usual anti-hypertensive therapy. Studies have shown that obesity, glucose intolerance and hyperinsulinemia can lead to high BP and can lower the effectiveness of anti-hypertensive treatment.[45,46]

11.4 Ischemic heart disease and congestive heart failure

A significant percentage of obese patients who present for intermediate- to high-risk non-cardiac surgery are likely to have cardiac disease: 45% of US veterans

presenting for intermediate- to high-risk non-cardiac surgery had IHD,[47] and >60% of patients who presented for vascular surgery had significant CAD.[48] The association between history of cardiac disease and post-operative cardiac morbidity and mortality was first reported by Butler *et al.* in 1930.[49] Practitioners were increasingly convinced of the association of pre-operative cardiac disease with poor post-operative outcomes; in 1972, Tarhan *et al.* established this association.[50] Subsequently, pre-operative cardiac risk indices were proposed to identify patients with increased risk of peri-operative cardiac events.[51–53] To date no specific cardiac risk index has been proposed for obese patients. Pre-operative cardiac assessment of obese patients follows the same sequence as for non-obese patients.

11.4.1 Pre-operative cardiac risk assessment

In 1977, Goldman *et al.* proposed the landmark cardiac risk index.[51] Though not prospectively validated, this index was used extensively for pre-operative cardiac risk assessment for the next two decades. In 1983, Jeffery *et al.* demonstrated that the incidence of cardiac complications in patients who had undergone abdominal aortic procedures was higher than that predicted by the cardiac risk index.[54] Subsequently, other cardiac risk indices were proposed and adopted in clinical practice for cardiac risk stratification and determination as to the need for further testing.[52,53] By the early 1990s, a confusing array of cardiac risk indices for pre-operative cardiac risk stratification had been proposed (Table 11.5). Some of these strategies were expensive and time consuming. Therefore, in 1996, a 12-member task force of the American College of Cardiology and American Heart Association (ACC/AHA) published guidelines with respect to the peri-operative cardiovascular evaluation of patients undergoing non-cardiac surgery.[55] In March 2002, these guidelines were updated based on new data.[9] The overriding theme of the original guidelines and the update is that "pre-operative intervention is rarely necessary simply to lower the risk of surgery, unless such intervention is indicated irrespective of the peri-operative context. "No test should be performed unless it is likely to influence patient treatment". Though no prospective randomized study has been conducted to prove the efficacy of these guidelines, some studies have suggested that there is utility in following them.[56,57]

The ACC/AHA guidelines provide an eight-step algorithm for determining the need for pre-operative cardiac evaluation, which should also be valid for obese patients. The first step assesses the urgency of surgery: the need for emergency surgery takes precedence over the need for additional workup. The second step assesses whether the patient has undergone revascularization; that is, coronary artery bypass grafting (CABG) or a percutaneous coronary intervention (PCI). The third step determines if and when the patient underwent invasive or non-invasive coronary evaluation. If the patient had revascularization within the last 5 years or had an appropriate coronary evaluation in the last 2 years – with no subsequent deterioration of cardiac status – then further cardiac evaluation is not warranted.

The next five steps of the ACC/AHA guidelines integrate risk stratification according to clinical risk factors, functional capacity and surgery-specific risk factors. Clinical risk factors – obtained by history, physical examination, and review of EKG – are grouped into three categories: namely (1) *major clinical predictors* (unstable coronary syndrome, decompensated heart failure, significant arrhythmias, severe valvular disease) mandate intensive management; (2) *intermediate clinical predictors* (mild angina pectoris, previous MI by history or pathological Q-waves, compensated or prior heart failure, diabetes mellitus (particularly insulin dependent), renal insufficiency) are well-validated markers of enhanced risk of peri-operative cardiac complications; (3) *minor clinical predictors* (hypertension, left bundle-branch block, non-specific ST–T-wave changes, history of stroke) are recognized markers of CAD that have not been proven to independently increase peri-operative risk.[9]

Functional capacity, also referred to as exercise tolerance, can be expressed in metabolic equivalent treadmill study (METs) levels. The oxygen consumption (VO_2) of a 70 kg, 40-year-old man in a resting state is 3.5 ml/kg/min or 1 MET. Peri-operative cardiac and long-term risks are increased in patients unable to meet a 4-MET demand during most normal daily activities ("poor" functional capacity). These people may be able to do leisure activities (for example, baking, slow ballroom dancing, golfing with a cart, walking at a speed of approximately 2–3 mph), but are unable to perform more strenuous (>4 METs) activity without developing chest pain or significant shortness of breath. Activities requiring >4 METs ("good" functional capacity) include climbing hills, ice skating and running a short distance. Activities requiring 10 or more METs include participation in sports, such as swimming, football, single tennis, basketball, and skating.[9]

Surgery-specific risk of non-cardiac surgical procedures is graded as high, intermediate, or low. *High-risk*

Table 11.5 Cardiac risk index

Cardiac risk index with variables	Points	Comments
Goldman cardiac risk index (1976)[51]		
1 Third heart sound or jugular venous distension	11	Cardiac
2 Recent MI	10	complication rate:
3 Non-sinus rhythm or premature atrial contraction on EKG	7	0–5 points = 1%
4 >5 premature ventricular contractions	7	6–12 points = 7%
5 Age >70 years	5	13–25 points = 14%
6 Emergency operations	4	>26 points = 78%
7 Poor general medical condition	3	
8 Intrathoracic, intraperitoneal, or aortic operation	3	
9 Important valvular aortic stenosis	3	
Detsky modified multifactorial index (1986)[52]		
1 Class 4 angina	20	Cardiac complication rate:
2 Suspected critical aortic stenosis	20	>15 = high risk
3 MI within 6 months	10	
4 Alveolar pulmonary edema within 1 week	10	
5 Unstable angina within 3 months	10	
6 Class 3 angina	10	
7 Emergency operation	10	
8 MI >6 months	5	
9 Alveolar pulmonary edema resolved >1 week ago	5	
10 Rhythm other than sinus or PACs on EKG	5	
11 >5 PVCs any time before surgery	5	
12 Poor general medical status	5	
13 Age >70 years	5	
Eagle's Criteria for cardiac risk assessment (1989)[53]		
1 Age >70 years	1	<1: no testing
2 Diabetes	1	1–2: send for non-invasive test
3 Angina	1	⩾3: send for angiography
4 Q-waves on EKG	1	
5 Ventricular arrhythmias	1	
Lee's modified cardiac (1999)[59]		
1 IHD	1	Each increment in points increases
2 CHF	1	risk of post-operative myocardial
3 Cerebral vascular disease	1	morbidity
4 High-risk surgery	1	
5 Pre-operative insulin treatment for diabetes	1	
6 Pre-operative creatinine >2 mg/dl	1	

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surgeries (emergent major operations particularly in the elderly, aortic and other major vascular surgery, peripheral vascular surgery, anticipated prolonged surgical procedures associated with large fluid shift and/or anticipated blood loss) are reported to have cardiac risk often >5%. *Intermediate-risk surgeries* (carotid endarterectomy, head and neck surgery, intraperitoneal and intrathoracic surgery, orthopedic surgery, prostate surgery) are reported to have cardiac risk generally < 5%. *Low-risk procedures* (endoscopic procedure, superficial procedures, cataract surgery, breast surgery) are reported to have <1% risk of cardiac events.[9]

These ACC/AHA guidelines are being widely adopted and have significantly helped in clarifying and streamlining the pre-operative cardiac assessment process. Institutions and practitioners can now conduct assessment and advise colleagues and patients in a consistent way, rather than follow a variety of different cardiac risk indices. However, one should keep in mind the limitations of the guidelines. The guidelines have not been prospectively tested,[58] though there is evidence that they are helpful.[56,57] The guidelines do not take into account the presence of multiple intermediate or minor risk factors even though presence of multiple

risk factors has been shown to increase the incidence of peri-operative cardiac morbidity.[59] Thus, if the guidelines are followed, the patient with multiple intermediate and minor clinical-risk factors and good exercise tolerance may not be considered for further testing prior to intermediate risk surgery, while a patient with one intermediate risk factor and low exercise tolerance would be (even if the exercise was limited by non-cardiopulmonary factors). In addition, although one of the implicit goals of the guidelines was to decrease testing, a recent analysis demonstrated that applying the guidelines led to 50% more testing (albeit with good post-operative results).[57] Furthermore, the list of risk factors is not all inclusive and some have modified it.[56,60] Finally, it is difficult to generalize: regional and ethnic differences should also be taken into account; and the surgical risk categories also may be modified based on specific institutional results, which are highly dependent on surgical skills, anesthetic care and nursing quality.[61,62] Though debated, there is evidence that significant differences exist between care and outcomes at different institutions for the same surgical procedure.[62–65] Once the patient has been identified as a candidate for further testing, the patient should be referred to a cardiologist or an internist. Obviously, most patients with a history of CAD who have not been tested in the past 2 years and have poor functional capacity likely will be referred for further testing prior to intermediate- or high-risk surgery (Table 11.6). Though utility of pre-operative stress testing has been questioned,[66–68] many consider it to be important in deciding further management strategy.[9,58]

It is evident that many obese patients who are scheduled for intermediate- to high-risk surgery would be candidates for cardiac evaluation as majority are likely to have limited functional capacity and intermediate- to low-risk clinical predictors. Any symptoms of heart failure (orthopnea, paroxysmal nocturnal dyspnea, pedal edema, jugular venous distension) would also warrant further evaluation of cardiac function. Comprehensive cardiac evaluation in obese patients should be focused to assess: a. cardiac function; b. presence and severity of IHD.

Cardiac function can be adversely affected in obese patients (*vide supra*). Evaluation of CHF by clinical signs can be extremely difficult in obese patients. Objective evaluation of ejection fraction and cardiac function by echocardiography and/or left ventriculography is usually necessary. Though resting LV function has not been found to be a consistent predictor of peri-operative ischemic events, the greatest risk of complication is noted in patients with LV ejection fraction of $<35\%$.[9] ACC/AHA recommendation for pre-operative non-invasive evaluation for LV function include: a. patients with current or poorly controlled heart failure; b. patients with history of heart failure and patients with dyspnea of unknown origin. Though no randomized study has been done in obese patients to determine the utility of routine evaluation of RV and LV function, it is expected that such evaluation, as guided by symptoms, prior to intermediate- and high-risk surgery, will be helpful in guiding intra- and post-operative management of the obese patients.

Evaluation for IHD requires stress testing. Though some obese patients may be candidates for exercise stress testing, many are likely to have poor functional capacity and are referred for pharmacological stress testing: stress echocardiography after dobutamine or atropine administration (DSE) or a dipyridamole thallium nuclear imaging study (DTS). Both DSE and DTS have high negative predictive value (94% and 88%, respectively) in non-obese patients.[69] The positive predictive value of DSE is better (67% vs. 37%)[60,70] and DSE is more physiologically representative of the post-operative state.[60] However, DTS effectively detects significant coronary occlusion and myocardium at risk and is probably a better test in patients who have baseline left bundle-branch block.[9] The effect of patient's body habitus (for example, breast attenuation in women and diaphragmatic attenuation in men) have long been recognized as factors which reduces the accuracy of myocardial perfusion studies.[71,72] Hansen *et al*. in a study involving 607 patients showed that obesity (BMI $>$ 30) was associated with decrease in accuracy (0.92 vs. 0.86 area under the curve) of quantitative SPECT thallium imaging.[73] However, weight and body surface area did not have any significant impact on the accuracy of the test.[73] Transthoracic echocardiography is also more challenging in obese patients due to body habitus. Transesophageal echocardiography has been reported to be safe in obese patients.[74] Dobutamine stress testing with transesophageal echocardiography has also been performed safely and reportedly has similar sensitivity and specificity as transthoracic dobutamine echocardiography.[75] This technique has been used successfully in obese patients, however, no large scale studies have been reported to date.[76]

Patients who have positive stress test are likely to be referred for coronary angiography. Many of the obese patients who complain of angina may not have significant occlusive coronary disease and angina is likely due to imbalance in oxygen supply and demand due to LV hypertrophy. An autopsy study showed that a considerable number of severely obese people have only fatty streaks and no marked stenosis in their coronary arteries, even at advanced age.[24] No significant stenosis was seen in circumflex or right coronary

Table 11.6 Summary of ACC/AHA guidelines for cardiac evaluation prior to non-emergent, non-cardiac surgery

Risk of surgery	Clinical predictors				
	Major clinical predictors	Intermediate clinical predictors		Minor clinical predictors	
		Poor functional capacity	Good functional capacity	Poor functional capacity	Good functional capacity
High					
• emergent major operations, particularly in the elderly • aortic and other major vascular surgery • peripheral vascular surgery • anticipated prolonged surgical procedures associated with large fluid shift and/or anticipated blood loss	Postpone or delay surgery	Testing indicated	Testing indicated	Testing indicated	Testing not indicated
Intermediate					
• carotid endarterectomy • head and neck surgery • intraperitoneal and intrathoracic surgery • orthopedic surgery • prostate surgery	Postpone or delay surgery	Testing indicated	Testing not indicated	Testing not indicated	Testing not indicated
Low					
• endoscopic procedure • superficial procedures • cataract surgery • breast surgery	Postpone or delay surgery	Possible testing	Testing not indicated	Testing not indicated	Testing not indicated

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Decision is based upon clinical predictors (clinical-risk factors), functional capacity (exercise tolerance), and risk of the given surgery.

artery in approximately half the cases. Anterior descending artery was the most commonly affected artery – 42% in men and 48% in women.[24]

11.4.2 Pre-operative management strategy after pre-operative cardiovascular assessment

Once the patient has been identified with IHD and the degree of IHD quantified by either invasive or non-invasive testing, three therapeutic options are available prior to elective non-cardiac surgery:

1 revascularization by surgery (CABG);
2 revascularization by PCI;
3 optimized medical management, typically with beta-blockers or alpha-2 agonists.

These treatments have effectively improved long-term outcomes in non-operative settings. Hence, many patients with significant IHD who present for non-cardiac surgery likely would be candidates for one or more of the above mentioned therapies whether they are scheduled for surgery or not. However, it may not be advisable to intervene pre-operatively (except with pharmacological therapy). Coronary revascularization should be guided by the patient's cardiac condition (that is, if there is unstable angina, left main CAD, three-vessel disease, decreased LV function and left anterior descending artery disease) as well as by the added risk of the coronary intervention and the potential consequences of delaying the non-cardiac surgery for recovery after the intervention.[9]

The Coronary Artery Surgery Study (CASS) showed that patients who had coronary revascularization prior to major risk surgery did better post-operatively.[77] The peri-operative mortality rate was twice as high in patients who were medically managed than in those who had undergone pre-operative CABG

surgery (3.3% vs. 1.7%, $P < 0.05$). Similar beneficial results were noted in selected group of patients in the Bypass Angioplasty Revascularization Investigation (BARI)[78] Trial and in evaluation of random sample of Medicare beneficiaries.[79] However, patients would have had to survive CABG surgery before they would undergo non-cardiac surgery. For CABG surgery to be beneficial, the institutional risk for non-cardiac surgery alone should be greater than the combined risks of coronary catheterization, coronary revascularization and the subsequent non-cardiac surgery. The decision analysis of Mason *et al*. showed that proceeding with vascular surgery was better than undergoing CABG surgery prior to elective non-cardiac vascular surgery.[80] On the other hand, Landesberg *et al*. showed that long-term mortality in patients who underwent CABG surgery prior to the vascular surgery was significantly improved at 5 years compared to patients who did not have CABG surgery (74.3% vs. 53.2%; $P = 0.006$).[81] Interestingly, there was no significant difference in the first 30 day outcome between the two groups (98.7% vs. 97.8%). This shows that short-term mortality is not affected by pre-operative revascularization; only long-term outcome is improved. Hence, the indications for coronary revascularization are aimed primarily at improving long-term survival and outcome and thus are the same as in the non-operative setting (unstable angina, left main CAD, three-vessel disease, decreased LV function and left anterior descending artery disease). There are also no data to suggest that indications for pre-operative cardiac revascularization are any different for obese patients than in non-obese patients. Moderately and extremely obese patients have higher incidence of deep sternal wound infection, renal failure, prolonged post-operative hospital stay, and operative mortality after coronary artery bypass surgery.[82–84]

Initial evaluations of PCI revealed that patients who underwent angioplasty prior to elective non-cardiac surgery had better outcomes.[85–88] However, angioplasty is now often accompanied by stenting, with post-procedure anti-platelet therapy to prevent acute coronary thrombosis and maintain long-term patency of the intervened vessel. Two recent reports strongly suggest that elective non-cardiac procedure surgery should be delayed for 4–6 weeks after PCI with stenting. Kaluza *et al*. reported eight deaths, seven MIs and 11 major bleeding episodes in a cohort of patients who had undergone non-cardiac surgery within 40 days after stent placement.[89] All deaths, MIs and eight out of 11 bleeding episodes occurred in patients who had stent placement within 14 days. More recently, Wilson *et al*. reported on 207 patients: eight suffered MIs, and six died.[90] All myocardial events or deaths occurred in patients who had PCI and stenting within 6 weeks of non-cardiac surgery, and were attributed to stent thrombosis. The authors concluded that it was prudent to delay elective non-cardiac surgery for 6 weeks after PCI, to allow for complete endothelialization of the stent and completion of aggressive anti-platelet therapy with GIIb/IIIa inhibitors.[90] The complication rate of the PCI in obese patients has not been reported to be different than in non-obese individuals and similar precautions should also be taken in obese patients.[91]

Several pharmacological agents have been used to reduce peri-operative cardiac injury, primarily because they have demonstrated, pharmacological efficacy in the management of coronary ischemia in non-surgical setting. Nitroglycerine was an obvious choice initially. As in the non-operative setting, nitroglycerine it may be helpful in the management of active peri-operative ischemia. However, prophylactic use of nitroglycerine has not been shown to be efficacious in reducing peri-operative morbidity and mortality.[92]

Peri-operative use of beta-blockers has been shown to be efficacious in reducing peri-operative morbidity and mortality.[93–96] The clinician should recognize that the strongest evidence for efficacy of peri-operative beta-blockers is based on studies with small number of patients.[97,98] Nonetheless, the ACC/AHA guidelines recommend initiating beta-blockers as early as possible, prior to high-risk surgery and titrating heart rate to 60 bpm.[9] Auerbach and Goldman have recommended peri-operative beta-blocker use in a larger range of patients[9,95] (Table 11.7). Their decision tree recommends the use of peri-operative beta-blockers in the following settings:

1. patients with one or more revised cardiac index risk factors despite a negative stress test;
2. patients with two minor risk factors, even with good functional status and/or negative non-invasive stress test.

In other patients, *pharmacological* therapy likely would not be sufficient. Even if they receive beta-blockers, patients scheduled for vascular surgery who have three or more clinical risk factors and significant myocardium at risk are still at appreciable risk of sustaining peri-operative MI or death.[100] According to the Auerbach and Goldman decision tree, these patients should be considered for revascularization.[95] Similarly patients with one or two revised cardiac risk factors or two minor risk factors, with poor or indeterminate functional capacity and a positive stress test should be considered for revascularization;[95] however,

Table 11.7 Eligibility criteria for use of peri-operative beta-blockers*

Have any *one* of the following: *(revised cardiac risk criteria)*

High-risk surgical procedure defined as follows:
- intrathoracic
- intraperitoneal
- suprainguinal vascular procedure

IHD defined as follows:
- History of MI
- History of current angina
- Use of sublingual nitroglycerine
- Positive exercise test results
- Q-waves on EKG
- Patients who have undergone PTCA or CABG and who have chest pain presumed to be of ischemic origin

Cerebrovascular disease defined as follows:
- History of transient ischemic attack
- History of cerebrovascular accident

Diabetes mellitus requiring insulin therapy

Chronic renal insufficiency, defined as a baseline creatinine level of at least 2.0 mg/dl

Have any *two* of the following: *(minor clinical criteria)*
- Aged 65 years or older
- Hypertension
- Current smoker
- Serum cholesterol concentration at least 240 mg/ml
- Diabetes mellitus not requiring insulin

* Suggested by Auerbach and Goldman[95,99] based on Lee *et al.*[59] Mangano *et al.*[98]

PTCA: percutaneous transluminal coronary angioplasty.

some would consider these patients eligible to proceed to surgery with intensive peri-operative beta-blocker therapy.[97]

Questions regarding peri-operative beta-blocker initiation and duration, choice of agent, and target heart rate are still unresolved. Controversy also persists as to the efficacy of acute peri-operative beta-blocker therapy vs. chronic beta-blocker therapy.[101–104] Moreover, despite widespread dissemination of the data as to the potential efficacy of beta-blockers, many patients do not receive them prior to surgery. In a recent analysis at our institution, pre-operative beta-blocker use was 50% in patients who were scheduled to undergo major- to intermediate-risk vascular surgery.[105] Furthermore, if heart rate of <60 bpm was considered a marker of adequate beta-blocker therapy, only 17% of the patients were noted to be adequately beta-blocked, *pre-operatively*.[105] Institutional protocols need to be developed to improve and standardize peri-operative beta-blocker use among the caregivers throughout the pre-, intra-, and post-operative periods.[106] These not only should take into account the indications for such therapy but also the potential adverse effects, alone or in the context of other medications, including hypotension, bradycardia, syncope, stroke, bronchospasm, and allergic reactions.

Evidence of the role of beta-blockers in the management of obese hypertensives and patients with cardiac dysfunction is scarce. Nevertheless, reductions in resting energy expenditure, thermic effect of food, exercise tolerance, non-exercise thermogenesis, increased tiredness, inhibition of lipolysis and exacerbation of insulin resistance are well-documented effects of beta-blockers.[107] All these factors can contribute to weight gain in obese patients who are receiving beta-blockers.[108] Short-term effects of peri-operative beta-blockers use in obese patients are not known. However, it is very likely that beta-blockers have similar beneficial peri-operative cardiovascular effects in obese patients, as in non-obese patients. Pharmacokinetics of beta-blockers is altered in obese patients, however, pharmacodynamic effects are of similar magnitude and pharmacokinetic differences are not considered clinically relevant.[109–111]

Alpha-2 agonists, by virtue of their central action, have analgesic, sedative, and sympatholytic effects. A study of 1897 patients with established CAD did not show a significant difference in cardiac morbidity and mortality between patients treated with the alpha-2 agonist mivazerol and the control group;[112] however, post-hoc analysis in a subset of vascular patients showed improved outcomes in treated patients. Hence, in patients in whom beta-blockers are contraindicated, alpha-2 agonists may be considered as an alternative to decrease peri-operative cardiac injury.

The evidence with respect to other pharmacological agents is less clear. A meta-analysis by Wijeysundera *et al.* suggested that calcium channel blockers are efficacious in reducing peri-operative cardiac morbidity and mortality.[113] However, Stevens *et al.* did not find a significant beneficial effect of calcium channel blockers in this context,[96] and trials in the non-operative setting have raised questions about their efficacy.[114]

It is likely that other agents with beneficial effects in the non-operative setting, such as ACE inhibitors, statins, and aspirin, may prove to be beneficial peri-operatively. Recently, a retrospective analysis by Poldermans *et al.* in patients who underwent vascular surgery indicated that statins improved long-term outcome.[115]

11.4.3 Intra-operative management

Hemodynamic response to anesthesia and surgery is altered in obese patients.[14,116] Obese patients demonstrated elevated intra- and post-operative right atrial, mean pulmonary artery, and pulmonary artery wedge pressures. Typically, the circulatory response to major surgery and general anesthesia consists of two phases: the operative phase and the post-operative phase. The first phase is characterized by depression of cardiac output and cardiac index, and second phase by elevation of cardiac output and cardiac index, particularly in the post-operative period. Obese patients, who underwent general anesthesia for their gastric procedure, demonstrated a greater decrease in cardiac index, right and left stroke work than non-obese patients, intra-operatively.[116] Furthermore, non-obese patients demonstrated an increase of cardiac index in the second period, the cardiac index remained low by an average mean of 13–22% in the obese patients. LV stroke work also remained depressed by an average of 30% in obese patients compared with normal values in non-obese patients.[116] Despite these hemodynamic changes, hemodynamic instability or increased incidence of post-operative cardiac morbidity was not reported in the immediate post-operative period.

While the goals of intra-operative management (for example, stable hemodynamics, normothermia, and avoidance of significant anemia) are generally agreed upon, it has been difficult to determine, if any particular anesthetic or monitoring technique is superior in this regard. As long as intra-operative management is guided by sound physiological goals, the outcomes in obese patients, in terms of peri-operative cardiac morbidity are not appreciably different among current anesthetic techniques or monitoring modalities.

General anesthesia with endotracheal intubation is considered a preferred technique by many practitioners. The primary advantage of general anesthesia is the assurance of adequate ventilation and oxygenation. Despite theoretic concerns based on lipid solubility and biotransformation of volatile anesthetics clinically significant delay in waking or prolonged recovery room stay has not been reported. As in non-obese patients, obese patient who receive sevoflurane or desflurane are likely to recover faster than patients who receive isoflurane[117–119] (see Chapter 22). Recovery with desflurane and remifentanil was noted to be faster than with sevoflurane and remifentanil.[120] However, one should keep in mind the bronchoconstrictive effects of desflurane at higher concentrations and subsequent effects on already compromised pulmonary mechanics in obese patients.[121] Total i.v. anesthesia has also been used safely in obese patients[122,123] (see Chapter 23). Though an earlier study reported higher incidence of hemodynamic instability and cardiac arrhythmia[124] during induction of general anesthesia, no difference in cardiac morbidity has not been reported between currently used inhalation anesthetics.[125]

Many problems associated with general anesthetics can be avoided with carefully administered regional anesthetics. Issues pertaining to airway management, protection of the airway and respiratory depression due to inhalational and systemic anesthetics can be avoided. Some reports have suggested that regional techniques may be advantageous in patients with IHD and cardiac dysfunction, but others have not confirmed this.[126,127] Other, potential benefits of a regional anesthetic include better pain control[128,129] and decreased incidence of deep vein thrombosis in patients who undergo lower limb orthopedic procedures.[130,131] However, the incidence of post-operative cardiac morbidity and mortality does not appear to be significantly different between general and regional anesthesia in non-obese population and has not been reported to be different in obese patients. Undoubtedly, one of the significant drawbacks to regional anesthesia in obese patients is its technical difficulty. Another problem is that the anesthetic levels during spinal or epidural anesthesia can be unpredictable. Higher than expected anesthetic levels can significantly compromise respiratory mechanics and gas exchange in obese patients. Epidural anesthesia may be preferable in obese patients, as it is more titratable than spinal anesthetic.[132]

Intra-operative monitoring must follow the basic American Society of Anesthesiologists (ASA) guidelines. Special attention should be given to monitoring respiratory parameters as respiratory mechanics, gas exchange and acid–base balance are closely linked to cardiac function (see Chapter 18). In a patient with known cardiac dysfunction it is critical to optimize respiratory indices. However, the issue of invasive cardiac monitoring is difficult to evaluate.[133] While it is important to monitor hemodynamic indices and maintain them within a narrow range, it is difficult to prove that the presence of a particular monitor significantly alters morbidity or mortality. This is highlighted by the persistent controversy over the use of a pulmonary artery catheter (PAC). Proponents cite the rationale for diagnosis and titration of treatment; opponents cite lack of data supporting its use and the risk of complications. In a study involving 1994 patients, Sandham *et al*. demonstrated no significant difference in outcome in high-risk surgical patients monitored with PAC vs. central venous catheter (mortality was 7.8% vs. 7.7%). Moreover, they noted a higher incidence

of pulmonary embolism in the PAC group ($P = 0.004$).[134] However, one should keep in mind the limitation of the study: if mortality is considered the primary outcome, it would require 14,240 patients to be randomized to detect a difference of 20% between the groups with 90% power.[135] The ultimate decision to employ a particular monitor is significantly influenced by case-specific factors, such as underlying disease, physician availability and expertise, as well as surgical and technical considerations. Invasive arterial monitoring should be used for the "super" obese (BMI $\geqslant 60\,kg/m^2$), those with severe cardiopulmonary disease, or for patients in whom the non-invasive BP cuff is unreliable. Non-invasive modalities to monitor BP should suffice in most other circumstances (*vide supra*). Transesophageal echocardiography has been used successfully in morbidly obese patients in non-operative setting[74] and can potentially be used intra-operatively to evaluate cardiac function and volume status.

Many patients' with clinically severe obesity have peripheral veins that are difficult to access, both for i.v. lines and for laboratory draws. Central venous catheters should be used in cases in which peripheral i.v. access cannot be obtained. In addition, central venous catheterization maybe needed if post-operative i.v. access is problematic. In the superobese patient where i.v. access (either central or peripheral) may be difficult to obtain, one should consider pre-operative placement of central access in the interventional radiology suite.

As volume status may be difficult to assess, a Foley catheter should be placed before the start of any major surgical procedure. Accurate urine output measurements throughout the patient's hospital stay may also be essential. In laparoscopic procedures (with carbon dioxide pneumoperitoneum), it may be especially difficult to corroborate urine output with volume status. Intra-abdominal carbon dioxide that diffuses into the blood stream leads to decreased renal blood flow via a centrally mediated constriction of the renal artery.[136] This can make urine output an unreliable indicator of the patient's overall volume status (see Chapter 14). Despite the negative effects of the pneumoperitoneum on urine output, intra-operative oliguria does not correlate with post-operative renal function.[136]

Beta-blockers have been used as intra-operative therapeutic agents to control hemodynamics, intra-operative ischemia, and cardiac arrhythmias.[93] Some studies investigating their prophylactic role have demonstrated decreased intra-operative ischemia.[137] Hemodynamic goals for intra-operative therapy with beta-blockers are far from clear, and potential interactions with anesthetics (which commonly cause myocardial depression and vasodilatation) must be taken into account (see Chapter 16). Poldermans *et al.* set their goals to maintain intra-operative heart rate at <80 bpm.[97] The general consensus appears to be that if beta-blockers are indicated peri-operatively, they should not only be given intra-operatively – they typically should be initiated pre-operatively and except in the presence of significant contraindications, should be continued post-operatively. Though pharmacokinetics of beta-blockers is affected by obesity, clinical impact is minimal as there is significant pharmacodynamic variability.[34,111] Dosage of beta-blockers should be initiated based on lean body mass and titrated to effect.

11.4.4 Post-operative management

Obese patients with pre-operative cardiac dysfunction are as much at risk for post-operative myocardial injury, infarction, and cardiac-related death, as non-obese patients. Surprisingly, higher incidence of peri-operative cardiac morbidity and mortality has not been reported in obese patients.[138,139] However, it is plausible that higher incidence of post-operative respiratory dysfunction can indirectly contribute to cardiac dysfunction in obese patients with compromised cardiac function. Similarly, in patients with established coronary atherosclerosis, BMI is independently associated with higher risk of acute coronary syndromes.[140] Though significant advances have been made in researching and refining pre-operative evaluation and management strategies, evidence-based strategies which can specifically be adopted in the post-operative period to improve outcomes still need to be developed. Our understanding of the pathophysiology of peri-operative MI is largely based on the information in the non-operative setting.

11.4.5 Peri-operative myocardial infarction

Pathophysiology

It has been estimated that each year 50,000 patients undergoing elective surgery suffer an acute MI.[141] The mortality after peri-operative MI has been quoted as high as 40–50%[141] though recent reports suggest the mortality has decreased to 10–15%.[142] The incidence of peri-operative cardiac injury is a cumulative result of the patient's pre-operative medical status, the specific surgical procedure, expertise of the surgeon, and the overall medical care at a particular institution. It also depends on the diagnostic criteria used to define an MI. Earlier observations suggested that most post-operative MIs tend to occur on the third post-operative day;[50,143–145] however, recent data suggest that most

MIs tend to occur within the first 48 h.[146] This discrepancy is thought to be related to the diagnostic criteria that were used in older studies; that is, late occurring MIs are predominantly Q-wave infarctions, while earlier MIs are non-Q-wave.[147]

In the past decade, significant advances have been made in the understanding of the pathophysiology and diagnosis of MI. Atherosclerosis is no longer considered a "passive plumbing problem" with clogging of the arteries by lipids.[148] It is now accepted as an active inflammatory process with an undulating course.[148] Almost all MIs in non-operative settings result from coronary atherosclerosis with superimposed coronary thrombosis.[148] A similar mechanism may be responsible for peri-operative MIs, with exacerbation by the acute stresses associated with surgery.[149] Endothelial injury at the site of a plaque triggers cascade of platelet aggregation and release of mediators, including thromboxane A2, serotonin, adenosine diphosphate (ADP), platelet activating factor (PAF), thrombin, tissue factor, and oxygen-derived free radicals. Aggregation of platelets and activation of inflammatory and non-inflammatory mediators potentiate thrombus formation and lead to dynamic vasoconstriction distal to the thrombus formation. The combined effects of dynamic and underlying narrowing cause ischemia and possibly infarction. In the post-operative period, changes in blood viscosity, catecholamines, cortisol, endogenous tissue plasminogen activator (t-PA) and plasminogen activator inhibitor (PAI) 1 create a prothrombotic state. Furthermore, changes in heart rate and BP can increase propensity to plaque fissuring and endothelial damage. In combination, these factors can precipitate harmful thrombus formation in an atherosclerotic vessel with the development of ST elevation and/or Q-waves (Figure 11.5).

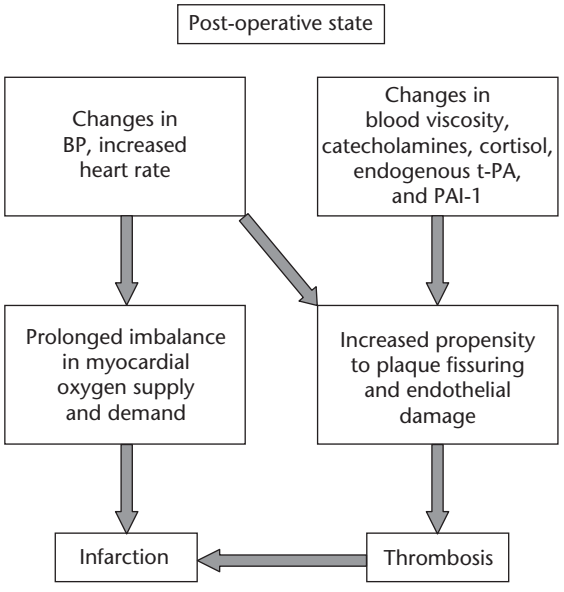

Figure 11.5 Predisposing factors in the peri-operative state that can contribute to endothelial injury and MI.

Alternatively, Landesberg *et al*. have suggested that most peri-operative MIs are not associated with ST elevation.[142] Instead, they are preceded by significant duration of ST depression and tachycardia. This may indicate that the injury develops as a consequence of increased demand (increased BP and heart rate) in the context of underlying compromised perfusion.

Challenges in diagnosis of peri-operative myocardial infarction

In 1979, the World Health Organization (WHO) developed criteria for diagnosis of acute MI[150] that required the presence of at least two of the following elements:

1. ischemic type chest pain;
2. evolutionary changes on serially obtained EKG tracings and;
3. rise and fall of cardiac markers (which at the time was CK/CK-MB).

However, one-third of patients do not present with classic chest pain; and it has been estimated that as many as 95% of post-operative ischemic episodes are silent and chest pain free.[141] Badner *et al*. reported only 17% incidence of chest pain in patients who sustained a peri-operative MI.[146] Additionally, 25% of the EKGs obtained post-operatively are considered non-diagnostic. Further complicating diagnosis, non-specific changes on the EKG, new onset arrhythmias and non-cardiac-related hemodynamic instability can obscure the clinical picture of acute coronary syndrome in the post-operative period. Thus, it has been more difficult to define the criteria for peri-operative MI, as two out of the three elements are either not frequently present or is not useful.[151]

In the non-operative setting, measurement of cardiac-specific troponins (cTns) now plays a significant role in the diagnosis of MI. This has prompted revisions of the evaluation and management of acute coronary syndromes[151] (Figure 11.6).

Although there is inconsistency with respect to interpretation of troponin values, most studies highlight the utility of cardiac troponins in the diagnosis of peri-operative MI.[146,152–162] These studies demonstrate increased sensitivity of troponins to

myocardial injury, that is not normally sufficient to cause CK-MB elevation, chest pain or EKG abnormalities.[155,158–160,163–165]

It is increasingly being recognized that, as in the non-operative setting, an acute increase in troponins above the cut-off for the assay should be considered an MI in the peri-operative setting. However, the association between peri-operative ischemia and the rise in cardiac troponin levels has not been conclusively proven. Neill *et al.*[157] and Rapp *et al.*[156] were unable to demonstrate the association between ischemia by Holter and rise in cardiac troponins. On the other hand, Landesberg *et al.* reported a good correlation between duration of ischemia and the rise in cTnI.[161] It also should be noted that the implications and clinical relevance of increases in troponins below the established cut-offs are still being investigated. First, should a small increase in troponin be considered a marker of myocardial ischemia or subclinical myocardial injury? Second, if present, are the small post-operative increases clinically relevant?

As is the case for non-surgical patients, there is a significant association between increased troponin levels with poor short- and long-term outcomes in surgical patients. Lee *et al.* and Lopez-Jimenez *et al.* have shown that increased levels of troponins translate to poor short- and long-term outcomes post-operatively (cardiac death, MI, myocardial ischemia, CHF, cardiac arrhythmias, and cerebrovascular accident).[153,154] Even minor cardiovascular complications (uncontrolled hypertension, palpitations, increased tiredness, or shortness of breath) were correlated to increased levels of cTnT. Kim *et al.* showed that, in patients who underwent vascular surgery, those with cTnI levels >1.5 ng/ml had a 6-fold increase in mortality at 6 months and a 27-fold increase in the risk of MI within 6 months.[162] Landesberg *et al.* evaluated a cohort of 447 patients who underwent major vascular procedures and concluded that rise in post-operative CK-MB and troponins, even at low-cut-off levels, were independent and complementary predictors of long-term mortality.[166] This suggests that the increase in cardiac troponins post-operatively, even in the absence of clear cardiovascular signs and symptoms, portends poor long-term outcome and that it is not simply a manifestation of an overly sensitive assay.

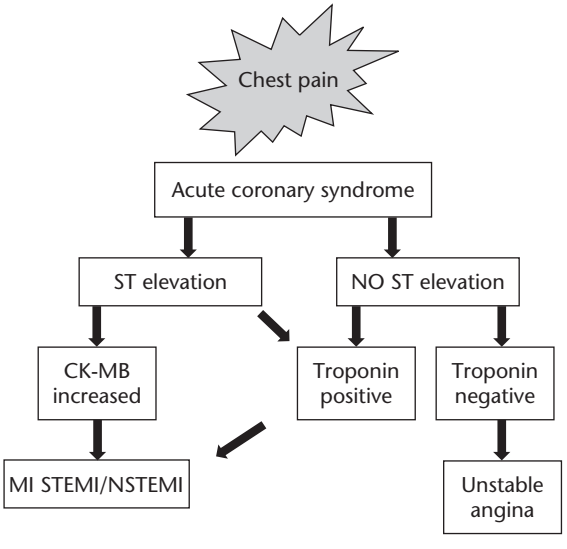

Figure 11.6 Terminology of acute coronary syndrome (reproduced with permission).[182]

Therapeutic interventions

The benefits of coronary revascularization immediately after non-cardiac surgery have been studied in only a limited number of settings.[9] The practice of carotid endarterectomy either concurrently with CABG surgery or immediately prior to CABG surgery is well documented; a significant difference between the two techniques has not been established.[167,168] The value of PCI post-operatively after non-cardiac surgery has not been addressed, largely because of the need for anti-thrombotic agents post-procedure.

Any clinical situation that leads to prolonged and significant hemodynamic perturbation can stress the heart. In patients with IHD who already have limited cardiac reserve and/or impaired coronary blood flow, prolonged and significant demand for increased cardiac output can lead to myocardial morbidity and mortality. Most cardiac events happen within the first 48 h, however, delayed cardiac events (within the first 30 days) still happen and could be the result of secondary stresses. Development of pain, respiratory failure, sepsis, or hemorrhage can lead to increased myocardial oxygen demand. The resulting oxygen supply/demand imbalance in patients with IHD can lead to myocardial ischemia, injury, infarction, or death. Interventions in obese patients that can decrease pain post-operatively, (epidural anesthesia) improve respiratory mechanics (elevated head and back, lateral position, supplemental oxygen) decrease wound infection and sepsis, would likely decrease the chances of oxygen supply/demand imbalance and preserve myocardial function. Furthermore, the aforementioned hemodynamic changes may be ameliorated with beta-blockers. It is imperative that patients who are on beta-blockers

pre-operatively continue to receive them post-operatively. Two studies have suggested that starting beta-blockers post-operatively can decrease cardiac ischemia.[169,170] However, it is not clear whether instituting beta-blockers post-operatively will achieve the benefits of initiating them pre-operatively and continuing them into the post-operative period.[97,98]

Prevention of hypovolemia and hypotension are universal goals in post-operative patients. It is important not only to maintain adequate intravascular volume but also to maintain an adequate hemoglobin (Hb) level. While an animal study suggests that myocardial dysfunction and ischemia occur earlier and to a greater degree in the context of anemia,[171] human data are inconsistent.[172] In two cohort studies, moderate anemia was poorly tolerated in peri-operative patients and critically ill patients with cardiovascular disease.[173,174] Wu *et al*. showed that short-term mortality in elderly patients was lower in patients who received blood transfusion after acute MI.[175] Nelson *et al*. showed that a hematocrit of 28% was the best threshold; morbidity increased in patients with values below this level.[173] Conversely, the Transfusion Requirement in Critical Care (TRICC) trial was not able to demonstrate a significant difference in 30 day mortality between patients who were "liberally" transfused (average Hb = 10.7 g/dl) vs. the "restrictive" group (transfused only if Hb dropped to <7 g/dl; average Hb = 8.5 g/dl).[176] Furthermore, an observational study by Vincent *et al*. demonstrated decreased mortality in patients who were not transfused.[177]

There is a lack of consensus as to the fluid of choice when non-Hb containing solutions are indicated. The controversy regarding the choice of fluid (colloid vs. crystalloid and the type of colloid or crystalloid) for resuscitation is still ongoing. A meta-analysis did not detect significant differences between types of fluids.[178] Hence, for patients with cardiac disease, a specific fluid cannot be advocated.

Timing of weaning and extubation in surgical patients is another much-debated aspect of care for which there is no one protocol that works for all patients. Early extubation is possible in many obese patients, as long as they fulfill the criteria for extubation (weaning parameters, appropriate mental status, adequate hemodynamics, adequate Hb, and adequate temperature). During prolonged intubation and subsequent extubation, there can be significant hemodynamic stress; wakefulness and hemodynamic stability need to be appropriately balanced. Many patients with IHD become ischemic during weaning, because of increased heart rate and rate pressure product.[179] Such hemodynamic perturbations should be managed with diligence and acute pharmacological therapy (for example, beta-blockers).

11.5 Conclusions

Due to changing demographics, increasing numbers of patients with obesity are presenting for non-cardiac surgery, and the risks of peri-operative cardiac morbidity and mortality are significant (see Chapters 2 and 30).

Structured management protocols which help assess, diagnose, and treat obese patients with CAD pre-operatively are likely to decrease post-operative morbidity and mortality. Augmented hemodynamic control with beta-blockers or alpha-2 agonists can play an important role in improving outcomes in many patients with IHD. Intra-operative anesthetic management which minimizes hemodynamic perturbations is important; however, choice of a particular technique typically is not critical.

Of critical importance is the post-operative management of the patient (see Chapters 25, 27, and 29).

Post-operative myocardial injury should be identified, evaluated, and managed aggressively. Secondary stresses, such as sepsis, extubation, and anemia that can increase demand on the heart should be treated or minimized.

Clearly optimal care of the patient with obesity and co-existing cardiac disease entails closely co-ordinated assessment and management throughout the pre-, intra-, and post-operative phases, if one is to optimize short- and long-term outcomes (see Chapter 1).

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DEEP VENOUS THROMBOSIS PROPHYLAXIS 12

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12.1 Introduction

The incidence of obesity in the US has increased substantially since the 1960s. More than half of the US adult population is considered overweight (body mass index, BMI $> 25\,kg/m^2$).[1]

It is estimated that approximately 300,000 deaths are attributed to obesity each year. Severe obesity ultimately results in a reduced life expectancy and is considered the second most preventable cause of death after cigarette smoking.[2]

Deep venous thrombosis (DVT) affects more than 250,000 patients per year with considerable morbidity and mortality.[3,4] Without prophylaxis 25% of the general surgery patients would develop DVT with a mortality of up to 17%.[5]

Both DVT and pulmonary embolism (PE) produce few specific symptoms and the first and only manifestation of the disease can be a fatal PE. Therefore, failure to provide adequate venous thromboembolism (VTE) prophylaxis should be avoided at all cost. The use of heparin in surgical patients has decreased the incidence of DVT and PE after surgical procedures.[6–8]

The addition of mechanical leg compression devices has not proven to enhance this reduction. However, it is common practice to provide both types of DVT protection. In the last few years low-molecular-weight heparin (LMWH) has showed to have better protection for DVT especially in patients considered to be at high risk of developing this entity.[8–11] Its use in trauma, orthopedic and neurological procedures has reported to be safe and to decrease the incidence of DVT when compared to historical controls.[12–13]

Morbid obesity is defined as BMI over 40 or $35\,kg/m^2$ if comorbidities are present. Obesity has been considered to be one of the risk factors for developing DVT. However, the prophylaxis used by the surgeons offering weight reduction surgery is far from uniform. We showed in a recent survey that most members of the American Society for Bariatric Surgery (ASBS) believed that their patients are at a higher risk of developing either DVT or PE.[14] Most of them have had a death related to PE in their surgical practice. The results of this survey raised more questions than answers, mainly due to the fact that the prophylactic method used by the surgeons that responded our survey was very heterogeneous. One interesting finding of our survey was that the reported incidence of DVT and PE was as low as the incidence reported in general surgery patients.[15,16] This finding is also supported by few studies in the literature that addressed the incidence of thromboembolic events in the perioperative period of obese patients. It was shown that the incidence of DVT and PE was not higher than in the general surgery population. There are a few explanations to these findings: first, that the risks for thromboembolic disease in the obese is not as high as commonly thought or second, that the incidence is low because most surgeons will provide prophylaxis

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to these patients. It is our belief that the second explanation is more plausible.

Despite the lack of a uniform prophylaxis for the morbidly obese we will try to explain in this chapter the different types of methods available, the pros and cons of each method and our suggestions based primarily in the literature and then in our experience.

12.2 Peri-operative assessment

Despite that very few respondents to our survey indicated that they did not use any method of prophylaxis except early ambulation, we strongly believe that there is enough data in the literature to support the use of some method of prophylaxis for the patient that is considered having a major general surgery procedure, especially an operation for the morbidly obese. In our opinion, the use of adequate VTE prophylaxis should be considered the standard of care. Despite the latter, a recent survey showed that although almost 100% of surgeons agreed with that statement, only one third of hospitalized patients received any type of prophylaxis.[17,18]

Before deciding what type of prophylaxis should be used for the morbidly obese, it is important to have a good pre-operative evaluation of the patients. One should look for factors that are well known to increase the risk of developing thromboembolism in the post-operative period. These factors are: history of previous DVT or PE, inadequate lower extremity circulation (that is, lymphedema, varices), poor ambulation (that is, severe osteoarthritis, need for walker, wheel chair, etc.), and age older than 55 years. In the presence of one or more risk factors, such patient should be considered to be at high risk.[19,20]

Another important factor before deciding what type of prophylaxis should be used is to consider the type of bariatric procedure offered to each patient. In our opinion, procedures such as gastric bypass (open or laparoscopic); restrictive procedures such as gastroplasties, or malabsorption procedures as the biliopancreatic diversion have a higher risk for thromboembolism than the adjustable band used in recent years in Europe, Australia and South America. The latter procedure is quicker and less invasive; therefore, the risks for DVT and PE are probably lower than with the previously mentioned procedures, where both anesthetic time and recovery time are more prolonged.

Education in the pre-operative period is of the utmost importance for the success of a bariatric procedure including the avoidance of a thromboembolic event. Patients should be aware of the importance of early ambulation and to keep on any compression device in the post-operative period. They need to know that prophylaxis does not end in the hospital, but it should continue at home especially during the first weeks after a major procedure, where the patient is still at risk to develop DVT or PE.

Each type of prophylactic method that used in our practice is discussed below and our suggestions on when to use it and why follows. Methods that are considered ineffective for DVT/PE prophylaxis according to the literature are also mentioned. It is worth reminding our readers that most methods are prophylaxing against DVT, considering that PE is an extension of this problem.

12.3 Vena cava filters

Traditionally vena cava filters (VCF) are used in patients diagnosed with DVT or PE and that either have a contraindication for anticoagulation or those who developed this problem while on heparin therapy. Its use as prophylaxis for PE has gained popularity and acceptance in the trauma literature. It is accepted in patients at high risk such as those with severe pelvic fracture, multiple long bone injuries, severe craneoencephalic injury, or spinal cord injury.[21–24] Its use is supported in the literature for these patients especially if they are older than 55 years. These filters are usually placed percutaneously in the operating room (OR) or in the interventional radiology department. Bed-side placements of such devices in the intensive care unit have been reported as a safe option. Nevertheless, VCF do not offer any prophylaxis against DVT and the risk of PE is still present albeit reduced.

PE is recognized as one of the two most common causes of mortality after bariatric surgery. The other is intra-abdominal abscess after a gastrointestinal leak. There is no data to support the use of VCF for prophylaxis of PE for the morbidly obese patients except in the instance of a patient with history of DVT and a contraindication for heparin therapy. However, we believe that VCF inserted percutaneously should be considered in a selected group of bariatric patients. At our institution, pre-operative placement of VCF is considered for patients with past history of DVT or PE, venous insufficiency, or poor ambulation due to severe arthralgia. These patients should also be older than 50 years because the patency and efficacy of these devices has not been clearly proven beyond 20 years after insertion. The incidence of complications with the insertion of this device in the general population is around 2–5%, being formation of a

small hematoma or bleeding the most common. Displacement of the VCF is a very unusual complication in the experienced hands.

We placed the filters in our patients at least a week pre-operatively in the radiology suite due to the difficulty in performing this procedure in the OR suite. To this date, VCFs were used in 3% of the last 400 patients with no adverse effects. Two patients developed DVT despite adequate use of prophylaxis but no patient showed evidence of PE.

There are new devices available in the market that offer the possibility of temporary insertion of a VCF for a short period of time and are manufactured for providing easy extraction. To date, there is no report of the use of such device in the morbidly obese population or any study comparing its use with the traditional filters. If the safety and efficacy are proven to be similar to the available permanent devices, the number of patients to be considered for placement of a prophylactic VCF could increase significantly.

12.4 Mechanical devices

Different mechanical devices are available for the prophylaxis of DVT. They include:

- graded compression elastic stockings (ES);
- intermittent pneumatic compression (IPC);
- foot pump (FP).

All the above-mentioned devices have been used as a method for DVT prophylaxis. There is evidence of the superiority of the compression devices applied in the calf or feet over placebo.[25,26] Its efficacy has been attributed to the pump effect that they produced over the venous circulation in the lower extremities. This circulation is diminished while the patient is convalescent in bed due to the lack of muscle contraction acting as a venous pump. This is the only confirmed manner that these devices produce the desire effect for DVT prophylaxis. There is no convincing evidence that they produce a fibrinolytic effect as reported by few in the past.[27] Therefore, their use in the upper extremities is not indicated.

There is plenty of support to the fact that they reduced the incidence of DVT in the surgical population when compared to no prophylaxis. Despite the lack of strong evidence of an improved effect with other therapies such as heparin, they are frequently used with other prophylactic method if possible.[28,29] The main reason to recommend this practice is because its efficacy depends in the reliability of the patient wearing the device when in bed or not ambulating. It has been shown in our institution that surgical patients wear these devices less than 12 h a day.

Another consideration when using these devices in the morbidly obese population is the fact that many standard sizes of ES or IPC will not fit large patients. It is important to discuss the availability of extra large sizes for the device selected. Due to the previous observations the use of FP for the morbidly obese patients is recommended. With this relatively new device, one size fits all patients and patients report better tolerance of the product. The FP device should be applied at the beginning of the surgical procedure, taken with the patient to the recovery room and should be applied when the patient is not ambulating until discharge from the hospital. It is possible that if another method of prophylaxis is used, the addition of this device may not decrease the risk of a thromboembolic event. A multicentric randomized study would be necessary in order to have this question answered.

12.5 Use of anticoagulation

The most frequent and probably most effective method for DVT prophylaxis is the use of an agent that impairs formation of clot in the venous system.

Aspirin, an antiplatelet agent, has generally been found to be ineffective in preventing VTE in general surgery patients, and should not be used as an appropriate prophylaxis regimen.[30,31] Although not extensively documented, the use of Warfarin in full therapeutic doses may be effective in preventing extensive DVT in surgical patients. However, the delayed onset of action, the constant need for blood tests in order to monitor therapeutic levels, the risk of drug interaction and the increased risks of bleeding complications if not closely monitored, makes Warfarin a poor choice when considering the availability of other effective agents for bariatric surgery. However, Warfarin has been used in orthopedic surgery with great success.[32,33]

The choice most surgeons selected in the survey conducted among members of the ASBS was either low-dose unfractioned heparin (LDUH) or LMWH.[14] The former has been the tool used by most physicians for several decades. However, there is a rapid grow of evidence in the literature supporting LMWH at least as effective and safe as LDUH. Multiple trials compared the use of LMWH to LDUH. There seems to be a consensus regarding the fact that the administration of either drug is equally efficacious in preventing DVT in general surgery patients.[34,35] With similar efficacy, cost becomes an important determinant in the choice of these drugs.[36,37] In the US, LMWH is

significantly more expensive than LDUH. Nevertheless, the fact that LMWH can be administered easily and that its mode of action is more predictable has convinced us that it should be used in our bariatric patients.[38] Our recommendation is to start its use just prior to surgery and to continue with a 30 mg twice a day subcutaneously (s.c.) until the patient is discharged home. Most patients who present with DVT will do so within the first 2–4 weeks after surgery. When the patient is discharged from the hospital the risk of developing a thromboembolic event is real. This has motivated us to continue the administration of LMWH in those patients who are discharged form the hospital and did not show adequate ambulation or suffered an intra-operative complication. The dose that we used in this group of patients is 40 mg of Lovenox daily as an outpatient.

We also consider the use of Lovenox after discharge in patients that develop a major complication such as anastomotic leak, re-operation or major wound infection.

It is important to indicate that the appropriate dose of LMWH has not been studied in the morbidly obese. The pharmacokinetics are also not well described, therefore, we may be "under-prophylaxing" these patients. More research is needed to answer these types of questions.

The protocol that we follow at the Center for Bariatric Surgery in Connecticut is described below. This protocol was developed after analysis of the results of our survey that showed a tremendous variance among bariatric surgeons regarding DVT prophylaxis. Prior to the implementation of this protocol a 57-year-old patient died of PE 2 days after discharge and just 7 days after a gastric bypass. The protocol includes placement of a VCF for those patients considered to be of high risk as described above. All patients received LMWH twice a day while at home, starting just before the surgical procedure. Patients that were not ambulating well and did not have a filter placed were kept on LMWH once a day until the first visit to our office. Initially all patients were screened with bilateral lower extremity Duplex ultrasonography between days 5 and 7. This study was carried out in the first 200 patients with no positive result. Moreover, during the study six patients who developed DVT after discharge were screened in the hospital with Duplex ultrasound and had negative studies. Thus it is our opinion that, in the absence of any clinical signs, Duplex ultrasonography is not indicated in the first days after the surgical procedure. The protocol described above was used in 318 patients who underwent gastric bypass procedure (GBP). Six patients were diagnosed with DVT at an average of 4 weeks after the procedure (range of 3–9). Two patients presented with PE. There was no mortality related to a VTE event. We believe that our protocol has eliminated the occurrence of clinically significant DVT during the early post-operative period. However one must remain vigilant for signs and symptoms of DVT or PE in the early period after hospital discharge. Those patients should be assessed immediately and diagnostic tests to rule out DVT or PE should be performed promptly.

12.6 Venous thromboembolism prophylaxis protocol

1 Pre-operative period:
   (a) Consider VCF in high-risk patients.*
   (b) LMWH (for example Lovenox 30 mg s.c.) 1 h before procedure.
2 Post-operative period:
   (a) FP
   (b) LMWH (for example Lovenox 30 mg s.c. bid).
   (c) Early ambulation.
3 After discharge:
   (a) Continue ambulation or if unable to ambulate adequately, follow b.
   (b) LMWH (for example Lovenox 40 mg qd in a.m.).
   (c) Maintain high level of suspicion for DVT/PE.

12.7 Conclusion

DVT prophylaxis in patients having bariatric surgery should be based on adequate risk stratification combined with knowledge of the literature and with clinical judgment. Risk factors are cumulative and morbidly obese patients represent a portion of the surgical population who usually present with multiple risk factors. Both DVT and PE can occur not only while the patient is in the hospital but could also occur several weeks after surgery. An effective and broadly implemented prophylaxis regimen should be the standard of care for any obese patient being submitted to a surgical procedure.

There is a high variation of prophylaxis among the surgeons performing bariatric surgery. There are several points in DVT/PE prophylaxis that are supported by the literature such as: every bariatric patient should have prophylaxis and the LMWH or LDUH should be the basis for the prophylaxis. The addition of FP to all patients although recommended here is still a controversial topic in the literature. Placement of VCF in all high-risk patients, the use of LMWH in those patients with limited ambulation or surgical complications after discharge is strongly recommended

*see text for risk stratification.

by our group despite the lack of published evidence. Close follow up in the early post-operative period and maintenance of a high index of suspicion for DVT or PE is extremely important in order to prevent dangerous complications.

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SURGICAL ANTIBIOTIC PROPHYLAXIS 13

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13.1 Introduction

In developed countries, almost 25% of nosocomial infections are related to wound surgical infections. As a consequence of this, medical costs are increased in 20–30% while hospitalization time is almost duplicated. On the other hand, this type of infections may cause permanent disability.[1–5]

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The term "prophylaxis" refers to the precautions and actions to be taken in order to prevent diseases.

Every year, a large number of patients are undergoing surgical procedures and, surgical antibiotic prophylaxis (SAP) is used to prevent post-operative infections.

Post-operative infections have always limited the development of new surgical techniques.

Antibiotics must be used before many surgical procedures besides other infection control measures, the administration of appropriate antiseptics and the understanding of the physiopathology of infections. Although the principles of pre-operative administration of antibiotics in surgery have been clearly established,[6] this subject is still controversial.

Infections are a constant risk in surgical procedures. Bacteria are found in 90% of surgical incisions, notwithstanding the technique used or the surgical site (even in laminar flow environments). Initially, bacterial count is low, but its development is stimulated by favorable local conditions (hematoma, ischemia, modifications in the oxidation–reduction potential) and the weakening of the host's immune defenses as well. In case of patients undergoing surgery, the objective of antimicrobial prophylaxis therapy is the reduction of surgical site infections (SSI) through the prevention of microbial proliferation.

Its efficacy is well documented. One third of hospital antimicrobial agents are used in SAP, and this proportion increases in huge surgical centers.[7–13] In spite of all these aspects, its appropriate administration does not exceed 40%.[14–17]

As it is mentioned above, the bacterial contamination of a wound is unavoidable. The development of SSI depends on the size of the bacterial inoculum and on the tissue environment that promotes the growth of these microorganisms.

The appropriate use of SAP prevents bacterial proliferation, significantly reducing the rate of SSI.[18] In some procedures, this reduction exceeds 50%.

SAP does not prevent hospital infections not related to surgical sites, and it does not substitute efficient and verified infection control measures. It is an adjunct to appropriate preparation of the patient, adequate pre-operative evaluation, good surgical techniques, safe operating rooms and post-operative care. On the other hand, its inappropriate use selects resistant microorganisms, exposes the patient to adverse effects and unnecessarily increases costs.[12]

13.2 General concepts about surgical antibiotic prophylaxis

13.2.1 The ideal antimicrobial agent

Nowadays, due to the great variety of surgical procedures, it is unlikely that a single antimicrobial agent will be effective in all cases. Some conditions are required to consider an antimicrobial appropriate for prophylaxis:

1. The antimicrobial *must be active against germs likely involved* (Table 13.1).[19] Most of the frequent germs that appear in infections that complicate the different surgical procedures are known, but their colonization and susceptibility levels may substantially differ from one institution to another, and these variations must be taken into account.
2. The antimicrobial *must have low potential resistance induction*. It has been demonstrated that the indiscriminated use of antibiotics may modify the predominant eco-system and may stimulate the appearance of high resistant strains. This is a good reason for using prophylaxis of short duration and antibiotics against the most dangerous germs. Some antimicrobials, like rifampicin and quinolone, must be avoided in prophylaxis because they can easily induce bacterial resistance of chromosomal type. As the resistance selection depends on the time of exposure, prophylaxis must be short.
3. The antimicrobial *must have effective tissue penetration*. When the surgical incision occurs, the tissue levels of antimicrobials at the tissues on risk must be appropriate.[8] It is difficult to estimate the best antimicrobial concentrations necessary to prevent post-operative infections in surgical sites. Although the antimicrobial preventive effects may be reached in tissue concentrations above or below minimal inhibitory concentration (MIC), many researches have determined a higher impact on the reduction of post-operative infections with microbial tissue concentrations above MIC.
4. Half-life of antimicrobials must be long enough to be effective during the whole surgical procedure (this subject will be developed below).[20]
5. *The antimicrobial toxicity must be as low as possible*. Unpredictable toxicity, not depending on the dose, like the Lyell Syndrome related to sulfonamide or agranulocytosis related to chloramphenicol, makes these antimicrobials not adequate for prophylaxis. Patients with a serious B-lactamase allergy should not use these antimicrobials for prophylaxis.
6. The antimicrobial *must not have pharmacologic interaction with anesthetic agents*, especially with neuromuscular relaxants (drugs like curare). This

Table 13.1 Antimicrobial prophylaxis: recommendations according to procedure

Procedure	Microorganisms	Recommended antibiotics	Adult dosages
Cutaneous	*S. aureus*, *S. epidermidis*	With no uniform recommendation*	
Head and neck	*S. aureus*, *streptococci*	Cefazolin#	1–2 g i.v.
Neurosurgery	*S. aureus*, *S. epidermidis*	Cefazolin#	1–2 g i.v.
Thoracic	*S. aureus*, *S. epidermidis*	Cefazolin#	1–2 g i.v.
Cardiac	*S. aureus*, *S. epidermidis*	Cefazolin#	1–2 g i.v.
Abdominal			
• Gastroduodenal	Gram-positive cocci, Gram-negative bacilli	High risk: cefazolin#	1–2 g i.v.
• Colorectal	Gram-negative bacilli, anaerobes	A. Oral: neomycin and erythromycin base B. Parenteral: cefotetan or cefoxitin#	A. 1 g oral (three doses). B. 1–2 g i.v.
• Appendectomy	Gram-negative bacilli, anaerobes	Cefotetan or cefoxitin#	1–2 g i.v.
• Biliary tract	Gram-negative bacilli	High-risk: cefazolin#	1–2 g i.v.
Gynecologic and Obstetric	Gram-negative bacilli, *Streptococcus* group B, anaerobes	Cefazolin#	1–2 g i.v.
Urologic	*S. aureus*, *S. epidermidis*	Cefazolin#	1–2 g i.v.
Orthopedic	*S. aureus*, *S. epidermidis*	Cefazolin#	1–2 g i.v.
Cardiovascular	*S. aureus*, *S. epidermidis*, Gram-negative bacilli	Cefazolin#	1–2 g i.v.
Breast and hernia	*S. aureus*, *S. epidermidis*	High-risk: cefazolin‡	1–2 g i.v.

In all parenteral prophylaxis cases, the antibiotic administration must occur 30 min prior to incision in the surgical site and must be repeated every 1–2 half-lives (for example, cefazolin, every 3–4 h).

* Appropriate local wound care is recommended. Cefazolin may be used.

Patients allergic to penicillin and cephalosporins may use vancomycin (1 g i.v.) to provide activity against Gram-positive cocci. If activity against aerobic Gram-negative enteric bacilli is needed, aztreonam (1 or 2 g i.v.) or AG in doses of 3 mg/kg/day i.v. may be added. If activity against anaerobic flora is needed, the alternative for patients with B-lactamase allergy is to use clindamycin 900 mg i.v. plus AG or aztreonam.

‡ Vancomycin may be used if high levels of methycilin-resistant staphylococci have been detected in hospital.

is the reason for not administering polymyxins or aminoglycosides (AG) for prophylaxis.

7 Antimicrobials *must be cost effective.* Cost effectiveness is calculated comparing the cost of antimicrobial prophylaxis and the cost of post-operative infection. Amoxicillin-clavulanate and first-generation cephalosporins are cost effective when they are administered in a single dose for prophylaxis in surgeries with less than 2% of post-operative infectious complications. In order to consider an antimicrobial prophylaxis of 24 h cost effective, the post-operative infection rate should be of 4% for first-generation cephalosporins, 6% for second- and third-generation cephalosporins, 20% for piperacillin and 30% for imipenem. In some cases, the use of drugs of broad-spectrum is recommended for prophylaxis: pre-operative hospital stays of more than 3 days, hospital outbreaks caused by with multi-resistant bacteria and previous surgical procedures.

According to these pharmacokinetic and microbiologic considerations, it can be said that, except in those situations of significant antianaerobe activity, the first-generation cephalosporin, especially cefazolin, is the antimicrobial that better meets those requirements since it provides a high peak concentration and also adequate and sustained levels for longer periods.[21] Due to these pharmacokinetic characteristics, it has better therapeutic effects during the period of bacterial contamination. Antimicrobials with narrow spectrum of activity, appropriate for a specific clinical situation, must always be used in order to reduce adverse effects, unnecessary cost and increase of bacterial resistance. Modern and broad-spectrum antimicrobials must be administered in special situations[18], supported by the Infection Control Committee (or team group that rationalizes antimicrobial administration), and when its benefits do not represent a risk for the community.

The use of third-generation cephalosporin's and antimicrobials that can easily stimulate the appearance of bacterial resistance, such as quinolone and rifampicin, is not recommended.[18] The glycopeptides (vancomycin and teicoplanin) must be used only in those situations

where there is no other alternative (high-risk clean procedures in institutions with high rates of infection caused by methycilin-resistant staphylococci), with the aim of reducing the risk of appearance of enterococci resistant to this group of agents.[22]

13.2.2 Route of administration

Intravenous (i.v.) route is the most frequently used. A low dose infusion of antibiotics diluted with a small volume of solvent provides rapid high plasmatic and tissue concentrations.

Intramuscular (i.m.) route is not the ideal, because absorption is slow and unpredictable, and tissue concentrations are low.[23] Topical administration has drawn considerable attention over the last few years, like the use of cements with antibiotics in orthopedic prosthesis even when its efficacy in the prevention of deep-seated infections remains controversial. Oral route is only used to decontaminate the gastrointestinal tract prior to scheduled colorectal[24] elective surgery and in some special cases of urologic and ophthalmic surgery.

13.2.3 Timing of administration and duration

In 1961, Burke established that antimicrobial prophylaxis is only useful if administered in the surgical site before bacterial contamination occurs.[25] Ideally, *the interval between i.v. administration of antibiotics (at induction of anesthesia) and surgical incision should be from 30 to 60 min*.[26–28] The exception to the rule is the cesarean procedure, in which SAP should be administered immediately after cross-clamping of the umbilical cord.

An earlier administration could cause low tissue concentrations at the end of surgery (without re-injections).[27,29]

Short prophylaxis causes fewer alterations in the endogenous flora and does not stimulate the development of resistant strains.[12] Most professionals recommend that antimicrobial prophylaxis should not exceed 24 h. Recent revisions to single dose prophylaxis regimens, by Di Piro and colleagues, mentioned more than 40 clinical studies showing that single dose prophylaxis regimens have proved to be as effective as multi-dose regimens.[30] It has been demonstrated that multi-dose regimens have not been very useful to prevent wound infections in colorectal, gastric and transurethral surgery and in hysterectomy and cesarean procedures although post-operative deep-seated infections (endometritis, pelvis or intra-abdominal abscesses) have been rarely studied. Preliminary data suggest that in orthopedic and cardiac surgeries, as well as in neurosurgery, single dose prophylaxis regimens have proved to be as effective as multi-dose regimens, although in order to recommend a single dose, more studies are needed.

The only evidence against single doses is appendectomy, but this may be a result of heterogeneous clinical manifestations (normal, inflamed, gangrenous and perforated appendix).

In these last situations, prolonged antibiotic therapy is required rather than prophylaxis.

When short half-life drugs are used (for example, cefoxitin and cefamandole), a dose every 2 or 3 h is required in order to be effective. The need of repeating the prophylactic antibiotic dose in lengthy procedures is not clearly stated in specialized bibliography. However, a large number of references mention the reduction in effectiveness of the single-dose prophylaxis in lengthy procedures where the tissue and plasmatic concentrations of antimicrobials may decrease at the end of it. Available information indicates that *an extra dose of antimicrobial should be administered at intervals of one or two times the plasmatic half-life of the drug used in order to ensure adequate tissue concentrations throughout the duration of the surgical procedure* (Table 13.2).

13.2.4 Indications

Antimicrobial prophylaxis is indicated when there exists post-surgical risk of infection. This risk mostly depends on the type of surgical procedure. *Nowadays, it is recommended to indicate antimicrobial prophylaxis for procedures where infection is less serious but more frequent, and for those where infection is not frequent but serious or life threatening.*

The contamination of the surgical wound is unavoidable phenomenon after incision and surgical manipulation that adding to temporary ischemia allows

Table 13.2 Half-life of the most common antibiotics used for prophylaxis

Antibiotic	Half-life (hours)
Cefazolin	1.8
Vancomycin	3–9
Cefoxitin	0.6–1
Cefotetan	3–4.6
Aminoglycoside	2
Metronidazole	8
Clindamycin	2.4–3
Ciprofloxacin	3–5

bacterial development in normally colonized areas. In this context, the possibility of development of a surgical wound infection depends on a complex interaction between different factors as initial bacterial load into the surgical site, patient factors and surgical techniques are surgical factors and patients factors.[3–5,31]

Surgical factors

Surgical procedures have been classified in categories (Altemeier categories) according to the post-surgical risk of infection:[32,33]

- **Category 1**: *Clean surgical procedure*: includes procedures in optimal conditions, with primary closure of surgical wounds without drains, without trauma or inflammation, good surgical technique and no compromise of oropharyngeal, digestive, urinary or respiratory tracts.
- **Category 2**: *Clean-contaminated surgical procedures*: includes procedures involving genitourinary tract (with a negative urine culture), respiratory tract, digestive tract in favorable conditions and without abnormal contamination (for example appendectomy), oropharingeal and biliary tract (not encountering infected bile).
  Procedures with minor break in asepsis standards and drains are also included in this category.
- **Category 3**: *Contaminated surgical procedures*: includes procedures involving recent trauma, perforation of biliar or urinary tract in presence of infected urine or bile, a high degree of contamination in the digestive tract, major break in asepsis standards and acute macroscopic non-purulent inflammation.
- **Category 4**: *Dirty surgical procedures*: includes procedures involving contaminated wounds, ischemic tissue, purulent bacterial infection, fecal contamination, foreign bodies and perforated viscera.

The risk of post-operative infection varies according to the different categories: It varies from less than 1% in clean surgical procedures to more than 30% in dirty surgical procedures (Table13.3). In a surveillance including more than 60,000 different surgical procedures, Cruse and his colleagues reported that the overall infection rate was 4.7%, ranging from 1.5% for clean surgeries to 40% or less for dirty surgeries. In the practice, more than 90% of surgeries are clean or clean-contaminated.[31]

Patients factors

The parameters used in the American Society of Anesthesiologists (ASA) *score* easily reflex the patient's health condition. This evaluation system is widely considered one of the most important methods to quantify this point before the surgery.[3–5,7,34–36]

13.2.5 Centers for Diseases Control risk of surgical infection score

Patients with risk of post-surgical infections must also be evaluated according to the post-operative risk of infection score stated by Centers for Diseases Control (CDC). According to National Nosocomial Surveillance System (NNIS), this evaluation is based on three independent factors associated with post-operative infection. Patients are classified from 1 to 3 according to the following description:

- 1 point: Class 3, 4 and 5 of the ASA[37] (Table 13.4).
- 1 point: Categories 3 and 4 of Altemeier.

Table 13.3 Classification of surgical procedures and risk of infection

Classification	Criteria	Risk (%)
Clean	Elective, non-emergency surgery, non-traumatic, primarily closed, no inflammation, no break in asepsis technique.	<2
Clean-contaminated	Emergency surgery: elective opening of respiratory, gastrointestinal, biliary or genitourinary tract; with minimal spillage (for example, appendectomy); not encountering infected urine or bile; minor break in asepsis technique.	<10
Contaminated	Macroscopic non-purulent inflammation, gross spillage from gastrointestinal tract; entry into biliary or genitourinary tract in the presence of infected bile or urine; major break in asepsis technique, penetrating trauma of less than 4 h old; open wounds to be covered or grafted.	~20
Dirty	Macroscopic purulent inflammation (for example, abscess); pre-operative perforation of respiratory, gastrointestinal, biliary, or genitourinary tract; penetrating trauma of more than 4 h old.	~40

Table 13.4 Anesthetic risk evaluation – ASA *score*

Class 1	Healthy patient
Class 2	Patient with mild systemic disease
Class 3	Patient with a severe systemic disease, which is not incapacitating
Class 4	Patient with an incapacitating systemic disease that is a constant threat to life
Class 5	Moribund patient not expected to survive more than 24 h, with or without surgery

"E" must be added to above if operation is an emergency

Adapted from Ref. [37].

Table 13.5 Surgical-time for some of the most frequent operative procedures

Operative procedure	Surgical time from incision (h)	Operative procedure	Surgical time from incision (h)
Cardiac surgery	5	Limb amputation	1
Thoracic surgery	3	Vascular surgery	2
Appendectomy	1	Joint prosthesis	3
Cholecystectomy	2	Mastectomy	2
Colon surgery	3	Herniorrhaphy	2
Gastric surgery	3	Prostatectomy	4
Laparotomy	2	Cesarean section	1
Open reduction fracture	2	Abdominal hysterectomy	3

Adapted from Ref. [7].

Table 13.6 Factors associated with increased risk of infection

Systemic factors	Local factors
• Diabetes	• Foreign bodies
• Corticosteroids use	• Electrocautery
• Obesity	• Injection with epinephrine
• Extremes of age	• Wound drains
• Malnutrition	• Hair removal with razor
• Recent surgeries	• Previous irradiation of surgical site
• Massive transfusions	
• Multiple (three or more) pre-operative medical diagnosis	
• ASA Class 3, 4 or 5	

Adapted from Ref. [36].

- 1 point: Duration of surgery $>$ *T*-hours (when surgery lasts *T*-hours more than its standard surgical duration, post-operative infection risk increases). Each surgical procedure has a standard duration established by NNIS (Table 13.5).

Post-operative overall risk of infection ranges from 1.5% to 13% from categories 0 to 3. Therefore, for patients with high score, antimicrobial prophylaxis may be recommended, even if it is not included in traditional guidelines.

Patients with special risk of infection must be identified before all surgical procedures (Table 13.6).[36] This group includes those patients that may be colonized with hospital flora (hospitalized more than 48 h prior to surgery), those patients previously treated with antibiotics or previously operated on for other than non-infectious reasons, and immunocompromised

Table 13.7 Prevailing rate of SSI over 59,352 hospitalized patients in 1975/76, according to wound class and risk factors

Wound class	Total (%)	High-risk (%)	Intermediate risk (%)	Low-risk (%)
Clean	2.9	15.8	3.9	1.1
Clean contaminated	3.9	17.7	2.8	0.6
Contaminated	8.5	23.9	4.5	–
Dirty	12.6	27.4	6.7	–

Adapted from Ref. [34].

patients (patients with a history of radiotherapy, steroidtherapy, chemotherapy, organ transplant, diabetes, elderly or *obese persons* or those who have lost weight).

Although the unfavorable influence of these factors on the incidence of post-operative infections is poorly documented, it cannot be discarded. In these cases, modified antimicrobial prophylaxis may be prescribed, for example, new cephalosporin or quinolone, but only for short periods, not beyond 24–48 h.

Finally, the specific risk of wound surgical infection can be well estimated with the combination of the three main evaluation systems: ASA score (patient factors), wound surgical type (as expression of the initial bacterial load) and *T* time-score (surgical techniques factor) (Table 13.7).

13.3 Recommendations regarding usage of surgical antibiotic prophylaxis

The following are specific considerations for each surgical procedure related to each surgical site.[8,18,22,26,29]

13.3.1 Orthopedics and traumatologic surgery

Antimicrobial prophylaxis is clearly recommended for certain orthopedics procedures: insertion of a prosthetic joint, revision of a prosthesic joint, hip fracture reduction, closed fracture reduction and open fracture reduction. In these procedures, post-operative risk of infection varies from 5% to 15%, and decreases to less than 3% with the use of antimicrobial prophylaxis. *Staphylococcus aureus and Staphylococcus epidermis* are the predominating germs in prosthesis infections and surgical wounds; therefore, the use of first-generation cephalosporins (cefazolin) is the appropriate prophylaxis. The additional use of aminoglycocides and the extension of prophylaxis for more than 24 h post-operative lack scientific evidence.

Regarding total hip joint replacement, the post-operative infection rate fluctuates between 3% and 5%. Antimicrobial prophylaxis can reduce this risk to less than 1%. These benefits become particularly significant when surgery occurs in environments with no laminar flow. Early re-operations due to non-infectious reasons (bleeding, dislocation) require an antimicrobial regimen different from the one used in the first surgery. In these situations, vanconycin is recommended. In some cases, it may be necessary to add prophylaxis against Gram-negative bacilli (for example, third-generation cephalosporins) according to the ecologic condition of the surgical center. Late re-operations due to non-infectious reasons (for example, mechanical problems) in ambulatory patients do not require modifications in the standard prophylaxis regimen.

13.3.2 Neurosurgical procedures

The risk of infection in craniotomy, without antimicrobial prophylaxis and not involving the placement of foreign bodies (*shunts*) varies between 1% and 5%. This risk increases at an average rate of 10% when a *shunt* placement occurs. Recently, after the revision of available data, prophylaxis indications have been limited only to craniotomy (because of the terrible consequences of these type of infections)[38] and *shunt* placement (because rates of infection could be reduced by 50%)[39]. The reduction in surgical infection risk is unquestionable in the case of craniotomy, and very probable in the case of surgery of *shunt* placement. Antimicrobial prophylaxis targets *S. aureus and S. epidermis*, and the antimicrobial regimens assessed have been the following: combinations such as cefazolin plus gentamycin, or single-agent therapy with cefazolin, vancomycin, piperacillin and cloxacilline, with no significant differences among them. Until further data are available, cefazolin is considered the appropriate agent.

13.3.3 Ophthalmologic procedures

The most dangerous infection in ophthalmologic surgery is endophthalmitis, which appears in elective ocular surgeries (scheduled) with very low incidence (three per 1000 in France). The administration of antimicrobial prophylaxis must not be indicated except for intra-ocular lens surgery or intra-ocular cataract surgery in cases of patients with diabetes.

13.3.4 Thoracic and peripheral cardiovascular procedures

Cardiac surgery is considered a clean surgery. The extracorporeal circulation, the procedure duration and its complexity, may increase the risk of sternal and/or mediastinal wound infection, high morbidity and mortality pathologies. The effectiveness of antimicrobial prophylaxis in cardiac surgery has been clearly demonstrated. First, second and third-generation cefalosporins and vanconycin in cardiac surgery prophylaxis have been studied, without observing any significant differences in their effectiveness, therefore, the drug generally used in these situations is cefazolin.

Vascular peripheral surgery is considered a clean surgery, except in the case of gangrene. The topographic proximity with the scarpa triangle, the re-operations or unfavorable conditions such as diabetes and obesity may increase the risk of infection, which is especially high when prosthesis material is placed. It has been clearly demonstrated that antimicrobial prophylaxis reduces the risk of wound infection in this kind of surgeries. Available information supports the use of prophylaxis in procedures with prosthesis placement and groin incisions. As *S. auereus and S. epidermis* are the predominant germs, cefazolin is the appropriate agent. Prophylaxis is not recommended for carotid endarterectomy.

Non-cardiac thoracic surgery may be a clean (mediastinal surgery) or a clean-contaminated surgery (when the respiratory: lobectomy, pneumonectomy or gastrointestinal tract is entered). In spite of the complexity of these situations and according to recent studies, the administration of antimicrobial prophylaxis is no longer controversial. Cefazolin is the agent recommended in these situations. Some authors recommended prophylaxis with cefazolin to placement a tube for pleural drainage after thorax trauma to reduce the incidence of pneumonia and empyema.[40]

The optimal duration of antimicrobial prophylaxis in thoracic surgery, cardiac or not, remains a debated topic: even though some clinicians insist on extending prophylaxis for more than 24 h or until the drainage tubes and catheters are removed, these actions lack scientific evidence. At present, prophylaxis is recommended only for 24 h post-procedure.

13.3.5 Gastrointestinal procedures

When the gastrointestinal tract is entered, the surgeries may be clean, clean-dirty or dirty.

Antimicrobial prophylaxis is recommended for most gastrointestinal procedures. The number of microorganisms and the proportion of anaerobic germs increase along the gastrointestinal tract, so the recommendation will depend on the segment of gastrointestinal tract entered during the procedure. The intrinsic risk of infection associated with procedures entering stomach, duodenum and proximal small bowel is quite low, but in cases of increased gastric pH (antacid, proton pump inhibitors or histamine H1 blockers) and in upper gastrointestinal bleeding or obstruction, where the surgical risk of infection increases, antimicrobial prophylaxis is recommended. Although the local flora may be altered in these situations, a single-dose of 1 g of cefazolin is recommended at induction of anesthesia. *To summarize, if the procedure enters the stomach (for example, gastric bypass, Scopinaro technique or duodenal switch) duodenum or proximal small bowel, antimicrobial prophylaxis is required when there has been previous use of antacids, proton pump inhibitors or H1 blockers (as frequently used to reduce volume and acidity of gastric content due to the eventually increased risk of gastric peri-anesthetic aspiration).*

Colorectal procedures have a very high intrinsic risk of infection (dirty procedures), therefore, antimicrobial prophylaxis is strongly recommended. Several studies have demonstrated efficacy in these procedures, with rates of post-operative infection decreasing from over 50% to less than 9%. Antibiotic spectrum is directed at Gram-negative aerobes and anaerobes bacteria. Different strategies using antibiotics, parenterally or orally administered, are used together with mechanical cleansing of the digestive tract with purgatives such as polyethylene glycol, mannitol, magnesium citrate or enemas. Those procedures reduce but do not eliminate the risk of infection, since with mechanical preparation only; the risk of infection is close to 30%. Therefore, additional prophylaxis is recommended: options include either oral (intraluminal) antibiotics given the day before operation or parenteral antibiotics, immediately before operation. Trials comparing intraluminal preparation with intraluminal preparation plus parenteral administration have produced mixed results. The common practice among surgeons in the US uses both intraluminal

(the day before) and parenteral (at induction of anesthesia) prophylaxis.[40,41]

Various intraluminal regimens appear to have similar efficacies according to controlled studies. One recommended regimen consists of erythromycin base and neomycin given at 1, 2, and 11 p.m. (1 g of each drug per dose) the day before a procedure scheduled for 8 a.m. (the first dose given 19 h before surgery). Erythromycin can be substituted for metronidazole and kanamycin can be substituted for neomycin. If parenteral prophylaxis is desired, a second-generation cephalosporin with activity against anaerobic organisms is recommended, such as cefoxitin.

To summarize prophylaxis of colorectal procedures includes the following:

- Mechanical cleansing of the colon, starting the day before surgery (until elimination of fecal matter, or until 4–6 h before surgery).
- Neomycin and erythromycin base (1 g of each medication orally at 1, 2, and 11 p.m. on the day before surgery, starting 19 h before the anticipated starting time of the procedure).
- Intravenous (i.v.) administration of 1 g of cefoxitin at induction of anesthesia (within 30 min before incision).

Prophylaxis is also recommended for appendectomy. Although the intrinsic risk of infection is low for uncomplicated appendicitis, the pre-operative status of the patient's appendix is not known. Cefoxitin is the recommended agent, but other acceptable alternatives are metronidazole combined with aminoglycoside or quinolone. For uncomplicated appendicitis, coverage needs not be extended to the post-operative period. Complicated appendicitis (for example, with accompanying perforation or gangrene) needs indication for antibiotic therapy for several days. In biliary tract surgeries, the prophylaxis recommendation depends on the presence of specific risk factors: in general, prophylaxis for elective cholecystectomy (either open or laparoscopic) may be regarded as optional. Risk factors associated with an increase incidence of bacteria in the biliary tract include: age (over 60 years), disease of the common bile duct, diagnosis of cholecystitis, presence of jaundice and previous history of biliary tract surgery.

13.3.6 Urologic procedures

Urologic procedures may be performed either with sterile urine (confirmed by a pre-operative negative urine culture) or with infested urine that requires therapy. In general, it is recommended to achieve pre-operative sterilization of the urine, if clinically feasible. For procedures entailing the creation of urinary conduits, recommendations are similar to those for procedures pertaining to the specific segment of the intestinal tract being used for the conduit. Procedures not requiring entry into the intestinal tract and performed in the context of sterile urine are regarded as clean procedures. However, it should be recognized that prophylaxis for specific urologic procedures has not been fully evaluated.

13.3.7 Obstetric and gynecologic procedures

Prophylaxis is clearly indicated for vaginal hysterectomy. For abdominal hysterectomy, and in spite of the different results of some studies, its similarity with abdominal surgery justifies the use of similar prophylaxis. For high-risk Cesarean section (emergency, membrane rupture for more than 12 h, previous fever), not withstanding the indicated prophylaxis regimen, it is agreed to administer it only after the cord is clamped (to avoid exposing the newborn to antimicrobials). Numerous clinical trials have shown a reduction in risk of wound infection and endometritis by as much as 70%. Despite the theoretical need to cover Gram-negative and anaerobic organisms, studies have not demonstrated significant differences between cefazolin and broad-spectrum antibiotics in prophylaxis. Therefore, cefazolin is the recommended agent.

As regards to breast surgery, there is only one study, which has demonstrated its efficacy. For this procedure, cephalosporin with activity against *Staphylococcus* (cefazolin, cefamandole, cefuroxime) is recommended (see below).

13.3.8 Oral and cervicofacial procedures

The risk of infection is high in cervicofacial procedures where buccopharyngeal cavity is entered (especially oncologic surgery). Many studies have clearly established the efficacy of antimicrobial prophylaxis in this type of procedures, with a reduction of approximately 50% in surgical wound infections.

In these cases, cefazolin is generally recommended. As it has been demonstrated by controlled studies, prophylaxis must not exceed 48 h. Drains, is not a valid reason for extending it.

Antimicrobial prophylaxis is not recommended for dentoalveolar procedures, unless for immunocompromised patients or patients who need to receive bacterial endocarditis prophylaxis (for example, valvular disease with insufficiency, previous endocarditis, etc.).

13.3.9 Plastic and reconstructive procedures

In the absence of appropriate controlled studies on this field, recommendations on Table 13.10 are suggested.

13.3.10 Cutaneous and superficial soft tissue procedures

Antimicrobial prophylaxis is not indicated for cutaneous and superficial soft tissue procedures. For patients with two or more significant risk factors (Table 13.6), prophylaxis is acceptable but optional.

13.3.11 Breast and hernioplasty procedures

In the past few years, several studies have mentioned the reduction of the rate of surgical wound infections in two situations of clean surgery: breast and hernioplasty procedures, whose intrinsic risk of infection, although low, can be reduced. This prophylaxis is considered optional. In radical and modified mastectomy, and in resection of nodules with axilla incisions, the risk of infection is higher and prophylaxis is recommended. Cefazolin is the recommended agent.

13.3.12 Laparoscopic and thoracoscopic procedures

Laparoscopic procedures follow similar indications to conventional procedures, due to their identical surgical techniques; only the entry changes. It must be considered that *any laparoscopic procedure may result in a laparotomy.*

There is no available data on the efficacy of antimicrobial prophylaxis in these procedures. Until new specific information is available, same indications as in similar open procedures are followed. It is useful to take account of the microbiologic flora of each site in order to choose the best antibiotic option in each endoscopy procedures (see Table 13.8).[23] Time ago, morbid obesity had been considered as a contraindication for video-assisted laparoscopic cholecystectomy. However, more recently it has been demonstrated that not only it can be performed with low rates of complications but also that many experts recommend this procedure as the best first approach for any surgical procedure including bariatric surgery in these patients. No major post-operative morbidity and no cases of mortality occurred among one group of 90 obese patients undergoing video-assisted laparoscopic cholecystectomy. Open conversion was not necessary among this group. It is important that conventional open surgery has been related to high rates of pulmonary and cardiovascular complications, thromboembolism and wound infections.[42]

13.3.13 Special procedures in obese patients

Laparoscopic Roux-en-y gastric bypass is a new and technically challenging surgical procedure for treating morbidly obese patients. Antibiotic prophylaxis must follow the general principles of laparoscopy and gastroduodenal surgery. Operative time and leaks decreased with experience and improved techniques. The main advantage of this procedure is a very low risk of wound complications including infections and hernia. In a recently published experience, 281 consecutive patients were evaluated. Only 1.5% developed a major wound infection following a re-operation

Table 13.8 Microbiology of post-operative infections

Surgical site	Microorganisms aerobes	Microorganisms anaerobes
Mouth, esophagus	*Streptococcus* spp.	Non-*fragilis Bacteroides*, *Fusobacterium* spp., *Peptostreptococcus* spp.
Stomach	*Streptococcus* spp., enterobacteria and/or other gram-negative aerobic bacteria	Same as above
Biliary tract	Enterobacteria and/or other gram-negative aerobic bacteria, *Streptococcus* group "D"	*Clostridium* spp.
Ileum, colon and feminine genital system	Enterobacteria and/or other gram-negative aerobic bacteria	*Bacteroides fragilis, Peptostreptococcus* spp., *Clostridium* spp.
Urinary tract	Enterobacteria and/or other gram-negative aerobic bacteria, *Streptococcus* group "D"	———
Orthopedic and cardiovascular	*Staphylococcus* spp., *Streptococcus* spp.	———
Other clean surgeries	*Staphylococcus* spp.	———

Adapted from Ref. [23].

for a complication or open conversion and 5.1% had an anastomotic leak with peritonitis and required open or laparoscopy repair and drainage.[43]

Laparoscopic adjustable gastric banding is another safe and effective treatment method for morbid obesity. Low rate of early complication (6%) including infections (4%) and a high rate of late complications (30%) as band slippage, gastric erosion with band migration and tubing leaks have been described after these procedures in diabetic patients.[44] In these patients, *S. aureus* colonization should be evaluated in pre-operative visit in order to treat and reduce the risk of infection.

Some complications as injection port dislocation, access port infection and tube perforation can require a re-operation and sometimes it is necessary to remove the band. A new technique was recently described to fix the port and avoid complications. The port is sutured onto a polypropylene mesh, which is then cut into shape and attached to the rectus fascia in the left hypochondrium with a Tacker stapling device. Stability reduces the risk of infection and incidental tube perforation.[45]

Well-known scientific societies have published recommendations about SAP (Surgical Infection Society, American Society of Hospital Pharmacy, French Society of Anesthesia and Intensive Care, Infectious Diseases Society of America, Sociedad Argentina de Infectología) and prestigious textbooks on infectology (Mandell Gl, Bennett JE and Dolin R. Principles and Practice of Infectious Diseases) show diverse opinions on certain subjects that still remain controversial (Table 13.9).

Widespread recommendations concerning antimicrobial prophylaxis are shown in detail in Table 13.10.

13.4 Controversies over surgical antibiotic prophylaxis

13.4.1 Cefazolin or cephalothin?

Based on scientific evidences, guidelines and recommendations on SAP in different countries include *cefazolin as the most frequently used antibiotic in most surgical procedures.* The principal benefits of this drug are its half-life (1.8 h) that permits its administration every 8 h, which is beneficial in long surgical procedures, and the high and sustained levels of serum and tissue achieved after its administration.[20] Despite cefazolin's well-known pharmacokinetic advantages and the scientific evidences supporting its use, in our country, cefalotin is usually recommended for prophylaxis due to economic reasons. A thorough analysis of specialized bibliography shows that there are not many works supporting the use of cefalotin for prophylaxis in certain surgeries. In central cardiovascular surgery, a less number of failures in prophylaxis using cefalotin rather than cefazolin has been shown, probably due to cephalothin's greater stability against B-lactamase.[46] However, in most surgical procedures, cephalothin has not proved to be effective in prophylaxis; therefore, using it instead of cefazolin is risky.

Recommendation: According to available data, the use of cefazolin as the cephalosporin of choice for SAP is recommended. The use of cephalothin is not contraindicated and is a valid alternative. Its use is probably preferred in central cardiovascular surgery. It is advisable for those hospitals that use cephalothin regularly, to elaborate strategies in order to check its replacement with cefazolin in the therapeutic form when sap is indicated. It is prudent to agree this measure beforehand with the surgical services in order to guarantee a successful implementation.

13.4.2 Antimicrobial prophylaxis in clean surgeries?

The use of SAP is controversial in surgeries where expected infection ranges from 3% to 5%. There is consensus on specifically recommending SAP in clean surgeries where an infectious complication would represent high morbidity or mortality, and high costs (such as morbid obesity); even with low rates of expected SSI (for example, central cardiovascular surgery). On the contrary, although exist studies supporting its use, its indication is controversial in surgeries where the risk of infection is low and the consequences of infectious complications are hardly associated to a higher rate of morbidity and mortality (for example, hernioplasty and breast surgery).[13,47,48] However, we must consider the fact that, in our country, the rates of SSI are higher than in those countries where the cost–benefit analysis has been made, and also that the cost of a single-dose of third-generation cephalosporin, appropriately administered, is not relevant, specially if it is compared to the cost of a post-operative infection.

Recommendation: To encourage the use of antimicrobial prophylaxis in those clean surgeries where the cost–benefit relation is uncertain, assuring through appropriate programs that only a pre-operative single dose of cefazolin is administered and its use discontinued post-operatively. Therefore, benefit is higher than costs and the potential risk of an increase in bacterial resistance, pharmacologic adverse effects and economic detriments is avoided. However, in hospitals with very low rates of infections in clean surgeries due to an appropriate system of surveillance, SAP

Table 13.9 Recommendations about prophylaxis according to different sources including scientific societies

Procedures	Principles and practice of infectious diseases (Mandell *et al.*)	Infectious Diseases Society of America (IDSA)	French Society of Anesthesia	Surgical Infection Society	American Society of Hospital Pharmacy	Sociedad Argentina de Infectología (SADI)
Cardiac	Yes: for median sternotomy, coronary artery bypass, grafting, valve surgery and permanent pacemaker insertion. Cefazolin. Cefuroxime, cefamandole or vancomycin if the rate of failure is high.	Yes: cefazolin. Vancomycin if the rate of oxacilin-resistant pathogens is high.	Yes: cefazolin or cefuroxime. Alternative: vancomycin.	Yes: cefazolin. Vancomycin if the rate of failure is high.	Yes: cefazolin or cefuroxime.	Yes: cefazolin or cephalothin. (with or without prosthesis material).
Non-cardiac thoracic	Yes for lobectomy and pneumonectomy. Cefazolin.	Yes: cefazolin.	Yes: cefazolin or cefuroxime. Alternative: vancomycin.	Yes: cefazolin.	Yes: cefazolin or cefuroxime.	Yes, cefazolin or cephalothin for lung resection, mediastinum surgery or placement of a tube pleural drainage.
Vascular	Yes: cefazolin or vancomycin. (In carotid artery surgery only when a rate of infection is high).	Yes: for aortic repair, abdominal or lower limbs surgery or prosthesis implant. Cefazolin. Vancomycin if the rate of oxacilin-resistant pathogens is high.	Yes: for major arteries, not for vein surgery. Cefazolin or cefuroxime. Alternative: vancomycin.	Yes: cefazolin.	Yes: for lower abdomen and vascular accesses surgery. Cefazolin.	Yes: cefazolin or cephalothin. Especially for aortic repair, abdominal or lower limbs surgery with prosthesis implant and permanent pacemaker insertion. No for vascular catheters insertion (Swang-Ganz, hemodialysis) or for vein surgery.
Orthopedic	Yes: for arthroplasty of joint including replacement, open reductions of fracture (Cefazolin). Open fracture are considerer contaminated and required treatment. For lower limb amputation (cefoxitin). Not for laminectomy and spinal fusion.	Yes: for implant of prosthesis material. Cefazolin. Vancomycin if the rate of oxacilin-resistant pathogens is high.	Yes: for all procedures including arthroscopy. Cefazolin or cefuroxime. Alternative: vancomycin.	Yes: for orthopedic prosthesis and open surgeries. Cefazolin.	Yes: for joint replacement of prosthesis and hip fracture repair. Cefazolin.	Yes: for implanted of prosthesis material and joint replacement (Cefazolin); exposures fractures (type I, II and III A: cefazolin or cephalothin); type III B and C: cefazolin/ cephalothin plus gentamicin); and for amputation (Clindamycin plus gentamicin or cefazolin plus metronidazole).
Neurosurgical	Yes: for craniotomy but only for high-risk procedures (re-exploration, microsurgery) Clindamycin or vancomycin	Yes: for craniotomy and placement of shunts. Cefazolin Vancomycin if the rate	Yes: oxacilin for shunts and craniotomy. Alternatives: cotrimoxazole: for	Yes: cefazolin.	Yes: for craniotomy or laminectomy. Not for shunts.	Yes: for craniotomy and laminectomy, procedures involving incision of pharyngeal or sinus mucosa

	plus gentamicin. TMP-SMX is recommended for shunting procedures in institutions with high rate of infections (>20%).	of oxacilin-resistant pathogens is high.	shunts. Vancomycin: for craniotomies.		Cefazolin.	(Cefazolin or cephalothin) procedures involving transesphenoidal access (Clindamycin; for Shunts insertion (TMP-SMX)).
Ophthalmic	Suggests topical antibiotic or antiseptics for extraction of lens and insertions of prosthesis (but without specific recommendations).	Not specified.	Yes: for lens implant, cataract extraction, penetrating trauma and not for other elective surgeries. Oral quinolones.	Not specified.	Not specified.	Yes: for penetrating trauma (oral ciprofloxacin) with the exception of B cereus risk exposure (add clindamycin); for lens implant, cataract extraction, (topical gentamicin or tobramycin plus subconjuntival and systemic cefazolin or cephalothin).
Head and neck	Yes: only for major procedures involving incision of pharyngeal mucosa or oral cavity. Clindamycin plus gentamicin. Cefazolin and third-generation cephalosporin have also proved to be effective.	Yes: for procedures with entry into the oropharynx or esophagus. Cefazolin.	Yes: cefazolin. Add aminopenicillin + BLI if the entry is through the oral cavity.	Yes: if mucosa is compromised and for major procedures Cefazolin.	Yes if mucosa is compromised. Cefazolin or clinda + genta.	Yes: only for major procedures involving incision of pharyngeal mucosa or oral cavity (Clindamycin + gentamicin or cefazolin); rhinoplasty with graft (cefazolin or cephalothin).
Gastro-duodenal	Yes: for gastric resection in high-risk patients (bleeding gastric or duodenal ulcer, obstructive duodenal ulcer, gastric ulcer and malignancy, morbid obesity) Cefazolin.	Yes: for high- risk procedures. Cefazolin.	Yes: cefazolin or cefuroxime.	Yes: cefazolin.	Yes: cefazolin.	Yes: cefazolin or cephalothin.
Biliary tract	Yes: for high risk procedures (age >60, previous biliary surgery, acute symptoms, jaundice (Cefazolin).	Yes: for high-risk procedures. Cefazolin.	Yes: cefoxitin or aminopenicillin + BLI	Yes: for open or laparoscopic procedures. Cefazolin	Yes: cefazolin.	Yes: cefazolin or cephalothin; endoscopy of biliary tract during obstruction: piperacillin.
Colorectal surgery and appendectomy	Yes: for elective procedures, erythromycin plus neomycin, (oral route), the day before. For non-elective or emergency: cefoxitin. Only for allergy: metronidazole plus gentamicin.	Yes: cefoxitin. For elective procedures: erythromycin + neomycin, oral route, the day before.	Yes: cefoxitin or aminopenicillin + BLI.	Yes: cefoxitin. For elective procedures: erythromycin + neomycin, oral route, the day before.	Yes: cefoxitin, cefotaxime or ceftizoxime. For elective procedures: erythromycin + neomycin, oral route, the day before.	Yes: metronidazole/ornidazol plus gentamicin or cefoxitin adding to mechanical preparation.
Hysterectomy	Yes: cefazolin.	Yes: cefazolin.	Yes: cefoxitin or aminopenicillin + BLI	Yes: cefazolin.	Yes: cefazolin.	Yes: cefazolin or cephalothin.

(*continued*)

Table 13.9 (*Continued*)

Procedures	Principles and practice of infectious diseases (Mandell *et al.*)	Infectious Diseases Society of America (IDSA)	French Society of Anesthesia	Surgical Infection Society	American Society of Hospital Pharmacy	Sociedad Argentina de Infectología (SADI)
Non-elective cesarean section	Yes: cefazolin after clamping the cord.	Yes: with PRM (premature rupture of membrane). Cefazolin.	Yes: cefazolin.	Yes: cefazolin.	Yes: cefazolin.	Yes: cefazolin or cephalothin after clamping the cord.
Elective cesarean section	No.	No.	Not specified.	Included in the general recommendations for cesarean section.	Yes: cefazolin.	Yes: cefazolin or cephalothin after clamping the cord.
Urologic	Not with sterile urine.	Not with sterile urine. For procedures that compromise the bowel, idem for colorectal surgery.	Yes: for prostatectomy, cistectomy, nefrectomy. Cefuroxime or gentamicin or tobramicin + quinolones. Quinolones only for prostatic biopsy.	Yes: for nefrectomy and cistectomy with construction of an ileal conduit. Not specified in other situations.	Yes: high-risk patients or hospitalized: cefazolin or cotrimoxazol, oral route, or cefalexin, oral route.	With non-sterile urine (treatment of infection for 7–10 days before surgery or at least for 72 h according to resistance pattern). For procedures that not compromise the bowel (like prostatectomy, cistectomy or nefrectomy) Cefazolin (alternative: oral norfloxacin); for procedures that compromise the bowel (systemic like colorectal surgery).
Trauma	For penetrating abdominal trauma: cefoxitin.	Not specified.	Yes: amino-penicillin + BLI.*	Yes: for abdominal trauma. Other trauma not specified.	Not specified.	Specified by type of surgery (orthopedic, ophthalmic, abdominal).
Other clean procedures	Yes: for pacemaker insertion. Not for the rest.	Optional for breast surgery and hernioplasty and for other clean procedures in patients with risk factors.	Yes: for reconstructive plastic surgery and pacemaker insertion. Acceptable for breast surgery.	Yes: for patients at high-risk due to the presence of co-morbilities.	Yes: for implant of prosthesis materials. Acceptable in inmuno compromised patients. Controversial in other circumstances.	Cefazolin or cephalothin for breast surgery. Optional for aesthetics surgery.

* BLI: B-lactamase inhibitors.[61] Modified and adapted from Zanetti G, Platt R. Guidelines for peri-operative antimicrobial prophylaxis. In: Abrutyn E, Goldman DA, Scheckler WE, editors. *Infection Control,* 2nd edition. WB Saunders Company; 2001; pp. 315–320.

Table 13.10 Antimicrobial prophylaxis recommendations for the most frequently used surgical procedures

Surgical procedure	Recommended prophylaxis regimen
Gynecologic surgery	
Cesarean section	Cefazolin 1 g i.v. after cross-clamping of the cord and other doses between 6 and 12 h later.
Dilation, curettage, abortion	Prophylaxis is not recommended for uncomplicated dilation or curettage. In abortions during the second trimester of pregnancy, 1 g of cefazolin is used before the procedure and other doses between 6 and 12 h after the procedure is recommended. In case of B-lactamase allergy, metronidazole 400 mg, oral route, before the procedure followed by two doses every 4 h is effective.
Vaginal or abdominal hysterectomy	Cefazolin 1 g i.v. pre-operatively and other doses 6 and 12 h later. Second or third-generation cephalosporins have not proved to be more effective. In case of B-lactamase allergy, doxyciclyne 200 mg i.v. pre-operatively, given as a single dose, is effective for vaginal or abdominal hysterectomy prophylaxis.
Bilateral occlusion of fallopian tubes	Not available data for prophylaxis recommendation.
Cystocele or rectocele repair	Antimicrobial prophylaxis has not proved to be effective.
Orthopedic surgery	
Arthroplasty, including replacements	For major joints repair (hip, knee), cefazolin 1 g i.v. pre-operatively and three more doses every 6 h (24 h). Cefazolin 2 g i.v. must be considered in prophylaxis for knee replacement with tourniquet. Non-available data for arthropic surgery.
Open reduction of fracture	Cefazolin 1 g i.v. pre-operatively and three more doses every 6 h (24 h). Complex open fractures are considered contaminated and, in such cases, the therapy is: cephalotin 1 g i.v. every 8 h for 10 days, starting when entering hospital.
Laminectomy	The use of antimicrobial prophylaxis has not shown to be effective.
Amputation of lower limb	Cefoxitin 2 g i.v. pre-operatively and every 6 h (a total of four doses in 24 h).
Ophthalmologic surgery	
Extraction of the lens, including prosthesis insertion	There are no appropriately controlled studies on ophthalmology. Retrospective revision of available data suggests that antibiotics and topical antiseptics may be effective, but their efficacy and the election of therapy is still a debated topic.
General surgery	
Colecistectomy	Cefazolin 2 g i.v. pre-operatively in high-risk patients: age $>$ 60, previous biliary surgery, acute symptoms or presence of jaundice. In case of B-lactamase allergy, gentamicin 80 mg i.v. pre-operatively and three more i.v. doses every 8 h.
Hernioplasty	Limited data. Routine prophylaxis is not recommended.
Colon surgery	Neomycin and erythromycin 1 g of each, oral route, at 1 and 2 a.m. and at 11 p.m. the day before surgery. For emergency colonic surgery and when oral administration is not possible, cefoxitin 2 g i.v. peri-operatively and three more doses every 4 h. In case of B-lactamase allergy, metronidazole 500 mg i.v. plus gentamicin 1.7 mg/kg i.v. pre-operatively and three more doses every 8 h post-operatively (24 h).
Liberation of adherences Laparotomy without entry into hollow viscus	Not available data for prophylaxis recommendation.
Appendectomy	Cefoxitin 2 g i.v. pre-operatively and every 6 h or three doses in case of non-perforated appendicitis. In case of perforated appendicitis, continue with antibiotic therapy for 3–5 days. In case of B-lactamase allergy, use metronidazole. In case of perforated appendicitis, continue with metronidazole every 8 h i.v. or oral route for 3–5 days.

(*continued*)

Table 13.10 (*Continued*)

Surgical procedure	Recommended prophylaxis regimen
Mastectomy (total or partial)	Limited data. Routine prophylaxis is not recommended.
Gastric resection	Cefazolin 1 g pre-operatively only in high-risk patients (bleeding duodenal or gastric ulcer, gastric neoplasia, morbid obesity). Prophylaxis is not indicated in case of non-complicated chronic duodenal ulcer. In case of B-lactamase allergy, a single-dose of gentamicin 120 mg and clindamycin 600 mg may be effective.
Surgery for penetrating abdominal trauma	Cefoxitin 2 g i.v. when entering hospital. In cases of patients with bowel perforation, 2 g of cefoxitin i.v. every 6 h for 2–5 days is effective.
Urologic surgery	
Peritoneal and transurethral prostatectomy	Prophylaxis is not recommended in patients with a pre-operative sterile urine culture.
Dilation of the urethra	Not available data for antimicrobial prophylaxis recommendation.
Pharynx, mouth and nose surgery	
Amygdalectomy	Not available data for prophylaxis recommendation.
Major surgery of head, neck and oral cavity	In major procedures requiring incision of pharyngeal or oral mucosa, gentamicin 1.7 mg/kg plus clindamycin 300 mg i.v. pre-operatively and two more doses every 8 h. Third-generation cefazolin and cephalosporins given for 24 h peri-operatively are also effective.
Rhynoplasty and nose repair	Prohylaxis has not proved to be effective.
Cardiothoracic and vascular surgery	
Median sternotomy, Coronary *by-pass* and valvular surgery	Cefazolin 1 g i.v. pre-operatively followed by 1 g i.v. every 4–6 h intra-operatively. Cefuroxime, cefamandole and vancomycin are alternatives for those institutions where wound infections caused by *S. aureus* persist although prophylaxis with cefazolin. Antimicrobial prophylaxis generally continues for 48 h although its optimal duration after surgery has not been established.
Pacemaker placement	Cefazolin 1 g pre-operatively and every 6 h after surgery for 24 h.
Thoracic surgery including lobectomy and pneumonectomy	Cefazolin 1 g pre-operatively and every 6 h after surgery for 24 h. In case of penetrating thoracic trauma and insertion of pleural tubes, antimicrobial prophylaxis has not proved to be effective.
Peripheral vascular surgery	Cefazolin 1 g pre-operatively and every 6 h after surgery for 24 h. Vancomycin is also effective. Efficacy of cefazolin in carotid surgery has not been established. Antimicrobial prophylaxis for carotid endarterectomy is not recommended.
Neurosurgery	
Placement of *shunts*	Prophylaxis is not recommended in institutions with low rates of infection. Trimethoprim (160 mg)-sulfamethoxazole (800 mg) i.v. pre-operatively and three more doses every 12 h have proved to be effective in institutions with high rates of infection.
Craniotomy	In high-risk procedures (re-exploration, microsurgery) clindamycin 300 mg i.v. pre-operatively and another dose after 4 h has proved to be effective. Vancomycin 10 mg/kg (maximum: 500 mg) i.v. and gentamicin 2 mg/kg (maximum: 120 mg) i.v. have been effective.
Miscellaneous	
Simple laceration of hand	Antimicrobial prophylaxis has not proved to be effective. In case of animal bites, amoxicillin/clavulanate 250/150 mg, oral route, every 6 h for 5 days may be effective.

could be used only in those special situations when the patient's own risk factors (for example, with an ASA score 3, 4 or 5) or of the surgery (prolonged surgeries, break in asepsis technique) justify its use.

13.4.3 Antimicrobial prophylaxis in endoscopic procedures?

In endoscopic procedures, the indication of SAP is accepted to prevent local infectious complications in the following situations:

- Urologic endoscopy with a positive urine culture.
- Retrograde endoscopic cholangiopancreatography with obstruction of the biliary tract.

In our country, there has been a rapid growth in the ambulatory surgery field, with a constant incorporation of new procedures and indications, including the placement of prosthesis elements by endoscopic methods. The use of SAP in these procedures is controversial because they have very low rates of infectious complications and the indiscriminated use of antibiotics could exert a great selective pressure, thus favoring the development of bacterial resistance.

Even though, in our country, SAP is regularly used in these procedures, it is possible to observe, with concern, that the processing of apparatus for high-level sterilization and disinfection is not made according with current recommendations. This fact constitutes a serious risk of SSI and the possible transmission of other microorganisms (hepatitis B virus, human immunodeficiency virus).

Recommendations: Do not use antimicrobial prophylaxis as a routine in endoscopic procedures, with the exception of immunocompromised patients or those who need to receive bacterial endocarditis prophylaxis (for example, valvular disease with insufficiency, previous endocarditis, etc.). For arthroscopic surgery the topic is still controversial.

Carry out surveillance of infectious complications and develop preventive policies based on own data, using SAP in hospitals with high rates of infection related to endoscopic procedures.

If prophylaxis is indicated, a single dose of antibiotic (cefazolin) is recommended immediately before the procedure, discontinuing its administration after it.

It is very important to make an adequate preparation of the patient and to make sure that the endoscope and its accessories are adequately processed (high-level disinfection or sterilization).[49,50]

13.5 Frequent mistakes in surgical antibiotic prophylaxis

Several studies concerning the use of antimicrobials have demonstrated high rates of inappropriate use in pre-operative prophylaxis, even in hospitals with their own guidelines on this subject. Most frequent mistakes are:

- absence of pre-operative dose;
- pre-operative dose administered more than 2 h before operation;
- prolonged post-operative prophylaxis;
- inappropriate choice of antibiotic regimen:
  - antibiotic with non-demonstrated efficacy,
  - broad-spectrum antibiotic,
  - combination of antibiotics;
- absence of intrasurgical dose (when it is indicated);
- mistakes in dosage, dose interval and route of administration.

The consequences of these inappropriate practices are:

- prophylaxis failure,
- resistance increase,
- more frequent adverse effects due to the use of antibiotics,
- SAP costs increase.

13.6 Other prevention measures

13.6.1 Classification

There are current measures sorted according to important scientific evidences. They can be classified as pre-operative (Table 13.11) and intra and post-operative measures. (Table 13.12) *Defined effectiveness* measures are of great value, and they are supported by studies that statistically demonstrate that their use modifies the SSI risk. Its use is strongly recommended, not withstanding the kind of surgery and the surgical center complexity. *Probable effectiveness* measures include recommendations based on less solid but rational evidences, therefore, their use is recommended unless until its effectiveness is clearly defined. *Possible effectiveness* measures are those that have not been verified or that are used in special situations. Their use is limited to specific indications. Finally, *definitely ineffective* measures are included in surgical traditional practices. Their use is not recommended because they increase costs bringing complications and no benefits[31] (Table 13.13).

Table 13.11 Effectiveness of *pre-operative* prevention measures for surgical sites infections

Defined	Probable	Possible
• Immunoprophylaxis for tetanus • Remote infections therapy • Hair removal limitation	• Underlying disease control (for example, diabetes) • Pre-operative reduction of stay	• *S. aureus* carriers control and identification • Patient's pre-operative bath with antiseptics

Adapted from Ref. [31].

Table 13.12 Effectiveness of *intra- and post-operative* prevention measures for surgical sites infections

Defined	Probable	Possible
• Appropriate surgical technique • Use of sterile materials • Pre-operative antisepsis • Antimicrobial prophylaxis • ↓ of surgical time • Use of gloves • Wounds treatment with aseptic techniques • Epidemiologic surveillance	• Hygiene of the area • Appropriate surgical attire • Air control and ventilation • Limitation in the use of electrobistoury • Restricted use of foreign materials • Reduction of homologous transfusions	• Limited use of drains • Autologous instead of homologous transfusions

Adapted from Ref. [31].

Table 13.13 Definitely *ineffective measures*

- Routine cultures of the environment.
- Personnel or microorganism carriers routine cultures.
- Exclusive use of operating rooms for contaminated and dirty surgeries.
- Cleaning methods and disinfectation of the area with aerosol or phormol.
- Use of carpets with or without disinfectant at the entrance or inside the surgical area.
- Extended use of antibiotics not supported by current standards.

13.6.2 Use and rational bases

Each of the measures listed above modifies any of the three variables that affect SSI. This aspect will be briefly analyzed.

Measures affecting the quality of surgical technique

The *quality of surgical technique and the reduction of operative time* are interdependent factors. Many experiences indicate that the surgeon's manual ability and clinical judgment ensure the making of right decisions during the procedure, the degree of compromise of local tissue, and the systemic repercussions of the surgery as well.[2–5]

Measures improving the host conditions

It has been mentioned that the patient's condition prior to the surgical procedure is a predominant factor for his future evolution. Therefore, if possible, the correction of risk factors, the underlying disease control and the therapy for remote infections before the patient undergoes an elective surgery is recommended. This is especially important in the case of patients that will undergo the placement of a vascular or orthopedic prosthesis.

The presence of *S. aureus* has shown to be related with an almost tenfold increase in SSI. Therefore, the search of this condition and later decolonization are indicated in every surgery with prosthesis placement, and in people with high risk of infection (diabetic and hemodyalized patients, drug addicts) before any scheduled surgery.[31] Obese patients are at risk of getting infections. Neuthrophils dysfunction has been detected: decreased levels of CD62L (one type of cellular receptors) reduce the neuthrophils's ability to activate and migrate to sites of inflammations. The

association between morbidly obesity and diabetes are very common. Both factors seem increase the risk for infections.[51]

Minimization of pre-operative hospital stay

Patients are colonized with hospital flora within 48 h after entering into hospital. These bacterial strains are frequently resistant and contaminate the skin of the surgical site before surgery. Therefore, it is recommended, if possible, to encourage ambulatory surgery and to reduce hospital pre-operative stay. The extension of pre-operative stay is a risk factor for the development of SSI. Pre-operative stay must be as short as possible.

Measures tending to minimize exogenous contamination of wounds

The objective of many of the control measures used within the surgical area is to avoid wound contamination with microorganisms from surgical environment or carried by the personnel. Severe control conditions that characterize modern operating rooms justify, unless partially, the secondary role that, according to bibliography, the environment performs in the origin of SSI.[6,52]

Within this group of measures, guaranteed sterilization of surgical material, selection and correct use of antiseptics, pre-operative washing of hands with antiseptic soap and the use of gloves constitute a universal valid basic standard and their implementation is not controversial.[31]

This group of measures implemented together with the objective of reducing aerial contamination, which is especially important in the origin of clean infected wounds, particularly when the surgery is long and when an extended area is exposed, deserves a special paragraph.

The number of particles in air depends on the number of people in the operating room, on their movement, on their conversation and on the turbulence caused by the opening and closing of doors. Therefore, *it is strongly recommended to reduce the number of people in the operating room during the procedure and their movements, to talk as less as possible and to keep doors closed once the procedure has started.*[6,47]

The adequate ventilation and climatization of the surgical area are very important factors in order to reduce the number of particles in air and to diminish, in an indirect way, the risk of exogenous wound contamination.[53] A reduction in temperature and an increase in humidity are related to an important raise in the rate of wound infections.

A standard ventilation system must be able to reduce the number of units that forms bacterial colonies to 15–20 per 30 cm^3 of air, and must provide the area with the following conditions:

- *Clean air* There must exist positive pressure within the surgical room with respect to the rest of the surgical area. There must be no windows communicating with the outside.
- *Remotion of contaminated air* There must be 20 air remotions within an hour, 20% of them with fresh air. It is better not to share the ventilation system of the surgical room with the rest of the institution. Some special air cleaning systems, like horizontal and vertical laminar flow, have proved to be useful in order to reduce infections associated with joint replacements with prosthesis. These systems are cost effective in units with a great number of joint replacement surgeries (more than 100 annual replacements). Laminar flow efficacy in the reduction of SSI in other kind of procedures has not been properly studied.
- *Climatization of the area* Temperature must be stable, within 18° and 24°C (64° and 75°F), with a humidity of 50–55%. Temperature must be higher in surgery rooms for neonatal surgery and lower in central cardiovascular surgery.
- *Independent control* It is recommended in every operating room.[6,29,46–48]
- *Surgical attire* Although there exist controversial data on the actual contribution of surgical attire (cap, mask, gown, shoe covers or special shoes for the area) to reduce wound infection risk, available evidences are not enough to abandon these practices that have the aim of reducing bacterial count in the air. This attire must be used within the area and must not be used outside it. It is also important to take into account the quality of the clothes to make sure that their production process are adequate.[6,47]
- Finally, it is important to mention that the personnel carrying *S. aureus* or *bethahemolitic streptococcus*, group A, may be a significant source of environment contamination. This is not important in normal situations, so systematic search is not indicated. Nevertheless, it must be considered that the possibility of a carrier to become a *disseminator* increases *in upper airway respiratory infections and when there exist active furunculosis or scaling skin diseases (eczema, psoriasis)*, specially when cutaneous lesions are large or affect the hands. In these circumstances *it is recommended to discontinue the carrier activity until clinical situation is under control.* Likewise, in infection outbreak periods, the search and therapy of the carriers can be useful.[5,31]

Patients and health professionals with upper airway respiratory infections may excrete *flügge* drops containing aggressive microorganisms like staphylococci and streptococci. People with respiratory infections must not be allowed to take part in surgical procedures.

Measures tending to reduce endogenous contamination of wounds

Antisepsis of surgical area and SAP, both of unquestionable value, are included within these measures.

With respect to the patient preparation, pre-operative skin cleansing constitutes a conventional routine, even though the value of the pre-operative bath with antiseptic soap (clorhexidin) has not been verified by important controlled studies. It can be cost effective in high-risk surgeries, like neurosurgery or cardiac surgery or implant of joint prosthesis.

Presence of hair does not increase the risk of infection of the surgical site, but hair shaving does.

This risk increases when the interval between shaving and surgery is extended. Hair must be removed only for technical reasons.

A careful *pre-operative antisepsis of the skin with antiseptics* (clorhexidin or similar), is important in order to reduce the patient's own flora (permanent and transitory). The covering of the surgical field must not allow the passage of bacteria and fluids. Plastic film coverings have not shown reduction in the rates of SSI.

Several studies demonstrate that hair shaving of the surgical area is related to an increase in wound infections. If possible, it is better not to remove the hair. If necessary, the use of a hair clipper or, eventually, a wet shaving within an hour before surgery is recommended.[5,29,32,54]

Post-operative contamination of surgical wound

Bloodstream infections, lymphatic route or direct inoculation after surgery are considered as a rare cause of surgical wound infection. However this mechanism is possible and must be taken account of an origin of wound infection.[3–5,55]

Epidemiologic surveillance

Permanent follow-up of patients undergoing surgery, detection of post-operative infections, obtaining of wound infection raw rates adjusted with risks factors, type of surgery and surgeon, have significantly reduced the incidence of SSI. The information obtained with this method is an adequate marker of the surgical team job quality, and it also helps to identify problems to be solved. Wound surveillance programs, with systematic feedback provided to the surgery team are very important in the SSI prevention.[3–5,31] Institutional programs related to rational use of SAP must be considered as one of the most important tool to reduce wound infections, medical cost and the emergency of bacterial resistance.[56] One of the main objectives of this kind of programs is to implement strategies for improving and increasing the rationale use of antibiotic in surgery.[57–59]

One effective control system is based on a selective blockade of the pharmacy in order to control antibiotic use for SAP allowing only those that were previously selected for each situation.[60]

13.7 Conclusions

As commented in other chapters, peri-operative morbidity and mortality are increased in morbidly obese population. The most frequent post-operative complications are: respiratory dysfunction, deep vein thrombosis (with or without pulmonary embolism) and surgical wound infection. Therefore, prevention should be focused in order to reduce all of them. Especially considering the increased possibility of wound infection, *it can be said, that the systematic use of all these measures implemented together can provide the patient a reasonable secure assistance.* The importance of each of them is hard to measure, but their isolated implementation will be, in any case, insufficient. Consequently, a multi-disciplinary approach (as in many other aspects involved in the peri-operative care of the morbidly obese surgical patients), seems to be the most appropriate way to obtain better outcomes (see Chapter 1).

Historically, the four landmarks that made a difference in the resolution of these problems are: *the improvement of surgical techniques, the development of asepsis, the development of antisepsis, and SAP.* If these measures are appropriately followed, the reasonable use of the rest of them will be an important contribution for achieving the final objective, which is to reduce the incidence of SSI as much as possible.

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RENAL DYSFUNCTION 14

D.M. Rothenberg & A. Rajagopal

14.1 Introduction

Renal function in the peri-operative period is often misunderstood. It is considered synonymous with the patient making "good urine". Treatment of renal dysfunction is also centered on methods to make urine appear. Understanding renal dysfunction requires a more analytic and physiologic approach to the patient, that is even more important in the morbidly obese patient who has other anatomical and physiologic variations.

We will review basic renal physiology and pathophysiology and its alterations in both the non-obese and obese patient as they relate to renal ischemia, pre-operative risk factors for developing post-operative acute renal failure (ARF), and finally, non-dialytic and dialytic modalities.

14.2 Basic renal physiology and pathophysiology

The kidney primarily functions to maintain internal homeostasis by regulating effective arterial blood volume (EABV), osmolality and ionic composition, and to concentrate and excrete the daily endogenous and exogenous load of nitrogenous waste. These actions are achieved by a complex interplay between glomerular filtration, tubular reabsorption and tubular secretion. The kidney also plays a vital role as an organ of endocrine function, regulating both red blood cell mass by the production of erythropoietin, and calcium and phosphorus homeostasis through the synthesis of vitamin D to its most active form, 1,25-dihydroxycholecalciferol.

The glomerular apparatus is a network of capillaries originating from the afferent arteriole and surrounded by an extension of the basement membrane of the proximal tubule called Bowman's capsule. The urinary space or Bowman's space (BS) separates the capsule from the glomerular tuft. The formation of urine begins with a protein-free ultrafiltrate of plasma passing through the glomerulus into BS. The rate of formation of tubular fluid (glomerular ultrafiltration rate or GFR) is dependent upon the hydraulic permeability of the glomerular capillary and the net ultrafiltration pressure across the capillary wall. GFR is a

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non-energy requiring process governed by "Starling forces" and is defined by the following equation:

$$GFR = K_f[(P_{GC} - P_{BS}) - \pi_{GC}]$$

The difference in hydrostatic pressure between the glomerular capillary (P_{GC}) and BS (P_{BS}) favors filtration, where as colloid osmotic pressure in the capillaries (π_{GC}) opposes it. As filtration of a protein-free fluid occurs, a progressive increase in π_{GC} ensues such that by the end of the capillary, ultrafiltration pressure becomes zero (that is, $P_{GC} = \pi_{GC} + P_{BS}$). This physiologic principle mandates that GFR be highly dependent upon renal plasma flow. The higher the flow rate, the slower the rise in π_{GC} and hence an increase in GFR.

Normal GFR is approximately 180 l/day and is due to the extensive surface area and permeability of the glomerular tuft. Despite large changes in mean arterial pressure, only small changes occur in GFR due to the process referred to as "renal autoregulation". Renal autoregulation occurs for both renal blood flow and GFR and is based on the afferent arteriole's intrinsic ability to sense transmural pressure and adjust wall tension to keep resistance proportional to pressure. Where as renal blood flow may fall at mean arterial pressures <50 mmHg, GFR tends to autoregulate at a higher pressure (70–80 mmHg). This concept becomes clinically relevant during deliberate hypotensive anesthesia (DHA) when mean arterial blood pressure is decreased below the autoregulatory threshold for GFR but not for renal blood flow, resulting in normal renal perfusion despite diminished urine output.

Relative to renal blood flow and perfusion, the kidney receives 20% of the normal cardiac output (Q_t), an amount far in excess of the kidney's overall oxygen and energy requirement. This percentage of Q_t is needed, however, to drive the processes of filtration. Relative to the proportion of overall renal blood flow, a marked disparity exists between the renal cortex and medulla. The cortex receives >90% of total renal blood flow, thus creating tissue oxygen tensions of approximately 50 mmHg compared to 8–10 mmHg in the medulla. Although necessary to prevent washout of the hypertonic interstitium and to preserve the osmotic gradient required for tubular secretion and reabsorption, preferential blood flow to the cortex leaves the medullary thick ascending limb of the loop of Henle (mTAL) highly susceptible to hypoperfusion-induced ischemia. Prevention of renal ischemia and ARF is, therefore, dependent upon maintaining oxygen delivery as well as minimizing oxygen demand. An intrinsic "tubuloglomerular" feedback system provides initial protection in the event of medullary hypoperfusion by renin-mediated afferent arteriolar vasoconstriction, which in turn leads to a decrease in plasma ultrafiltration and hence a decrease in energy expenditure of the cells of the mTAL.[1] Prolonged periods of hypoperfusion may overwhelm this process leading to erythrocyte sludging in the medulla and eventual tubular obstruction from necrotic cellular debris. The resulting increase in intratubular pressure ($\uparrow P_{BS}$) in association with the decrease in glomerular capillary pressure ($\downarrow P_{GC}$) may eventually result in *progressive azotemia not amenable to manipulation of EABV, Q_t or other extra-renal factors*, that is, ARF.

GFR, and hence urine formation, may therefore be diminished by the following factors:

1. a decrease in K_f from exposure to nephrotoxins;
2. a decrease in P_{GC} from hypoperfusion;
3. an increase in P_{BS} from intratubular obstruction due to cellular debris;
4. an increase in π_{GC} from concentration of proteins due to dehydration.

While the decrease in GFR will result in a decrease of urine output, the opposite is not necessarily true; that is, *a decrease in urine volume does not always mean a decline in GFR, nor does it imply the diagnosis of ARF*.

The additional processes of tubular reabsorption and secretion further refine urine formation. Homeostasis is maintained by transforming the plasma ultrafiltrate into urine of variable volume, osmolarity and composition via a complex interaction between the renin–angiotensin–aldosterone system, the sympathetic nervous system and other hormonal and physical factors.

The proximal, distal and collecting tubules each modulate and control various functions. Of primary significance to anesthesiologists is an understanding of sodium and water homeostasis relative to maintenance of EABV. Despite the enormous amount of sodium that is filtered on a daily basis (140 mEq × 180 l = 25,200 mEq) <1% is generally excreted in the urine. The bulk of sodium reabsorption, and therefore volume and osmotic control, occurs in the proximal convoluted tubule, the loop of Henle and the distal tubule. During periods of hypovolemia these segments fractionally reabsorb >99% of the filtered load of sodium and thus fractionally excrete <1%. (This concept of fractional excretion of sodium will be addressed in more detail in the section on perioperative renal evaluation.)

Urine is ultimately refined by the effect of antidiuretic hormone (ADH) on the collecting duct to reabsorb water thereby helping to maintain plasma tonicity (normal range 280–295 mOsm/kg H_2O). Hypertonicity stimulates osmoreceptors in the hypothalamus to

release ADH. Changes in EABV will also lead to a baroreceptor-mediated release of ADH. Finally, postoperative pain, anxiety and/or nausea may also stimulate the release of ADH independent of osmolarity or EABV. As would be expected, these patients characteristically manifest low urine outputs despite having normal renal function. In this setting, efforts to increase urine production by inappropriate volume challenges may result in hyponatremia and/or pulmonary edema.

14.3 Renal physiology and pathophysiology in obesity

Obesity initiates a cascade of interlinked disorders including hypertension, diabetes, dyslipidemia and chronic renal disease. Essential hypertension is commonly caused by obesity. Currently 30–35% of the adult US population above the age of 50 is obese with 50% having essential hypertension.[2–5] Data from the Framingham Heart Study suggest that approximately 78% of hypertension in men and 65% in women can be directly attributed to being overweight.[6] Central to the development of hypertension is the role of renal pressure natriuresis.[7–9] Renal pressure natriuresis is the mechanism by which the body regulates extracellular fluid sodium levels, which in turn determines intravascular volume in the body. Obese patients require a higher than normal arterial pressure to maintain a balance between intake and urinary output of sodium.[8,9]

Obesity, through a number of mechanisms, impairs renal pressure natriuresis.

The mechanisms include:

1 activation of the renin–angiotensin system;[10]
2 activation of the sympathetic nervous system;[11]
3 renal medullary compression.[9]

Obese subjects have higher plasma renin and angiotensin converting enzyme (ACE) activity, and plasma angiotensinogen, and angiotensin II levels.

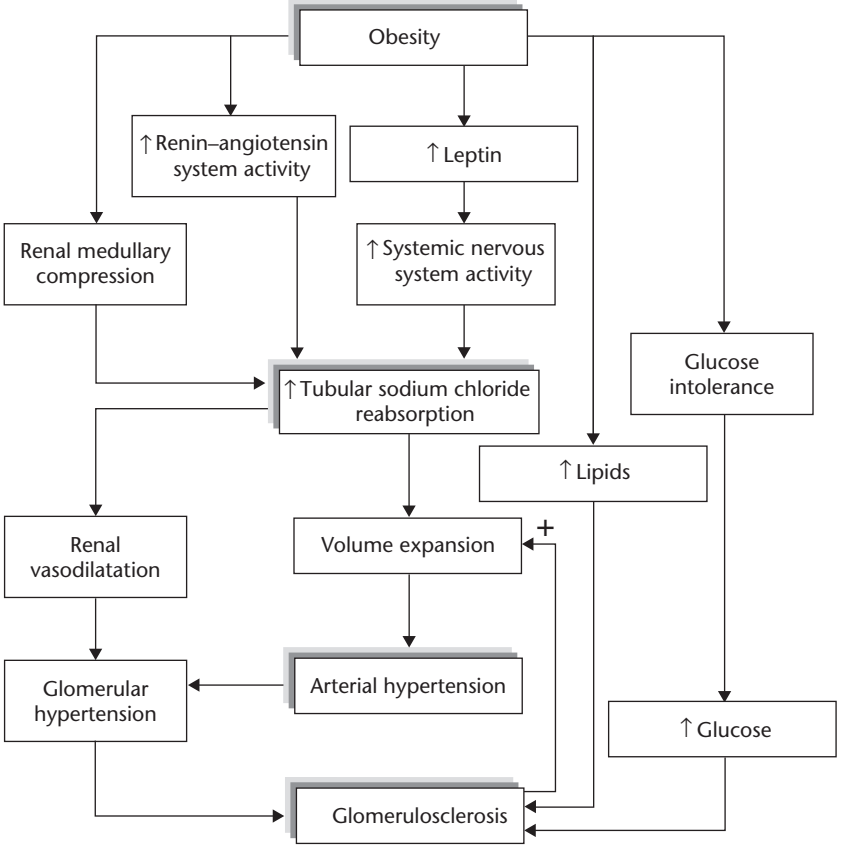

Figure 14.1 Summary of mechanisms by which obesity increases renal tubular sodium reabsorption, impairs pressure natriuresis and causes hypertension as well as progressive glomerular injury. Reprinted with the permission of John E. Hall, Novartis lecture: The kidney, hypertension and obesity. *Hypertension* 2003; **41[Part 3]**: 625–633.

Robles *et al.* demonstrated that treatment of obese dogs with an angiotensin II antagonist or an ACE inhibitor blunts sodium retention, volume expansion and results in an increase in arterial pressure. ACE inhibitors are also effective in treating hypertension in obese humans.[12,13] Sympathetic nervous system activation also contributes to obesity-induced hypertension. Obese subjects having elevated sympathetic nervous system activity as assessed by both direct and indirect methods support this assumption.[10,14,15] Studies have demonstrated that pharmacologic regulation of adrenergic activity leads to a greater reduction in blood pressure in obese vs. lean subjects, and renal denervation decreases sodium retention and the development of obesity-induced hypertension in experimental animals fed with high fat diets.[16,17] Activation of the sympathetic nervous system in obesity has many proposed mechanisms including hyperinsulinemia, hyperleptinemia and sleep apnea causing hypoxia and hypercapnia.[7,8]

Anatomic changes seen in the kidneys in obesity include an increase in adipose tissue, which encapsulates the kidney.[18,19] This along with a rise in intra-abdominal pressure causes an increase in intra-renal forces impairing pressure natriuresis.[18–20] Marked increase in the mesangial matrix causes compression of the medulla also impairing pressure natriuresis. A relatively non-compliant capsule surrounds the kidney and an increase in the extracellular matrix causes compression of the thin loops of Henle, reducing blood flow in the vasa recta and increasing tubular reabsorption.[21,22] This hypothesis is supported by the measurement of markedly elevated renal interstitial fluid pressures in obese dogs.[18,19] Compensatory mechanisms in the obese for overcoming increased sodium reabsorption include renal vasodilation, increase in GFR and a higher blood pressure. These changes in the long term cause glomerular injury leading to glomerulosclerosis. A review of 7000 renal biopsies from 1990 to 2000 showed a 10-fold increase in obesity-related glomerulopathy (glomerulomegaly and glomerulosclerosis).[23] A summary of the pathophysiology of obesity and progressive glomerular injury is noted below (Figure 14.1).

14.4 Pre-operative renal risk factors

Despite inconsistencies in the medical literature in defining criteria for establishing pre-operative renal risk factors,[24] virtually all-recent studies assessing peri-operative renal risk factors have established pre-operative renal dysfunction, as defined by an elevated serum creatinine, as the single greatest risk for developing post-operative ARF. Creatinine, a breakdown product of muscle creatine, is primarily filtered with only minimal reabsorption and secretion and therefore is reflective of GFR. A more accurate assessment, however, would employ creatinine as part of a calculated or measured creatinine clearance (detailed in section on peri-operative renal evaluation). Studies tend to define pre-operative renal dysfunction as a serum creatinine >1.35–1.5 mg% (120–130 mmol/l). The incidence of post-operative ARF is $<1\%$ in patients with normal renal function undergoing routine, elective surgery. However, depending on the degree of renal insufficiency, the type of surgery and peri-operative complications, this incidence may approach 20% and be associated with a 30–80% post-operative mortality.[25–34] In patients with chronic, non-dialysis-dependent renal dysfunction, the etiology of the underlying renal disease is far less critical than their level of overall dysfunction. The pre-operative renal risk of a patient with lupus nephritis and a creatinine clearance of 25 ml/min is therefore no different than a patient with hypertensive nephrosclerosis with a similar creatinine clearance.

Advanced age also constitutes a risk factor for developing post-operative renal dysfunction and ARF.[25–30] Multiple studies have concluded that age >63 years is an independent variable for developing post-operative renal failure and may be related to the diminished nephron mass that occurs routinely with aging as well as loss of autoregulatory ability.

Exposure to nephrotoxic agents may also contribute to post-operative renal insufficiency. Radiocontrast agents presumably induce calcium-mediated vasoconstriction leading to medullary ischemia, which is accentuated in high-risk individuals.[35] Azotemic, diabetic patients, who undergo cardiac, vascular, or biliary tract surgery and receive radiocontrast as part of their pre-operative work up, are at particularly high risk for developing ARF. Delaying elective surgery is advisable if the serum creatinine increases >0.5 mg% within 48 h following exposure given the additional inherent surgical risk of post-operative ARF. Drugs with nephrotoxic side effects, such as aminoglycosides and cyclosporine, may also cause ARF when serum levels are not properly monitored in the peri-operative period. The use of non-steroidal anti-inflammatory agents *per se* does not seem to influence the incidence of post-operative ARF provided that pre-operative renal function is normal.[36]

Major trauma and burns also pose significant pre-operative risk for developing post-operative ARF.[31] Vivino *et al.*, in a prospective study of 153 patients admitted to an intensive care unit (ICU) after major

trauma, identified rhabdomyolysis (creatinine phosphokinase, CPK > 10,000), hemoperitoneum and the need for prolonged mechanical ventilation as risk factors for developing ARF.[31] This most likely relates to intratubular precipitation of urinary myoglobin, and/or renal hypoperfusion from hemorrhage, hypovolemia or abdominal compartment syndrome.[37] Patients who sustain significant burns and who develop ARF have been noted to have 80–100% mortality. Holm *et al.*, in a retrospective analysis over a 4-year period, identified the extent of surface burn and the presence of inhalation injury, as risk factors for ARF, but do not speculate upon the cause and effect.[32] ARF appears to play an important role in both the development of and response to this critical injury, given that most of these patients die from multiorgan system failure.[38]

Sepsis is also considered a renal risk factor, presumably related to a combination of factors including a direct effect of inflammatory mediators, hypovolemia, myocardial depression and maldistribution of renal blood flow. The mortality of sepsis-associated ARF is in the range of 70–80%.[33]

Finally, the association between obstructive jaundice and post-operative ARF has been well described.[34] ARF occurs in up to 10% of patients undergoing biliary tract surgery and is associated with a 70–80% post-operative mortality. Bile constituents (for example, bilirubin and bile acids) are not direct nephrotoxins, but rather appear to exert their effects on the cardiovascular system by sensitizing the kidney to developing pre-renal failure and acute tubular necrosis in patients with obstructive jaundice. Experimental evidence suggests that endotoxemia in association with obstructive jaundice produces excessive levels of nitric oxide, which, in turn, disrupts renal autoregulation leading to ARF.[39]

14.5 Operative renal risk factors

The surgeries most commonly associated with post-operative renal failure are listed in Table 14.1.

Renal dysfunction following cardiopulmonary bypass (CPB) is relatively common, with dialysis-dependent ARF developing in 1.2–13% of patients depending upon their pre-operative GFR.

Table 14.2, lists recent prospective studies assessing mortality in patients who develop either renal dysfunction (increase in serum creatinine >0.7–1.0 mg%, or an increase >50% of baseline) or dialysis-dependent ARF (ARF-D) following cardiac surgery[25,26,28–30] (Table 14.2).

Intra-operative renal risk factors included low output syndrome, need for intra-aortic balloon counterpulsation and prolonged CPB times >130–180 min. More recently, Dávila-Román *et al.*, using intra-operative epiaortic ultrasound, identified ascending aortic atherosclerosis as an additional independent risk factor for developing post-operative renal dysfunction.[40] The authors studied 978 patients with normal pre-operative renal function undergoing open heart surgery and noted that the incidence of post-operative renal dysfunction increased with the degree of ascending aorta atherosclerosis from 4.1% with normal-mild to 9.0% with moderate, to 17.1% with severe disease. Although not assessed in this study it is postulated that this may relate to renal atheroembolism.

Recently, prospective studies describe the incidence of ARF-D following aortic surgery to range from 2.7% to 15%.[41–44] In addition to direct renal hypoperfusion from suprarenal aortic cross clamping, the pathophysiology of renal dysfunction from aortic cross clamping and unclamping at any level appears to be related to a complex interplay between the renin–angiotensin

Table 14.1 Operative renal risk factors

- Cardiac surgery
- Aortic aneurysm surgery
- Major trauma/burns
- Biliary tract surgery
- Transplantation (liver, kidney and heart)

Table 14.2 Prospective studies in patients undergoing cardiac surgery: mortality relative to degree of renal dysfunction

Number of patients	Mortality		
	Creatinine <1.5 mg%	Creatinine >1.5–2.5 mg%	ARF-D
2009	0.4	1.3	44[5]
775	0.8	9.5	44[6]
42,773	0.5–0.8	1.8–4.9	63.7[8]
2222	0.9	19	63[9]
2843	1.0	14	28[10]

system, the sympathetic nervous system, prostaglandin pathways, oxygen free radicals, the complement cascade, and the release of cytokines and other inflammatory mediators.[45,46] Mathematical models have been constructed to describe the types of, as well as to predict the incidence of, ARF following aortic aneurysm surgery.[41,47] As has been previously mentioned, both pre-operative renal function and age contribute significantly to renal outcome, but a duration of >30 min of left renal ischemia and intra-operative blood loss requiring >5 units of packed red blood cells are also predictive of developing ARF-D following aortic surgery.[43] Mortality in patients who sustain ARF-D after aortic surgery remains high (50–60%) despite various intra-operative interventions such as left atrial to femoral bypass, renal artery cold perfusion and deep hypothermic circulatory arrest.[48]

Finally, relative to the influence of anesthetic techniques and/or agents on post-operative renal function, those that merit consideration include DHA, epidural anesthesia and sevoflurane. DHA is employed to limit intra-operative blood loss and improve visualization of the surgical field. Theoretically renal hypoperfusion may occur when mean arterial pressure is maintained below the autoregulatory threshold for renal blood flow. Williams-Russo *et al.*, recently addressed this concern in a study consisting of 235 patients, either elderly (age > 70) or middle aged with either cardiac disease, hypertension or diabetes mellitus, undergoing total hip replacement employing epidural anesthesia to induce variable degrees of DHA.[49] Results failed to show any significant change in renal function (as defined by an increase in serum creatinine of >20% from baseline for >48 h) irrespective of the level of DHA; that is, mean arterial pressure of either 45–55 or 55–70 mmHg. The authors do not provide pre-operative serum creatinine or creatinine clearance levels, thus limiting the study's predictive value in those patients with pre-operative renal insufficiency. It may be presumed, however, that the population studied was likely at risk given their age or underlying disease. In addition to discounting the deleterious effects of DHA on renal function, this study, as well as previous others fail to show the renal protective effects of epidural anesthesia. Epidural anesthesia-induced sympathetic blockade fails to improve renal function following aortic cross clamping implying a less critical role of the sympathetic nervous system in regulating GFR and renal blood flow during this type of surgery.[50]

Finally, the issue of sevoflurane nephrotoxicity has been a topic of heated debate in the anesthesia literature. Sevoflurane is a fluorinated anesthetic, which undergoes oxidative defluoridation resulting in the release of potentially nephrotoxic free fluoride ions. Previous experimental data suggest a threshold for fluoride-induced nephrotoxicity to be 50 μM of inorganic fluoride. Compound A, a by-product of the breakdown of sevoflurane by soda lime and barium hydroxide lime has also been shown experimentally to be nephrotoxic. Despite these experimental data, there are currently no reports of *clinically relevant* renal dysfunction occurring in patients receiving sevoflurane even during prolonged exposure, at low flow rates, for DHA, or in those with pre-operative renal insufficiency.[51–53] In this regard, sevoflurane should *not* be considered nephrotoxic.

An additional peri-operative renal risk for patients undergoing bariatric surgery is the potential fatal complication of rhabdomyolysis. Bostanjian *et al.* in a series of six patients undergoing bariatric surgery described the development of rhabdomyolysis caused by necrosis of the gluteal muscles. Three of six patients eventually died of renal failure. The author recommended the use of padding under the gluteal muscles and the use of aggressive hydration and mannitol diuresis for serum levels of CPK > 5000 IU/l. The need to perform serial CPK measurements in these patients was also recommended.[54]

Jejuno-ileal bypass procedures are an alternative for morbid obesity. Mole *et al.* described a series of eight patients who developed renal failure attributable to renal calculi caused by hyperoxaluria. Of these eight patients, three required renal-replacement therapy (RRT).[55]

Pneumoperitoneum created during laparoscopic gastric bypass has been associated with decreased urine output. Nguyen *et al.* in a study compared intra-operative urine output, levels of ADH, plasma renin and aldosterone levels in open vs. laparoscopic gastric bypass. Laparoscopic gastric bypass was associated with a significantly lower urine output compared to open gastric bypass. The levels of ADH, plasma renin and aldosterone were not different between the groups. Post-operative blood urea nitrogen and creatinine levels remained in normal range in both groups.[56] Therefore, high abdominal pressures generated during laproscopic gastric bypass do not appear to significantly affect renal function in the post-operative period.

14.6 Peri-operative evaluation of renal function

Peri-operative assessment of renal function invariably focuses on the volume of the patient's urine with a post-operative decline in urinary output often heralding a work up for ARF. *Oliguria* is defined as an abnormal

reduction in urine output of <400 ml/day, the amount necessary to excrete the normal daily solute load. Critical care physicians and anesthesiologists have further defined oliguria on an hourly basis, as a urine output of <0.25–0.33 ml/kg/h. This is based on the presumption that hourly urine output measurements are essential in order to detect renal hypoperfusion, especially in hypovolemic oliguric patients, before permanent damage occurs. Although there are no data to support this concept, hourly urinary volume measurements is the standard in most operating rooms, post-anesthesia care units and ICUs. If hourly assessment of urine volume is necessary then the question that must be asked is does peri-operative oliguria predict post-operative ARF? Based on the majority of clinical studies the answer would be a resounding, no! Both Alpert *et al.*, and Knos *et al.*, studied patients undergoing aortic reconstructive surgery and found no correlation between intra-operative urine volume and post-operative renal dysfunction.[57,58] None the less both groups of authors administered furosemide when the anesthesiologists or surgeons became "uneasy" with a diminished urine output, despite clinical data suggesting normal EABV and $\dot{Q}_t$. Zaloga and Hughes recognizing that oliguria could simply be a manifestation of either hypovolemia or normovolemia with stress-induced ADH secretion studied 18 critically ill oliguric patients all of whom had normal renal function.[59] Not surprisingly the hypovolemic patients responded to a rapid intravenous saline bolus by increasing urine output. However, the oliguric, normovolemic patients had no response in urine output to the fluid challenge. Instead, 33% of these otherwise normovolemic patients developed pulmonary edema as a manifestation of ADH-induced free water reabsorption. These studies tend to perpetuate the myth that in patients with normal EABV and $\dot{Q}_t$, untreated oliguria will cause ARF.[60]

There are three key concepts that are imperative to the understanding of assessing oliguria:

1. Oliguria and renal perfusion are not analogous to ST-segment elevation and myocardial perfusion in that immediate therapy of oliguria is not crucial in preventing renal ischemia and ARF.
2. Adequate or "good" urine output does not exclude the possibility of impending renal dysfunction. On the contrary, non-oliguric ARF is commonly observed peri-operatively, occurring during or after surgery for burns, trauma, and aortic or coronary revascularization.[61–63]
3. Oliguria may be a sign of renal hypoperfusion, and while efforts are made to ensure adequate EABV and $\dot{Q}_t$, further diagnostic studies must be elicited to distinguish its etiology before any form of renal protective therapy is considered.

A number of simple, rapid and inexpensive diagnostic tests are useful to distinguish acute, pre-renal oliguria from impending ARF. A urine sample should be analyzed by dipstick for proteinuria, and sediment examined for microscopic evidence of renal tubular epithelial cells, cellular debris and pigmented granular casts, all of, which are indicative of ARF.[64] Although serum creatinine levels will not change acutely, calculating the patient's baseline creatinine clearance with the Cockcroft–Gault formula and comparing it to a measured creatinine clearance will assist in differentiating the oliguric patient with renal insufficiency from the patient with ADH-induced oliguria[65] (Appendix 1). The use of the Cockcroft–Gault formula also helps to appreciate that the calculated creatinine clearance in a 70-year old, 60 kg female (with a creatinine of 1.2 mg%) is significantly less than a 40-year old, 70 kg male (with the same creatinine); 41 ml/min vs. 81 ml/min, respectively. In the obese patient, the Cockcroft–Gault formula tends to overestimate the creatinine clearance when using the actual body weight, and underestimates the creatinine clearance when using the ideal body weight.[66,67] Twenty-four hour urine collections to measure creatinine clearance, however, are cumbersome and time consuming. However, the peri-operative uses of 30 min, 1 and 2 h creatinine clearances have been shown to be accurate in estimating changes in GFR.[62,66–69] Urine indices that determine osmolality, creatinine and sodium concentration, coupled with simultaneously obtained serum levels of these corresponding measures, help to further differentiate pre-renal oliguria/azotemia from ARF. Summarizing, the typical urinary diagnostic indices used to distinguish these two entities are shown in Table 14.3.

Miller *et al.*, originally described the use of urinary diagnostic indices in a prospective study of patients with ARF, including non-oliguric and obstructive forms, and concluded that these tests were of diagnostic value predominately in oliguric patients.[70] Patients with

Table 14.3 Urinary diagnostic indices: pre-renal oliguria/azotemia vs. ARF

Urinary diagnostic indices	Pre-renal	ARF
Osmolality (mOsm/kg H_2O)	>500	<350
Sodium concentration (mEq/l)	<20	>40
FE_{Na^+} (%)	<1	>1
Urine sediment/dipstick	–	Pigmented granular casts/ proteinuria

pre-renal oliguria/azotemia were shown to have a urine osmolality >500 mosm/kg H_2O, urine sodium <20 mEq/l and fractional excretion of filtered sodium (FE_{Na}+) <1% (Appendix 2). This signifies, preserved concentrating and reabsorptive capacity of the kidney. In contrast, patients with oliguric ARF had a urine osmolality <350 mOsm/kg H_2O, urine sodium >40 mEq/l and FE_{Na}+ >1% representative of impaired renal function. Although FE_{Na^+} is highly sensitive and specific, a value <1% has been reported in patients with myoglobinuria, radiocontrast nephropathy, sepsis or urinary tract obstruction.[64,71] The clinical utility of these indices are further limited when applied to patients who are non-oliguric, have received diuretic therapy, or who have obstructive uropathy. Ultrasound imaging is particularly useful in oliguric or anuric (urine production <40 ml/day) patients suspected of urinary tract obstruction.

In addressing the differential diagnosis of post-operative oliguria, urinary tract obstruction (including the bladder catheter) decreased EABV or Q_t, and excess secretion of ADH should be considered prior to pursuing the diagnosis of ARF. Simple irrigation of a bladder catheter may unravel the mystery of diminished urine production. In addition to accidental surgical ligation of the ureters during abdominal or pelvic surgery, increased abdominal pressure from ascites, hemorrhage or abdominal compartment syndrome, may cause oliguria/azotemia due to both ureteral and vena caval compression.[37,72] Measuring intra-abdominal pressure via a transurethral bladder catheter has been shown to be a useful technique in determining the need for abdominal re-exploration.[72,73] Extracellular volume depletion and acute blood loss remain the most common causes of peri-operative oliguria/azotemia. Central venous or pulmonary artery catheters, and/or transesophageal echocardiography may be necessary in order to assess both EABV and Q_t and appropriately direct therapy. Although measuring ADH levels is impractical in a clinical setting, one may assume that a patient who has no pre-operative renal risk factors, who has not undergone a high renal risk procedure and who has no evidence of obstruction, hypovolemia or low cardiac output, is oliguric on the basis of excess ADH. These patients will correct over time as the levels of ADH decrease and therefore do not require any medical intervention.

14.7 Pharmacologic interventions in acute renal failure

The major goal in choosing any mode of prophylactic therapy is to ARF-D. While it is universally acknowledged that patients with spontaneously induced non-oliguric ARF have significantly less morbidity and mortality, a pharmacologically induced increase in urine volume does not have similar predictive implications. Despite the vast array of agents studied, none have conclusively or consistently shown outcome benefit in either preventing ARF-D or death. The agents commonly employed to improve renal perfusion in patients suspected of having ARF are listed in Table 14.4.

Table 14.4 Pharmacologic therapy for prevention/treatment of ARF

Sympathomimetic amines
- Dopamine
- Dopexamine
- Fenoldopam

Natriuretics
- Furosemide
- Mannitol
- ANP

Calcium channel antagonists
- Diltiazem
- Nifedipine

Other
- Endothelin antagonists
- Growth factors

Low-dose dopamine (LDD), often inappropriately referred to as "renal-dose" dopamine, has been shown experimentally, in doses 0.5–3.0 μg/kg/min, to stimulate dopamine-specific receptors in the renal vasculature promoting vasodilatation, while inhibiting sodium reabsorption in the proximal tubule causing natriuresis. However, in the few prospective, randomized, controlled clinical studies LDD fails to alter outcome in patients after cardiac, aortic or biliary tract surgery.[74–77] Therefore, the routine peri-operative use of prophylactic LDD does not seem warranted.[78] Its use should also be tempered with the knowledge of the drugs potent side effects. LDD has been shown to cause nausea and vomiting by central nervous system stimulation of dopamine receptors, promote post-operative arrhythmias following cardiac surgery[79] and suppress circulating levels of anterior pituitary-dependent hormones,[80] including prolactin, which plays a major role in modulating cellular immune function.[81] Perhaps a situation in which LDD does appear to have some beneficial effects is in offsetting norepinephrine-induced renal hypoperfusion in patients with systemic inflammatory response syndrome (SIRS)-induced hypotension.[82,83]

Dopexamine, a synthetic sympathomimetic amine, stimulates adrenergic β_2 and dopaminergic DA_1

receptors thus exerting both a systemic as well as renal vasodilating effect. Studies in healthy volunteers, as well as in patients undergoing aortic and cardiac surgery have shown modest improvement in creatinine clearance in doses of 0.5–1.0 μg/kg/min of dopexamine.[84,85] Berendes *et al.* also reported on dopexamine's role in decreasing proinflammatory cytokines following cardiac surgery as a result of this dual receptor stimulation.[86] This agent therefore may prove even more advantageous than LDD when administered concomitantly with norepinephrine in patients with SIRS.

Fenoldopam is another synthetic dopamine agonist that binds selectively to DA_1 receptors causing both systemic and renal vasodilatation.[87] Clinical studies describe its use primarily for the treatment of hypertensive emergencies including post-cardiac surgery hypertension. Theoretically, fenoldopam should augment renal blood flow following CPB, or during aortic cross clamping or DHA,[88] but to date there are no clinical studies documenting improved renal outcome. Unlike dopamine, fenoldopam does not affect the release of anterior pituitary hormones.[89]

Loop diuretics such as furosemide have been used for decades to prevent and/or treat both experimental and clinical ARF. Furosemide acts by inhibiting the active transcellular transport of chloride and sodium thus producing a natriuresis and associated diuresis. Experimental data suggest that by reducing active transport, furosemide decreases cellular oxygen demand thus reducing damage to the mTAL. The diuretic effect may also increase clearance of necrotic cellular debris thereby diminishing tubular obstruction. Unfortunately, clinical studies are lacking in validating these potential therapeutic effects in patients with either impending or established ARF. In a recent prospective, randomized, double-blind, placebo-controlled study, 92 patients with ARF,[90,91] randomized to receive furosemide, torasemide or placebo in addition to LDD and mannitol, had significant improvements in urine flow rates but no change in their overall dialysis-free survival.[90] Interestingly, those patients who converted from an oliguric to a non-oliguric state had lower mortality, but they were also noted to be significantly less ill and have less severe renal failure. It is critical to recognize that in attempting to promote a diuresis, furosemide may worsen renal function by decreasing EABV and Q_t or by occasionally causing interstitial nephritis. Excessive and prolonged use may also cause ototoxicity, which is usually reversible.

Mannitol is an osmotic diuretic that when administered prior to an ischemic insult, such as CPB or aortic cross clamping, has been purported to decrease renal injury. Proposed mechanisms of action include a "flushing" effect of necrotic tubular debris, oxygen free radical scavenging and improves medullary blood flow by reducing endothelial edema. In comparative studies of prophylactic therapy, however, mannitol imparts no greater renal protection than maintaining EABV with intravenous fluids.[92,93] None the less, mannitol is often administered prior to aortic cross clamping in doses of 0.25–1.0 mg/kg. Monitoring serum electrolytes is necessary as hyponatremia, hypokalemia and hypomagnesemia can occur.

Atrial natriuretic peptide (ANP) is a hormone synthesized by the cardiac atria that has been shown experimentally to improve renal function in models of ARF. ANP dilates afferent arterioles thus increasing P_{GC} and therefore GFR. ANP also inhibits the tubular reabsorption of chloride and sodium, redistributes medullary blood flow and blocks the effects of endothelin on the renal vasculature. Allgren *et al.*, in a multicenter, randomized, double-blind, placebo-controlled clinical trial administered ANP via a 24-h infusion to patients with ARF.[94] Results of this large study showed an increase in dialysis-free survival only in those patients with oliguric ARF. Patients with non-oliguric ARF fared worse presumably due to hypotension from the ANP infusion. In a subsequent study in critically ill patients who developed ARF following major abdominal surgery, urodilatin, a derivative of ANP, failed to improve renal function when administered to patients concomitantly receiving infusions of LDD and furosemide.[95] Currently ANP does not appear to be beneficial in the prevention or treatment of ARF.

Calcium channel antagonists have also been studied in both experimental models as well as clinical trials. Wagner *et al.* evaluated the effects of diltiazem in preventing ARF following cadaveric renal transplantation.[96] Diltiazem was added to the preservative solution as well as given as a pre-operative intravenous injection, followed by maintenance therapy. The diltiazem-treated group had a 10% incidence of ARF vs. a 41% incidence in the control group, and accordingly had significantly less dialysis treatments. Antonucci *et al.* studied the effects of the calcium channel antagonist, nifedipine vs. LDD, in patients undergoing aortic surgery with infrarenal cross clamping.[97] Results of this study showed that nifedipine but not LDD improved GFR with evidence supporting the drug's role in enhancing the vasodilating prostaglandin E_2, suppressing the vasoconstricting prostaglandin thromboxane B_2 and by modulating the vascular synthesis of endothelin. These results are similar to experimental data showing the beneficial effects of an endothelin

antagonist on renal function following aortic cross clamping in a dog model.[98]

Finally, there appears to be a role for agents designed to promote proximal tubule restoration following acute tubular necrosis. Insulin-like growth factor (IGF-I) is known to bind to specific receptors in the proximal tubule and regulate proliferative responses in these cells. Preliminary work by Franklin *et al*. in patients undergoing suprarenal cross clamping suggest that IGF-I administered subcutaneously after surgery may improve renal function.[99] Future multicenter studies will need to validate these results.

14.8 Renal-replacement therapy for acute renal failure

There are a number of complications of ARF that may require the institution of RRT in the forms of either dialysis of hemofiltration. Clinical indications for RRT include pulmonary edema, symptoms of uremia, severe metabolic acidosis, hyperkalemia and accidental drug overdoses.[64] The decision with respect to which mode of RRT to select (for example, hemodialysis, peritoneal dialysis or hemofiltration) is often based on the patient's hemodynamic stability and catabolic state. Patients with multiorgan system failure, including ARF, who are hemodynamically unstable, may benefit from the use of continuous venovenous hemofiltration (CVVH).[100] This technique involves establishing a large venous access (for example, subclavian or femoral vein) with a double lumen dialysis catheter, through which blood passes under the control of an occlusive pump to an extracorporeal hemofiltration circuit. Blood passes under pressure through a highly permeable membrane that allows water and solutes of molecular weights as great as 20,000 Da to be filtered. In contrast, dialysis membranes only allow for smaller molecules to be cleared and then at a much slower rate. Hemofiltration offers other possible advantages such as the removal of cytokines, and the ability to administer continuous nutritional support.[101] Disadvantages include the need for continuous anticoagulation and meticulous plasma ion replacement.

The more recent development of biocompatible dialysis membranes[101] is that RRT appears to have significantly altered the survival rates in critically ill patients with ARF; however, the overall mortality for ARF remains high.[102] Indeed hemodialysis-induced hypotension may paradoxically prolong the course of ARF by causing transient periods of renal ischemia.[47] Preliminary studies suggest that CVVH may improve survival rates in critically ill patients with ARF;[103] however, its precise role has not yet been defined.

Finally, peritoneal dialysis can be used in the setting of ARF but is limited by the increased risks of peritonitis, atelectasis and pneumonia.

14.9 Conclusion

Obese patients with associated hypertension, diabetes and chronic renal disease have an increased risk for developing peri-operative renal failure (see Chapters 10 and 11). Too often, in the setting of post-operative oliguria, clinicians become engrossed in the process of making urine appear. If intravenous fluid boluses fail, furosemide is usually administered, a routine that can be euphemistically termed "endothelial lavage". However, management of post-operative renal dysfunction and in particular oliguria, requires a more detailed risk assessment including calculation of a baseline creatinine clearance, assurance of adequate EABV and Q_t, exclusion of urinary tract obstruction, and if need be, determination of urinary diagnostic indices to distinguish pre-renal insufficiency from ARF. Obese patients suspected of ARF need to have their oxygen delivery maximized, medications adjusted in accordance to GFR and agents with potential nephrotoxicity avoided. Although most physicians will attempt to pharmacologically convert oliguiric to non-oliguric ARF, clinical evidence validating this approach remains unsubstantiated.

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Appendix 1

Cockcroft–Gault formula

$$C_{\mathrm{Cr}} = \frac{(140 - \mathrm{age}) \times (\mathrm{kg})}{72 \times S_{\mathrm{Cr}}} \ (0.85 \text{ female})$$

where age is given in years; C_{Cr} is creatinine clearance and S_{Cr} is serum creatinine. Multiply the value by a factor of 0.85 for females due to less muscle creatinine production than males.

Appendix 2

Fractional excretion of sodium

$$\mathrm{FE}_{\mathrm{Na}^+} = \frac{U/P\,\mathrm{Na}^+}{U/P\,\mathrm{Cr}} \times 100$$

where U/P is urine to plasma ratios of sodium and creatinine.

PHARMACOLOGY

SECTION 5

PHARMACOKINETICS AND PHARMACODYNAMICS:ESSENTIAL GUIDE FOR ANESTHETIC DRUGS ADMINISTRATION

15

L.E.C. De Baerdemaeker, E.P. Mortier & M.M.R.F. Struys

15.1 Introduction

Morbidly obese patients undergoing general anesthesia represent a challenge for the anesthesiologist as multiple co-morbidity might compromise their physiological status. Therefore, special anesthetic approaches have to be considered when anesthetizing morbidly obese patients. In addition to the physiological challenges, pharmacological changes associated with obesity might lead to alterations in the distribution, binding and elimination of many drugs. The net pharmacokinetic effect in these patients is often uncertain, making drug titration even more difficult and unpredictable.[1]

Beside kinetics, pharmacodynamic changes can be seen in morbidly obese patients. Additionally, many package inserts, including a wide variety of drugs like benzodiazepines, opioids, intravenous (i.v.) anesthetic agents, volatile anesthetic agents, muscle relaxants, local anesthetics and other drugs such as those influencing the cardiovascular system, explicitly provide per-kilogram adult-dosing guidelines. Doesn't this tell us that the drugs should be given per kilogram of body weight? That is the message, but it may be wrong.[2] One of the problems in providing anesthesia for morbidly obese patients is how does obesity influence the pharmacokinetics and pharmacodynamics compared to non-obese patients. As a result, multiple questions have to be answered: Can pharmacokinetic-based drug administration be used as safely in obese patients as it is being used in the non-obese or do we need to correct them and in what way? What about pharmacodynamics and pharmacodynamic monitoring, if available?

15.2 Changes in pharmacokinetics

In clinical anesthesia practice, most drugs are given using standard-dosing guidelines without applying

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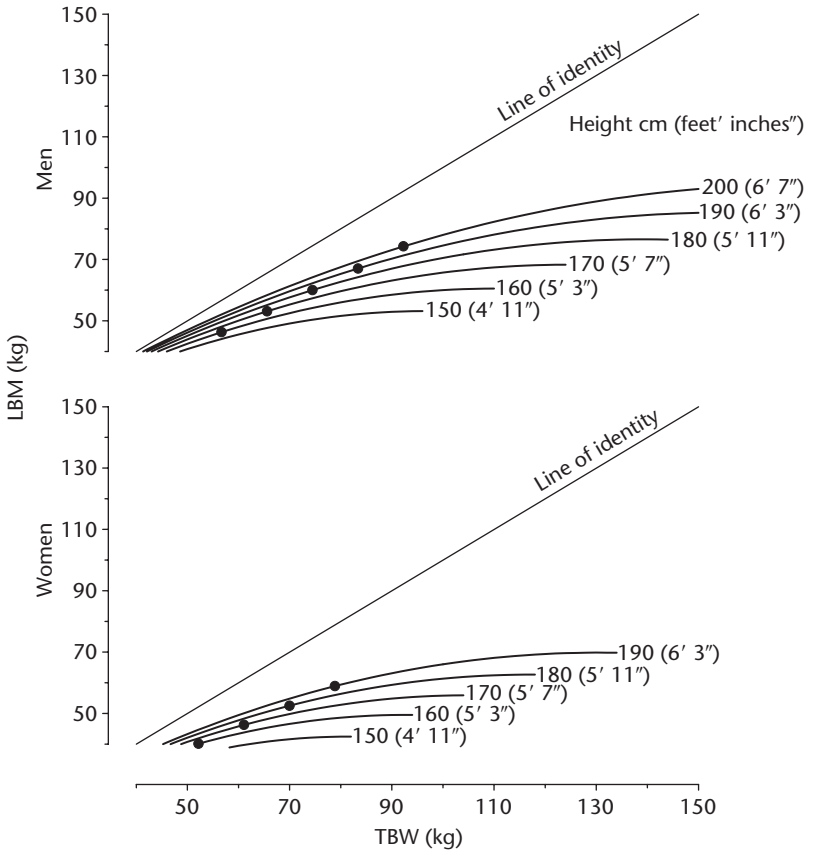

Figure 15.1 A nomogram relating TBW, height, and gender to LBM. (The dots show the IBW at each height, computed from standard formulas.) (Reprint from Ref. 2, with permission.)

knowledge of their pharmacokinetics to control their administration. Drugs are sometimes administered with the rationale: "Give some drug and observe your patient to see what happens". In addition, administration of drugs in obese patients is difficult since dosage based on pharmacokinetic data obtained in normal-weight individuals could induce errors. Physiopathological modifications in obese patients are likely to affect drug distribution and elimination. Even if not correct, anesthesiologists have become highly skilled at titrating toxic drugs within their narrow therapeutic window towards their specific therapeutic and clinical effect. Using these skills, it might be observed that most anesthesiologists reduce doses in obese patients based on experience and intuition alone.[2]

One might ask if "size does matter"? Before being able to answer this question, the clinician has to know what "weight" has to be used to calculate dosage: total body weight (TBW), lean body mass (LBM) or ideal body weight (IBW)? Mostly, dosage recommendations in the package inserts are scaled to TBW (not to LBM or IBW) and the assumption is made that pharmacokinetics are weight proportional. Therefore, different strategies of adjusting the dosage in obese patients are developed: scaling to TBW, LBM, IBW, not adjusting at all. In their editorial, Bouillon and Shafer[2] show which of these weight approaches (as a function of patient sex, height and TBW) can be used clinically when we are unsure about the true relation between size and pharmacokinetics (Figures 15.1 and 15.2).

This weight can then be multiplied by the published doses scaled to TBW. These figures also show that weight scaling is important in persons heavier than IBW. Below IBW the TBW and the weight that should be used to scale by LBM are not very different.

Classical pharmacokinetic parameters such as volume of distribution (V_d), clearance (Cl) and protein binding can change for some drugs in morbidly obese patients.[1] Highly lipophilic substances such as barbiturates and benzodiazepines show significant increases in V_d for obese individuals relative to normal-weight individuals. Less lipophilic compounds have little or no change in V_d with obesity. Certain exceptions to this rule include

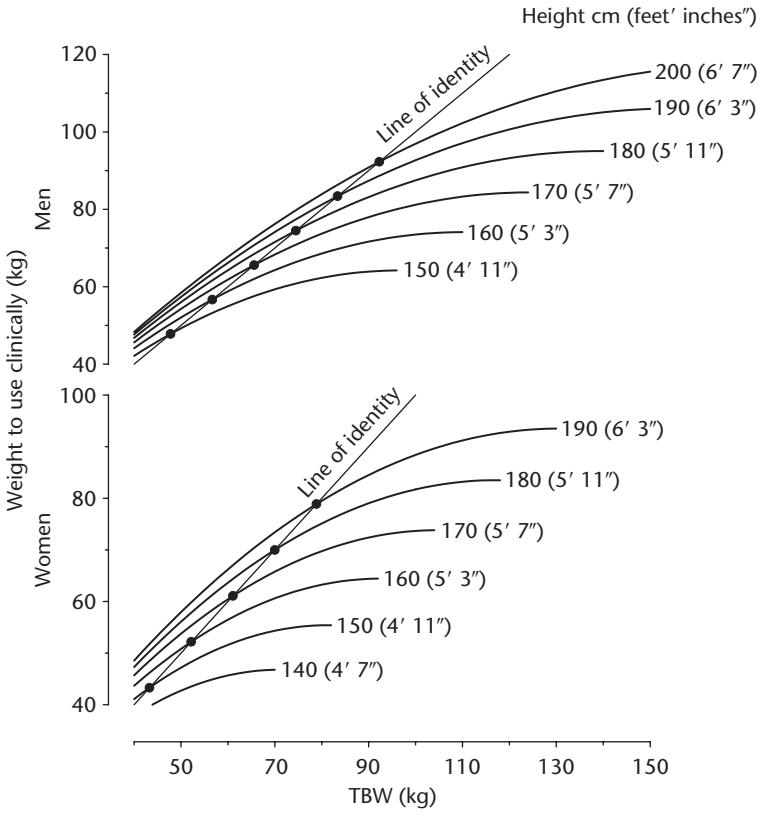

Figure 15.2 A nomogram relating TBW, height and gender to the body weight that should be used to calculate dose from recommendations that are scaled to TBW. (The dots show IBW, as in Figure 15.1.) (Reprint from Ref. 2, with permission.)

remifentanil which is a highly lipophilic drug but with no systematic relationship between the degree of lipophilicity and the distribution in obese individuals. Consequently the absolute V_d remains relatively consistent between obese and normal-weight individuals and the dosage should be calculated on the basis of IBW. Drugs with weak or moderate lipophilicity can be dosed on the basis of IBW or more accurately on LBM. These values are not identical because 20–40% of an obese patient's increase in TBW can be attributed to an increase in LBM. Adding 20% to the estimated IBW dose of hydrophylic medication is sufficient to include the extra lean mass. Non-depolarizing muscle relaxants can be dosed in this manner. Succinylcholine is an exception, dosage should be done on TBW. The majority of anesthetic drugs are strongly lipophilic. Increased V_d is expected for lipophilic substances but this is not consistently demonstrated in pharmacological studies because of factors such as end-organ clearance or protein binding.[3] Blouin *et al.* observed that the V_d of water-soluble agents is less affected by obesity than lipophilic compounds.[4] Drugs with high affinity for fat tend to have an increased V_d in the obese.

Albumin binding of drugs is unchanged in the obese, but plasma protein binding may be influenced by obesity-associated increases in fatty acids, triglycerides and alpha$_1$-acid glycoprotein. This means that the free fraction of acidic drugs is unchanged, the free fraction of basic drugs can be increased.

Most obese patients have fatty infiltration of the liver or even non-alcoholic steatohepatitis (NASH). This may affect the clearance of high extraction compounds. Obesity does not affect phase 1 metabolism. Drugs with phase 2 conjugation pathways appear to be cleared faster in the obese. Both renal glomular filtration and tubular secretion are increased in the obese, and renally excreted drugs may need increased dosage.[4]

15.3 Changes in pharmacodynamics

An equally important consideration when developing a dosing strategy for obese individuals involves the consideration of drug efficacy. It is important to note that with the plethora of probable genetic, pathophysiological and nutritional changes associated with obesity, changes in receptor expression or affinity for ligand could be altered resulting in differential

pharmacotherapeutic effects in obese individuals as compared to lean individuals.

15.3.1 Gamma-aminobutyric acid (A) receptor and obesity

Gamma-aminobutyric acid (GABA (A)) is the major inhibitory neurotransmitter in the vertebrate brain and acts by binding to GABA receptors. Food intake and ingestive behavior is not only controlled by central monoaminergic systems (norepinephrine, dopamine and serotonin) also by neural peptides and GABA. Cortisol secretion is partially controlled by GABA. Rosmond *et al.* studied the association of allelic variants of the GABA (A) alpha-6 receptor and abdominal obesity caused by increased cortisol secretion.[5] Their conclusion was that allelic variants of GABA receptors may predispose to hypercortisolism and abdominal obesity. The pathophysiology may involve various environmental factors, particularly stress that destabilizes the GABA hypothalamic pituitary adrenal systems in those with genetic vulnerability. In individuals with either Prader–Willi or Angelman syndrome, elevated plasma GABA was measured by Ebert *et al.*[6] Possibly this represents a compensatory increase in presynaptic GABA release in response to hyposensitivity of a subset of GABA receptors. This could produce an increased postsynaptic activation of other normal-GABA receptor subtypes resulting in complex alterations of GABAergic function throughout the brain. Lee *et al.* studied the GABAergic modulation of ventilation and peak oxygen consumption in obese Zucker rats.[7] They concluded that the reduced exercise capacity in obese rats may be attributed to altered GABAergic mechanisms. These findings suggest that GABAergic tonic inhibition may be potentially responsible for the "obstructive hypoventilation syndrome" in obese patients. In addition to GABA, complex interactions among various neurotransmitters and neuromodulators involved in the etiology of obesity such as leptin, neuropeptide Y, dopamine, opioids, adenosine and several hormones, may be directly or indirectly involved in GABAergic regulation. Additional studies are required to address the role of GABAergic mechanisms in morbidly obese humans.

15.3.2 Opioid receptors, endogenous opioids and obesity

Levels of endogenous opioids, particularly beta-endorphin are increased in morbidly obese humans and obese rats. Endogenous opioids are important neuromodulators and are involved in a wide range of functions including food intake, body weight and ventilatory control. Cole *et al.* and Marin-Bivens *et al.* showed that chronical central administration of opioid receptor subtype antagonists resulted in weight loss and reduced intake.[8,9] Mu-opioid agonists preferentially increase the intake of highly palatable food. Smith *et al.* investigated the changes in mu-opioid binding in feeding and reward related brain regions in rats given palatable diet for 17 weeks.[10] In all investigated brain regions, binding was significantly correlated with plasma leptin and insulin. The authors suggest that increased mu-binding reflects decreased release of endogenous opioid peptides. This may represent a failed homeostatic attempt to limit overeating and eventually obesity.

Evans *et al.* demonstrated that the density of beta-endorphin and delta opioid receptors in muscles was greater in obese mice.[11] Boudarine *et al.* investigated the activity of mu- and kappa-receptors in mice with late onset obesity due to a point mutation in the carboxypeptidase E (responsible for the biosynthesis of neuropeptides).[12] They found that mu-receptor activity was altered in select brain regions. The natural ligand for these mu-receptors was found to be Met-Enk. Met-Enk and mu-receptors may contribute to the development of obesity in these mice.

15.3.3 Neuromuscular blockade and obesity

Varin *et al.* showed that even though obese individuals were exposed to significantly higher plasma concentrations of atracurium, no change was seen in the duration of neuromuscular blockade. The authors attributed these changes in sensitivity to a combination of protein-binding effects and desensitization of acetylcholine receptors. Desensitization of acetylcholine receptors has been associated with chronic inactivity.[13]

15.3.4 Beta-receptors and obesity

The peripheral sympathetic nervous system is a key factor in the regulation of energy balance in humans. Differences in sympathetic nervous activity may contribute to variations in 24 h energy expenditure between individuals. Beta-adrenoceptors play a more important role than alpha-adrenoceptors in this regulation. The involvement of both beta-1 and beta-2 adrenoceptors subtypes has been demonstrated, the role of the beta-3 subtype is not yet clear.[14] Obesity does have an influence on beta-receptors. Cabrol *et al.* assessed the cardiac beta-adrenoceptors in a canine model of obesity and hypertension.[15] Left ventricular beta-adrenoceptors came under a specific desensibilization independent of plasma noradrenaline levels. This functional decoupling of beta-adrenoceptors may account for the progressive systolic dysfunction of hypertensive cardiomyopathy in obese patients.

Merlino *et al.* studied the total and surface beta-adrenergic receptor (BAR) density and their relationship with hemodynamics and left ventricular function in young subjects with central or peripheral obesity.[16] Total and surface density of BAR were significantly lower in both obese groups compared to lean individuals. Plasma Norepinephrine levels were higher in the central obese type. Carroll *et al.* found that obesity related decreases in responsiveness of the isolated heart to isoproterenol are not associated with alterations in beta-receptor density and affinity.[17] In addition adenylyl cyclase activity appeared unchanged in ventricular preparations from obese rabbits. Decreased responsiveness to isoproterenol in obesity may be due to effects downstream of adenyl cyclase activation of cAMP. Recently, genetic evidence about the involvement of adrenoceptors in obesity has become available. Gln27Glu beta-2 adrenoceptor, a genetic variant of the beta-2 adrenoceptor, confers resistance to agonist-induced desensitization and enhanced vasodilator response to isoprenaline. This variant could not be linked to hypertension but to overweight, stressing the importance of beta-adrenoceptors and their role in obesity.[18] Although the results of association and linkage studies on polymorphisms in the beta-2, beta-3 and alpha-2 adrenoceptors genes are inconsistent, the functional correlates of some of these polymorphisms (changes in agonist promoted downregulation, protein expression levels, lipolytic sensitivity basal metabolic rate, sympathetic nervous system activity) suggest that they may be important in the etiology of obesity.[19]

15.3.5 Dopamine and obesity

Recent evidence provided a clear association between obesity and the decrease in the expression of D2 receptors in the brain of obese persons. Dopamine, a neurotransmitter that modulates rewarding properties of food is likely to be involved. Wang *et al.* used positron emission tomography (PET) scan and C11 raclopride (a radioligand for D2 receptors) to demonstrate that the availability of D2 receptors in the striatal areas of the brain was decreased in obese individuals in proportion to their body mass index (BMI). Dopamine deficiencies may perpetuate pathological eating as a means to compensate for decreased activation of these circuits.[20]

15.3.6 Leptin and obesity

Leptin is a protein produced by adipose tissue that interacts with receptors in the hypothalamus to provide information about the energy status of the body and to inhibit eating. Leptin might have therapeutic potential for obesity related breathing disorders associated with a relative deficiency in leptin or a leptin resistance. Most obese subjects have high serum levels of leptin, suggesting that the major problem is leptin resistance rather than leptin deficiency.[21]

15.4 Application of pharmacokinetics in the obese patient

Obesity is common enough to constitute a serious medical and public health problem. As these patients require anesthesia even more often due to co-morbidity, anesthetists have to be able to manage these patients in a safe way. Therefore, the above described information on altered pharmacokinetics and pharmacodynamics in obese patients has to be translated to a practical application for our daily anesthetic practice.

15.4.1 Propofol

Propofol has a favorable pharmacological profile for the induction and maintenance of anesthesia or sedation.[22] It is known for its fast onset and offset. Classically, propofol bolus injection or continuous infusion are guided on a weight base.[23]

When applying propofol in morbidly obese patients, alterations in kinetics and dynamics have to be questioned. For induction of anesthesia with propofol, dosage can be calculated on IBW.[24–26] When using propofol to maintain anesthesia in elective patients, Hirota *et al.* measured the plasma propofol concentration at the end of surgery after a fixed rate infusion of propofol and found that plasma concentrations were dependent on TBW.[27] This may imply that when obese patients are anesthetized with propofol based on TBW, deep anesthesia and deleterious cardiovascular effects may result. Servin *et al.* used a specific-dosing scheme and demonstrated that propofol does not accumulate in morbidly obese patients.[28] Although they concluded that the dosage of propofol for maintenance of anesthesia in obese subjects expressed in mg/kg/h are the same as in normal patients, an empirical formula was used to calculate weight: corrected weight = ideal weight + (0.4 × excess weight).

Propofol pharmacokinetics have been studied extensively using classical and compartmental pharmacokinetics in non-obese patients.[29–31] These models have been implemented into pharmacokinetic-based drug infusion, also called target-controlled infusion (TCI) devices. The idea behind TCI techniques is to use pharmacokinetic modeling and calculations to predict a set concentration in one of the pharmacokinetic

compartments (plasma or effect site). These TCI devices will rapidly achieve and maintain this desired predicted concentration in the specific compartment. The specific target concentration and patient demographics are set by the anesthetist. In a clinical setting, the first device that became commercially available for propofol infusion was "Diprifusor®" (AstraZeneca, London, UK) using the weight-adjusted three compartmental model published by Marsh *et al.*[32] As this model was not developed for morbidly obese patients, one might ask which weight has to be dialed into the system. Most anesthetists feel that obese patients may be at risk of overdose when TBW-adjusted infusion schemes are used. Gepts *et al.* recommends the corrected body weight being the ideal weight + (0.4 × excess weight) as published previously by Servin *et al.*[28] Although no evidence has been found in the literature to defend or reject this clinical practice, two cases of intraoperative awareness during propofol anesthesia when using the Diprifusor® device with adjusted body weight are reported.[33]

The recently developed three compartmental models in non-obese patients suggest using LBM instead of TBW or IBW. Schüttler *et al.* made an estimation of the pharmacokinetics of propofol with respect to the covariates age, body weight and gender and at the same time made an evaluation of the inter- and intraindividual pharmacokinetic variability.[34] Age and weight were covariates of his three compartmental model. The influence of body weight on all clearances and compartmental volumes could best be modeled by a power function with an exponent smaller than 1. For those patients whose heights were known, the individual pharmacokinetic parameters did not correlate better with LBM than with body weight. This is in contrast to the work of Schnider *et al.* who found that inclusion into his model of weight, height and LBM improved his fit significantly compared to inclusion of any combination of just two of these three covariates.[35] Recently, this model has been implemented in a new commercial device (Primea-Base, Fresenius-Vial, Grenoble, France). More studies are required to optimize propofol TCI in morbidly obese patients.

15.4.2 Midazolam

Greenblatt *et al.* demonstrated that V_d and elimination half-time increases in line with body weight but they did not find significant change in total metabolic clearance.[36] Thus midazolam should be administered in larger absolute doses, but in the same doses per unit body weight. A prolonged sedation can occur from the larger initial dose needed to achieve adequate serum concentrations. The rate of continuous infusion, however, should be adjusted to the ideal rather than the total weight.[37]

15.4.3 Thiopental

Thiopental has an increased V_d and a longer elimination half-time but clearance values are unchanged in obese patients. A dosage of 7.5 mg/kg IBW is adequate.[38]

15.4.4 Volatile anesthetic drugs

Halothane is known to have considerable deposition in adipose tissue and an increased risk of reductive hepatic metabolism, increasing the risk of halothane hepatitis.[39] Enflurane has a blood : gas partition coefficient which falls with increasing obesity. This means possibly lowering the minimal alveolar concentration (MAC) of enflurane. The inorganic fluoride concentrations rise twice as fast in obese individuals, increasing the risk of fluoride nephrotoxicity following prolonged administration of enflurane.[40] Due to their lower blood : gas solubility, sevoflurane and desflurane pharmacokinetics seem not to be influenced by obesity and they have been used safely and without major problems in obese patients.[41] Some investigators observed significantly higher concentrations of fluoride metabolites in obese patients anesthetized with sevoflurane than in non-obese patients, whereas others have found no differences. Major metabolites of desflurane are inorganic fluoride and trifluoroacyl chloride, which may bind to tissue proteins or and up as trifluoroacetic acid in the urine. Only a single case of desflurane hepatotoxicity has been reported.[42]

Øberg *et al.* consider isoflurane as the drug of choice in obese patients due to less fluoride levels and less organ toxicity.[43] Others have suggested desflurane as the inhaled anesthetic of choice in morbidly obese patients because of its more rapid and consistent recovery profile and the fact that it has the lowest solubility in fat tissues.[44] Rapid elimination and analgesic properties make nitrous oxide a good choice during bariatric surgery, but high oxygen demand in the obese limits its use.[45]

Two defining effects of inhaled anesthetics (immobility in the face of noxious stimulation and absence of memory) correlate with the end-tidal concentrations of the anesthetics. Such defining effects are characterized as MAC (the concentration producing immobility in 50% of patients subjected to a noxious stimulus) and MAC-awake (the concentration suppressing appropriate response to command in 50% of patients, memory is usually lost at MAC-awake).

These defining effects of inhaled anesthetics may be monitored by the end-tidal concentrations and the results displayed if the concentrations are known and corrected for the effects of age and temperature. Weight correction seems not to be necessary.[46]

The major advantage in administering inhaled anesthetics compared with i.v. drugs is found in the availability of inspired and end-tidal concentration on-line. Although the end-tidal partial pressures of volatile anesthetics are greater than the drug concentration in arterial blood the ratio of the arterial partial concentration and the end-tidal partial pressure is remarkably stable. By knowing the end-tidal concentration, optimization in inhaled drug administration by using "inhalation bolus technique" and closed-circuit anesthesia systems is possible even in morbidly obese patients.[47,48]

15.4.5 Analgesics, opioids and patient-controlled analgesia

Theoretically, obesity significantly affects the protein kinase (PK) profiles of lipophilic drugs including alfentanil, fentanyl and sufentanil. This is because the peripheral compartments are characterized by a high amount of adipose tissue which could result in a prolonged beta-elimination half-life ($t_{½}\beta$). Bentley *et al.* studied the PK of fentanyl on obese vs. non-obese and found no significant differences.[49] The author suggested administering fentanyl on an LBM basis. In other work, the same author showed that obesity decreases clearance and prolongs $t_{½}\beta$ of alfentanil but did not appear to affect the maximum plasma concentration or V_d.[50] He suggested that loading dose and maintenance dose of alfentanil should be calculated on LBM because of its prolonged half-time in obese patients. When applying compartmental pharmacokinetics for TCI purposes, Maître *et al.* found obesity had no effect on alfentanil clearance but a direct relationship with the central compartment volume.[51] In his model, TBW should be used.

In a study in morbidly obese patients comparing the effects of remifentanil, alfentanil and fentanyl on the cardiovascular responses to tracheal intubation, Salihoglu *et al.* used corrected weight = IBW + (0.4 × excess weight) for all opioids. After induction of anesthesia, arterial pressures were decreased in all groups but within acceptable limits.[52]

Controversy in the literature still exists whether the pharmacokinetics of sufentanil are altered in the obese patient or unchanged. Schwartz *et al.* found that obese are characterized by an increased V_d and a prolonged $t^{½}\beta$.[53] These changes correlate with the severity of obesity. One might speculate that a higher fat mass may result in larger V_d at steady state and a longer $t^{1/2}\beta$. In contrast, V_d/kg TBW was similar in the obese and non-obese group. This suggests that the drug was distributed at least as extensively in the excess body mass as in LBM. The author recommends that loading dose must account for TBW, maintenance dose must be prudently reduced. In contrast, in their study of pharmacokinetics and model estimation of sufentanil Gepts *et al.* and Hudson *et al.* found that neither weight nor LBM was a covariate in their model.[54,55] These studies excluded morbidly obese patients, so Hudson concluded that none of these models should be assumed applicable to patients with this condition. Slepchenko *et al.* found that the pharmacokinetic parameter set of Gepts *et al.* derived from a normal-weight population accurately predicted plasma sufentanil concentrations in morbidly obese patients.[83] For BMI > 40, the model overestimated the plasma sufentanil concentrations. When using sufentanil TCI with the pharmacokinetic set of Gepts *et al.*, no weight correction has to be made when punching in weight data.

For remifentanil, it is clear that weight is an important consideration in the formulae of the dosing schemes (see Chapter 16). While developing their compartmental model for remifentanil, Minto *et al.* found that age and LBM were significant demographic factors that must be considered when determining a dosage regimen for remifentanil.[56,57] The essential findings of the study by Egan *et al.* are that remifentanil's pharmacokinetics are not appreciably different in obese vs. lean subjects and that remifentanil pharmacokinetics are therefore more closely related to LBM then to TBW.[58] Clinically this means that remifentanil-dosing regimens should be based on LBM and not TBW. The investigators also recommend the use of a computer-controlled infusion pump to implement their remifentanil model that scales some parameters to LBM. Interestingly, scaling all parameters to LBM or TBW did not result in the best performing models. Other parameters needed to be involved too. In clinical practice, when applying the Minto model for TCI, one should just dial in the TBW of the patient, together with age, height and gender. The TCI device will calculate this towards LBM to be used into the model.

Paracetamol (acetaminophen) disposition is affected by obesity and gender. Acetaminophen V_d is increased in obesity and in men relative to women, but the drug's distribution into body weight exceeding IBW is less extensive than that into IBW. Acetaminophen clearance increases with body weight and therefore is much greater in obese patients and men.[59] The area under the curve (AUC) for oral administration in

obese patients when normalized to IBW was more consistent with that in normal subjects than when normalized to TBW. Administration of a normal dose of acetaminophen to an obese patient should yield plasma levels in the same range as persons of normal weight. Dosing according to TBW rather than IBW could lead to toxic effects.[60]

An important consideration when managing analgesia in morbidly obese patients is the route of administering the drugs[1,61] (see Chapter 29). Regional anesthesia provides safer and more effective postoperative analgesia, but due to contraindications or anatomical considerations it is not always feasible. Anesthesiologists often have to resort to i.v. analgesics. The intramuscular route is not recommended as it is unpredictable and has been shown to provide poorer analgesia than other routes. If the i.v. route is to be used, then a patient-controlled analgesia system (PCAS) is the best option. Doses should be based on IBW, Choi *et al.* prospectively investigated the efficacy of i.v. morphine PCA in morbidly obese patients and found that it provided good analgesia without deleterious effects on oxygen saturation, blood pressure, heart rate or respiratory function.[62] Supplemental oxygen and close observation, including pulse oximetry are still recommended.

15.4.6 Muscle relaxants

When using succinylcholine, dosage should be done on TBW, due to an increase in cholinesterase activity proportional to body weight. This rule applies not only to adult patients, but also to obese adolescents. It has been reported that a smaller total dose of suxamethonium (doses of 120–140 mg) provided satisfactory conditions for tracheal intubation in patients weighing more than 140 kg.[63,64] No data are available on the application of mivacurium in morbidly obese patients. Since it has the same hydrolysis by plasma cholinesterase at a rate of 70–88% that of suxamethonium, one can presume that dosage can be calculated on TBW, yet no available data can confirm this.

Rocuronium in a dosage of 0.6–0.9 mg/kg can be used as alternative for suxamethonium. The long duration of action can be a disadvantage in case of difficult intubation. Pühringer *et al.* advises to administer rocuronium on the basis if IBW.[65] The onset is faster and the duration of action is longer in obese patients. Spoelders *et al.* evaluated the spontaneous recovery from a standardized infusion of rocuronium based on IBW in morbidly obese patients.[66] They concluded that the recovery of rocuronium-induced neuromuscular blockade is comparable to the recovery of neuromuscular blockade in patients with normal BMI, provided rocuronium is administered in a dose calculated to the patient's ideal weight.

Reports concerning the pharmacology of atracurium in obese patients are conflicting. Weinstein *et al.* and Varin *et al.* claim the duration of action of atracurium to be independent of body constitution.[67,68] Their recommendation is to calculate dose on TBW. But several data question this statement. Beemer *et al.* concluded that the clearance scaled to TBW (absolute clearance/TBW) is significantly smaller in obese than in normal-weight patients.[69] Also, absolute V_d in patients weighing between 45 and 98 kg does not increase with increasing TBW.[70] When calculated according to normal weight, the ED 95 of atracurium showed no differences between underweight, normal weight or overweight patients. The dosage necessary to maintain a 95% twitch depression correlated with LBM.[71] In a study of Kirkegaard-Nielsen *et al.* the authors found that the duration of action of atracurium neuromuscular blockade (NMB) was prolonged in obese patients.[72] TBW divided by surface area and TBW were the best predictors for duration of action. The authors propose an atracurium dosage regimen where the initial dose of atracurium (0.5 mg/kg) is reduced with 2.3 mg for each 10 kg TBW more than 70 kg. For the supplement dose (0.15 mg/kg) a reduction of 0.7 mg/10 kg TBW more than 70 kg is proposed. Data on the use of cisatracurium in obese patients is sparse.

When looking to antagonists of muscle relaxants in obese patients, it is known that neostigmine has a maximum ceiling effect. The exact maximum dose in humans is not known, but is probably between 35 and 70 μg/kg. Kirkegaard-Nielsen *et al.* concluded in his study that reversal time of neostigmine is independent of TBW and BMI.[73] TBW can be used to calculate antagonism dosage.

15.5 Application of pharmacodynamics in the obese patient

In contrast to pharmacokinetics, which focused on the relation between administered dose and plasma concentration, pharmacodynamics focus on the relation between effector organ concentration and clinical effect (see Chapter 19). The objective of any drug administration is to obtain the desired clinical and therapeutic level as accurate as possible. The importance of accuracy in controlling this dose–response relation is directly related to the importance of optimizing the efficacy and quality of anesthesia while minimizing adverse drug effects. As said above, multiple pharmacodynamic changes like altered levels of endogenous

agonists and antagonists, changes in the number of drug receptors and their sensitivity (increased or decreased), etc. will result is an huge pharmacodynamic variability among patients. If this variability is "multiplied" by the pharmacokinetic changes due to the coupling between pharmacokinetics and dynamics, optimizing drug administration in morbidly obese patients might become very difficult. If the clinician is willing to optimize drug administration on a patient individualized base, pharmacological effect monitoring might become important. Hereby, the ideal method of individualizing drug administration would be a continuous non-invasive measure of the degree of therapeutic drug effect. Thus, one would examine the pharmacodynamic effect (the drug effect) instead of the pharmacokinetics which are the driving force for the drug effect.

Unfortunately, anesthesia is a complex state of the human body. What constitutes anesthesia is still hotly debated, with no sensor able to measure changes in "overall depth of anesthesia".

Depth of anesthesia is an elusive concept. The notion is based on classical theories of anesthesia, which suppose that there is a continuum of anesthetic action related to the dosage of the corresponding agent. As highlighted by Kissin, several observations on the interaction of anesthetic drugs make a revision of this approach necessary.[74] Since different agents act via different mechanisms and these mechanisms contribute to different components of the state of general anesthesia, it is highly improbable that a single reliable index of depth of anesthesia can be designed. However, since the idea of depth of anesthesia and the subsequent problem of controlling it, goes back to the beginning of our discipline and since the concept has found its way into the language, it will be very hard to eradicate it.

For the hypnotic-anesthetic drugs, various electroencephalographic and mid-latency auditory evoked potential (MLAEP)-based indices have become commercially available. Using the electroencephalogram (EEG), several computerized univariate parameters like spectral edge frequency (SEF) and median frequency (MF) can be extracted.[75] However, several investigators have found disadvantages when using these indicators.[76,77] More recently, the bispectral index (BIS, Aspect Medical Systems Inc. Newton, MA) has been tested and validated as a promising measure of the hypnotic component of anesthesia.[78] BIS combines several features extracted from EEG including higher order spectra of the signal which can reveal phase coupling of single waveforms. Multivariate statistics were used to combine the different features into a single indicator. Although not ultimately perfect, BIS offers a sensitivity of 100% and a specificity of around 55% to measure loss of consciousness at values lower than 53 during propofol administration.[79] Beside BIS, other EEG derived indicators are currently developed such as approximate entropy and Shannon entropy.[80,81] Previously, Kenny and colleagues used a derived indicator from the MLAEP, called AEP index, as controlled variable.[82] Until now, one other MLAEP derived indicator is commercially available, namely the AEP monitor (Danmeter, Odense, Denmark). They used a new method for extracting the MLAEP from the EEG signal by employing an autoregressive model with an exogenous input (ARX) adaptive method. This method allows extraction of the AEP signal within 15–25 sweeps of 110-ms duration, resulting in only a 6-s response delay time. A new variable, called the A-line ARX index (AAI), is then calculated from this fast extracted MLAEP wave.[79] In contrast to the hypnotic component, no specific commercially available measure exists for measuring analgesia. Therefore, hemodynamic stability and changes in response to a noxious stimulus has to be used as "analgesia titrator". For the muscle relaxants, a direct measure exists and should be applied whenever possible. During bariatric laparoscopic surgery, complete muscular relaxation is crucial to facilitate ventilation and to maintain an adequate working space for visualization and safe manipulation of laparoscopic instruments. Complete relaxation also facilitates the introduction of surgical equipment and extraction of excised tissues. Unfortunately, inaccurate recovery after muscle relaxation due to large pharamcological variability might result in postoperative residual curarization, hereby compromising adequate ventilation in these already respiratory compromised patients.

15.6 Conclusions

When faced with obese patients, anesthesiologist do not always have correct information on how to scale the drug dose to the patient's size.

Regulatory organizations such as the American Food and Drug Administration and the European Pharmaceutical Inspections are very strict on giving their approval for new drugs to be marketed. But on the other hand, adult-dosing recommendation of most drugs are scaled to weight and approved without any scientific evidence that the pharmacokinetics are weight proportional.

Although our knowledge concerning the pharmacological alterations in this challenging population is

still incomplete, we do start to have some insight and understanding. Calculation of dosage based on IBW or to IBW with some fraction of excess weight is a handy tool. For some anesthetic drugs the known pharmacokinetic models have been evaluated on weight as a covariate. Usually, the gap in our knowledge is filled up by the anesthesiologist's experience and intuition. Ideally, pharmacokinetic models should be adjusted not only to this population, but also individually.

This is where pharmacodynamic monitoring such as neuromuscular transmission (NMT) monitoring and EEG or MLAEP derived monitoring and others can help to individualize our anesthetic management. In the future, we hope to see the development of pharmacodynamic monitors that can measure the antinociceptive effect as well. Measuring the clinical effect could help overcome the shortcomings of the pharmacokinetic models that try to estimate plasma or effect site concentrations.

To our opinion, superobesity (BMI $>$ 55) and morbidly obese patients with high co-morbidity (for example biventricular failure) are a subpopulation that would benefit most of these future developments, since perioperative mortality is still very high among these patients and surgery is usually there only alternative to dying under their own weight.

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REMIFENTANIL IN MORBIDLY OBESE PATIENTS 16

A.O. Alvarez

16.1 Introduction

The use of opioids is almost essential in the anesthesiological practice nowadays. Many clinical benefits can be observed by the use of morphins, such as autonomic stability, blocking response to surgical stress, good to excellent hemodynamic conditions to improve myocardial oxygenation and capability to reduce the required doses of other agents (such as hypnotics) between others. Unfortunately, use of opioids in this particular population (principally in large doses or long lasting infusions) is limited and even dangerous due to pharmacokinetic and -dynamic alterations[1] (see Chapter 15).

Latter distribution might result in variable adverse effects, such as delay in recovery, respiratory depression, muscle rigidity, cardiac dysfunction, nausea, vomiting and "resedation phenomenon".[2] This is related to the redistribution of lipophilic/sedative agents from the fatty tissue back into the bloodstream. The resedation phenomenon is compounded by the very high risk of obstructive sleep apnea (OSA) and upper airway resistance syndrome (UARS) seen in these patients.

Respiratory system function is significantly altered in the obese (see Chapter 4). It has been noted that a body mass index (BMI) of one standard deviation above the mean is associated with a 4-fold increased risk of obstructive sleep apnea syndrome (OSAS).[3]

Prevalence of OSAS in general USA population is 2% in women and 4% in men, but increases up to 3–25% in women and 40–78% in men if they are morbidly obese.[4–8]

Patients with OSAS are more sensitive to the consequences of the depressant effects of hypnotics and opioids on airway muscle tone and respiration.[9] Consequently, post-operative opioid administration to obese patients with OSAS may develop fatal respiratory complications.[10,11]

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In fact, because of a large prevalence of sleep apnea between obese individuals, it has been recommended presuming that "all morbidly obese patients" have OSAS, and all should be treated accordingly.[12]

Prominent cardiac dysfunctions are also evident between obese individuals, and the degree of impairment seems to correlate with the increasing BMI and duration of obesity[13,14] (see Chapter 5).

These patients may have limited cardiac reserve, consequently if any additional functional demand is imposed to the heart, such as exercise or surgical stress, an increase in left ventricular filling pressure could develop, thus exceeding the threshold for pulmonary edema.[15]

Summarizing pain control is essential in the perioperative care of the morbidly obese in order to avoid increases in catecholamine activity and its consequences, but opioid administration could promote dangerous respiratory misadventures.

So, for many years, there has been the necessity of developing a drug with which, common related risks of narcotics could be reduced, but still maintaining the possibility of enjoying all their clinical benefits.

In this chapter it will be analyzed how remifentanil would fit in this context.

Unfortunately, at the time this book is being written, no randomized-controlled trials have been yet performed and/or published to give irrefutable evidence even about many basic issues regarding peri-operative care in the morbidly obese patient. Due to the paucity of published literature data, observations extrapolated from general population studies will be applied. Some own data and experience will also be presented, rather than trying to accomplish impossible consensus.

When providing anesthesia in any circumstance but mainly in a morbidly obese, tactics and anesthetic techniques have to be carefully planned and discussed between the anesthesiologist and the surgical team, in order to reduce the increased risks factors.[16]

In first place, two facts have to be taken into account:

- Patient's physiological condition.
- Type of surgery (mainly, estimated time of the procedure and intensity and timing of surgical stimuli).

Once patient's condition is well known and type of surgery has been decided, anesthesiologist would be in position to select:

- Drugs to better achieve desirable levels, at the desired time, of hypnosis, muscular relaxation and analgesia for every particular situation (considering pharmacological properties of the drugs, such as onset, offset, potency, metabolism, dosing schemes, potential adverse effects, interactions with another agents between others).
- Best way to administer the selected drugs according to the relationship between three aspects: pharmacokinetics and -dynamics of the selected drug, surgical necessities and patient's physiological condition.

16.1.1 Patient's physiological condition

Even this topic is deeply considered in other chapters, a brief summary would help to understand why and how remifentanil could become an excellent choice for clinical application in the morbidly obese.

Cardiac, respiratory, metabolic and digestive dysfunctions are the most important regarding pharmacodynamics. Body composition, renal and liver dysfunctions are the most prominent regarding pharmacokinetics.

Cardiac function

Hemodynamic instability could happen when providing anesthesia to a morbidly obese.[15] Preload, postload and arterial blood pressure are frequently higher among these patients. In addition coronary artery disease is more frequent in overweight individuals, especially in central obesity[17–19] (see Chapters 6 and 11).

Possible mechanisms involved are vascular compromise secondary to systemic hypertension, hyperlipidemia and/or associated diabetes mellitus. Morbidly obese have lower functional reserve to face increased physiological demands. Consequently, intra-operative analgesia should be profound in order to avoid increases in plasma catecholamines levels which could promote heart failure and/or myocardial ischemia.

Respiratory function

Morbidly obese is well known for suffering respiratory malfunctions. Due to a decrement in functional residual capacity and alterations in pulmonary compliance, in the obese patient, pre-oxygenation is less effective and, following apnea, the time to hemoglobin desaturation below 90% is reduced.[20,21] Consequently, trachea should be quickly intubated to avoid dangerous hypoxia. In addition laryngoscopy is one of the highest stimuli for adrenergic response, therefore considering the circulatory performance above mentioned, autonomic stability during laryngoscopy would be highly desirable. A narcotic with high versatility to be easily titrated according to every clinical situation would be the agent of choice in this scenario. Also if tracheal intubation is impossible or difficult (morbid obesity is associated with higher incidence of difficult intubation

and mask ventilation mainly if OSAS co-exists) the possibility for a quick reversion of respiratory depression could become essential[11,22–24] (see Chapter 21).

During recovery, high tolerance to tracheal tubing (as observed with narcotics) would be very helpful to allow a full recovery of consciousness and respiratory function with the airway protected but without neither increases in catecholamine plasma levels nor risk of prolonged respiratory depression.

Digestive function

Gastro-oesophageal functional and anatomical alterations are frequently present in the morbidly obese (see Chapter 8). They are responsible for an increased risk of gastric aspiration.[25] Good conditions for a quick and secure tracheal intubation and successful extubation are mandatory in these cases. A potent and versatile narcotic with fast onset and offset is extremely useful in order to allow a quick induction and recovery thus reducing the time when airways are not protected by full reflexes.

Metabolic function

Diabetes mellitus is much more frequent among obese population.[26,27] Increases in catecholamine plasma levels could promote an increment of plasmatic glucose. High levels of analgesia are desirable to avoid increases in plasmatic concentrations of stress hormones (such as catecholamines, cortisol and growth hormone) and consequent hyperglycemia and its threatening complications. In addition, tight blood glucose control has been associated with improved outcomes in diabetic patients[26] (see Chapter 10).

Body composition

Highly lipophilic substances such as most of opioids or barbiturates that could accumulate in adipose tissue should be avoided. A narcotic with no possibility of accumulation and possible latter redistribution would be an excellent choice for these subjects, since quick and full recovery is essential for early ambulating and sufficient ventilatory function.

Renal and hepatic function

Morbidly obese are at a higher risk of liver and/or renal malfunction. One for fatty infiltration and the other for vascular nephropathy secondary to systemic hypertension and/or diabetes. A review of 7000 renal biopsies from 1990–2000 showed a 10-fold increase in obesity-related glomerulopathy (glomerulomegaly and glomerulosclerosis)[28] (see Chapter 14).

Opioids with metabolic pathways not affected by renal and/or hepatic function would be more than desirable in this clinical situation.

Systems mainly affected, dysfunctions, related risks and anesthetic targets and/or recommendations are summarized in Table 16.1.

16.1.2 Type of surgery

At this point it is important to consider that surgical procedures are usually longer in the obese due to anatomical reasons between others. Estimated time of the procedure has to be taken into account for the selection of the opioid since context-sensitive half-life is highly dependent on the duration of infusion. In addition the magnitude and timing of surgical stimuli have to be evaluated as well. So, a potent narcotic with an onset of 1.3 min and a context-sensitive half-life of 3.5 min seems to be suitable for the morbidly obese. This unique versatility of remifentanil among the actually available opioids allows to follow step by step the changing stimuli levels of every surgical procedure minimizing the risk of delaying recovery.

16.2 Pharmacological properties of remifentanil

16.2.1 General considerations

Remifentanil is an effective agonist at the μ opioid receptor and produces a profound analgesia. Being a pure μ opioid agonist its actions are typically antagonized by naloxone. The drug differs from existing highly effective μ opioid agonist in its rapid metabolism by non-specific red cell and tissue esterases, rather than in any novel properties at the opioid receptor. In fact remifentanil arose from a deliberated attempt to develop a 4-anilido piperidine compound with opioid effects and a very short duration of action. This unique pharmacokinetic characteristic is due to its chemical structure in which an ester link that is essential for its opioid activity is also susceptible to hydrolysis by non-specific esterases to a metabolite that is 4600 times less potent (in dogs) than the parent compound.[29,30]

The esterase metabolism suffered by remifentanil is not related to pseudo-cholinesterase, which terminates the action of suximetonium. Remifentanil is not a substrate for pseudo-cholinesterase and patients who are deficient in this enzyme and in consequence susceptible to long muscular relaxation after suximetonium, metabolize remifentanil normally.[31] The extensive metabolism occurs in red cells and muscle. Morbidly obese often have a higher absolute (not proportional) lean body mass (LBM) than lean people,

Table 16.1 Systems, dysfunctions, potential risks, and anesthetic targets and/or recommendations

	Dysfunction	Potential risk	Anesthetic target and recommendations
Cardiac	Increased blood volume Increased preload Increased afterload Reduced oxygen offer for increased oxygen demand Ventricular diastolic dysfunction Ventricular systolic dysfunction	Hemodynamic instability Myocardial ischemia Ventricular failure	Hemodynamic stability Low myocardial oxygen demand High myocardial oxygen offer Low ventricular work
Respiratory	Reduced functional residual capacity Increased closing capacity Impairment in diaphragmatic impedance Increased pulmonary shunt Ventilation/perfusion mismatch Impairment in neurological control of respiration Decrease in total respiratory system compliance Increase in airway resistance Anatomical airway alterations	Quick development of oxygen desaturation Hypoxemia Hypercapnia Post-operative respiratory dysfunction Difficult airway management Difficult mask ventilation	Supplementary oxygen through all peri-operative period Meticulous pre-oxygenation Proper precautions for difficult airway management Semi-recumbent position Avoid drugs that could interfere with consciousness and respiratory function recovery
Digestive	Anti-reflux system impaired Increased gastric content More acid gastric content	Gastric aspiration	Secure and fast intubation Extubation with full protected reflexes adequately recovered
Metabolic	High incidence of diabetes	Hyperglycemia, diabetic ketoacidosis Higher incidence of infections	Avoid increments in catecholamine plasma levels Meticulous control of glucose plasmatic level Meticulous fluid therapy Prophylactic infectious measures
Body composition	Increased adipose tissue Increased LBM	Lipophilic drugs accumulation Delay in recovery Re-narcosis	Avoid drugs with tendency to accumulate in adipose tissue Drugs with short context-sensitive half-life and rapid onset and offset are of choice Dosing based upon IBW
Renal and hepatic	Nephropathy due to arterial hypertension and/or diabetes Liver dysfunction due to fatty infiltration and esteatosis	Alterations in drugs elimination pathways Delay in recovery Toxic effects Impairment in fluid management	Drugs with metabolic elimination different than hepatic and renal Non-acting metabolites Avoid nephrotoxic or hepatotoxic drugs or metabolites Meticulous fluid management Avoid arterial hypotension

may be as a result of the higher weight they have to carry to move themselves. This might be the reason to a best correlation of doses when they are calculated considering ideal body weight (IBW) instead of LBM, as it was referred by Egan and co-workers.[32]

Also polycythemia is frequent secondary to chronic hypoxemia, so both places where metabolic processes take place are enhanced in these subjects.

Remifentanil is 70% bond to α-1-glycoprotein. The high protein banding contributes to its volume of distribution at steady state of 0.3–0.4 l/kg, which is smaller than that of other opioids. Due to this, and its rapid metabolism and large clearance of 1741/h, the terminal elimination half-life of remifentanil is extremely short, with a mean of 9.52 min.[30] Consequently, remifentanil must be delivered by continuous

intravenous (i.v.) infusion. Even when any other opioid could be diluted and continuously infused by i.v. tubing, only remifentanil until now between all available opioids satisfies the requirements of a drug necessary to make rate-controlled delivery worthwhile:[33]

1 short elimination half-life,
2 no active metabolites,
3 offset by metabolism or excretion and not redistribution,
4 concentration–effect relationship,
5 narrow therapeutic index.

Another distinction between remifentanil and other opioids is the behavior after prolonged infusions. This is known as context-sensitive half-time, where context refers to the duration of infusion and the half-time is the time required for the drug concentration in the central compartment to decline by half after a particular duration of infusion.[34]

Currently available opioid receptor agonists, different from remifentanil, are known to accumulate when administered for prolonged periods or by continuous infusion.[34]

However, because of the unique metabolism of remifentanil, its effective biological half-time of 3–5 min is unchanged, regardless of the total dose or infusion duration. Hence, there is no accumulation, even after prolonged administration.[35]

Paraphrasing Dr. Gavin Kenny, "remifentanil has a *context-insensitive* half-life".

This characteristic confers on remifentanil many potential benefits over traditional opioids, including the option for rapid titration of dose for profound analgesia during surgical stimuli without the risk of post-operative respiratory depression.[36]

Remifentanil as it was mentioned above has a rapid onset of action. This is because time to equilibration between blood concentration and site effect is short and constant ($t_{1/2}\ k_{e0} = 1.34$ min). Thus any desired increment in analgesic effect can be rapidly achieved according to changes in surgical stimuli that could result in undesirable higher catecholamine activity. So remifentanil is the most versatile opioid actually available with the unique property to modify quickly the analgesic level, being possible to follow moment to moment the changing intensities of surgical stimuli.[30]

When comparing alfentanil with remifentanil, Cartwright and co-workers observed that patients who have received remifentanil performed significantly better in post-operative psychometric and psychomotor tests (trigger dot test and digit symbol substitution test) than alfentanil-treated patients, which suggests that patients anesthetized with remifentanil were likely to be more coordinated and alert after surgery. The quality and speed of recovery with remifentanil, as assessed by the above tests, must be regarded as a consequence of its rapid metabolism (terminal elimination half-life <10 min) compared with alfentanil (the shortest-acting opioid until remifentanil appeared), which is eliminated predominantly through hepatic metabolism, with a terminal half-life of 1.2–1.9 h. It may be that immediate recovery after brief anesthesia is virtually indistinguishable among opioids, but later psychomotor and psychometric recovery seem to be better after remifentanil than after other opioids because there is no tendency for recurrent sleep or sedation after remifentanil.[37]

16.2.2 Opioid selection and pharmacokinetic modeling

In clinical practice, propofol is usually combined with one of the currently available synthetic opioids to provide total i.v. anesthesia.[38,39]

Alfentanil, fentanyl, sufentanil and remifentanil all interact in a similar synergistic manner with propofol for the suppression of responses to surgical stimuli and for the return of consciousness post-operatively.[40,41] So is interesting to find out which one of them could be the best for every clinical situation and mainly when providing anesthesia to a morbidly obese.

In the absence of adjuvant agents, the blood propofol concentration that is associated with loss of consciousness in 50% of patients is 3.4 μg/ml, whereas concentration in excess of 10–15 μg/ml are needed to suppress responses to surgical stimuli.[42]

Opioids decreased the required propofol concentration associated with return of consciousness.[38,43] Distinct propofol and alfentanil concentrations have been defined to obtain 50% probability of no response to surgical stimuli. Speed of recovery varies with different intra-operative propofol and alfentanil concentrations even when these are equipotent intra-operatively as was observed by Vuyk and co-workers.[43]

It has also been observed by computer simulation, that the time from termination of a 180 min infusion of propofol and alfentanil to awaking was found to be shortest (10 min) after infusion of a constant target propofol concentration of 3.5 μg/ml combined with a constant target alfentanil concentration of 85 μg/ml.[43] On the basis of the same model Stanski and Shafer determined the infusion rates to maintain optimal propofol concentrations when combined with alfentanil or remifentanil.[44]

For anesthetic management of morbidly obese patients, opioid selection is essential in order to:

1 achieve high levels of analgesia during surgery to prevent adrenergic responses that could promote hemodynamic instability;
2 assure quick and successful recovery to prevent respiratory complications and to allow early ambulating capacity.

Because pharmacokinetics of propofol and the various opioids are different, it is logical to believe that the optimal intra-operative propofol concentration would also be different with the selected opioid and the duration of infusion.[45] In a special article published by Vuyk and colleagues, it was evaluated by pharmacokinetic and -dynamic computer simulation, the implications of opioid selection and duration of infusion on the rate of recovery for combinations of propofol with alfentanil, fentanyl, sufentanil and remifentanil.[45]

In contrast to the other opioids studied, for all durations of infusion, the effect-site propofol concentration decreases much less (by 25%) in the time span to return of consciousness compared with the effect-site remifentanil concentration (by >60%). The reduction in the effect site remifentanil concentration is much steeper than that of the other opioids and that of propofol, especially with infusions in excess of 300 min. In addition, at extremes of the concentration axes displaying the simulations of high remifentanil–low propofol or high propofol–low remifentanil anesthesia, recovery is much less postponed with high effect-site remifentanil concentrations of 7–12 ng/ml (it takes 9 and 10 min for 50% of patients to awaken after infusions of 300 and 600 min, respectively) than with high effect-site propofol concentrations of 11–12 μg/ml (it takes 18 and 21 min for 50% of patients to waken after infusions of 300 and 600 min, respectively). For all combinations of propofol and remifentanil associated with adequate intra-operative anesthesia in 50% and 95% of patients and for all durations of infusion, recovery after propofol–remifentanil anesthesia is much faster than when propofol is combined with one of the other opioids at equipotent concentrations.

The time to return of consciousness after propofol opioid anesthesia seems to depend basically on the selected opioid and only marginally on the duration of infusion.

For infusion durations of 15–600 min the context-sensitive half-times of the opioids decrease in the order of fentanyl > alfentanil > sufentanil > remifentanil. The longer the context-sensitive half-life of the opioid relative to propofol, the more the opioid delays the return of consciousness and the more the propofol–opioid combination shifts to higher propofol concentrations and correspondingly lower opioid concentrations. As a result, the optimal propofol concentration decreases in the order: fentanyl > alfentanil > sufentanil > remifentanil. Propofol concentrations necessary to allow the most rapid return of consciousness are lower when propofol is combined with remifentanil than when combined with either alfentanil, fentanyl or sufentanil. The target concentrations or the infusion rates of propofol and of the opioid with which propofol is combined should be adjusted in relation to the selected opioid and the duration of the infusion to allow an optimal rapid return of consciousness.[34,45] From Vuyk's study it also can be inferred, that to avoid delayed return of consciousness, the intra-operative responses can be best counteracted by additional propofol when combined with fentanyl, alfentanil or sufentanil and by additional remifentanil during propofol–remifentanil anesthesia. It is also notable that in these pharmacokinetics simulations, the optimal effect-site propofol concentrations are below those that assure hypnosis in the absence of remifentanil. *Such low effect-site concentrations of propofol can only be given in the presence of remifentanil at adequate doses*.[45]

In this situation (propofol–remifentanil anesthesia) and considering that a huge inter-individual variability exists between patients, pharmacodynamic monitoring (bispectral index (BIS), auditory evoked potential (AEP) or others) should be highly desirable in order to avoid intra-operative awareness and to achieve the best possible titration of every drug according to surgical necessities (see Chapters 19 and 23).

In clinical practice, adjustments should be made to factors such as patient's condition and mainly stimulus intensity. For instance, in the cardiovascularly compromised patient (such as many morbidly obese) the hemodynamic function may become less depressed in the presence of higher than optimal effect site of the opioid and correspondingly lower than optimal effect-site propofol concentrations. In contrast when spontaneous breathing is desired, lower than optimal effect-site opioid concentrations in the presence of correspondingly higher than optimal effect-site propofol concentrations should be given.[45]

In morbidly obese population, as it will be considered in the paragraph below, Egan and co-workers have demonstrated that remifentanil pharmacokinetics are not significantly affected by patients weight, in consequence dosing schemes have to be based upon IBW instead of total weight.[32] So, if body weight does not affect pharmacokinetics of remifentanil, and lean and morbidly obese patients show similar responses at equal

doses (lean = total body weight (TBW), obese = IBW), observations from pharmacokinetic and -dynamic simulations performed by Vuyk and colleagues could be coherently extrapolated at least theoretically to obese subjects. Nevertheless, it has to be assumed that those findings are just obtained from computer simulations and ideally it should be confirmed in clinical studies not only in obese population but also in lean.

At this point it can be hypothesized that remifentanil could be an interesting choice as the narcotic compound of anesthesia for the morbidly obese, and also that if used for total intravenous anesthesia (TIVA) associated with propofol, anesthesia should be based mainly on higher doses of remifentanil and lower doses of propofol in order to obtain a faster recovery and more stable hemodynamic performance. Pharmacodynamic monitoring would be more than desirable in these cases in order to prevent awareness during surgery, since propofol concentrations required for adequate anesthesia could be below those that assure hypnosis in the absence of remifentanil. Finally, taking this fact into account, all precautions should be taken to assure a constant and secure opioid infusion. As has previously reported for TIVA techniques, the most common reasons for intra-operative awareness involve technical problems such as infusion pumps malfunctions or disconnection of the i.v. tubing.[46,47]

16.2.3 Demographic factors and co-morbidities

The effect of many patients' demographic factors and co-morbidities traditionally considered when formulating dosing schemes has also been examined for remifentanil.

Weight

Regarding weight (essential topic to discuss in this book), there is an excellent study in which it was demonstrated that remifentanil's pharmacokinetics are not appreciably different in obese vs. lean subjects and that remifentanil pharmacokinetic parameters are, therefore, more closely related to LBM than to TBW.[32] Clinically this means that remifentanil dosing regimens should be based on IBW or LBM and not TBW.[32]

The simulations also support the conclusion that remifentanil dosing ought to be based on LBM (or IBW) and not TBW.[32] Calculating remifentanil dosage based on TBW in an obese patient results in concentrations that are grossly higher than those needed for clinical purposes.[32,48] This is in harmony with the observation that the only significant adverse hemodynamic events (that is, bradycardia with hypotension) in Egan and co-worker's study occurred in two patients from the obese group who received substantially higher doses and thus reached significantly higher remifentanil concentrations than the patients in the lean group.[32] Similarly, the results of the 50% and 80% decrement time simulations suggest that for a given remifentanil plasma level, obese and lean patients groups would not exhibit widely different times to recovery.[32] Although remifentanil appeared to be slightly shorter acting in the obese group, this may be a function of a larger absolute amount (not proportionally) of LBM in obese subjects compared to lean.[32]

The findings of this analysis are consistent with current knowledge regarding the effect of body weight on pharmacokinetics. There is mounting evidence to suggest that LBM is a better predictor of metabolic capacity than TBW.[49] This is probably related to the fact that >90% of the body's metabolic processes are thought to occur in the lean tissue.[50]

Age

With regard to age like the other fentanyl congeners, remifentanil's central clearance and distribution volume are somewhat lowers in the elderly population, whereas remifentanil potency increases with advancing age. In elderly population remifentanil dosing should be calculated at a third of an adult health subject.[51]

Gender

Gender does not impact remifentanil pharmacokinetics or -dynamics.[52]

Renal and/or hepatic disease

Remifentanil's pharmacokinetics are not appreciably altered by renal or hepatic insufficiency.[53,54] This is important among morbidly obese population because both functions, renal and hepatic, could be affected more frequently than in lean subjects. Liver can be infiltrated with adipose tissue with or without dysfunction (esteatosis) and kidneys could be affected by diabetes or chronically systemic hypertension (both well known and highly frequent co-morbidities in morbid obesity).

16.2.4 Adverse effects

Like with any other μ opioid agonist, usual adverse opioid-related adverse effects have been demonstrated

in remifentanil application, such as respiratory depression, sedation, nausea and vomiting, muscle rigidity, bradycardia and pruritus.[30,55,56] But like the analgesic effect of remifentanil, adverse effect rapidly disappeared after stopping infusion, and they are antagonized by naloxone.[57]

It has to be taking into account that muscle rigidity and apnea appeared rapidly after a single high dose or after a significant increment of infusion rate with the possibility of occurrence of a life-threatening situation. Thus administration should be in infusion, starting with doses below 1 μg/kg/min, with later increments if necessary within 5–10 min intervals. Hypotension could be considered as an adverse effect if it is not part of the anesthesiological target. A decrement between 25% and 30% is common, and it is not associated with histamine release.[58]

Finally it is essential to consider that bradycardia and hypotension could be extreme when remifentanil administration is associated with β-blockers. Morbidly obese frequently suffer hypertension and could be medicated with these drugs. In this situation remifentanil infusion should start at a 25–50% of the standard dose, and then carefully titrated according to hemodynamic response.

16.2.5 Tolerance development

Regarding tolerance during remifentanil infusions, in an article published by Vinik and Kissin it is claimed that studies in experimental animals have demonstrated a rapid development of acute tolerance to the analgesic effect of opioids administered by continuous i.v. infusions.[59] In their study performed between 13 paid volunteers, the analgesic effect of remifentanil, infused at a constant rate of 0.1 μg/kg/min for 4 h, was evaluated by measurement of pain tolerance. The authors noticed that after reaching a maximum in 60–90 min, the analgesic effect of remifentanil began to decline despite the constant rate infusion, and after 3 h of infusion, it was only one-fourth of the peak value. So the conclusion of their study was that tolerance to analgesia during remifentanil infusion is profound and develops very rapidly.[59] However, based on data collected during an evaluation of clinical efficacy of alfentanil and remifentanil, Schraag and colleagues found that the target concentrations of the opioids required to produce post-operative analgesia and the cumulative opioid doses administered over the course of the clinical observation, suggested that even the requirements for both analgesic drugs in individual patients had large variation (200%) there was no evidence of tolerance to the analgesic effects of the opioids.[60] In addition in Vinik and Kissin study the exclusion of almost one quarter of the patients for inappropriate analgesic responses suggest that the results obtained from it may not be reliable and should not be applied to the clinical situation.[60] Finally Schraag *et al.*'s study is based on the results observed in 30 remifentanil patients followed for 6 h and 51 alfentanil patients followed for 24 h compared with only nine followed for 240 min as studied by Vinik.[60]

So in my opinion, findings about lack of tolerance development during remifentanil and alfentanil infusions are much more consistent. In fact our observations based on unpublished data among 156 patients treated with remifentanil infusions for intra-operative analgesia are coincident with lack of tolerance development.

16.3 Clinical applications

16.3.1 Narcotic compound of inhalational anesthesia

Remifentanil is not recommended as a sole anesthetic agent and should be given in association with an inhalational or i.v. agents.[61] It is indicated for use as a supplement to general anesthesia during induction (co-induction) and as an analgesic during maintenance of anesthesia (co-maintenance).[62] It is effective in blunting hemodynamic responses to stimuli during anesthesia. Clinical studies have compared heart rate and systemic arterial blood pressure in groups of patients given remifentanil and alfentanil as the opioid compound, in part of an anesthetic technique balanced by muscle relaxants and inhalation or i.v. anesthetic agent.[63] There were consistently fewer responses in the remifentanil-treated group than in the alfentanil-treated one in the doses used. Responses to intubation and skin incision measure by raises in heart rate and blood pressure occurred in 8–15% of patients given remifentanil 1 μg/kg and then 0.5 μg/kg/min, and 17–28% when alfentanil was administrated.[63]

During outpatient laparoscopic surgery, 11% of patients given remifentanil 1 μg/kg/min then 0.5 μg/kg/min responded to trocar insertion compared with 32% of the patients given alfentanil.[64] Responses at any time during surgery were demonstrated by 53% of remifentanil patients vs. 71% of the alfentanil group.[64]

The amount of anesthetic supplement required to achieve anesthesia is considerably reduced by remifentanil. Using computer-controlled infusions to achieve target remifentanil concentrations of 0–32 ng/ml, remifentanil 1.37 ng/ml achieved a 50% reduction in minimum alveolar concentration (MAC) of isoflurane, required to prevent movement on skin incision.[65] Remifentanil 2–4 ng/ml reduced 70% the MAC

isoflurane and 32 ng/ml, 91%.[65] Even at very high plasma concentrations of remifentanil it did not provide adequate anesthesia if it was not associated with isoflurane.[65] At steady state, when infusion rate = concentration at steady state × blood clearance, remifentanil 0.038–0.048 μg/kg/min would be required to achieve a 50% reduction in MAC for isoflurane.[65] This is at the lower end of the dose range recommended for clinical anesthesia.

The use of remifentanil as the mainstay of an anesthetic technique, with doses of anesthetic agents much lower than those required when using small opioid supplement, forms the basis of anesthesia based on "esterase metabolized opioid" advocated by Glaxo Wellcome.

The excess of inhalational or i.v. agents in the presence of remifentanil at times of minimal surgical stimulation may be responsible for episodes of hypotension and/or bradycardia, seen during remifentanil infusion.[66] Anyway this episodes promptly reverse if remifentanil infusion is stopped.

16.3.2 Narcotic compound of total intravenous anesthesia

Until a few years ago, alfentanil was the shortest-acting opioid available, but more recently several clinical studies showed that remifentanil is highly effective in providing profound intra-operative analgesia and faster recovery than alfentanil.[67,68] In a clinical trial it was tested the hypothesis that using 1 : 4 ratio of remifentanil to alfentanil, a remifentanil infusion would provide better suppression of intra-operative responses and similar recovery than an alfentanil infusion. Both drugs were used as part of total i.v. anesthesia, for laparoscopic procedures lasting more than 30 min.[64] Due to the pharmacokinetic differences between the two opioids (mainly their context sensitive half-life), it was not possible to administer alfentanil infusions at an equipotent dose to remifentanil because of the risk of delayed recovery and prolonged respiratory depression.[64] Also, and for similar reasons, the infusion of alfentanil was not maintained until the end of surgery. Alfentanil and propofol were discontinued at 10 and 5 min, respectively, before the anticipated end of surgery while remifentanil was discontinued just at the end of the surgical procedure. The remifentanil and propofol infusion rates were chosen based on effective anesthesia in previous studies.[69] It was also evaluated the interaction between propofol and remifentanil, and the results showed that as the dose of remifentanil increased, propofol dose requirements for anesthesia decreased.[64] As it should be expected smaller proportion of remifentanil patients than alfentanil patients had any intra-operative responses, had responses to trocar insertion, or required dosage adjustments during maintenance. Remifentanil provided better intra-operative hemodynamic stability than alfentanil, because remifentanil was dosed to higher levels of opioid effect (1 : 4 ratio), with similar recovery.[64] Recovery times calculated from the end of surgery showed that awakening times were not significantly different between the two studied groups. Since remifentanil can be administrated until the end of surgery, it may be useful for procedures where high levels of surgical stimulation persists until the end of surgery (for instance: port fixation in laparoscopic adjustable gastric banding) and for surgery of unknown duration.[64] (see Chapter 23).

It is important to consider that regarding post-operative pain control, more patients in the remifentanil group received fentanyl and they needed it sooner than alfentanil treated patients.[64] This finding is coherent with the fact that remifentanil shows a shorter elimination half time than any other opioid actually available. Consequently, when remifentanil is used as the narcotic compound of general anesthesia, a transitional intra-operative to post-operative analgesic regime has to be conceived and applied in order to avoid early post-operative pain. Pre- or intra-operative administration of analgesics according to duration of the procedure and magnitude of surgical stimuli, rather than in response to pain, should provide appropriate patient comfort after remifentanil-based anesthesia.

16.3.3 Awake tracheal intubation

According to physiological and anatomical alterations related to obesity, and the impressive relationship between morbid obesity and OSAS, airway management is an essential topic to be considered (see Chapter 21).

OSAS is associated with difficult laryngoscopy and difficult mask ventilation.[10,11,22–24]

Morbidly obese have been considered as patients with certain or potential difficult airway management since 13% of difficult tracheal intubation has been reported among them.[70]

In addition, obese patients have reduced oxygen stores because of their diminished expiratory reserve volume.[71,72] The combination of these factors could promote serious respiratory misadventures, if a rational and meticulous plan for airway management is not conceived in advance.

In patients with anticipated difficult tracheal intubation, it is advisable to maintain spontaneous ventilation and a patent airway. The best way to accomplish this,

and nowadays standard method, is fiberoptic guided awake endotracheal intubation.[73] Successful tracheal fiberoptic intubation in an awake patient depends on the skill and experience of the intubating person, but also on the proper preparation of the patient.[74] The traditional way is to prepare the patient, apart from topical anesthesia, by combined use of opioids and benzodiazepines, but other options have been analyzed with different results, to achieve the best comfort and security of the patient.[74–76]

Before performing this kind of intubating procedure, incidence and causes of failure and problems with the use of flexible fiberoscope have to be considered.[77]

The appropriate level of analgesia and sedation is a challenge because an overdose of medication results in the loss of spontaneous ventilation in the face of a difficult airway. On the other hand, insufficient medication may result in patient discomfort, pain, coughing, hemodynamic and respiratory disorders, making the tracheal intubation technically more difficult, if not impossible. Effective and also secure dose of opioids like fentanyl is limited in these cases due to a huge inter-individual variability in pharmacokinetics and -dynamics, and to a great interpatient variability, which is impossible to identify before the procedure. With the routine dosing schemes of drugs based upon weight, morbid obesity amplifies the possibility of undesirable situations.[78] Consequently it seems to be licit to use an opioid as the single i.v. drug, avoiding administration of combined sedatives. A potent opioid, easy to titrate, short acting with rapid onset and rapid offset qualities, can be more easily tailored to the patients' individual needs. Effects of opioids, as pain relief and suppression of laryngeal reflexes, must be better utilized to improve this intubating technique. In the case of an overdose, there must be a fast way back from inadvertent excessive respiratory depression or loss of the patent airway. Remifentanil meets these requirements in a unique fashion and has been already successfully utilized for awake fiberoptic tracheal intubation in the morbidly obese.[78,79]

Studies have already proved that 0.1 μ/kg/min provides satisfactory analgesia and comfort in preparation for regional anesthesia, while preserving respiratory rate and responsiveness.[80,81] The use of remifentanil as unique i.v. medication for nasotracheal fiberoptic awake intubation was effective, secure and well tolerated as it has been demonstrated by Puchner and co-workers, in a morbidly obese patient with a severe neck inflammation process.[78] The patient was calm and co-operative, obeying verbal commands to take deep breaths during the procedure, cardiovascular performance and oximetry confirmed an excellent preparation of the subject by the combination of remifentanil and topical anesthesia.[78]

In fact we have performed similar preparation (low infusion rate of remifentanil associated with topical pharyngeal and laryngeal anesthesia and bilateral transoral blockade of the lingual branch of glossopharyngeal nerve) for awake orotracheal intubation under direct laryngoscopy, in patients with full stomach (two cases) or predicted difficult airway management (one case). It has to be noticed that the tolerance to tracheal tube resulted to be excellent in all cases. This is of enormous importance not only during intubation, but also during tracheal extubation, because these are the two moments during which, gastric content aspiration occurs more frequently. During recovery, with such an excellent tolerance to tracheal cannula, anesthesiologist will be able to wait until ventilatory performance is sufficient and consciousness is recovered enough to obtain proper responses to verbal commands before extubating the trachea. Thus, patients have their airway protected by full reflexes during the most dangerous periods for gastric aspiration.

16.3.4 Post-operative analgesia

A major disadvantage of remifentanil is the appropriate transition to post-operative pain control, as the rapid offset of action has been shown to produce inadequate immediate post-operative analgesia which may adversely affect recovery and outcome.[82] Consequently, a transition must be made from remifentanil to some other long-acting analgesic for surgeries that result in significant post-operative pain. To overcome the disadvantage of immediate painful conditions after stopping infusion of remifentanil, which occurs significantly earlier compared with other opioids, several studies examined different approaches to achieve a safe and effective post-operative transition pain control scheme, including the feasibility of a manually controlled remifentanil infusion.[64]

Bowdle and co-workers, performed a clinical trial in which infusion rate of remifentanil were reduced from an anesthetic dose to an analgesic dose at the conclusion of surgery, with titration of the analgesic infusion in the recovery room for 30 min followed by a gradual transition to a longer-acting opioid (morphine).[83] They compared different infusion rates (0.05–0.15 μg/kg/min) and the effect of incremental bolus doses of remifentanil in this multicenter study. They found adequate analgesia (0–1 on a 0–3 scale) in 64% of the studied subjects, but adverse respiratory effects (oxygen saturation by pulse oximetry <90 or respiratory rate <12) were a notable problem (29% of patients, 7% apnea). One possible factor was the

mechanical details of the remifentanil infusion since remifentanil was administered from a syringe pump containing a concentration of 50 μg/ml, connected into a standard i.v. infusion line.[83] The "dead space" of the main i.v. tubing between the port where the remifentanil was inserted into the main i.v. tubing and the patient's vein could have varied from 1 to 5 ml depending on the type of tubing and the site of insertion of the remifentanil infusion. Thus, changes in the rate of flow in the main i.v. tubing could have a substantial impact on the amount of remifentanil delivered moment to moment. Nausea occurred in 35% of the patients and emesis in 8%, with a peak incidence right after finishing remifentanil infusion when morphine was administered. The authors of the trial concluded that as it was described it was not practical for routine clinical use because of the occurrence of apnea in 7% of the patients.[83]

In other multicenter investigation, Yarmush and co-workers compared in a double-blind double-dummy study, a post-operative transition pain control scheme, using either morphine bolus doses (0.15 mg/kg) and placebo infusion and increments, with remifentanil infusion (0.1 μg/kg/min) and increments (0.025 μg/kg/min) and placebo bolus doses.[84] Transient respiratory depression, apnea or both were the most frequent adverse effect in the remifentanil group (14%). Successful analgesia: no or mild pain with adequate respiration (respiratory rate >8 and pulse oximetry >90) was higher in remifentanil-treated patients (58%) compared with morphine ones (33%).[84]

Taking into account the results of the above mentioned clinical trials, at least theoretically it seems that manual bolus administration of remifentanil could promote an uncontrolled increase in plasma concentrations and consequently adverse effects specially related to respiratory function.[85] It is reasonable to consider that a target-controlled infusion (TCI) of remifentanil, which increases by a controlled stepwise titration of only small boluses of drugs according to pharmacokinetic specific models, may avoid these undesirable overdoses.[85] As remifentanil has a fast effect-site equilibration, every new target results in rapid onset and rapid achievement of a stable level of drug effect. In fact in none of the 30 patients participating in a very interesting clinical trial performed by Shraag, Mohl, Georgieff and Kenny with a TCI/patient-controlled analgesia (PCA) of remifentanil, sufficient analgesia (3 or less score in a 11-point visual analog scale) was achieved in reasonable time (18.9 min).[85]

Facing these promising results, confronted with other methods for transition analgesia in the early post-operative period after remifentanil-based anesthesia, TCI/PCA of remifentanil seems to be the most effective and secure procedure. Anyway, further controlled studies (specially in morbidly obese patients) are needed to include this analgesic scheme in clinical regular practice.[85]

Despite of which analgesic drug is chosen for post-operative pain control it is unquestionable that when remifentanil is used for intra-operative analgesia, a post-operative analgesic strategy has to be priorly elaborated. For a rational strategy it has to be considered:

1. patient physiological state (OSAS, BMI, cardiac function, age, gender, etc.),
2. magnitude of pain stimuli,
3. onset of the selected analgesic drug,
4. offset of remifentanil.

If analgesic action of remifentanil ceases before post-operative analgesic drug achieves its peak effect, post-operative significant pain will appear and so unwanted consequent reactions. No randomized-controlled trials are available regarding post-operative pain management in the morbidly obese population. Nevertheless, there exists some evidence that regional techniques provide safer and more effective post-operative analgesia, but due to absolute or relative contraindications or anatomical alterations it is not always feasible.[86–92]

The intramuscular route is not recommended as it is unpredictable and has been shown to provide poorer analgesia than other routes. If the i.v. route is to be used, then a patient-controlled analgesia system (PCAS) could be the best option. Choi *et al*. prospectively investigated the efficacy of i.v. morphine PCA in morbidly obese patients and found that it provided good analgesia without deleterious effects on oxygen saturation, arterial blood pressure and heart rate.[93]

In order to obtain a better pain relief and specially to reduce the risk of post-operative respiratory depression and to allow fast post-operative mobilization we believe, and in fact always applied to obese patients, a multimodal analgesic scheme (see Chapter 29).

For open surgery if possible we prefer to set an epidural catheter pre-operatively and deliver an intra-operative bolus dose (volume depending on the level desired) of 0.1% bupivacaine 15 min before the estimated time of the end of surgery, then a continuous infusion of the same solution starts at 12 ml/h and thereafter titrated according to pain score and motor blockade. One microgram per kilogram based upon IBW of fentanyl is administered i.v. 10 min before the estimated time of the end of surgery and remifentanil infusion rate is set at that moment at 0.05 μg/kg based upon IBW and maintained until consciousness is recovered and patient responses to verbal commands

are obtained. We always applied complementary systemic analgesic agents 1 h before the surgery starts (ketorolac, 1 mg/kg based upon IBW, and then a continuous i.v. infusion of the same drug, that is maintained during 48 h at the maximum recommended dose per day based upon IBW). A prophylactic bolus dose of ranitidine (2 h before the surgery starts) and a continuous infusion is also applied to prevent gastritis and to reduce gastric volume and acidity. With this scheme we have observed good results regarding transition from intra-operative remifentanil to post-operative analgesia.

For laparoscopic surgery, we use the same systemic scheme but combined with pre-incisional wound infiltration with 0.25% bupivacaine and a reinforcement before the end of surgery. A bolus dose of dextropropoxyphen 1 mg/kg based upon IBW is administered 20 min before the surgery ends and then starts a continuous infusion of the same drug at standard doses per day. If an adjustable gastric banding is performed, 20 min before the surgery ends we administer a standard dose of hyoscine in order to prevent gastric upper pouch spasm and its related pain. Most post-operative treatment programs focus on unimodal therapies, nevertheless a multimodal approach, would lead to more effective pain relief and faster return of patient mobility.[94] Multimodal analgesia involves the use of combined formulations of various analgesic drugs, such as opioids, and anti-inflammatory agents, with different and/or complementary mechanisms of action. Evidence exists that anti-inflammatory agents may increase the analgesic properties of opioids. When used in combination, opioids and anti-inflammatory analgesics may have additive effects. The different sites of analgesic action found with non-steroid anti-inflammatory drugs (NSAIDs) and opioids suggest additive, or possibly even synergistic effects and in clinical practice they are often used in combination.[95]

The opioid sparing effect of NSAIDs may lead to a reduction in opioid-induced side effects.[96,97] In particular, nausea, vomiting, ileus, pruritus and respiratory depression have been reported.[98,99]

This increment in clinical effect allows the use of lower doses of both analgesics and thereby reduces the *severity* of dose-related side effects normally associated with the use of a single analgesic agent. This is of main concern when facing the increased risk of respiratory depression associated with opioid therapy specially in morbidly obese with OSAS. Optimal management of post-operative pain could only be achieved by multimodal regimens (balanced analgesia).

Local anesthetic agents combined with opioids epidurally/intrathecally may act synergistically, thus reducing even more the total dose of each drug.[100,101]

16.4 Practical recommendations

- Do always pre-oxygenate adequately and position the patient semi-recumbent prior starting any anesthetic drug administration. Maintain supplementary oxygen delivery and semi-recumbent position continuously during post-operative period to avoid respiratory misadventures.[102]
- Have all the proper equipment for airway management ready.
- Use recommended solution to dilute remifentanil (D 5% or saline).
- Consider IBW and not TBW for dosing remifentanil.
- Apply dosing correction in elderly, critically ill patients and those medicated with β-blockers.
- Use continuous infusion or TCI (avoid bolus injection).
- Connect remifentanil infusion to main i.v. line without dead space.
- Do not connect to the same tube for other infusions (mainly if red cells are being administered through them).
- Use adequate monitoring of ventilatory and hemodynamic performance (specially during the immediate post-operative period after tracheal extubation).
- Conceive a rational and secure strategy for transition from intra-operative to post-operative analgesia.

16.5 Our experience with the use of remifentanil in morbid obesity

Due to the heterogeneity observed between our patients (regarding BMI, severity and type of co-existing diseases, chronic consumption of other medications, American Society of Anesthesiology (ASA) physical status, and type or duration of every surgical procedure), it is difficult to analyze every factor influencing in post-surgical-anesthetic outcomes. Therefore, in order to evaluate the eventual advantages or disadvantages of the use of remifentanil as the narcotic compound of general anesthesia in this population, a retrospective view of my experience with 156 patients has been chosen (unpublished data). TIVA, TCI propofol, midazolam, remifentanil BIS-guided anesthesia was provided in 141 patients; sevoflurane, remifentanil BIS-guided anesthesia was the technique applied

Table 16.2 End points analyzed and results

Range of end-tidal sevoflurane during maintenance	0.3–0.8
Range of remifentanil required	0.5–2 μg/kg/min (IBW)
Severe immediate peri-operative cardiac complications	None
Severe immediate peri-operative respiratory complications	None
Necessity of vasoactive therapy (more than one efedrine rescue dose)	None
Necessity of vasodilatators according to arterial blood hypertension events not responding to remifentanyl increments	None
Necessity of pharmacological hemodynamic support	None
PACU discharge time	46.06 min
Necessity of assistance to move themselves (when transferring from operating table)	None
Necessity of intensive care unit	None
Necessity of mechanical ventilation	None
Awareness with recall (post-operative questionnaire)	None

in the other 15. Simple end points have been considered according to evaluate the outcomes. These end points are clearly related to the most frequent complications or misadventures that the anesthesiologist has to deal with, when providing general anesthesia to a morbidly obese patient.

Results, demographic particularities and anesthetic technique for TIVA can be seen in the respective chapter, in consequence it will not be further analyzed here (see Chapter 23).

In the following section, it will be discussed why sevoflurane, remifentanil BIS-guided anesthesia was the technique of choice in patients under inhalational anesthesia, demographic characteristics of the studied population will be shown and results will be presented in Table 16.2.

16.5.1 Anesthesia technique

Delay in recovery could happen after inhalational anesthesia in these individuals, depending on:

- the duration of the procedure,
- the inhaled concentration,
- the solubility of the agent,
- the respiratory impairment of the patient.

Adipose tissue has slower uptake than organs and muscle, because of its poorer blood flow, thus equilibration for anesthetic concentrations will take minutes for the organs but hours for fat. On the other hand, it has a great affinity for inhaled anesthetic agents, so the amount of excessive fat tissue will interfere not only on the uptake and distribution, but also on the elimination of the anesthetic. In consequence when the longer the procedure and the higher the inhaled concentration of the agent more chances for accumulation in "adipose compartment" will appear. In addition, the various inhalational agents in common clinical use have distinct solubility characteristics that will bear on the rapidity of onset of action, and the speed of recovery after their administration. The more soluble the anesthetic the slower the induction and the more prolonged the recovery. But the major factor to slow recovery seems to be the reduced capability to remove alveolar gas due to alterations in respiratory function. Air trapping have been demonstrated in obese individuals by obtaining higher values of total lung capacity (TLC) when measured by plethysmography as compared with the value of TLC by the Helium dilution technique.[103]

As a conclusion it could be assumed that, morbidly obese patients have excessive amounts of adipose tissue that may act as a reservoir of the volatile agent. This way, once administration is suspended, fat tissue will continue to contribute anesthetic to maintain blood concentrations. This remaining concentration may be sufficient to promote post-operative oversedation and or respiratory depression which could be of devastating consequences in this particular population. Impaired post-operative ventilation with reduced removal of alveolar gas will contribute to slow recovery from inhalational anesthesia by delaying the elimination of the anesthetic agent. Because of the restrictive lung defect that is common in the obese, this effect is exaggerated.

Considering the factors influencing in eventual delayed recovery after volatile anesthesia, it is possible to take actions to minimize this unwanted situation. In first place agents with low solubility (such as sevoflurane or desflurane) should be selected. It has been demonstrated that they have better recovery profiles than other agents in obese patients.[104–107] Nevertheless, desflurane does not bronchodilate like other inhalational agents.[108] Particularly in smokers, there can be increased respiratory resistance and potential respiratory compromise in obese patients managed with desflurane. It has been observed that obese subjects are more likely

to report wheezing and other asthma-like symptoms.[109–111] Desflurane may also increase heart rate, which could be undesirable in cardiac compromised patients. Consequently, sevoflurane would be a better choice for morbidly obese.

Second, it is advisable to reduce the inhaled concentration of the agent, but still providing enough hypnotic effect. Association of remifentanil, as discussed before, has shown a significant reduction of the MAC of inhalational agents.[65]

Finally in order to provide sufficient hypnosis, BIS has shown to be a suitable monitor of anesthetic depth, and also allowing a further reduction in the doses required.[112]

In fact, sevoflurane, remifentanil BIS-guided anesthesia was already used for the anesthetic care of morbidly obese patients. Paventi used this technique for laparoscopic cholecystectomy in 40 morbidly obese patients. The patients were divided into two groups, one treated with sevoflurane titrated by end-tidal concentrations and the other with sevoflurane and a continuous infusion of remifentanil, titrated according to BIS values. BIS-guided anesthesia showed, shorter awakening time, extubation time and speed of orientation and transfer to recovery room.[113]

In conclusion, sevoflurane, remifentanil BIS-guided anesthesia was the technique of choice in these population.

16.5.2 Demographics

All of the 15 patients were morbidly obese scheduled for different elective bariatric procedures (laparoscopic adjustable gastric banding and laparoscopic gastric bypass). Demographic particularities are summarized below:

Gender: males, 6 (40%); females, 9 (60%)
Age: range, 23–60 years old (median 40.66)
BMI: range, 35.2–61.4 (median 44.64).

16.5.3 Results

End points analyzed and results are summarized in Table 16.2.

Even not included as an end point, it was clinically evident that awaking was much more abrupt when compared with TIVA technique. This may be a consequence of not administering midazolam in the inhalational group. No complications were observed but it has to be considered that there were just 15 cases. Randomized-controlled trials with bigger populations have to be developed in order to achieve reliable conclusions.

16.6 Summary

Remifentanil is a potent opioid with unique properties regarding offset of action. It has a rapid onset (time to equilibration between blood and site effect concentration = 1.34 min) and a rapid terminal half-life (10 min) so it makes it highly versatile in order to achieve profound levels of intra-operative analgesia without the risk of delay in recovery. Its time of clinical action is predictable according to its context-insensitive half-time (3.5 min) and is not prolonged even though high doses or long lasting infusions are applied. For dosing no special precautions have to be taken with the exception of age (30% reduction) associated use of β-blockers (50% reduction) and critical clinical situations (smooth individual titration is recommended). Gender, weight, renal and hepatic failure do not affect the dosing schemes (dosing schemes have to be based upon IBW). It is the most efficient narcotic to prevent responses to tracheal intubation and surgical stimuli. It has a remarkable tolerance to tracheal tube, becoming suitable for awake tracheal intubation and allowing a comfortable extubation with the airway protected until reflexes and consciousness are totally recovered.

Even if it is not recommended for use as a sole agent for anesthesia, it has shown synergistic actions with volatile agents, being possible to reduce >50% the MAC of them even at low opioid infusion rates. It also has synergistic actions with propofol and midazolam, agents of common use in TIVA techniques. So remifentanil allows to achieve sufficient levels of anesthesia with much less hypnotics (volatile or i.v.). This property gives the possibility to perform co-induction and co-maintenance schemes in which as the total amount of drugs is much lower so should be their adverse effects.

Recovery is fast and predictable with better performance in psychometric and psychomotor post-operative test compared with alfentanil, the shortest-acting opioid until remifentanil appeared.

16.7 Conclusions

At this moment considering all pharmacological properties and clinical applications of remifentanil, in my opinion, this opioid is the one clearly indicated for the morbidly obese.

Of course all precautions have to be taken for administration.

Remifentanil administrated under all precautions mentioned above is capable to provide:

- Rapid intubating conditions with low hemodynamic variation.

- Possibility of a comfortable and secure awake tracheal intubation according to certain clinical situations (full stomach or predicted difficult airway management).
- Rapid and successful recovery of respiratory function and consciousness.
- Enough tolerance to tracheal tube during extubation until full recovery of protective reflexes and consciousness.
- Absence of post-operative over-sedation and/or respiratory depression.
- Quick recovery of spontaneous ambulating capacity.
- Easy and quick handling of different levels of analgesia according to changes in nociceptive stimuli.
- Avoid increments of plasmatic catecholamine levels that may increase ventricular work and myocardial oxygen consumption.
- High levels of analgesia even at the end of the surgical procedure without delaying recovery (important in long surgeries or those of uncertain duration).
- Adequate peri-operative hemodynamic stability.
- No risk of delay in recovery in patients with severe hepatic and/or renal malfunction.

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MONITORING

SECTION 6

ELECTROCARDIOGRAPHY 17

M.A. Alpert

17.1 Introduction

There is a worldwide epidemic of obesity in developed nations that involves virtually all ages, races and socioeconomic classes. In the US alone nearly one-third of the population is overweight or obese. Consequently, it is logical to assume that a comparable proportion of patients presenting for anesthesia and analgesia will be overweight or obese, and will be subject to the complications of this increasingly common malady. A resting 12-lead electrocardiogram (ECG) is routinely performed on obese patients who present for medical or surgical evaluation. Obesity is associated with a wide variety of ECG abnormalities. Some of these are innocuous. Some may represent alterations in cardiac morphology associated with obesity and/or its co-morbidities. Still others may serve as markers of risk for sudden cardiac death. Many of these alterations are reversible with weight loss. This chapter describes ECG abnormalities associated with obesity. Morbidly obese patients receive special attention because of the large body of information available concerning the ECG in this group. In addition to reviewing alterations in heart rate, axis, waves and intervals, this chapter addresses the issue of arrhythmogenesis by discussing ventricular repolarization, the signal-averaged ECG and heart rate variability. Arrhythmias associated with obesity are also reviewed. Finally, ECG abnormalities and arrhythmias associated with dietary therapy, bariatric surgery and currently available anorexiant drugs are described.

17.2 Definition of obesity

The World Health Organization (WHO) classifies obesity in terms of body mass index (BMI). The classifications are as follows: lean or normal range (18.5–24.9 kg/m^2), pre-obese or overweight (25.0–29.9 kg/m^2), obese class I (30.0–34.9 kg/m^2), obese class II (35.0–39.9 kg/m^2), and obese class III or morbid obesity ($\geq$40.0 kg/m^2). This classification system is used in this review to define the presence of leanness and the severity of obesity. Severity of obesity is

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provided for studies in which it was specified. Unless otherwise stated ECG alterations described herein were derived from resting ECGs performed at a speed of 25 mm/s. Except when otherwise specified, the studies discussed in this review were conducted in adults.

17.3 Heart rate

Resting heart rate in obese persons is usually normal.[1–4] Bradycardia at rest (usually sinus bradycardia) has been reported in 0–19% of obese subjects (<5% in most studies).[1–5] Resting tachycardia has been reported in up to 0.5% of obese persons.[1] The presence of bradycardia or tachycardia in obese persons should elicit a search for such factors as congestive heart failure, cardiac arrhythmias, use of heart rate modifying drugs, metabolic disturbances (for example, hypothyroidism) and the sleep apnea syndrome. Most studies comparing obese (including morbidly obese) and lean subjects have reported no significant difference in heart rate.[2,3] However, some studies have reported higher heart rates in obese than in lean individuals.[2,3] These differences have rarely exceeded 7 bpm and are not clinically important in most cases. Similarly, heart rate changes little with weight loss in obese subjects because the decrease in cardiac output, which is elevated in obesity, occurs primarily due to a decline in stroke volume.[4]

17.4 Axis

Leftward shifts in the P wave, QRS and T wave axes were originally reported by Proger in 1931.[5] Subsequently, Eisenstein *et al.* reported that mean P wave, QRS and T wave axes were normal, but somewhat leftward in 144 obese subjects (≥50% overweight) compared to 100 normal lean controls.[2] Frank and colleagues reported a normal, but leftward mean QRS axis in 1029 obese subjects which became more pronounced with increasing obesity.[1] Alpert and co-workers reported mean P wave, QRS and T wave axes of 33 ± 16°, 28 ± 14° and 35 ± 17°, respectively, in 100 asymptomatic normotensive morbidly obese patients.[3] Corresponding mean P wave, QRS and T wave axes in 100 lean healthy controls were 46 ± 14°, 52 ± 10° and 48 ± 18°. These differences were statistically significant.[3] A subsequent study by Alpert and co-workers demonstrated that substantial weight loss in 60 morbidly obese patients produced rightward movement of the mean P wave, QRS and T wave axes from their leftward location.[4] These findings confirmed prior observations by Eisenstein *et al.* in 58 less severely obese subjects.[2] The cause of this axis shift is uncertain, but may relate to a leftward and more horizontal orientation of the heart due to the diaphragmatic pressure from visceral obesity.[2–4] The presence of overt left or right axis deviation in obese persons suggests severe left ventricular hypertrophy (LVH) or right ventricular hypertrophy (RVH), conduction system disease or co-existent structural heart disease.

Thus, obesity is associated with a leftward shift in P wave, QRS and T wave axes that is directly related to severity of obesity and is reversible with substantial weight loss. Left and right axes deviation *per se* are uncommon in persons with uncomplicated obesity.

17.5 P wave morphology and duration

Lavie *et al.* studied P wave morphology in normotensive and hypertensive obese and lean subjects using the P-terminal force in lead V_1 as a diagnostic marker of left atrial abnormality.[6] Mean P-terminal force was significantly greater (more negative) in normotensive obese (0.020 ± 0.007 mm s than in normotensive lean subjects (-0.0058 ± 0.0004, $P = 0.01$).[6] Similarly, mean P-terminal force was significantly greater (more negative) in hypertensive obese (-0.026 ± 0.004 mm s) than in hypertensive lean subjects (-0.008 ± 0.003 mm s, $P = 0.01$).[6] The authors concluded that the greater (more negative) P-terminal force noted in obese subjects probably reflected left atrial distension due to left ventricle (LV) diastolic dysfunction.

Alpert and co-workers reported significant differences in left atrial morphology on ECG between 100 normotensive morbidly obese patients and 100 lean healthy controls.[3] Each of the morphologies studied qualifies as a marker of left atrial abnormality. P-terminal force in lead $V_1 \geq -0.04$ mm s was present in 18% of morbidly obese subjects but was not detected in controls.[3] P wave duration in lead II > 110 ms was noted in 24% of morbidly obese subjects and five controls. P wave duration >120 ms in lead II was observed in 17 morbidly obese subjects and no controls.[3] An interpeak notch >40 ms in lead II was present in 11 morbidly obese patients and no controls. All of these differences were statistically significant. When considered as continuous variables, only mean P-terminal force was significantly different (more negative) in morbidly obese subjects (-0.16 ± 0.008 mm s) than in controls (-0.0003×0.0001 mm s).[3] In their study of 60 normotensive morbidly obese subjects, Alpert and co-workers noted a significant decrease in P-terminal force with substantial weight loss.[4]

Right atrial morphology has not been extensively studied in obese subjects. Alpert and co-workers reported

that the frequency of P wave amplitude >2.5 mm in lead II (2%) in 100 normotensive morbidly patients was not significantly different from that observed in 100 lean healthy controls (0%).[3]

17.6 PR interval

Alpert *et al.* reported no significant difference between the mean PR interval of 100 normotensive morbidly obese patients (0.15 ± 0.03 s) and 100 lean healthy controls (0.14 ± 0.02 s).[3] Frank and co-workers also reported normal PR intervals in most of the 1029 obese subjects in their survey, but noted a progressive increase in PR interval duration with increasing severity of obesity.[1]

17.7 QRS alterations

17.7.1 QRS duration

Alpert and co-workers reported mean QRS durations of 0.06 ± 0.02 and 0.06 ± 0.01 s, respectively, in 100 asymptomatic normotensive morbidly obese patients and 100 normal lean controls.[3] Frank and colleagues reported progressive QRS widening with increasing obesity in their survey of 1029 obese subjects.[1] However, this study did not exclude hypertensive patients or those with underlying structural heart disease.[1] Bundle branch block is discussed in the section on arrhythmias and conduction disturbances.

17.7.2 Low QRS voltage

Proger was the first to report low QRS voltage in obese patients in 1931.[5] Alpert *et al.* reported an 11% incidence of low QRS voltage (≤5 mm in the standard leads and ≤10 mm in the precordial levels) in 100 normotensive morbidly obese patients compared to a 1% incidence in 100 normal lean subjects ($P < 0.001$).[3] In contrast, Eisenstein and colleagues reported no significant difference in the incidence of low voltage between 144 moderately to severely obese patients and 100 normal controls.[2] Frank and co-workers reported a 3.9% incidence in 1029 subjects whose obesity ranged from mild to severe.[1] The reason for the discrepancies among these studies is uncertain. Speculation exists that low voltage, when present, is due to excessive chest wall fat and in some cases, increased epicardial fat. Subjects in Alpert's study were more severely obese than those in Eisenstein's or in Frank's study.[1–3] It is possible that differences in these variables may account for the disparate findings in these studies. Alpert *et al.* reported significant reduction of the frequency of low voltage (from 13% to 2%) with substantial weight loss in 60 normotensive morbidly obese patients.[4]

17.7.3 Left ventricular hypertrophy

Nath *et al.* studied 65 normotensive morbidly obese patients without underlying heart disease to determine the sensitivity and specificity of various ECG criteria for LVH.[7] ECG criteria used were: Romhilt–Estes point score ≥5, $SV_1 + RV_5$ or $RV_6 > 35$ mm or RaVL > 11 mm (Sokolow–Lyon index), RV_5 or $RV_6 > 26$ mm, RaVL > 7.5 mm, RaVF > 20 mm, (RI–RIII) + (SIII–SI) ≥ 17 mm, $SV_1 > 24$ mm, SaVR > 14 mm, and onset of intrinsicoid deflection in V_5 or $V_6 > 0.07$ s.[7] M-mode echocardiography was used to diagnose LVH. Echocardiographic criteria for LVH were increased ventricular septal and/or LV posterior wall thickness (>1.1 cm), increased LV mass (Penn convention) or increased LV diastolic dimension in diastole (>5.6 cm).[7] Sensitivities of ECG criteria for LVH ranged from 0–13%, when increased LV wall thickness was used, 0–20% when increase LV mass was used and 0–12% when LV chamber dilation was used to diagnose LVH.[7] Corresponding specificities were 73–100%, 87–100% and 83–100%.[7] Combining criteria did not appreciably affect sensitivity or specificity.[7] The authors concluded that the surface ECG criteria employed in this study were limited in their ability to detect LVH in morbidly obese patients.

Alpert *et al.* studied 100 normotensive morbidly obese subjects or organic heart disease (mainly women) and 100 normal lean controls.[3] The frequencies of the 10 previously described ECG criteria for LVH[7] were compared in morbidly obese and lean subjects.[3] Frequencies of these ECG criteria in the morbidly obese group ranged from 9% ($SV_1 > 24$ mm) to 25% ($SV_1 + RV_5$ or $RV_6 > 35$ mm).[3] Frequencies for all of the ECG criteria for LVH were significantly greater in morbidly than in lean patients.[3] However, when these ECG criteria were treated as continuous variables only RaVL and SaVR voltage were significantly greater in obese than in lean subjects.[3] The authors concluded that ECG criteria that do not rely primarily on left or right precordial voltage may be more reliable markers of LVH than those that rely on left or right precordial voltage for diagnosis.

Okin *et al.* studied the performance of various ECG criteria for LVH in detecting LVH based on a variety of echocardiographic measures of LV mass in obese and non-obese patients.[8] The Cornell voltage (SV_3 + RaVL ≥ 28 mm in men and ≥20 mm in women), Cornell product (Cornell voltage × QRS duration > 2436) and Framingham-adjusted Cornell voltage were selected as ECG criteria for LVH.[8] LVH

was defined as LV mass indexed to body surface area, height alone or height to the power of 2.7.[8] The sensitivity values of the Cornell product were significantly higher than those of the Cornell voltage.[8] The sensitivity of the adjusted Cornell voltage was significantly greater in obese (50–59%) than in non-obese subjects (18–24%, $P < 0.01$) but was associated with high variability.[8] The Cornell product appeared to provide the best combination of overall accuracy and low variability among the three criteria studied.

Okin and co-workers studied 8417 patients entered into the Losartan Intervention for Endpoint (LIFE) Reduction in Hypertension Study including 2519 overweight and 1573 obese subjects.[9] Compared to normal weight patients, obese and overweight patients had lower Sokolow–Lyon index voltage and a lower prevalence of LVH on ECG using the Sokolow–Lyon index (10.9% vs. 16.2% vs. 31.4%).[9] In contrast, obese and overweight subjects had higher mean values of the Cornell product and a higher prevalences of LVH on ECG using the Cornell product (75.1% vs. 60.6% vs. 60.7%).[9] Obese patients had a greater than two-fold greater risk of LVH on ECG using the Cornell product and a four-fold lower risk of LVH on ECG using the Sokolow–Lyon index.[9] Overweight individuals had intermediate levels of risk.[9] Thus, the Cornell product appears to be far superior to the Sokolow–Lyon index in detecting LVH on ECG in overweight and obese subjects.

Abergel studied 380 hypertensive patients to determine the relation of the Sokolow–Lyon index and Cornell voltage to LV mass index and LV mass/height index in obese and lean subjects.[10] Cornell voltage correlated positively and significantly with LV mass ($r = 0.48$).[10] There was a similar, but less robust relation between Sokolow–Lyon index voltage and LV mass ($r = 0.36$).[10] However, in obese subjects, the correlation coefficients for Sokolow–Lyon index voltage and LV mass were 0.10 in men and 0.21 in women.[10] The correlation coefficients for Cornell voltage and LV mass were somewhat higher at 0.22 for men and 0.36 for women (both were statistically significant).[10] The sensitivity of Sokolow–Lyon index voltage for echocardiographic LVH was <10%.[10] Although neither ECG criterion performed well in obese subjects, Sokolow–Lyon index voltage was particularly weak. The authors concluded that it should not be used to diagnose LVH in obese subjects.

Norman *et al.* demonstrated that adjusting Cornell voltage for age and obesity increases gender specific criteria for LVH.[11] Okin and colleagues expanded on this observation by noting a lower overall performance of the Cornell voltage in women when adjusted for age and obesity.[12] This observation persisted regardless of which echocardiographic criterion was used to diagnose LVH.[12]

Lavie and co-workers noted that mean Sokolow–Lyon index voltage was significantly lower in normotensive obese than in normotensive lean patients (19.7 ± 2.0 mm vs. 25.9 ± 1.4 mm, $P = 0.01$).[6] Similarly, the mean Sokolow–Lyon index voltage was significantly lower in hypertensive obese than in hypertensive lean patients (22.6 ± 1.5 mm vs. 30.0 ± 2.3 mm, $P = 0.01$).[6] In contrast, the mean Romhilt–Estes point score failed to discriminate obese from lean normotensive or hypertensive patients.[6]

Hayashi and co-workers studied 18 obese children before and after weight loss achieved by diet and exercise.[13] Transthoracic echocardiograms were performed at baseline and at 1 year.[13] ECGs were performed at baseline, at 3 months and at 1 year.[13] At 1 year there was an increase in LV internal dimension in diastole, but no change in LV wall thickness.[13] $SV_1 + RV_5$ voltage decreased at 3 months, but returned to baseline levels at 1 year.[13]

The preponderance of evidence suggests that ECG criteria for LVH that rely heavily on left or right precordial voltage perform less well than those that either do not rely or rely little on left or right precordial voltage. Among those studied to date, the Cornell voltage and product appear to be the best ECG criteria for diagnosing LVH in obese persons. However, it is important to understand that all of the ECG criteria for LVH including the Cornell voltage and product underpredict LVH. Approximately two-thirds of asymptomatic normotensive morbidly persons obese have LVH (mainly eccentric), yet studies of ECG criteria for LVH in such individuals have reported frequencies that are much lower than those observed in echocardiographic studies. In such patients, it is likely that the increased QRS voltage generated by the hypertrophied LV is offset to a variable degree by the presence of chest wall and epicardial fat.

17.7.4 Right ventricular hypertrophy

Alpert and co-workers assessed the frequency of nine previously described criteria for RVH in 100 asymptomatic normotensive morbidly obese subjects and 100 normal lean controls.[3] There were no significant differences in the frequency of any ECG criterion for RVH between the two groups.[3] When criteria were considered as continuous variables, only mean R/S in V_1 or V_2 was significantly greater in morbidly obese than in lean subjects.[3] The failure of ECG criteria to diagnose RVH may be due in part to the absence of a reliable non-invasive diagnostic standard for RVH.

17.8 ST segment

Frank and co-workers reported non-specific ST and T wave abnormalities in 11% of 1029 obese patients.[1] These findings were more prevalent with increasing age and blood pressure.[1] In a study of 100 normotensive young morbidly obese patients and 100 young normotensive normal controls, ST segment depression with or without T wave inversion occurred rarely.[3] There were no significant differences in the frequency of ST depression between the two groups.[3]

ST elevation has not been described in obese persons in the absence of acute myocardial infarction, pericarditis or early repolarization.

17.9 T wave

T wave flattening and inversion in obese patients were originally described by Jaffee *et al.* in 1938.[14] In a later study, Eisenstein and co-workers reported T wave inversion in lead III in 28% of 144 obese subjects and in 21% of 100 lean persons.[2] Flattened T waves in the inferolateral leads were noted in 49% of obese patients, but were not observed in normal subjects.[2] In this study T wave abnormalities that occurred in the 58 patients who lost weight returned to normal.[2] A more recent detailed analysis by Alpert and co-workers showed that T wave flattening in the inferior leads occurred in 58% of 100 normotensive morbidly obese patients and in 2% of 100 normal lean controls.[3] T wave flattening in the lateral leads occurred in 29% of morbidly obese patients and 1% of controls.[3] T wave flattening in the inferolateral leads was noted in 44% morbidly obese subjects and in 1% of controls.[3] All of these differences were statistically significant.[3] In contrast, there was no significant difference in the frequency of T wave inversion (which occurred rarely) between the two groups.[3] In a subsequent study by Alpert and co-workers substantial weight loss was associated with reversal or marked reduction of T wave flattening among 60 morbidly obese patients following bariatric surgery.[6] Thus, reversible T wave flattening in the inferior and lateral leads is commonly observed in morbid obesity and is presumed to occur due to leftward and horizontal displacement of the base of the heart due to excessive abdominal adiposity.

17.10 QT interval

Esposito and colleagues studied 70 obese and 25 lean women to determine if differences existed in QT interval duration and nocturnal in blood pressure between the two groups.[15] Thirty-eight obese patients had a waist-to-hip ratio >0.85.[15] Obese women with a waist-to-hip ratio of >0.85 had a significantly longer mean corrected QT interval, mean corrected QT interval dispersion and blunted fall in nocturnal blood pressure than lean women or obese women with a waist-to-hip ratio of <0.85.[15] Heart rate variability was adversely altered in centrally obese women compared to peripherally obese and lean women.[15] The authors concluded the co-existence of prolonged cardiac repolarization and a blunted nocturnal fall in blood pressure may contribute to cardiovascular risk in centrally obese persons and speculated that autonomic dysfunction may be the common mechanisms for this association.

El-Gamal *et al.* studied 742 moderately to morbidly obese subjects to determine the effects of obesity on the corrected QT interval.[16] There was a significant positive correlation ($r = 0.311$, $P < 0.00002$) between BMI and corrected QT interval using Bazzett's formula.[16] To determine the effect of body fat composition on the corrected QT interval Park and colleagues studied 22 obese premenopausal women and nine lean premenopausal women.[17] Obese women were further classified as having upper body obesity or lower body obesity.[17] Corrected QT intervals were significantly longer in women with upper body obesity than in those with lower body obesity (at equivalent levels of body fat) or those who were not obese.[17] The authors concluded that abdominal obesity is a risk factor QT interval prolongation in premenopausal women.

Corbi and co-workers studied 66 obese patients, 30 whose waist-to-hip ratio was >0.85 and 36 whose waist-to-hip ratio was <0.85.[18] These investigators reported that the longest QT intervals occurred in those with the highest plasma levels of free fatty acids. The corrected QT interval correlated positively with plasma free fatty acid levels in the group with a waist-to-hip ratio >0.85. Dietary weight loss resulted in significant decreases in the mean corrected QT interval and mean plasma free fatty acid level for 1 year. Thus, in centrally obese persons QT interval alterations appear to be closely related to plasma free fatty acid levels. The clinical implications of this observation are uncertain.

Girola and colleagues studied 54 uncomplicated obese (mean BMI: $38.1 \pm 0.9\,kg/m^2$), 35 overweight and 57 lean patients to determine if differences exist in QT interval dispersion among these three groups.[19] Mean QT interval dispersion values were comparable among the three groups.[19] There was no correlation with BMI, waist circumference on abdominal sagittal diameter in any of the groups.[19] QT interval dispersion correlated only with the corrected QT interval.[19] This study suggested that in uncomplicated obesity there is

no relation between QT interval dispersion and BMI or body fat distribution.

These studies provide potent evidence that obesity is associated with corrected QT interval prolongation. The evidence is mixed concerning the relation of obesity and QT interval dispersion. Based on these studies, obesity should be considered a risk factor for delayed ventricular repolarization, which is a potential substrate for the development of ventricular tachyarrhythmias.

17.11 Signal-averaged electrocardiogram

The signal-averaged ECG analyzes multiple QRS complexes and is capable of providing detailed information on ventricular conduction following depolarization. Its greatest clinical use involves analysis of the terminal portion of the QRS complex for small, high-frequency waves called late potentials. The most important measurements are QRS duration, root mean square and low amplitude signal. The presence of abnormal root mean square and low amplitude signal suggests the presence of late potentials. These alterations are thought to predispose to ventricular tachyarrhythmias.

Lalani *et al.* studied 105 subjects whose BMI was $\geqslant 30\,kg/m^2$ and 43 patients whose BMI was $<30\,kg/m^2$.[20] All patients were free from clinical heart disease.[20] The objective of the study was to determine whether obesity was associated with an abnormal signal-averaged ECG.[20] Obese subjects had significantly more abnormalities (increased QRS duration, high root mean square or low amplitude signal) on their signal-averaged ECG than non-obese controls (55.0% vs. 4.6%).[20] Within the obese group, the prevalence of abnormalities increased as BMI increased and was 100% in patients whose BMI was $>50\,kg/m^2$.[20] Increasing BMI was an independent predictor of an abnormal signal-averaged ECG.

Mizia-Stec and colleagues studied 62 moderately to severely obese patients (mostly females) and 15 healthy lean controls to determine if differences existed in QT interval dispersion between the two groups.[21] Mean QT interval dispersion values (observed and corrected) and echocardiographic LV mass were significantly longer/greater in obese than in lean patients.[21] Late potentials detected using signal-averaged ECGs were detected in six obese patients, all of whose QT interval dispersion values were among the highest in the study.[21] The authors concluded that increased QT interval dispersion is associated with LVH and is particularly high in those with late potentials on their signal-averaged ECG.

In a study of 40 healthy medical residents Matsui and co-workers found that increasing subadipose tissue as well as increasing BMI correlated positively and significantly with the duration of the low amplitude signals, in many cases producing false positive test results.[22] These studies suggest that obesity is commonly associated with the presence of late potentials on the signal-averaged ECG, which may predispose to ventricular tachyarrhythmias. However, false positive tests may occur due to excessive subadipose fat accumulation.

17.12 Heart rate variability

Multiple studies have addressed the issue of heart rate variability in obese subjects.[23–26] Techniques that measure heart rate variability are thought to represent the relation of sympathetic and parasympathetic influences on the heart. Reduced heart rate variability is thought to be predispose to sudden cardiac death in selected disease states. Studies in obese adults[23–25] and children[26] have consistently shown evidence of decreased parasympathetic influence and/or increased sympathetic influence.[23–26] This has been attributed variously to decreased adrenoreceptor responsiveness, withdrawal of parasympathetic tone (or vagal withdrawal), and/or increased sympathetic activity.[23–26] One study showed correction of alterations in heart rate variability with weight loss.[25] The results of these studies suggest that obesity may be associated with autonomic abnormalities that increase the risk for lethal cardiac arrhythmias.

17.13 Cardiac arrhythmias and conduction disturbances

There are several case reports of sudden death in morbidly obese patients, most of whom also had cardiomegaly and congestive heart failure with no other causative factors.[27–29] MacGregor *et al.* reported five such cases among 22 morbidly obese subjects.[30] Similarly, Warnes *et al.* reported sudden death in five of 12 morbidly obese subjects, many of whom were hypertensive and most of whom had congestive heart failure.[31] In each of these cases LVH was present.

Messerli and co-workers studied mildly to moderately obese subjects with and without eccentric LVH (detected echocardiographically) who were matched with lean healthy subjects.[32] The prevalence of ventricular premature beats was 30 times higher in obese than in lean patients.[32] Those with LVH had higher Lown grades of ventricular ectopy than those without LVH.[32]

Thus, eccentric LVH associated with obesity with or without hypertension is arrhythmogenic.

The sleep apnea syndrome is known to be associated with atrial and ventricular arrhythmias regardless of weight.[33] These include atrial and ventricular premature beats, atrial fibrillation and a variety of brady-arrhythmias.[33] Although many of the patients in studies assessing the risk for cardiac arrhythmias in those with sleep apnea are obese, relatively few studies have focused entirely on obese populations. Valencia-Flores *et al.* studied 52 consecutive morbidly obese subjects using polysomnographic monitoring to determine relation of cardiac arrhythmias to the apnea–hypoxia index.[34] Ninety-eight percent had an apnea–hypoxia index >5 (mean 51 ± 37) and 33% had severe sleep apnea with an apnea–hypopnea index ≥ 65 with a mean oxygen desaturation time $<65\%$ over 135 min.[34] Cardiac arrhythmias (profound sinus bradycardia as well as ventricular and atrial arrhythmias) were noted in 31% and their frequency correlated positively with severity of sleep apnea based on the apnea–hypopnea index.[34] Laabun and colleagues studied 60 morbidly obese patients using polysomnography and continuous ECG monitoring.[35] Twenty-five had an apnea–hypopnea index ≥ 16 and thus qualified as having the sleep apnea syndrome.[35] Thirty-five did not.[55] There were few arrhythmias noted and there was no significant difference in their frequency between the two groups.[35] Thus, conflicting information exists concerning arrhythmias and the sleep apnea syndrome in obese subjects.

Bharati and co-workers performed post-mortem studies on seven young obese people who had died suddenly and unexpectedly.[36] None were morbidly obese, but three had a history of sleep apnea.[36] There was cardiac hypertrophy in all patients and all had a distinct ventricular septal bulge.[36] The epicardial coronary arteries were normal in all subjects.[36] All had focal mononuclear cell infiltration in and around the sinus node or it approaches.[36] Three had marked fat infiltration throughout the conduction system.[36] Fibrosis of the atrioventricular node or left bundle branch was present in five.[36] Focal fibrosis and mononuclear cell infiltration were present in the ventricular conduction system in six.[36] Atherosclerosis of intramural coronary arteries was present in four and myocardial disarray was present in three.[36] The findings suggest that significant, potentially arrhythmogenic pathologic abnormalities are present in the conduction systems of young obese people who have suffered sudden death. However, bundle branch block has not occurred with disproportionately high frequency in studies of unselected or asymptomatic populations of obese subjects.[1–3]

17.14 Effect of weight loss regimens on the electrocardiogram

17.14.1 Starvation diets

Information concerning the arrhythmic complications and ECG abnormalities of starvation diets has been derived primarily from case reports and small series.

Garnett *et al.* reported a case of sudden death in a 20-year-old obese woman treated with a therapeutic starvation diet supplemented with vitamins and minerals.[37] The patient lost 60 kg during therapeutic starvation.[37] She experienced cardiac arrest on the seventh day of a refeeding regimen.[36] Her post-resuscitation ECG showed marked QT interval prolongation.[37] She subsequently died of ventricular fibrillation.[37] Post-mortem examination showed a paucity of myofibers.[36] Those present showed gross myofibrillar fragmentation.[37]

In a study by Spencer, two of 12 obese patients treated with starvation diet died of ventricular fibrillation.[38] Post-mortem examination showed LVH without other abnormalities.[38]

Severe shock without arrhythmia occurred in a patient treated with a starvation diet that was supplemented by vitamins and minerals.[39] Hypotension occurred and was accompanied by a marked decrease in QRS voltage and a marked increase in the corrected QT interval.[39]

Pringle *et al.* studied 11 women and two men whose ages ranged from 19 to 35 years.[40] All were morbidly obese and all were treated with a starvation diet for 53 to 136 days.[40] Weight loss ranged from 20 to 49 kg.[40] Progressive reduction of mean QRS voltage was observed by week 7.[40] The corrected QT interval became prolonged in all patients by week 8 and became frankly abnormal in seven subjects.[40] QT interval prolongation increased progressively for 3 weeks after cessation of starvation in two patients.[40] One of the women with QT interval prolongation experienced syncope during the diet and then two episodes of *torsades de pointes* during refeeding.[40] She was successfully cardioverted, treated with phenytoin, and survived.[40]

A study by Zuckerman and colleagues assessed cardiovascular status in 11 obese patients whose BMI exceeded 35 kg/m^2 in each case.[41] All patients received a 0 kcal/day diet for 10 days.[41] No clinical cardiac complications or ECG abnormalities were reported.[41]

17.14.2 Low- and very-low-calorie diets

Case reports and small series documenting sudden death during starvation stimulated investigative interest

aimed at determining whether such complications occurred with low- and very-low-calorie diets and whether an ECG substrate for sudden death could be identified. Multiple case reports and small studies have described abnormalities that might be attributable to the diets.

Michiel *et al.* reported the case of a 38-year-old woman who weighed 153 pounds.[42] Against medical advice, she partook of a 600-kcal/day, very-low-calorie diet of beef-hide extract supplemented with folic acid and potassium.[42] After 8 months on the diet, she developed presyncope and then syncope.[42] Shortly thereafter, she was discovered unresponsive.[42] After she was revived, the corrected QT interval progressively increased.[42] She subsequently developed ventricular tachycardia and fibrillation that was refractory to multiple antiarrhythmic drugs.[42] Her post-mortem study showed normal coronary arteries, a dilated LV, diffuse reduction of cardiac myofiber size, myofibrillar fragmentation, and lipofuscin deposition.[42] Skeletal myofibers were also reduced in size.[42]

Brown *et al.* described the case of an individual who developed cardiovascular complications during a protein sparing modified fasting diet.[43] The patient experienced syncope, hypotension, persistent QT interval prolongation, and a decrease in QRS voltage before the development of fatal ventricular tachycardia.[43] Necropsy showed antemortem thrombi attached to LV endocardium and a fenestrated aortic valve.[43]

Pietrobelli and co-workers studied the effects of short-term dietary weight loss on the corrected QT interval in 30 healthy overweight and obese subjects before and after weight loss (3.9 ± 1.7 kg) on a 1120 kcal formula diet.[44] The mean corrected QT interval decreased from 0.411 ± 0.028 to 0.404 ± 0.0025 s ($P = 0.11$) with weight loss.[44] The corrected QT interval normalized in three patients with a prolonged QT interval prior to weight loss.[44]

Carella and co-workers performed a prospective and retrospective study on 522 obese patients (average weight: 116 kg) to determine the effect of weight loss (various methods) on the QT interval.[45] Patients were serially monitored if the corrected QT interval was >0.44 s or if they lost >23 kg.[45] The mean baseline QT interval was 0.41 ± 0.02.[45] In this group 53% had a corrected QT interval >0.42 s and 24% had a corrected QT interval >0.44 s.[45] Weight loss produced significant shortening of the corrected QT interval.[45] Regression analysis showed that fat mass above normal predicted corrected QT interval prolongation.[45]

Mshui and co-workers studied 36 obese subjects and 36 normal lean controls to assess the comparative effects of weight loss on the QT interval and QT interval dispersion.[46] Weight loss was achieved with a very-low-calorie diet (370 kcal/day).[46] Maximum mean corrected QT interval was 445 ± 32 ms prior to weight loss and decreased significantly to 434 ± 28 ms after weight loss.[46] Minimum mean corrected QT interval also decreased with weight loss.[46] There was, however, no significant change in mean corrected QT interval dispersion.[46]

Gupta and co-workers studied 63 obese patients who had completed 26 week liquid protein diet therapy.[47] QT dispersion decreased after weight loss in 89.5% and increased in 10.5%.[47] In the former group the decrease in QT dispersion was associated with an increase in the minimum QT interval.[47] In the latter group the increase in QT dispersion was associated with an increase in the maximum QT interval.[47]

Moyer and colleagues reported the results of a study of 24 women whose ages ranged from 21 to 55 years and who were treated with a very-low-calorie diet (660–720 kcal/day) for 294 days.[48] Patients received 1 g of protein as well as supplementation of potassium, calcium, magnesium and copper.[48] There were no changes in either QRS voltage or the corrected QT interval, but one patient developed isolated ventricular premature beats during stress testing.[48]

Lantigua *et al.* reported the results of a study on 45 women and one man who were treated with a very-low-calorie (300 kcal) collagen protein diet for 40 days.[49] Their ages ranged from 21 to 42 years.[49] Weight loss ranged from 13.0 to 14.5 kg.[49] Each patient received 75 g of protein and 1.2 g of potassium per day.[49] Three subjects developed complex ventricular ectopy on Holter monitor recordings on day 10.[49]

Amatruda *et al.* studied five women whose ages ranged from 42 to 58 years.[50] Each patient received a very-low-calorie diet (420 kcal/day) for 40 days.[50] Weight loss ranged from 7.5 to 13.2 kg.[50] Each patient received 23 g of protein per day and appropriate supplementation of potassium and magnesium.[50] No changes in either QRS voltage or the corrected QT interval were noted.[50] One patient developed a three-beat run of ventricular tachycardia.[50]

In 1979, Isner reported the results of a study of 17 previously healthy obese persons who died suddenly on a liquid protein, modified fast diet between July 1977 and January 1978.[51] These 17 were drawn from a group of 60 patients who had died suddenly on this diet.[51] However, other potential causes of sudden death were identified in 28 and the data were incomplete in 15.[51] There were 16 women and one man.[51] The average age was 37 years and the average weight loss was

41 kg over an average of 5 months.[51] Eight had a history of syncope while on the diet.[51] Twelve-lead ECGs were available in 10 patients before their sudden death episode.[51] Nine and possibly 10 had prolongation of the corrected QT interval and nine had low voltage.[51] Ventricular tachycardia was documented in 11 patients; four of these were episodes of *torsades de pointes*.[51] Cardiac histologic studies were available in 14 patients.[51] Cardiac myofiber size was decreased in 12 patients and lipofuscin pigment was increased in 11 patients.[50] Those who lost ⩾40% of their body weight experienced greater myofiber attenuation than those who lost lesser amounts of weight.[51] There were mononuclear infiltrates suggesting myocarditis in three patients.[51] It is notable that similar histologic abnormalities were observed in 16 cachectic patients, but not QT interval prolongation or ventricular tachycardia.[51] Van Itallie *et al.* reviewed the data from the preceding study.[52] There was a significant positive correlation between BMI and the duration of survival on the diet.[51] The authors reasoned that more severely obese persons were able to conserve body (including myocardial) protein better than their less obese counterparts.[52]

In contrast to these reports, numerous studies of various types of very-low-calorie diets showed no clinical or ECG abnormalities. Cumulatively, these studies consisted of 84 patients whose ages ranged from 21 to 60 years.[53–57] The types of very-low-calories diets used were as follows: a 350-kcal/day meat diets; the Optifast diet (472 kcal/day; Delmark Co., Minneapolis, MN) in two subjects; a non-specific 850-kcal/day diet; a 420-kcal/day diet consisting of collagen or soy protein; a 420-kcal/day high-quality protein diet; and a 420-kcal/day diet consisting of Carnation Instant Breakfast (Nestle USA, Inc., Glendale, CA) plus low-fat milk. The duration of these diets ranged from 4 to 789 days and weight loss ranged from 2.7–35.0 kg. Protein intake ranged from 51 to >70 g/day. Appropriate mineral, electrolyte and vitamin supplementation was provided in all cases. In one study, the corrected QT interval was prolonged in eight patients before weight loss and normalized during the course of dietary therapy.

All of the aforementioned reports concerning the ECG effects of starvation, low- and very-low-caloric diets on the ECG involved adults. Little information is available concerning dietary therapy in children. Zwiauer *et al.* performed weekly 24 ECG monitoring on 36 severely obese children and adolescents during a 3 week 525 kcal mixed diet.[58] There were no arrhythmias.[58] Mean average and minimum heart rates decreased, respectively, from 84 ± 9 to 75 ± 9 and from 53 ± 6 to 45 ± 6.[58] Mean maximum heart rate increased during the 2nd week, but returned to baseline by the end of the study.[58] Schmidinger and co-workers studied nine obese children (74.2% overweight) who were treated for 3 weeks with a high-quality protein very-low-caloric diet (240 kcal commercially available diet in eight and a homemade 500 kcal diet in one).[59] Mean weight loss was 9.4 kg in those on the commercial diet and 8.7 kg in the patient on the homemade diet.[59] Frequent Holter monitor recordings detected no arrhythmias in patients on the commercial diet, but showed ventricular couplets and non-sustained ventricular tachycardia in the patient on the homemade diet.[59]

Fisler has provided an explanation for sudden cardiac deaths associated with severe caloric restriction that serves as a modification of a previous hypothesis by DeSilva.[60,61] She postulated that myocardial hypertrophy from obesity predisposes to ECG abnormalities such as QT interval prolongation. Rapid or pronounced weight loss is thought to produce a decrease in myocardial fiber size. Relative lack of protein, electrolytes or micronutrients may contribute to myofibrillar damage. Such damage is thought to provide a substrate for electrical instability because of regional inhomogeneities of conduction and generation of ectopic impulses. Transient extracardiac stimuli (for example, stress) might alter sympathetic nervous system activity. Catecholamines may then act on structurally abnormal myocardium to provoke life-threatening arrhythmias. This hypothesis does not require a single provoking event to explain sudden death and therefore serves as an attractive explanation for cases of sudden death reported in the literature.

Most of these case reports and small studies were published prior to 1990. Whether safety has improved with currently used very-low-calorie diets is uncertain due to the paucity of recent published studies in this area. Clearly however, such diets have the potential to produce ECG abnormalities and arrhythmias that may serve as markers of increased cardiovascular risk during anesthesia and surgery.

17.14.3 Bariatric surgery

Drenick *et al.* surveyed mortality among 50,134 morbidly obese patients referred for bariatric surgery.[62] This study included patients who had undergone various forms of gastric bypass and those who had undergone jejunoileal bypass.[62] There were 60 sudden deaths.[62] The calculated annual mortality was 40 times greater in those undergoing bariatric surgery than in the matched lean population.[62] Eight of these deaths occurred before surgery.[62] Twenty-two occurred within the first 10 days after surgery and the remaining 30 occurred up to 22 months after surgery.[62] Post-mortem studies were performed in 26 cases.[62] Increased heart

weight and increased LV wall thickness were described in nine of the 14 patients for whom these variables were described.[62] Ventricular tachyarrhythmias accounted for all of the sudden deaths for which ECG monitoring was available.[62] Arrhythmias included ventricular fibrillation, monomorphic ventricular tachycardia and torsade de pointes (in three cases).[62] The corrected QT interval was mildly prolonged in 29 of the 38 available ECG tracings.[62] No other precipitating factors for sudden cardiac death were identified.[61]

Peiser and co-workers studied 14 subjects with obstructive sleep apnea who were 222 ± 38% overweight prior to and after gastric bypass surgery to determine the effect of weight loss on arrhythmias in such patients.[63] The mean apnea index pre-operatively was 84 ± 44.[63] Follow-up ECG studies (12 h of telemetry) were performed 6 weeks after surgery.[63] Prior to surgery all patients had sinus arrhythmia and four had severe sinus bradycardia.[63] Following weight loss sinus arrhythmia persisted in only seven and none had brachycardia.[63] Multifocal ventricular premature beats and nonsustained ventricular tachycardia were noted in all patients pre-operatively, but were present in only two (in milder form) after weight loss.[63] The authors concluded that surgically induced weight loss in morbidly obese patients is an effect method for abolishing potentially life-threatening ventricular arrhythmias.

Rasmussen *et al.* studied 22 women whose age ranged from 21 to 53 years.[64] These women were treated with gastroplasty and dietary modification.[64] They were observed for 180 days and lost 14 to 38 kg.[64] Protein intake ranged from 19 to 202 g/day and potassium, calcium and magnesium were supplemented to maintain normal serum levels.[64] The corrected QT interval became prolonged within 3 months in seven patients.[64] Low voltage was not reported.[64]

17.14.4 Anorexiant drug therapy

The two most commonly prescribed drugs for obesity are orlistat and sibutramine hydrochloride. Orlistat has no direct effect on the ECG and has not been shown to provoke arrhythmias. Sibutramine hydrochloride has been shown to raise blood pressure and heart rate in some patients.[65] Non-specific T wave abnormalities have been described in some patients receiving sibutramine hydrocholoride.[66] In addition, a variety of cardiac arrhythmias have been described in patients treated with sibutramine hydrochloride including ventricular premature beats, atrial fibrillation and ventricular tachycardia.[65,66] Much of this information however, has been derived from case reports, uncontrolled studies or reports to regulatory agencies. Whether sibutramine is arrhythmogenic remains uncertain at this time.

17.15 Summary

Obesity, particularly morbid obesity, has been associated with a wide variety of ECG alterations. These include leftward shifts of the P wave, QRS and T wave axes, enhancement of the P-terminal force in lead V_1 and prolongation of P wave duration and the interpeak notch in lead II, possible prolongation of the PR interval, possible prolongation of the QRS duration, low QRS voltage, LVH (particularly when ECG criteria that do not rely heavily on left or right precordial voltage are used), T wave flattening in the inferior and lateral leads, prolongation of the corrected QT interval, increased in QT interval dispersion, an abnormal signal-averaged ECG and abnormal heart rate variability. Case reports and small studies have documented a variety of cardiac arrhythmias and conduction disturbances in morbidly obese patients and in less severely obese patients with LVH or sleep apnea. Starvation diets place obese patients at high risk for ventricular tachyarrhythmias and sudden death. Some older studies of obese patients undergoing very-low-calorie diet therapy reported QT interval prolongation and nonsustained ventricular arrhythmias, while others reported no ECG abnormalities. Older studies of patients undergoing bariatric surgery suggested an increased risk for the development of ventricular tachyarrhythmias. Little information exists in the literature concerning the effects newer dietary regimens and bariatric surgical techniques of the ECG and on arrhythmogenic risk. Concern exists regarding the arrhythmogenic potential of sibutramine hydrochloride.

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RESPIRATORY MONITORING 18

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18.1 Introduction

As much as one-third of the population in the US weigh 20% or more than the ideal body weight at the present time. One measure of obesity is body mass index (BMI) equal to the ratio of weight (kg) divided by the square of the height (m). An index value over 27 in women and 28 in men represents a weight excess of 25% over ideal, and a BMI of 31 or higher is commonly accepted to represent morbid obesity. The clinical consequences of obesity involve all major organ systems: animal models have been developed in rats to study the metabolic changes induced by obesity and physiological changes can be readily verified in man because they can be induced by overfeeding in normal subjects and can be reversed by dietary restrictions. Therefore, it is possible to reduce some of the extreme risks in morbid obese patients facing elective surgery by a weight reduction diet and judicious postponement of elective procedures.

Obesity is a significant health risk, which leads to overall overuse of health resources, increased hospitalization, and increased perioperative risks. In this chapter we focus to review the respiratory system and the related monitoring strategies: first we describe the altered respiration physiology in obese patients, then pre-operative evaluation, intra-operative monitoring, and post-operative strategies. Finally, we discuss surveillance after surgical procedures. We selected recent key references narrowly related to the anesthetic field.

18.2 Peri- and intra-operative respiratory changes

18.2.1 Respiratory mechanics

The effect of obesity on pulmonary function is influenced by several factors: most importantly the degree of obesity, followed by the patient's age, and distribution of body fat – either centrally or peripherally (see also Chapter 4). The degree of obesity influences the impairment in pulmonary function directly. In patients with mild to moderate obesity that are otherwise healthy, vital capacity (VC), total lung capacity (TLC), and functional residual capacity (FRC) are generally indistinguishable from normal non-obese

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patients. In grossly overweight patients these parameters can be reduced up to 30%.[1,2] These changes occur predominantly in patients with central obesity.

Compared to the normal weighting patient, the morbidly obese has significantly lower static respiratory system compliance, decreasing exponentially with increasing BMI[3] and increased respiratory resistance in the supine position at least while he is ventilated and anesthetized[4] his FRC is significantly lower[5] and may even decrease within or below closing capacity in the supine position.[6,7] During general anesthesia the loss of respiratory muscle tone causes a reduction of the transverse cross-sectional area. The cephalad displacement of the diaphragm, due to the increased body fat in the abdominal region, leads to compression atelectasis in the dependent lung tissue, thereby reducing FVC.[8] Application of positive end-expiratory pressure (PEEP) is probably effective in recruiting lung volumes by increasing FRC via recruitment of atelectatic regions of the lung. During upper abdominal laparoscopic surgery it is essential to adequately restore ventilated volumes in these patients.[9–11] On the other hand, voluntary respiratory efforts might be maintained at normal level or even enhanced, such as forced expiratory volume in one second (FEV_1) to FVC ratios, if spontaneous ventilation is preserved, even in the supine position.[4,10]

18.2.2 Alveolar ventilation and pulmonary gas exchange

When the FRC volume decreases below closing capacity (CC), ventilation and perfusion undergo a mismatch and gas exchange in the dependent parts of the lung deteriorate because of the narrowing or even closure of the small airways. The shunt fraction increases and the alveolo-arterial oxygen gradient widens accordingly.[8]

Because of these factors which are exacerbated during paralysis and controlled ventilation, the more obese a patient, the greater the alveolo-arterial gas difference becomes, and less expiratory gas measurements will correlate with blood gas analysis.

Even with higher inspiratory oxygen concentrations, the morbidly obese patient will not be able to reach the same PaO_2/F_iO_2 ratio as the normal weight patient. Morbid obesity decreases the arterial oxygenation index even further, yet leaving $PaCO_2$ values unaffected[3] if the patient does not suffer the pickwickian syndrome. This is mainly due to intrapulmonary shunts in the atelectatic dependent lung areas. This problem is accentuated as soon as the patient is in the supine position and even more if he is anesthetized and ventilation patterns changes from spontaneous to controlled. Denitrogenation of the lung prior to tracheal intubation has shown to decrease the PaO_2/F_iO_2 ratio, whereas non-denitrogenated lungs do not demonstrate sufficient improvement with intra-operative application of PEEP. These differences, however, were noted in moderately obese subjects compared to normal patients[8] and have not yet been verified in the extremely obese.

Other contributing factors to inadequate gas exchange are a marked decrease in ventilatory drive, eventually leading to obesity-hypoventilation syndromes (OHS). These patients are usually extremely obese and develop marked alveolar hypoventilation such they often require intensive care unit (ICU) admission postoperatively. Two main theories about the pathogenesis of OHS have been developed. The first theory suggests that hypoventilation is a result of excessive mechanical load caused by obesity on the inspiratory muscles, leading to hypoventilation. However, this mechanical disadvantage is not seen in all obese patients, as most obese patients can hyperventilate spontaneously when requested and can normalize their arterial carbon dioxide concentration. The second theory proposes that the alveolar hypoventilation is a result of blunted ventilatory drive.[12] Patients with OHS have dramatically reduced hypoxic and hypercapnic ventilatory drives compared to normal individuals. The exact mechanism is unknown but the respiratory chemosensitivity varies individually among normal adults and factors that influence the respiratory chemosensitivity includes age, sex, body size, changes in body weight, acid–base status, high altitude sojourning, and smoking habits.[13]

18.3 Consequences for respiratory monitoring

The more obese the patients, the lower his FRC and the higher the intrapulmonary shunt fraction, the less expiratory gas concentrations will reflect arterial blood gas concentrations. With the effects accentuated in general anesthesia and in the supine position, arterial blood gas analysis becomes increasingly important because blood gases reflect the respiratory status more accurately than the expiratory gas measurements.

Is there a need for invasive or special monitoring of respiration in the obese patient? Capella found, in review of 521 morbidly obese patients undergoing bariatric surgery, no need for invasive monitoring.[14] However, morbid obesity does influence the decision to initiate intra-arterial monitoring, because ventilatory assessment will be of greater importance.

18.4 Pre-operative assessment

To be able to develop an anesthetic strategy, the patient's respiratory situation has to be accurately assessed pre-operatively (see Chapter 9). History of obstructive sleep apnea (OSA) syndrome should raise a flag and will alter the intra- and post-operative narcotic use, as this has shown to be a major factor for complications in this group of patients.[15] An assessment of nocturnal overnight pulse oxymetry by means of continuous measurement of the oxygen saturation may be indicated in severely obese patients at risk.

Pulse oxymetry or even arterial blood gas analysis in the awake obese prior to premedication and anesthesia will provide a reference value for data acquired during the intra- and post-operative period, as anesthesia and ventilation will always have a negative impact on oxygenation and alveolar ventilation. OHS can only be assessed by means of obtaining a pre-operative $PaCO_2$ value by arterial blood gas analysis.

18.4.1 The obstructive sleep apnea syndrome

Approximately 3% of obese patients suffer from OSA, during sleep in room air demonstrate apneas in excess of 10 sec more than five times per hour with a periodic SpO_2 drop exceeding 4%. This usually leads to disrupted night sleep and increased sleepiness during the waking hours. An even larger number of patients suffer from less extreme symptoms with more dispersed episodes of apnea (obstructive sleep hypopnea, OSH). Obesity is linked to both these syndromes, but a firm diagnosis can be confirmed only with a formal sleep study: therefore, at the present time well over 95% of obese patients with either form of the syndrome are only presumptively diagnosed. A possible suspicion can be elicited by an overt history of snoring, or the chance observation of SpO_2 periodic desaturation during a resting period. It is quite likely than anesthesiologist might be the first physician to face the decision to treat the patient as suffering from OSA.[16] For the diagnosis to exist, the history in the adult obese patient must be positive for snoring/snorting and apnea during sleep and sleepiness during daytime. This diagnosis is further supported by a history of hypertension, a large neck circumference (>40 cm), nocturnal diaphoresis, frequent nocturia and morning headache. In these patients at high risk, regional anesthesia might be worth considering, as the awake patient can spontaneously maintain a patent airway during surgery and especially in the post-operative period.

If general anesthesia must be used in OSA, preparation must be done for a difficult intubation, at times requiring awake intubation (in approximately 8% of some series). This is often observed after a first failed attempt at intubation, if excess tissues are present at the pharyngeal and retroglossal opening, which might be difficult to visualize. This also can herald a danger of post-extubation upper-airway obstruction. After loss of consciousness, these patients represent a difficult mask fit, often requiring three- or four-handed mask ventilation. The pre-oxygenation phase of these patients must be prolonged and is best accomplished with the head elevated, with steep dependency of the abdomen, with prolonged spontaneous ventilation, and a sufficient number of personnel ready to help during intubation. SpO_2 will decrease precipitously during apnea, because of reduced lung volumes.

Extubation of this high-risk patients must be conducted with care and with an eye toward the chance of requiring re-intubation in often less than optimal situations (see also Chapter 25). The patient should be awake, fully reversed from paralysis, 30–45° upright, with 2-person mask ventilation ready to be applied, oral or nasal airway in place. An exchange catheter can be left in place in the trachea following extubation after appropriate topical anesthesia. Some patients will require nasal continuous positive airway pressure (CPAP) application immediately post-operatively. Often this group of patients can be recognized, as they use CPAP at night for sleep.

18.5 Intra-operative monitoring

The normal, routine non-invasive monitoring will be sufficient for most of the morbidly obese patients. In some patients however, such as for example, neurosurgical patients, where adequate ventilation within small range of arterial blood gas pressures is important, $PaCO_2$ may have to be assessed either by frequent blood gas analyses or by transcutaneous measurements and ventilation has to be adjusted accordingly.

Satisfactory tissue oxygenation can not only be assessed by pulse oxymetry or PaO_2 alone, but is also reflected by lactate and pH values or an increasing anionic gap, that may be indicative of insufficient tissue oxygenation or low tissue perfusion.

In severely obese individuals, transcutaneous CO_2 measurement has proven to be more accurate with lower mean differences from $PaCO_2$ than $EtCO_2$.[17] However, the success of transcutaneous CO_2 monitoring depends on several technical and operator factors such as trapped air bubbles, temperature,

appropriate placement, adequate calibration, or even variations in skin thickness. To minimize issues related to subcutaneous fat, the probe can be placed on the ventral aspect of the forearm where the subcutaneous fat is the least.

The decision of whether or not to establish invasive monitoring should be based on the type of surgery and on type and severity of concomitant diseases, where morbid obesity should be counted as "concomitant disease". This implicates that the more obese the patient, the more beneficial invasive monitoring will be.

There are certain situations during anesthesia that require special mention. During induction, due to the reduction in FRC, the obese patient will desaturate much more rapidly than normal individuals. A working pulse oxymetry is crucial during apnea. The strategy for induction of anesthesia in the morbidly obese is in most cases a rapid-sequence induction or awake fiberoptic intubation because of the increased risk of pulmonary aspirations.[18] During both maneuvers, involuntary movement either due to fasciculations or out of distress is not uncommon and may influence accurate reading of the pulse oxymeter. Similar considerations apply also during emergence from anesthesia. Only the awake and adequately responding morbidly obese patient should be extubated, because the airway management in the severely obese may be difficult and apneas are usually associated with rapid decreases in SaO_2.

18.6 Post-operative surveillance

Like every other patient, the degree and duration of post-operative surveillance depends on the surgical intervention, the course of anesthesia and the patient's condition and concomitant diseases. Obesity and OSA syndrome are concomitant diseases that will influence post-operative respiratory surveillance.

The monitoring should at least include pulse oxygen saturation and respiratory rate in the immediate post-operative period. In selected cases, especially in patients with decreasing oxygen saturations in the post-operative period, ABG analysis, and chest X-ray may be useful in finding atelectasis and to guide the need for continuous positive pressure application.

Sudden onset of distress, chest pain, and dyspnea may be indicative not only of cardiac events, but also of pulmonary embolism, which represents one of the leading causes of death following bariatric surgery, according to a retrospective analysis of over 5000 patients.[19]

Obese patients have an increased relative risk of 2.28 to experience complications related to respiration, such as hypoxemia, hypoventilation, and airway obstruction in the post-operative period. The overall rate of critical respiratory events in obese patients was 3% in a recently published study,[20] much higher than in normal subjects.

Another recent retrospective study showed no significant increase of adverse peri-operative events in patients with polysomnographically confirmed OSA when the levels of wakefulness are carefully maintained.[21] In a previous study, Gupta and colleagues found 2 years earlier about twice as many post-operative complications in a retrospective analysis of 101 cases with serious complications, almost three times as high in the OSA as in the control group. Most of the complications occurred within the first 24 h post-operatively.[22]

We believe that OSA, documented at the time of the intervention or just suspected, is a condition that requires careful observation. In the post-operative care, this may warrant prolonged surveillance in the post-anesthesia care unit (PACU) or even admission to the ICU in selected cases, especially in prolonged surgery (>4 h) and in patients with critical co-morbidities. The main reasons for admittance to the ICU in morbidly obese patients are disturbances in pulmonary gas exchange,[23] which can be prevented by more prolonged one-on-one surveillance.

18.7 Conclusion

The exact management of respiratory monitoring for each obese patient intra- and post-operatively is continuously dependent on history, type of surgical trespass, post-operative pain control, and especially body position (see Chapters 20 and 29). All efforts must be made to recognize OSA patients and to recover them in an appropriately monitored environment.

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CORTICAL ELECTRICAL ACTIVITY MONITORING

19

G.M. Gurman

19.1 Introduction

One of the most difficult tasks of modern anesthesia is to assess how much anesthetic drugs administration influences on central nervous system (CNS) function.

Clinical signs, such as blood pressure and heart rate are not always reliable parameters, since they vary according to many other factors (cardiovascular patient's condition before and during anesthesia, influence of non-anesthetic drugs on hemodynamic function, etc.). In addition, not all anesthetic drugs produce the same kind of hemodynamic changes when administered for obtaining analgesia or pharmacological hypnosis.

When the anesthesiologist solely relies on clinical signs for guiding anesthetic drugs administration, the analysis of the cortical electrical activity showed a large variation among individuals, mainly when a certain group of patients were considered, like pregnant women undergoing Cesarian section and general anesthesia was provided.[1]

Particular clinical conditions which would demand special precautions in order to avoid unwanted episodes of superficial anesthesia are showed below (Table 19.1).

Morbid obesity is on the list of the high risk patients for whom the use of clinical hemodynamic parameters might be not enough to guide anesthetic drugs dosing.

19.2 Cortical electrical activity monitoring in the morbidly obese: its importance

19.2.1 Epidemiologic factors

The prevalence of obesity is permanently increasing. Modern society offers easy approach for food consumption, especially fast food, which is rich in calories, lipids and carbohydrates.

This is one of the reasons why the incidence of obesity among the age group 18–29 years increased in the US from 12% in 1991 to 18.9% in 1999.[2]

Indications for surgery in obese patients include general surgical procedures, elective as well as emergent.

But in the last decade more and more obese patients, mainly young and without a significant co-morbidity, are brought to the operating room for bariatric surgery.

Their number increases in the same proportion with the rate of failure of non-surgical methods of weight loss.

So it is supposed that in the near future an increasing number of obese patients will need general anesthesia in Western civilization.

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Table 19.1 Clinical situations with a higher incidence of awareness during general anesthesia

Clinical condition	Possible explanation
The patient	
American Society of Anesthesiologist grades IV and V	Fear of affecting cardiovascular stability
Morbid obesity	Lack of evidence-based recommendations on dosage calculation
Difficult or prolonged intubation	The effect of induction drugs wore off
Hemodynamic instability during surgery and anesthesia	Almost every single anesthetic drug might produce hypotension
Enzyme induction (alcohol, barbiturates and benzodiazepines)	More rapid enzymatic metabolism
Pre- and intra-operative use of drugs with influence on autonomic system	The hemodynamic parameters (blood pressure and heart rate) are influenced by these drugs and they are not reliable anymore for detecting awareness
Type of surgery	
Obstetrics	Fear to affect fetal respiratory drive and uterine tonus
Bronchoscopy	Frequent interruption of inhalational drugs during bronchoscopic maneuvers
Cardiac surgery	Fear to administer anesthetics immediately after bypass
Trauma surgery	Fear of aggravating hemodynamic instability
Techniques of general anesthesia	
Total i.v. anesthesia	Non-use of inhalatory agents in the absence of a reliable guide for titrating i.v. drugs
Use of no pre-medication	Especially when associated with one of the above patient's clinical conditions
Excessive use of neuromuscular blocking agents, or delayed reversal	Abolishes movements as a sign of superficial anesthesia
Equipment	
Vaporizer failure	In both situations the inhalatory drug is not administered in the desired concentration
Anesthetic circuit leak	

19.2.2 Pharmacokinetic factors

In the absence of clear recommendations for anesthetic dosing "anesthesiologists reduce doses in obese persons based on experience and intuition alone".[3]

So administrating general anesthesia to an obese patient could be a real challenge for the professional (see Chapter 15).

The current absence of clear guidelines for dosing anesthetic drugs in obese patients could lead to inappropriate administration and eventual under or overdoses with consequently unwanted effects.

The smaller proportion of body water and muscle mass and the greater proportion of fat to body weight in the morbid obese patient leads to changes in the proportion of drug distributed between the different body compartments.

Usually recommendations regarding anesthetic drugs dosage in obese patients include, ideal body weight (IBW) or ideal lean body mass (LBM) as a term of reference rather than the actual (total) weight of the patient, i.e. total body weight (TBW).[4] But in a significant percentage of obese patients, the increase in TBW could be explained not only by the quantity of fat tissue in excess but also by the increase in the LBM. This would mean that, as per today, there is no efficient way to know accurately the real LBM of the obese patient.

Thus this recommendation cannot be successfully used for establishing the correct regimen of anesthetic drugs in obese patients. Lack of precision in establishing anesthetic dosages, especially those administered intravenously (i.v.), can be attributed to the fact that adipose tissue could act as a reservoir for many anesthetic drugs and therefore would empty slowly when anesthesia finishes. This pharmacological fact not only affects the calculation of the necessary dose for each drug and for each obese patient but also could lead to a maintenance of subclinical blood concentrations which might increase the effect of hypnotic, opioids or other anesthesia compounds previously administered, and thus delay recovery. Highly lipophilic anesthetic drugs show significant increases in their volumes of distribution (V_d) for obese individuals relative to normal-weight persons.[5–7]

In addition to increase the complexity of this scenario, there are data showing an evident impairment of metabolism and elimination of anesthetic drugs in the obese patient. The hepatic function is affected by obesity. Up to 90% of morbidly obese patients showed histological abnormalities of the liver, one-third of them having fatty changes involving more than 50% of hepatocytes.[8] In a study on morbidly obese patients Ramsey-Stewart found that 75% of them had histological changes compatible with the diagnosis of hepatic steatosis.[9] In 20% of the 127 patients included in the study the degree of steatosis was severe and diffuse.

Finally, renal clearance of anesthetic drugs is enhanced in obesity due to an increased renal blood flow.[10]

Each factor listed above might reduces accuracy when calculating doses of anesthetic drugs in obese patients.

19.2.3 Controversial drugs dosing regimes

Gepts *et al.* proposed in 1987 that propofol dosage should result from a combination between a fixed dose and a body weight-related dose.[11] For instance, propofol dosage for induction can be calculating according to the patient's IBW but the maintenance dose has to be referred to TBW. Some years later, in 1993, Servin *et al.* used an empiric formula for calculating propofol dosage for maintenance of general anesthesia: corrected weight = ideal weight + (0.4 × excess weight).[12] When using this formula, they showed no accumulation of propofol in morbidly obese patients and their conclusion was that dosage of propofol for these patients can be established on the same basis as in lean subjects.

Thiopental and benzodiazepines have a significant higher V_d in obese than in lean patients. Due to this particular characteristic, the elimination half-life of thiopental was found significantly higher in obese patients than in lean patients, which means that its dosage per body weight has to be reduced in order to prevent delay in recovery.[5]

Prolonged sedation after administration of midazolam is to be expected from the same reason and there is data showing a necessity for initial larger doses in order to achieve adequate serum concentrations.[4] Greenblatt *et al.* observed that in spite of a similar metabolism of this drug in obese and non-obese patients, midazolam had a significant longer elimination half-life in overweighed patients.[13] The explanation was the increased V_d. Their recommendation was to increase midazolam doses in obese patients, at least in proportion to total weight and "possibly more, since V_d increases disproportionately with degree of adiposity".

Other studies suggested that the only group of i.v. anesthetic drugs not influenced by obesity regarding dosage seemed to be the opioids. In spite of a higher V_d, dosage calculation of different opioids such as fentanyl or sufentanil can be done by using TBW as a reference term.[14,4]

Nevertheless, when Bentley *et al.* calculated fentanyl doses in obese patients in order to achieve certain blood concentration of the drug, it was necessary to double the dose in this group compared with the non-obese control group patients.[15]

Remifentanil was found as an exception to this rule. Minto *et al.* and Egan showed that remifentanil pharmacokinetics correlate better with LBM, or even IBW rather than TBW.[16,17]

Since obese patients are at high risk of both aspiration and acute upper airway obstruction after tracheal extubation, rapid recovery is therefore highly desirable in order to ensure early efficient coughing and to decrease the rate of postoperative complications[18] (see Chapter 8). In spite of the feeling that administration of volatile agents can be easier managed in obese patients, since removal of these drugs can be accomplished actively by ventilating the patient, data from the literature are not always consistent with this hypothesis (see Chapter 22). The old inhalational agents have been found as producing delayed recovery when administered in obese patients. Wahrenbrock *et al.* in 1974 emphasized the fact that kinetics of inhalational agents depends, among other factors, on the proportion of different tissues in body composition.[19] In 1982 Bentley *et al.* studied biotransformation of halothane in obese and non-obese patients.[20] They found differences between the two groups, among them a higher blood concentration of fluoride and bromide in obese subjects, most probably as a result of enhanced metabolite production and slow release of the drug from fat tissue in this group of patients.

But recent studies on newer inhalational agents such as sevoflurane and desflurane are more encouraging.

Juvin *et al.* compared isoflurane with desflurane regarding the postoperative recovery parameters.[21] They found that desflurane produced an earlier recovery regarding time to extubation, to eye opening and stating name. Extubation, emergence and response times were found to be significantly shorter in Torri *et al.* study when sevoflurane was used, comparing with the group in which isoflurane was used.[22]

Summarizing the multitude of data regarding the cumbersome way of calculating anesthetic regimens for obese patients, it is evident that the clinical anesthesiologist does not possess exact data for deciding upon the anesthetic drug regimen to be properly applied in this special category of patients.

In the absence of a simple and reliable way of calculating the dosage of anesthetic agents for the obese patient, the solution could be specific, on-line monitoring of at least one parameter reflecting the electrical cortical activity during general anesthesia.

19.3 Electroencephalographic parameters as monitors of anesthetic depth

19.3.1 General considerations

The continuous effort done for introducing instrumental tools in the daily practice of modern anesthesia could be easily explained by the drawbacks of the so-called "classical signs" of depth of anesthesia and by the obvious importance of quantifying in real time the influence of general anesthesia on CNS.

Measuring adequacy (or depth) of general anesthesia is supposed to offer significant advantages in clinical practice these days. It may prevent, in a vast majority of cases, episodes of awareness (explicit memory) and storage of subliminal negative information during anesthesia (implicit memory). It may also contribute to a better cardiovascular stability and also to optimize anesthetic drugs regimens, thus reducing costs and shortening recovery time.[23,24] Cardiovascular stability was evident in an intensive care unit (ICU) setup in patients sedated by continuous propofol i.v. infusion after abdominal aortic surgery,[25] guided by an EEG parameter.

Naturally, clinicians and researchers led their studies towards the use of electroencephalography (EEG) during general anesthesia, since EEG is a complex of signals representing the cortical electrical activity.

Unfortunately its chaotic appearance with random waves, amplitudes, frequencies or shapes made the classical EEG difficult to be used in clinical practice. But the raw aspect of EEG can be translated into its digital counterpart for mathematical analysis and transformed into a much more friendly way of presentation, easier to interpret and useful for taking clinical decisions.

19.3.2 Spectral edge frequency and other power spectrum-derived parameters

When the complex EEG waves, with their amplitude and frequencies, are analyzed by using the method called Fourier fast transformation (FFT) a power spectrum with several parameters is obtained.

Among them, spectral edge frequency (SEF) got in the last two decades a special place regarding the use during anesthesia. SEF represents a frequency in which 90% or 95% of the area of the waves's histogram is below it. It was described for the first time by Rampil *et al.* in dogs.[26] In their report it correlated well with end-tidal concentrations of halothane and isoflurane. In subsequent studies SEF proved to vary in the same direction with thiopental serum concentrations, as well as with the pressure response to laryngoscopy and tracheal intubation.[27–29]

In our earlier studies we used SEF for various aims. This EEG parameter was first used by us as a measure of the effect of general anesthetics on CNS when we intended to compare two completely different anesthetic drugs used for maintenance of general anesthesia: propofol and isoflurane.[30] The monitor used by us, Cerebrotrac 2500 (Israel, SRD) is a dual channel bipolar device which utilized FFT to convert EEG waves from the time domain, as in raw EEG, to the frequency domain.[31] Five electrodes, one neutral, two frontal and two parietals, were used in order to obtain two symmetrical temporo-parietal channels. This monitor displays both amplitude and frequency (SEF) from each one of the channels. We used an SEF range from 8 to 12 Hz as a target value for titrating the main anesthetic drug used, and have demonstrated that in condition of equipotency (defined as different anesthetic regimens producing the same level of SEF) the use of propofol for maintenance of general anesthesia was accompanied by a more significant hemodynamic stability[32] (Table 19.2).

The usefulness of continuous SEF monitoring was also proven during continuous propofol i.v. administration, both as a supplement to epidural anesthesia for surgery and as the only drug for postoperative sedation after aortic surgery.[25]

Table 19.2 The frequency of a blood pressure event[a] during anesthesia with propofol or isoflurane when SEF was kept between 8 and 12 Hz

Parameter	Propofol group[b] (n = 20)	Isoflurane group[b] (n = 23)	P
Number of events per case	0.45 (0.69)	0.96 (0.82)	0.04
Number of events per hour of anesthesia	0.34 (0.72)	0.72 (0.59)	0.03
Mean duration of an event (min)	5.55 (11.28)	16.87 (19.6)	<0.01
% event time of total anesthesia	0.06 (0.12)	0.20 (0.23)	0.03

[a] Definition of a blood pressure event: deviation of mean blood pressure more than 20% from the baseline, more than 2 min.[30]

[b] Values are mean (±standard deviation).

By recording the mean values of SEF during general anesthesia for various surgical procedures (Cesarian section, laparoscopic surgery)[1,33] we found out, in both series, that there was a correlation between the length of time SEF remained in the desired range (8–12 Hz), and the doses of morphine needed during the immediate postoperative period. Longer the period of SEF in the "normal" range, lower the needed morphine dose requested by the patient.

Finally, we used SEF for assessing the magnitude of implicit memory by measuring the time the patient needed for completing a pair of words heard during general anesthesia (the so-called reaction time, RT).[34] The 9 Hz cut-off point divided our patients into two groups, that with a short RT (that is, learning during anesthesia) and that with a significantly longer RT, which was accompanied by a lower SEF when compared with the first group.

The use of SEF during general anesthesia was accompanied by criticism of the method. Some studies failed when proving accuracy of the parameter. No correlation was found between SEF and methohexital blood levels in a small group of patients.[35] Also Arden *et al.* described a poor relationship between SEF and blood concentrations of etomidate.[36] Rampil (SEF's pioneer in clinical practice) recently claimed an explanation for the limits of this EEG parameter.[37] SEF calculation is sensitive to changes in spectral distribution, but since only 90–95% of the waves are included in the algorithm, there would always be some energy left in the low-frequency range. Even more, some general anesthetics might produce burst suppression without slowing the waves present during those bursts which are not suppressed. This aspect of EEG during anesthesia is not reflected when using SEF.

From the power spectrum, several other parameters beside SEF have been derived to indicate the influence of various anesthetic regimens on the cortical electrical activity. Median or mean frequency can be calculated and clinical ranges for routine general anesthesia can be used for describing the anesthetic effects on the cortex.

19.3.3 Bispectral index

Recently a new EEG frequency parameter, bispectral index (BIS), was developed and used for measuring the effect of anesthetic drugs. Bispectral analysis incorporates a set of EEG characteristics, each selected to cover a specific range of CNS anesthetic effect. For instance two parameters measure the amount of burst suppression in the electrical cortical activity during "deep" anesthesia. Two other components cover the high EEG bands (beta), characteristic of light anesthesia levels. BIS combines all the above and translates the data, by using a special nonlinear algorithm, into a scale from 0 to 100 in which 100 reflects full consciousness.

Several studies showed a good correlation between BIS and movements produced by surgical incision.[38,39]

Similarly to SEF, BIS has proven to predict hemodynamic response to laryngoscopy and tracheal intubation.[40] Most of the studies in which anesthetic agents titration was performed according to BIS values (BIS-guided anesthesia) showed a significant reduction in the concentrations and amount of drugs[41,42] (see Chapter 23). Accordingly, several studies found that BIS titration of general anesthetic agents shortens emergence from anesthesia, and improves patient's orientation on arrival at recovery room.[42,43]

Johansen *et al.* retrospectively studied more than 1500 patients receiving general anesthesia, some under BIS guidance and others for whom anesthesia monitoring did not include BIS.[24] They showed that anesthetic emergence, recovery times and the amount of volatile agents used were significantly reduced or shortened when BIS values were maintained between 50 and 65. Nevertheless the use of BIS in general anesthesia for improving its adequacy, by preventing awareness or optimizing drug regimen, has not become a routine monitoring in the operating room yet. Some reasons concur for explaining the reticence on using BIS on a larger basis. First, most of the clinical studies regarding BIS performance, used single anesthetic regimens (propofol or isoflurane) or incomplete combinations of anesthetic drugs, like a volatile agent and N_2O. The restricted use of anesthetic agents could be explained by the fact that administration of opioids could make interpretation of BIS unreliable. For instance addition of alfentanil to propofol resulted in loss of consciousness at higher values of BIS than those observed during anesthesia with only a volatile agent.[44]

When prevention of recall/awareness/explicit memory could be considered the main aim of using BIS during general anesthesia, several reports showed contradictory results.

In a review article Sandler suggested that BIS offers additional information regarding depth of hypnotic state, when induced by midazolam and ketamine.[45] Lehmann *et al.*, in 62 patients undergoing aortocoronary bypass grafting, found no explicit memory during anesthesia when BIS was kept around 40–50.[46]

In spite of the accepted recommendation that BIS below 50 would prevent recall during general anesthesia,

some trauma patients lost explicit memory when BIS was even higher than 80.[47] On the other side, a similar group of trauma patients displayed memory for words presented at BIS values between 40 and 60.[48] Barr *et al.* studied 10 volunteers who have been presented with pictures, sounds and smells at different BIS values under propofol administration.[49] They concluded that it was not possible to establish a threshold value or zone for discriminating between wakefulness and loss of response to verbal command, in spite of the fact that no volunteer could explicitly recall any of the stimuli presented during the period of wakefulness. There are reports in the literature on sporadic cases in which BIS was kept into the desired range but the patient had episodes of awareness during general anesthesia.[50] BIS could not differentiate between patients with or without awareness, when it was kept between 50 and 60 in 20 patients studied by Schneider *et al.*[51] O'Connor *et al.* considered that BIS effectiveness in preventing awareness is less than 100%, and in order to demonstrate the precision of the method the number of patients to be recruited in such a study would be too large.[52]

Summarizing, we feel that in spite of the drawbacks of each of the proposed parameters, the use of a monitoring tool to evaluate CNS electrical activity might improve the quality of the anesthetic act and optimize the administration of anesthetic drugs.

19.4 Electroencephalographic monitoring in morbidly obese patients

Reckoning the danger of awareness during anesthesia in morbidly obese patients, one could expect getting reliable recommendations resulting from studies done on this topic.

But the literature is scarce in providing data on EEG monitoring during anesthesia for the obese patient.

Juvin *et al.* used BIS as a measure of electrical cortical activity level when comparing desflurane, propofol and isoflurane in morbidly obese patients anesthetized for gastric banding.[21] In that study BIS was not used for guiding the anesthetic regimen, but only to proof the similitude between the three groups at discontinuation of anesthesia (a method used by us in 1994).[30] So Juvin *et al.* could prove that at equal BIS value at the end of anesthesia, desflurane showed a significant quicker recovery. Recently Paventi *et al.* used BIS during anesthesia for laparoscopic cholecystectomy in 40 morbid obese patients.[53] The patients were divided into two groups, one treated with sevoflurane titrated by end-tidal concentrations and the other with sevoflurane and a continuous infusion of remifentanil, titrated according to BIS values. They found that by using BIS for guiding remifentanil infusion, shorter awakening time, extubation time and speed of orientation and transfer to recovery room were obtained.

Based on previous studies which showed a reduction in the need for immediate postoperative analgesia after Cesarian section and laparoscopic cholecystectomy, we questioned the efficacy of monitoring cortical electrical activity during anesthesia in morbid obese patient in the same direction of postoperative use of opioids.[1,33,54] We used SEF as a EEG parameter in 71 obese patients planned for gastric banding under general anesthesia with isoflurane, N_2O, fentanyl and vecuronium. There was no intention to titrate the anesthetic regimen according to the SEF values, which have been kept hidden from the anesthesiologist in charge. SEF recorded during maintenance of anesthesia was analyzed retrospectively and correlated with the patient's request for morphine in the immediate postoperative period. A SEF range of 8–12 Hz was considered compatible with a normal level of surgical anesthesia.[32] Retrospective analysis of SEF recordings used a 80% anesthesia maintenance time for dividing the studied patients into two groups: one in which SEF remained into the "normal" range of 8–12 Hz for more than 80% of the time and the second one in which SEF was found to stay less than 80% of the maintenance time into that range. Pain was measured at admission to and discharge from recovery room. Total doses of morphine requested by patients during

Table 19.3 A comparison between three groups of patients monitorized with SEF during maintenance of general anesthesia

Group	Number of patients	Number of patients with SEF 8–12 Hz: anesthesia maintenance time		% of total maintenance time in which SEF remained between 8 and 12 Hz
		>80%	<80%	
Orthopedic surgery	39	35 (89%)	4 (11%)	87
Laparoscopic cholecystectomy	40	22 (55%)	18 (45%)	83
Gastric banding for morbid obesity	71	38 (53%)	31 (47%)	68

their stay there were also evaluated. The group in which SEF stayed at least 80% of the maintenance time into "normal" range had a significantly lower pain score (visual scale from 0 to 10) and also a reduced need for opioids during immediate postoperative period.

A possible explanation for these differences could be found into the higher end-tidal isoflurane concentration used in that group in which SEF was kept at least 80% of the time in the "normal" range. But a striking result was found when we compared that group of 71 obese patients with two other groups of patients in whom SEF was used during general anesthesia for either orthopedic surgery or laparoscopic cholecystectomy.[23,33]

SEF monitoring was used during maintenance of general anesthesia in all the three groups, but the SEF screen was kept hidden from the view of the anesthesiologist in charge with each patient.

Results of the comparison regarding the percentage of patients in whom SEF remained in the "normal" range (8–12 Hz) at least 80% of the maintenance time as well as the total anesthesia time with SEF between 8 and 12 Hz for each group are shown below (Table 19.3).

The comparison of the three groups confirmed that regarding the obese patients, keeping the electrical cortical activity (measured by SEF) into the so-called normal range becomes a more difficult task for the clinical anesthesiologist than in other groups of patients. The percentage of patients kept into "normal range" SEF as well as the total anesthesia time in which SEF was kept between 8 and 12 Hz was lowest in the morbidly obese group than in the other two.

These findings strengthen the clinical impression and data from the literature that a desired level of anesthesia is hard to be achieved in surgical obese patients.

19.5 Conclusions

The number of morbidly obese patients who need general anesthesia for various surgical procedures is continuously increasing.

In most cases anesthesia for the morbidly obese is not simple. Technical difficulties related to the problematic anatomic landmarks, tracheal intubation or even assuring a venous access, are all known by the clinical anesthesiologist. It could be added to this list the complexity of the process of titrating the anesthetic dosage among obese patients. In the absence of a reliable clinical or an instrumental tool for measuring the adequacy of anesthesia, this task seems to be much more difficult when the patient is overweighed. Suggestions offered by the literature regarding the anesthetic agents dosage are more recommendations than guidelines "larger absolute dose, smaller dose per unit of body weight", on thiopental, "larger absolute dose, same dose per unit body weight" on midazolam, or "smaller concentration" on enflurane.[55]

The danger of awareness during general anesthesia is more evident between these patients. Overdosing could be easily encountered during anesthesia in the morbidly obese, with drastic consequences such as cardiovascular instability or prolonged recovery. Insufficient anesthesia can be accompanied by an increased necessity for postoperative analgesia, with its undesired secondary effects.

All the above lead to the conclusion that the obese patient qualifies high on the list of situations for which it becomes necessary to use any of the available methods for measuring the adequacy of general anesthesia.

New technology, based on EEG computerized analysis is on its way to the daily clinical practice.

We cannot but agree with Rampil's conclusions on the review article on EEG signals processing during anesthesia: "The exact role and limitations of this new technology will be determined by additional clinical experience".[37] The obese patient is one of the first who would fully benefit from technology progress in the field of monitoring the adequacy of general anesthesia. Even if this benefit is not yet evident, we are persuaded that monitoring any EEG parameter during general anesthesia in obese patients presents some advantages, as presented in the respective table (Table 19.4).

Table 19.4 The possible benefit of EEG monitoring during general anesthesia for morbid obesity

Advantages	Comments	References
Prevention of overdosing, quicker recovery and less anesthetic drugs used	Currently guidelines regarding anesthetic dosage are not precise	24, 41–43, 53
Better hemodynamic stability	Not studied in obese patients	23
Better postoperative analgesia	Large doses of opoids in postoperative stage could lead to respiratory depression	54
Prevention of awareness	Controversial data in the literature	44–52

One cannot but hope that in the near future new instruments, and also the use of more than one single parameter, would provide more clear guidelines regarding the anesthetic regimen to be applied in morbid obesity (see Chapter 30).

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INTRA-OPERATIVE MANAGEMENT

SECTION 7

POSITIONING THE MORBIDLY OBESE PATIENT FOR SURGERY

20

J.B. Brodsky

20.1 Introduction

The incidence of significant obesity is rising throughout the entire world.[1–3] As a result every anesthesiologists must be familiar with the management of morbidly obese patients, not only for bariatric procedures but for all types of surgery.[4,5]

Any surgical patient can experience serious physiologic impairment and even physical injury if improperly positioned during surgery. Positioning considerations are even more important for the morbidly obese patient. It is therefore surprising that many reviews on the peri-operative management of the obese patient fail to discuss the effects of position on cardiopulmonary physiology.[7–9]

This chapter reviews the implications of the different intra-operative positions on the morbidly obese patient. A patient is considered to be morbidly obese if their body mass index (BMI = weight (kg)/height (m^2)) is greater than 39 kg/m^2.[6]

20.2 General considerations

For any procedure clear and open communication and careful planning between the anesthesiologist and the surgical team is essential.[10] All needed equipment must be identified, be available, and be in working condition before the start of the surgery.

Operating room gurneys are usually too small or too uncomfortable for a very obese patient. Transfer of a morbidly obese patient, both to and from the operating room, is best accomplished with the patient on a hospital bed. Special beds are available to accommodate patients heavier than 200 kg.

Sufficient manpower must also be available before attempting to move a very obese patient. Transfer to the operating room table(s) or turning the patient from the supine to the prone or lateral positions requires the coordinated help of many people.

Conventional operating room tables are not designed for very large patients, and one table may not be wide enough. Two standard tables can be placed side-to-side to accommodate a very large patient[11] (Figure 20.1).

Lifts can be placed beneath the tables for added support (Figure 20.2).

A "staircase" to the operating table can be built using lifts. This can allow the patient to get off the bed and position themselves (Figure 20.3).

If the patient is going to position themselves, it is important that they receive no pre-operative sedative medication which could impair their ability to cooperate (Figure 20.4(a–c)).

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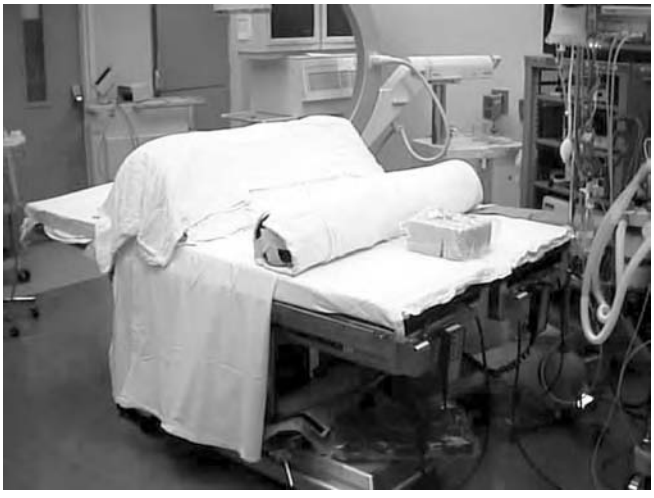


Figure 20.1 Conventional operating room tables are not designed for extremely obese patients and one table may not be wide enough. Two standard tables can be placed side-to-side to accommodate very large patients. Special operating room tables are available for patients weighing over 200 kg.

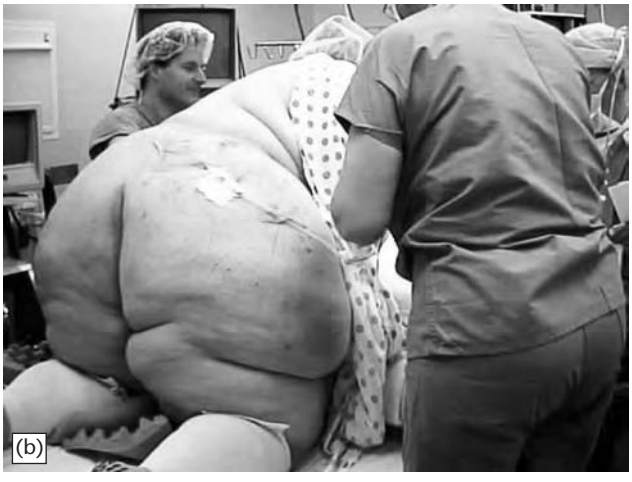
Figure 20.2 Lifts can be placed beneath the operating room table(s) for added support.

Figure 20.3 Lifts can be used to build a "staircase" to the operating table to allow the patient to position himself or herself.

All potential pressure points must be adequately padded after the patient is positioned on the operating table before the induction of anesthesia. The risk of pressure sores and neural injuries from prolonged stasis during surgery is higher in an obese patient than in a normal weight patient,[12] and for the diabetic obese patient these risks are further increased. Normal amounts of padding may be insufficient to prevent the increased weight of the adipose tissue from injuring nerves and vascular structures.[13]

20.3 Cardiovascular and pulmonary physiology

Obesity itself is normally associated with significant physiologic changes, and each of the different surgical positions can further alter baseline cardiovascular and pulmonary function[14] (see also Chapters 4 and 5).



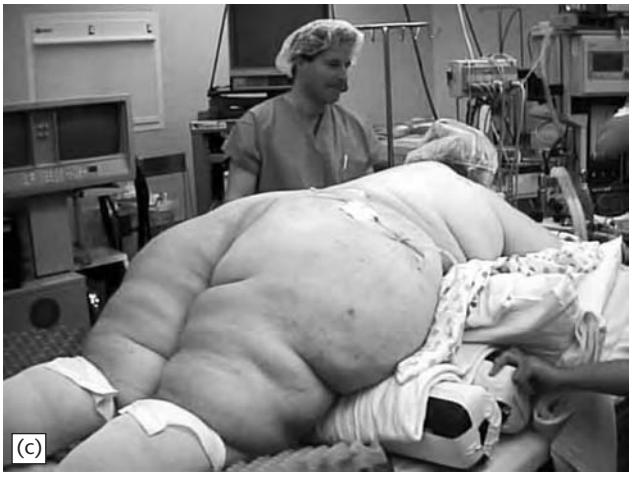


Figure 20.4 An un-premedicated patient can position himself or herself. (a) The patient gets off the transport gurney. (b) Then climbs the "stairway" onto the operating table. (c) She then positions herself prone on the table. While awake, she can identify any pressure points that require additional padding or support.

Awake, spontaneously breathing obese patients have decreased chest wall compliance and inefficient respiratory muscles.[15] Work of breathing increases with increasing obesity, and is associated with increased oxygen consumption and carbon dioxide production.[16] Obese patients require greater diaphragmatic excursion than normal weight patients to effect the same ventilation.[17]

With increasing weight, intra-abdominal pressure increases and functional residual capacity (FRC), expiratory reserve volume (ERV) and total lung capacity (TLC) all decrease in obese patients compared with normal weight patients.[18–20] These changes are usually attributed to mass loading of the thoracic and abdominal components of the chest wall and splinting of the diaphragm.[21] Airway closure occurs during normal tidal ventilation producing air trapping, shunting and a lower PaO_2 than would be expected in similar normal weight patient.[22]

In morbidly obese patients, cardiac output,[23] systemic and pulmonary artery pressures, and left and right ventricular pressures are all increased.[24] These changes manifest themselves clinically as arterial hypertension, and with advancing age as ischemic heart disease and right and left heart failure.[25,26] The incidence of pre-existing, often severe, cardiovascular disease in obese patients scheduled for elective bariatric surgery is claimed to be as great as 20% in some series.[7,8]

20.4 Supine position

In any patient, simply changing from standing or the sitting position to the supine position causes an increase in venous blood return to the heart. Cardiac output, pulmonary blood flow and arterial blood pressure all increase after assuming the supine position. The abdominal contents limit diaphragmatic movement reducing FRC. In normal weight patients (BMI < 29) there are statistically significant declines in spirometry values when changing from the sitting to supine positions.[27] General anesthesia with muscle paralysis causes a further reduction of lung volumes in every patient.[28]

In obese patients these cardiorespiratory changes are exaggerated.[29,30] The increased diaphragmatic load causes a marked reduction in expiratory flow and an increase in intrinsic positive end-expiratory pressure (PEEP).[31] Supine obese patients have relative hypoxemia and significant alterations in the mechanical properties of their respiratory system with marked reductions in lung volume.[32] In the supine position intra-abdominal pressure is increased causing a splinting effect of abdominal contents on the diaphragm.[33]

The supine obese patient has a proportionally greater decrease in FRC, total respiratory system and pulmonary compliance, and a larger ventilation/perfusion (V/Q) mismatch than normal weight patients. All these changes increase with increasing BMI.[33]

In order to avoid these problems, induction of anesthesia in the lateral decubitus position has been recommended for morbidly obese patients.[34]

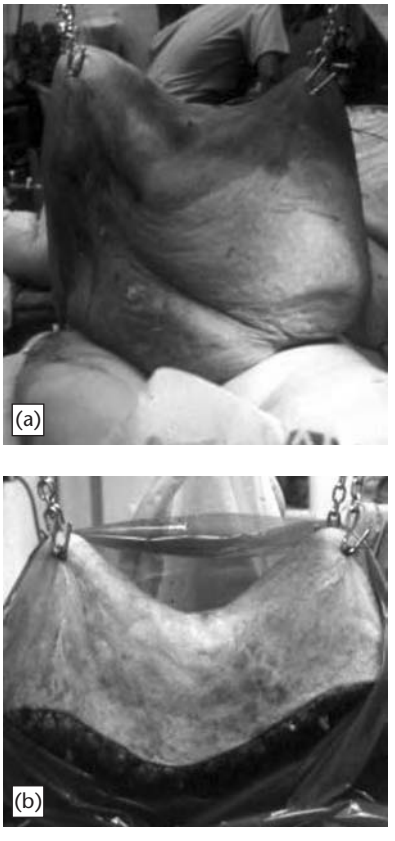


Figure 20.5 (a) In the supine position if the high intra-abdominal pressure is reduced, FRC and oxygenation will improve. This was dramatically demonstrated in this supine 340 kg patient. (b) Without any changes in ventilatory parameters, mechanically lifting the panniculus relieved intra-abdominal pressure and increased PaO_2 markedly.

The application of PEEP can improve respiratory function in mechanically ventilated supine morbidly obese patients.[35,36]

Relieving or reducing the high intra-abdominal pressure increases FRC and improve oxygenation.[37] This was dramatically demonstrated in a supine extremely obese patient[38] (Figure 20.5(a,b)).

Without any other changes in ventilatory parameters, mechanically lifting her panniculus during surgery relieved intra-abdominal pressure and PaO_2 increased markedly. Similarly, in morbidly obese patients undergoing laparotomy, simply opening the abdomen leads to an increase in pulmonary compliance and lung volumes return towards normal values.[39,40] Many morbidly obese patients cannot tolerate the supine position (Figure 20.6).

In a study of cardiovascular changes in obese patients scheduled for gastric stapling surgery, changing from

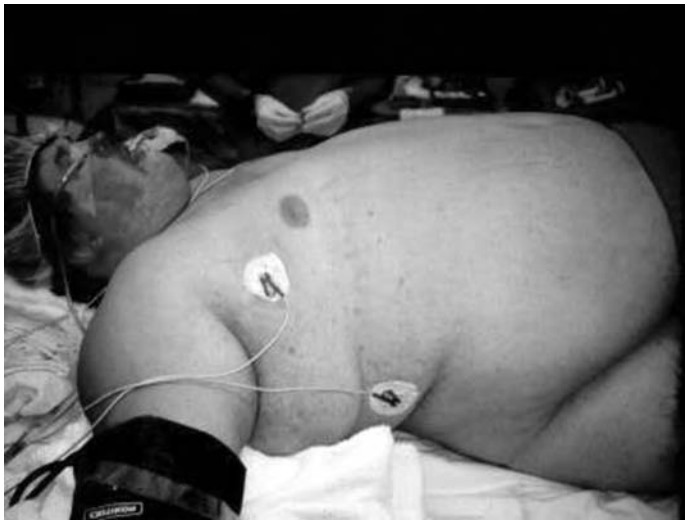


Figure 20.6 Most morbidly obese patients cannot tolerate the supine position. Changing from the sitting to supine position causes significant increases in oxygen consumption, cardiac output and pulmonary artery pressure. By lying down, a decrease in already reduced chest wall compliance, a further increase in ventilation to perfusion mismatch and a sudden shift of blood to the heart can occur.

the sitting to supine position caused significant increases in oxygen consumption, cardiac output and pulmonary artery pressure. By lying down, a decrease in already poor chest wall compliance, further V/Q mismatch, and a sudden shift of blood to an already hyperactive, borderline hypoxic heart occurred.[41] These changes can lead to fatal cardiorespiratory decompensation (obesity supine death syndrome) in obese patients with inadequate cardiac reserve.

Compression of the inferior vena cava, which reduces venous return to the heart, must also be avoided. This can be accomplished by tilting the operating room table or by placing a wedge under the patient. These maneuvers are similar to those performed during Cesarian section to reduce the pressure of the gravid uterus on the inferior vena cava.

20.5 Head-down (Trendelenburg position)

In the Trendelenburg position the patient's head is below the horizontal plane. During selected surgical procedures this position improves operative exposure and can reduce bleeding.

Obese patients generally do not tolerate the Trendelenburg position. There is an auto-transfusion of blood from the lower extremities into the central and pulmonary circulation. The added weight of the abdominal contents pressing on the diaphragm plus the weight of the chest wall further decrease total compliance and FRC, which in turn leads to atelectasis and hypoxemia (Figure 20.7).

Arterial blood gas samples were obtained from morbidly obese patients undergoing jejuno-ileal bypass procedures. Patients were placed in the supine and then in a 15° head-down (Trendelenburg) position.[42] Ventilation with an F_iO_2 of 0.4 did not uniformly produce adequate arterial oxygenation in either position. A change from supine to the Trendelenburg position resulted in a significant decrease in PaO_2. The combination of Trendelenburg position with placement of sub-diaphragmatic packs, which further impeded diaphragmatic excursion, was particularly dangerous.

In any patient, a change from supine to the Trendelenburg position can result in advancement of the tip of the endotracheal tube deeper in the airway.[43] The potential for tube misplacement is greater in morbidly obese patients, and when it occurs it can result in bronchial intubation which results in further decreases in pulmonary compliance and oxygenation.

The Trendelenburg position should be avoided if possible in a morbidly obese patient. If an anesthetized obese patient must be placed head-down, their trachea should be intubated and ventilation should be mechanically controlled.

20.6 Head-up (semi-Fowler's and reverse Trendelenburg) positions

Extremely obese patients should never be allowed to lie completely flat. Their upper body should be elevated 30–45° in the semi-recumbent (semi-Fowler's) or with the entire operating room table tilted in the reverse Trendelenburg position to allow adequate ventilation.

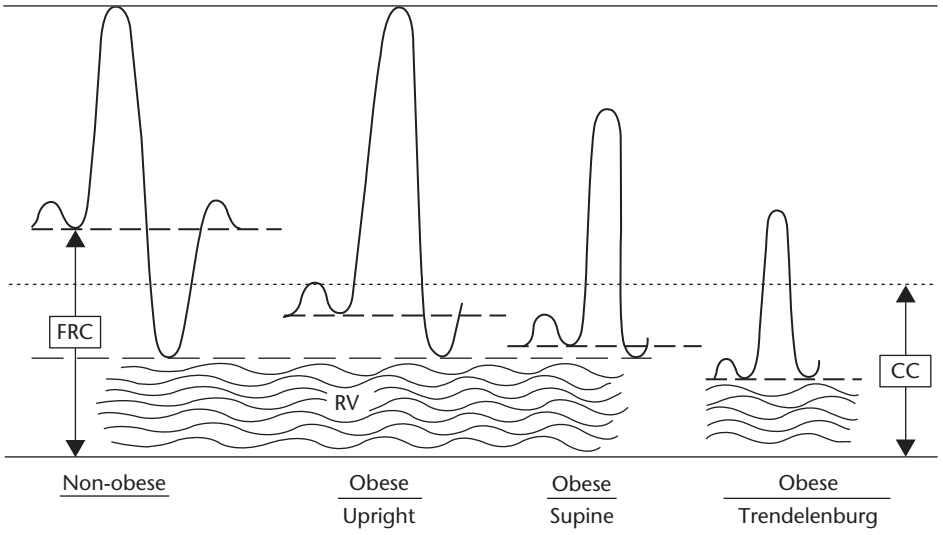


Figure 20.7 Effect of position change on various lung volumes in non-obese subject compared with markedly obese subject. Obese patients cannot tolerate the Trendelenburg position. The added weight of the abdominal contents pressing on the diaphragm plus the weight of the chest wall decrease total compliance and FRC, which in turn leads to airway closure and hypoxemia. RV, residual volume; CC, closing capacity.

Figure 20.8 Prior to induction of general anesthesia, the patient should be positioned with pillows or towels under their shoulders (stacked), with their head and upper body elevated in a semi-recumbent or reverse Trendelenburg position. This position improves pulmonary compliance, allows easier mask ventilation and improves conditions for tracheal intubation.

A head-up position results in an unloading of the weight of the intra-abdominal contents from the diaphragm. Morbidly obese patients in the reverse Trendelenburg position had an increased pulmonary compliance and FRC, and oxygenation returned towards baseline values compared to the same patients supine.[44]

Prior to induction of general anesthesia, the obese patient should be positioned with pillows or towels under their shoulders, with their head and upper body elevated in a semi-recumbent or reverse Trendelenburg position (Figure 20.8). This "stacked" position improves pulmonary compliance while allowing easier mask ventilation and improving conditions for tracheal intubation.[45,46]

Hypoxemia during induction of general anesthesia for the morbidly obese patient is a real concern for the anesthesiologist. During anesthetic induction in morbidly obese patients, the 30° reverse Trendelenburg position provided a longer safe apnea period than the 30° semi-Fowler's and supine positions.[47] Mask ventilation and occasionally tracheal intubation can be difficult in obese patients, and patients can experience

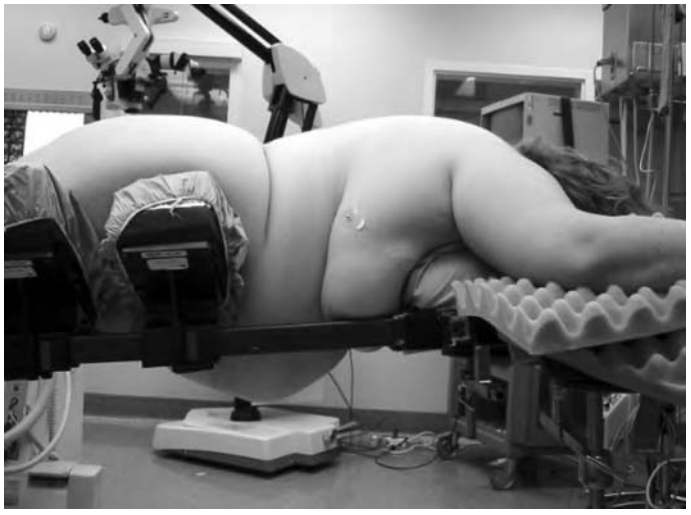


Figure 20.9 In the prone position if the abdomen is not free to move, it will impede the diaphragm and restrict chest wall movement. If the abdominal wall is allowed to hang freely as illustrated, there is a reduction in cephalad displacement of the diaphragm with re-opening of atelectatic lung segments. The prone position is tolerated by obese patients as long as their upper chest and pelvis are adequately supported to ensure free abdominal movement.

rapid arterial oxygen desaturation during induction of anesthesia.[48] Since the reverse Trendelenburg position allows extra time to secure the airway before arterial desaturation can occur, this position has been recommended as the optimal position for induction of general anesthesia in morbidly obese patients.[47]

The efficacy of PEEP and the reverse Trendelenburg position were compared in morbidly obese patients undergoing bariatric procedures.[49] Both PEEP and the reverse Trendelenburg position improved oxygenation and total respiratory compliance. There were no significant differences with regard to gas exchange, but both PEEP and the reverse Trendelenburg position were associated with a drop in cardiac output. Any beneficial effects on oxygenation could be offset if cardiac output decreased significantly. Since the same research group previously reported no adverse cardiovascular changes in morbidly obese patients placed in the reverse Trendelenburg position, whether the actual reduction in cardiac output is clinically important is not known.[44]

Combining the reverse Trendelenburg position and pneumoperitoneum during laparoscopic gastric bypass surgery reduces femoral blood flow and increases venous stasis, increasing the risk of pulmonary embolism.[50] The use of sequential compression devices was only partially effective in reversing the reduction in femoral peak systolic velocity.

If hemodynamically stable, the trachea should be extubated with the patient's upper body elevated 30–45°. The patient should be transferred from the operating room while in a semi-recumbent or tilted reverse Trendelenburg position.[51]

Following abdominal surgery obese patients have a greater reduction in lung volumes compared to normal weight patients.[52] Patients should be kept in a head-up position to minimize intrapulmonary shunting.[53] Post-operatively on days 1 and 2, change from the semi-recumbent to the supine position resulted in significant decreases in PaO_2. Obese patients should always convalesce in the semi-recumbent position while receiving supplemental oxygen.[54]

20.7 Prone position

In an anesthetized and paralyzed normal weight patient in the prone position, oxygenation is improved compared to the same patient in the supine position.[55,56] If the abdominal wall is allowed to hang freely, there is a reduction in cephalad displacement of the diaphragm and a re-opening of atelectactic lung segments. However, if the abdomen is compressed and not free to move, it will impede the diaphragm and restrict chest wall movement.[57,58]

The prone position is usually well tolerated by obese patients, as long as the upper chest and pelvis are adequately supported to ensure free abdominal movement[59] (Figure 20.9).

The unloading of abdominal viscera significantly reduces pressure on the diaphragm, which in turn leads to an increase in FRC. For very large patients the thorax and pelvis may have to be raised as high as 2 ft (60 cm) above the operating table. This is accomplished using large pelvic and chest supports.[60]

When properly positioned, cardiovascular function is maintained in normal weight prone patients.[61,62]

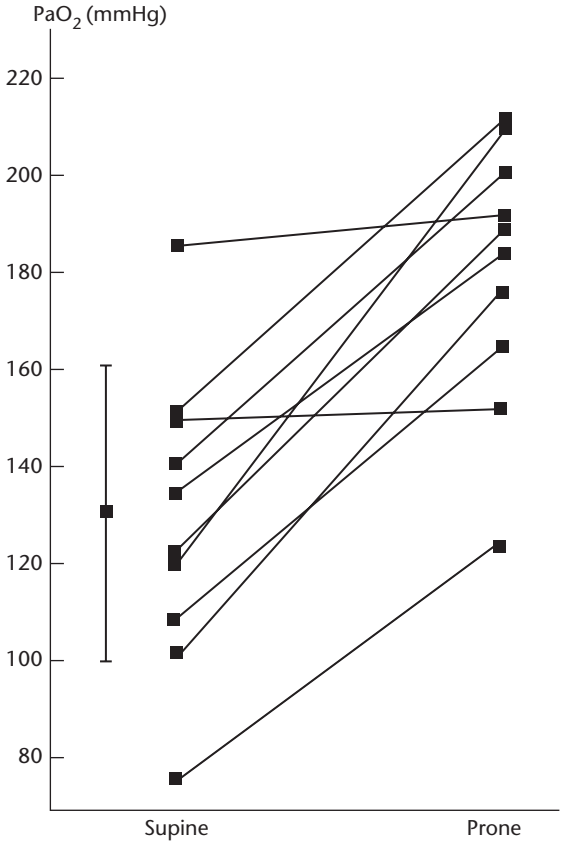


Figure 20.10 In mild to moderately obese patients lung volumes and oxygenation all increased when changing from the supine to prone position. Less airway pressure is required to ventilate the lungs of prone morbidly obese patients compared to those same patients supine.

The abdominal viscera must be free in order to reduce pressure on the inferior vena cava. If the inferior vena cava or femoral veins are compressed then venous return to the heart will decrease resulting in decreased left ventricular filling and hypotension.[63] Blood pressure may be further decreased from the increased intrathoracic pressures generated during mechanical ventilation in an improperly positioned prone patient.[64]

In mild to moderately obese patients (average BMI: 34, range 30–46) respiratory mechanics, lung volumes and oxygenation all increased when changing from the supine to prone position (Figure 20.10).

Less airway pressure is required to ventilate the lungs of prone morbidly obese patients compared to the same patients when supine.[65]

In a study of anesthetized obese patients (BMI $>$ 30), measurements of respiratory function were made in the supine and prone positions. Tidal volume ventilation (VT = 12 ml/kg ideal weight), respiratory rate (RR = 14/min) and F_iO_2 of 0.4 were maintained in both positions. There was an increase in FRC and lung compliance and a significant increase in PaO_2 when the patients were changed from supine to prone.[66] The authors concluded that the prone position improves pulmonary function, increases FRC, lung compliance and oxygenation in anesthetized and paralyzed obese patients.

For procedures in the prone position the trachea can be intubated while the patient is still awake. The patient can then turn him or herself and settle in a comfortable position before induction of general anesthesia. An awake patient can identify areas that require additional padding, decreasing the chances of soft tissue or nerve injuries.

Prolonged surgery in the prone position, especially in a poorly positioned patient, can cause complications. If the abdomen is compressed impairing vena caval flow, collateral venous drainage will engorge the vertebral and epidural veins. This coupled with arterial hypotension can compromise spinal cord perfusion producing spinal cord ischemia.[67] At least one case of ischemic optic neuropathy from venous engorgement was reported in an obese, diabetic patient in the prone position.[68] The arms must be carefully supported to avoid stretch or compression that can lead to brachial plexus injury.[69]

20.8 Lateral decubitus position

Due to the potential difficulty in positioning morbidly obese patients, procedures routinely performed in the prone patient are often done in the lateral decubitus position.[70] There are few clinical studies of how obese patients under general anesthesia tolerate the lateral position.

In normal weight patients changing from supine to the lateral decubitus position is not associated with any significant hemodynamic effects. If a kidney rest is used, cardiac output can be reduced due to a decrease in venous return and an increase in systemic vascular resistance.[71]

In normal weight patients there is a decrease in lung compliance in the lateral position.[72] In an experimental study of five morbidly obese volunteers, changing from the seated position to the lateral decubitus position resulted in a reduction in the volume of the dependent lung. The mechanism for this change,

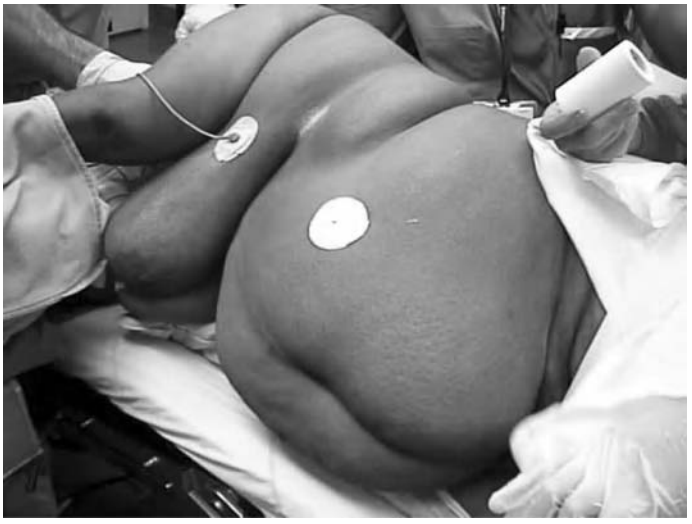


Figure 20.11 Morbidly obese patients tolerate the lateral position because their panniculus is displaced off the abdomen reducing intra-abdominal pressure and allowing greater diaphragmatic excursion during mechanical ventilation.

whether due to position alone or mechanical dysfunction of the diaphragm or intercostal muscles, was not determined.[73]

Morbidly obese surgical patients tolerate the lateral position, perhaps because their panniculus is displaced off the abdomen reducing intra-abdominal pressure and allowing greater diaphragmatic excursion during mechanical ventilation[74,75] (Figure 20.11).

Oxygenation with one-lung ventilation was satisfactory during thoracotomy in the lateral decubitus position.[74,75]

Regional anesthesia is often difficult in obese patients due to problems identifying landmarks.[76] The distance from the skin to the epidural space increases with increasing BMI. After placing an epidural catheter in a sitting patient, changing to the supine, lateral or lithotomy positions for surgery can increase the distance from the skin to the epidural space (Figure 20.12).

With the epidural catheter taped to the skin, position changes can dislodge the catheter and result in inadequate analgesia.[77]

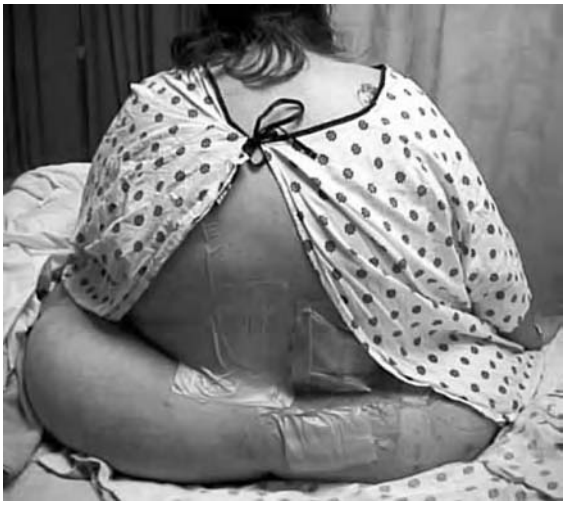


Figure 20.12 The distance from the skin to the epidural space increases with increasing BMI. The epidural catheter is usually placed in a sitting patient and is then securely taped to the skin. Changing to the supine, lateral or lithotomy positions for surgery increases the distance from the skin to the epidural space. This can cause catheter dislodgement and result in inadequate analgesia.

20.9 Lithotomy position

In the lithotomy position the patient is on their back with the legs and thighs flexed at right angles. The patient may also be head-down (Trendelenburg position) (Figure 20.13).

Vital capacity decreases in normal weight patients breathing spontaneously in the lithotomy position because of the restriction of diaphragmatic movement. Venous return to the heart is increased causing an increase in cardiac output and increased pulmonary blood flow.

These changes were exaggerated when a morbidly obese patient in the lithotomy position was positioned with his knees-to-abdomen similar to the "Heimlich Maneuver".[78] This markedly increased intra-abdominal pressure and compressed the lungs further reducing chest wall compliance.

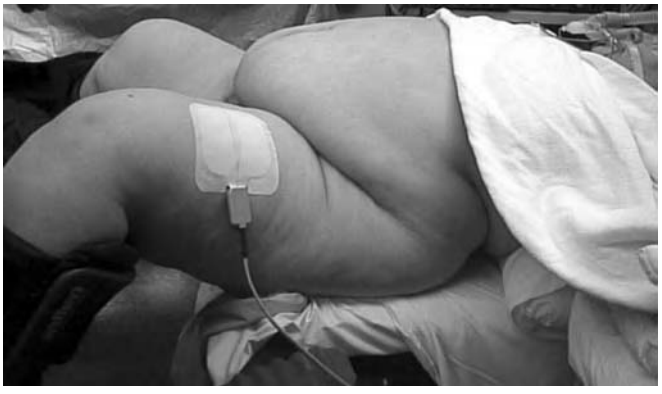


Figure 20.13 In the lithotomy position the patient is on their back with their legs and thighs flexed at right angles. The patient may also be head-down. In spontaneously breathing patients, vital capacity decreases because of the restriction of diaphragmatic movement. Venous return to the heart is also increased causing an increase in cardiac output and increased pulmonary blood flow. For morbidly obese patients, positive-pressure ventilation is recommended to compensate for the decreases in lung volume in the lithotomy position.

For morbidly obese patients undergoing procedures in the lithotomy position, positive-pressure ventilation with an endotracheal tube is recommended to compensate for the decrease in lung volume.

Depending on the method of leg support used, the lithotomy position can cause changes in intra-compartment pressure in the calf or knee. Compartment syndrome, a condition in which increased tissue pressure within a limited tissue space compromises the circulation and function of the contents in that space, is a potential complication of prolonged positioning in the lithotomy position.[79,80] The longer the patient is in the lithotomy position, the greater the chances of developing a lower extremity neuropathy or compartment syndrome. Due to the heavier weight of their lower extremities, obese patients in the lithotomy position are at increased risk for compartment syndrome.[81,82] The use of intermittent external compression devices can reduce intra-compartment pressure.[83] The obese patient in lithotomy is also at a greater risk from transient neurologic symptoms, particularly following spinal anesthesia.[84]

Adequate padding with pillows and foam is always important. Backache after procedures in the lithotomy position is common, but its incidence in the obese surgical population is unknown. The combination of obesity and the lithotomy position may also increase the risk of gastric reflux and pulmonary aspiration.[85] Venous stasis with thrombo-embolism is common with the lithotomy position, and obesity increases the risk of this complication as well.[86]

20.10 Pneumoperitoneum for laparoscopy

Many surgical procedures, including bariatric operations, are now routinely performed by laparoscopy (see also Chapter 7). In supine patients, oxygenation, lung and chest wall compliance all decrease and peak inspiratory and mean airway pressures all increase during carbon dioxide pneumoperitoneum.[87] All values quickly return to normal values after deflation.

Similar changes are seen in obese patients, and changing to a 25° reverse Trendelenburg position did not have any beneficial effects on lung function.[88] Not surprisingly, morbidly obese patients in the Trendelenburg position undergoing laparoscopy can experience even further decreases in lung volume.[89]

Respiratory mechanics are altered in obese patients undergoing laparoscopy. Compliance is reduced and resistance is increased compared to non-obese controls. Position (head-up or head-down) did not induce additional alterations in respiratory mechanics. Pneumoperitoneum was the major factor for impaired ventilation.[90] Increasing tidal volume ventilation or ventilatory rate did not improve oxygenation in morbidly obese patients undergoing laparoscopy.[91] Again, changes in position were not as significant determinants of respiratory parameters as weight alone.

Morbidly obese patients (average BMI: 45) with otherwise normal lung function tolerate laparoscopic gastroplasty.[92] Although there was a decrease in respiratory system compliance, an increase in peak and plateau pressures, and an increase in $PaCO_2$, arterial hemoglobin saturation remained unchanged. The authors of this study found that the relative degree of alterations in pulmonary mechanics were proportionately less than those observed in non-obese patients. Cardiac output did not decrease despite an increase in intra-abdominal pressure after carbon dioxide insufflation. Mean arterial pressure, mean pulmonary artery pressure and central venous pressure all increased.

The effects of obesity, pneumoperitoneum and body position on cardiac function during laparoscopy were studied by trans-esophageal echocardiography.[93] Normal weight and morbidly obese patients were

compared in the supine, the Trendelenburg and the reverse Trendelenburg positions before and after pneumoperitoneum. Systolic blood pressure was not different between groups prior to creation of the pneumoperitoneum, but increased significantly only in the obese group after abdominal insufflation. Postural changes had no further impact on cardiac function in either group. The slight increase in cardiac output that occurs during laparoscopic surgery is believed to be due to sympathetic stimulation.[94]

Other studies have reported no differences in oxygenation and respiratory mechanics,[95] and no impairment in cardiac function [96] between morbidly obese patients undergoing laparoscopic procedures compared to those undergoing open bariatric procedures.

Pneumoperitoneum and the reverse Trendelenburg position during laparoscopic bariatric surgery each decrease femoral blood flow which can result in venous stasis.[50] When patients undergoing laparoscopic bariatric procedures were compared to a control group undergoing an open procedure, prolonged pneumoperitoneum was associated with reduced intra-operative urine output.[97] Although there were no differences in the total amount of fluid administered during surgery, urine output was 30–50% lower in the laparoscopic group. There were no differences in post-operative renal function.

Abdominal insufflation, as well as changes in operating room table position (usually to Trendelenburg's position),[43] can cause cephalad movement of the diaphragm and can lead to migration of an initially correctly positioned endotracheal tube.[98] This phenomenon in morbidly obese patients undergoing laparoscopy can result in right endobronchial intubation and intra-operative hypoxemia.[99]

20.11 Conclusion

The care and management of the morbidly obese patient undergoing any surgical procedure is always a challenge for the anesthesiologist. However, with an understanding of the pathophysiology of obesity and with special consideration for how position can further impact cardiopulmonary function, even patients with extreme obesity can successfully undergo the most complex procedures.[100]

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AIRWAY MANAGEMENT 21

A.P. Reed & D.C. Kramer

21.1 Introduction

Conventional wisdom relates morbid obesity to difficult mask ventilation (DMV) and difficult intubation. Is this born out in the literature? Yes. Difficult intubation is the second most frequent cause of malpractice claims against American anesthesiologists.[1] Death or brain damage resulted in 57% of 283 claims involving difficult intubation, compared to 43% in all other claims. Obesity was a factor in 31% of difficult intubation claims, compared to 14% of all other claims. In obstetric patients, critical events related to the respiratory system were significantly more common among obese patients (32%) than non-obese patients (7%).[2] This data substantiates what practitioners have known for years.

Difficult direct laryngoscopy occurs in 1.5–8.5% of intubations and failed intubation occurs in 0.13–0.3% all general anesthetics.[3] The predictive role of obesity as an independent risk factor for difficult intubation remains somewhat controversial.[4,5] Several large studies suggest that obesity may be a risk factor for difficult intubation in general surgical[3,4] and obstetrical patient.[6] Although obesity is well defined, the difficult airway is not. Consequently, it becomes problematic to study the incidence of difficulty airway in morbidly obese patients. Rose and Cohen addressed the issue of nomenclature in a study of 3325 consecutive patients for direct laryngoscopic intubation.[7] They noted the difficult airway has been defined as difficult visualization of the airway, 3 or more attempts at intubation, or failure to intubate by direct laryngoscopy. All patients who could not be intubated in their study demonstrated Cormack Lehane Grade 3 or 4 laryngoscopic views[8] and underwent more than three laryngoscopic attempts. In that study, the incidence of true failure to intubate was 0.1%. In a follow-up study, the same authors examined 18,205 records of patients who underwent direct laryngoscopy. The incidence of failed intubation was 0.3% and multiple attempts at intubation occurred in 2.5% of patients.[9] Obesity was an independent risk factor predicting difficult and failed intubation. Another study examining 1833 intubations among all patients undergoing general anesthesia, revealed that obesity provided a 20.2% predictive value of difficult intubation compared to patients with normal body mass indices (BMIs). When obesity and Mallampati classification[10,11] were used to calculate predictive value of difficult intubation, the estimate rose to 66.7%.[4] The authors concluded that obesity contributed to difficult intubation because of

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a disproportionately large tongue base. In contrast, Brodsky *et al.* prospectively studied 100 consecutive morbidly obese patients. All of their patients possessed BMIs $> 40\,kg/m^2$ and all presented for bariatric surgery. The Brodsky team concluded that neither BMI nor absolute weight were predictors of difficult intubation.[5] Twelve percent of patients were classified as having had problematic intubations. In their study, both large neck circumference and high Mallampati score predicted problematic intubation. Unfortunately, the patient population was too small to determine a specific neck size that might predict difficult intubation. Only one patient (1% of the study population) was a true failed intubation. This patient required fiberoptic intubation. Rocke *et al.* found that short neck might be related to difficult intubation. In their study, short neck was associated with morbid obesity.[6] Hiremath *et al.* found that symptoms of obstructive sleep apnea (OSA) were associated with difficult intubation.[12] The most common reason for OSA found in adults is obesity.

The relationship between obesity and difficult airways remains controversial. Available data is inconclusive. In actuality many anesthesiologists engaged in busy bariatric practices report good results with rapid sequence inductions and cricoid pressure, for the vast majority of their patients. However, just as a small incidence of failed intubation exists in the lean patient population, it also exists in the morbidly obese group. This chapter will discuss some airway management alternatives to traditional tracheal intubation in morbidly obese patients.

21.2 Tracheal tube placement

Before tracheal intubation, it is common practice to provide some type of aspiration prophylaxis to morbidly obese patients. A non-particulate antacid by itself or in combination with other agents can be administered. The most reliable method of delivering positive pressure ventilation to morbidly obese patients is via a cuffed tracheal tube. Several methods of tracheal intubation exist. Selection among them is predicated on the airway examination and individual practitioner preference.

21.2.1 Conventional direct laryngoscopy

If the airway examination does not predict difficulty, rapid sequence induction with cricoid pressure remains the most common intubation technique for morbidly obese patients. Positioning is the first concern. For over 70 years, McGill's sniffing position ("sniffing the morning air position") has been recommended to align the three visual axes of the upper airway.[13]

Recently, Adnet[14] and Chou[15] have challenged that concept, freeing us from the dogma that previously existed. A common problem encountered during laryngoscopy of morbidly obese patients is positioning the laryngoscope in the mouth. Oftentimes, the laryngoscope handle abuts the patient's chest and prevents proper placement. This issue is overcome by supporting the patient's head and upper back on a ramp. Ramps bring the head anterior to the chest, thereby allowing space to correctly place the laryngoscope over the chest (Figure 21.1).

The second concern is oxyhemoglobin desaturation during induction and intubation. Morbidly obese patients suffer reduced functional residual capacity (FRC). FRC acts as a bank of oxygen from which patients draw, during periods of apnea. The more oxygen deposited, the longer the time to desaturation and the longer the time to perform intubation.[16] To optimally store oxygen in the FRC, preoxygenation (denitrogenation) is carried out. Preoxygenation is accomplished by administering 100% oxygen through an anesthesia face mask with an airtight seal. Gaps between the mask and skin allow room air to enter the mask and dilute the oxygen. The larger the air leak, the lower the effective F_iO_2 delivered to the lungs. Lean patients require about 3 min of breathing 100% oxygen to optimally fill the FRC.[17] The time to optimal preoxygenation in morbidly obese patients is a multifactorial issue. Rather than guess, the authors prefer to measure end-tidal oxygen, using an expired concentration of 90% as their endpoint.

Induction doses seem to influence intubating conditions. Deep anesthesia provides better laryngoscopic

Figure 21.1 Ramp used for positioning the head anterior to the chest, during rigid laryngoscopy.

views than light levels of anesthesia.[18] Highly lipophilic substances, with large volumes of distribution, such as barbiturates, can be dosed according to total body weight.[19,20] The most popular induction agent today, propofol, is dosed based on ideal body weight.[21] Even though large doses of non-depolarizing neuromuscular blockers can provide more rapid onset than conventional doses, succinylcholine remains the relaxant of choice. Among all available neuromuscular blockers, succinylcholine offers the most rapid onset and profound relaxation. Plasma cholinesterase activity increases in proportion to body weight, so succinylcholine doses are based on total body weight.[19]

No laryngoscope blade has been shown advantageous over others in morbidly obese patients. It is best to have a variety of blades available. Intubators should start out using the blade with which they are most expert. The distance between teeth and epiglottis does not increase with increasing weight. Long blades, such as Macintosh 4s or Miller 3s, are rarely required. Limited experience exists with Wu Scopes, Bullard Laryngoscopes, Gluidescopes, and other retraction blades in the morbidly obese population.

21.2.2 Flexible fiberoptic laryngoscopes

Although most morbidly obese patients do well with rapid sequence induction and traditional laryngoscopy, some patients do not. The goal is to predict, which patients will prove to be difficult intubations, before induction of general anesthesia. To accomplish this, difficult intubation prediction criteria are applied. When difficulty is anticipated, fiberoptic intubation is recommended. In lean patients with easy mask airways, fiberoptic intubation under general anesthesia remains an option. Morbidly obese patients, however, are different. Two factors dictate the need for awake flexible fiberoptic intubation in morbidly obese patients. They are the anticipation of difficult intubation and DMV.

Flexible fiberoptic laryngoscopes have a long and enviable history with difficult intubations. Their use is applicable to morbidly obese patients under certain circumstances. Although not considered the preferred method of laryngoscopy for rapid sequence induction, fiberoptic intubation is a reasonable choice following a limited number of failed rigid laryngoscopies, usually with Macintosh or Miller blades.[22] Multiple attempts at rigid laryngoscopy could result in bleeding, swelling, vomiting and aspiration. Early intervention with flexible fiberoptic laryngoscopes might prevent these problems. Cricoid pressure, jaw thrust and tongue protrusion can be provided by one or two assistants. More commonly, flexible fiberoptic intubation in morbidly obese patients is used electively for awake intubations. Profound airway anesthesia provides considerable patient comfort during fiberoptic intubation. Awake intubation with flexible fiberscopes offers many advantages. Spontaneous ventilation is maintained, allowing for nearly normal oxygenation and ventilation. Intubation can progress in a slow deliberate manner without the risk of hypoxia. Awake patients can sit up and expel vomitus from the airway. They can follow instructions to breath deeply thereby dilating the airway, allowing the larynx to move posteriorly to improve visualization, and abducting the vocal cords for passage of the fiberscope. Although rigid laryngoscopes can be used for awake intubation, fiberscopes are gentler and result in less hypertension and tachycardia than rigid blades.[23] Fiberscopes are applicable to the oral or nasal route. Nasal approaches tend to be easier than oral approaches, but risk epistaxis, which can be serious. Oral routes risk biting on the scope, which is prevented by employing any one of numerous bit blocks/oral airways.

21.2.3 Lighted stylets

Lighted stylets generally consist of three components: a handle, a stylet and an illumination source. Most commonly, batteries serve as the power source and are stored in the handle. The stylet is generally malleable and functions as a guide for the tracheal tube. Illumination frequently comes from a distally placed light bulb. Many models exist. The Trachlight™, with numerous other features, has emerged as a popular and useful design[24] (Figure 21.2).

Lighted stylets have been used in conjunction with intubating laryngeal mask airways (ILMAs) for tracheal intubation,[25] but this technique has not found its way into widespread use. Presently, lighted stylets have

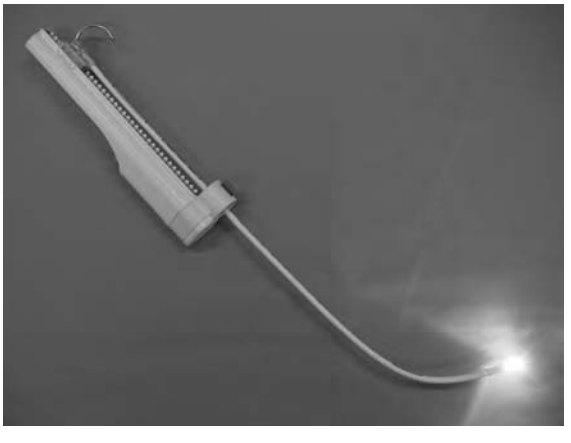

Figure 21.2 Trachlight™.

limited application to morbidly obese patients. For those undergoing rapid sequence induction with cricoid pressure, lighted stylets are not generally employed. Few practitioners are expert enough to rely upon them for elective use during rapid sequence inductions. However, in the event of failed intubation with first choice techniques, lighted stylets might be considered among several alternatives. Cricoid pressure could make lighted stylet intubations technically more difficult.[26] Morbid obesity adds additional problems to the use of lighted styles.[27] Excess adipose tissue overlying the anterior neck reduces the amount of transilluminated light, thereby limiting the usefulness of an important endpoint. Many obese patients have short necks which require careful measurements to determine where to place the bend in the stylet. Additionally, these patients do best with a pillow under the shoulders and neck to help facilitate intubation.[25] Lighted stylets are applicable to awake intubations, but have not emerged as a popular method in this arena.

21.3 Esophageal–tracheal combitubes

Esophageal–tracheal combitubes (ETCs) are not tracheal tubes, but they provide many of the advantages of tracheal intubation. ETCs are generally inserted blindly, although some have advocated placement under laryngoscopic visualization. They are applicable to elective and emergent situations. At the time of this writing, ETCs are manufactured in two sizes: Combitube SA 37F for patients 4–5½ft (123–168 cm) tall and Combitube 41F for patients over 5½ft (168 cm) tall.[28] The device is a double lumen tube, equipped with two balloons – one for occlusion of the oral and nasal cavity and another for occluding the trachea or esophagus. ETCs offer an esophageal lumen, with a patent proximal orifice and an occluded distal tip. Along the surface of the esophageal lumen, small perforations are situated between the two balloons. These perforations allow supraglottic pulmonary ventilation when the device is situated in the esophagus. The tracheal lumen is patent at the distal and proximal ends. A wall separates both lumens. If placed in the trachea, the lumen open at both ends is used as a small tracheal tube (Figure 21.3).

ETCs do not require sniffing position for placement. The tube is usually inserted blindly into the mouth. Lifting the anterior tongue and mandible facilitates passage around the base of tongue. Once resistance to passage is encountered, it is left in place. Opaque rings on the proximal third of the ETC generally lie at the dentition line. The proximal cuff is inflated with 100 cc of air and then the distal balloon is inflated

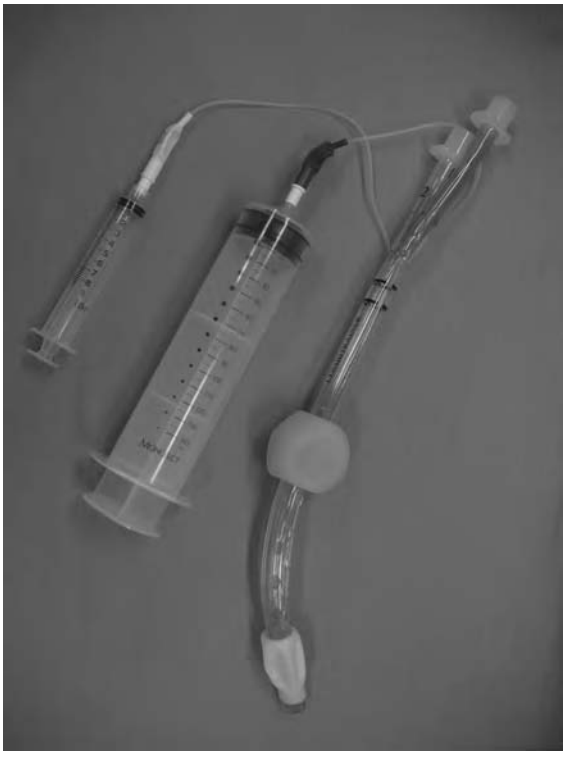

Figure 21.3 ETC.

with 5–15 cc of air. The ETC enters the esophagus 95% of the time. In the esophageal position, gas is administered via the lumen with a proximal opening and a distal occlusion. Gas exists the perforations, situated behind the larynx, and enters the trachea. Breath sounds may be auscultated over the lung fields. Gas should not enter the stomach. If breath sounds are absent while using this lumen, then the ETC may reside in the trachea. In that case, the lumen open at both ends is employed for ventilation. The lungs are auscultated once again to confirm proper ventilation.

Contraindications to ETCs are:

- Intact gag reflexes (regardless of the level of consciousness);
- Height <4 ft (121 cm);
- Esophageal pathology or after ingestion of caustic substances;
- Foreign body in the airway;
- Airway tumors or friable tissue in the airway;
- Latex allergy.

The combitube has been associated with esophageal and piriform lacerations, subcutaneous emphysema, pneumomediastinum and pneumoperitoneum.[29] These complications are more likely when the distal cuff is inflated beyond the manufacture's recommendations

of 5–15 cc of air. In the esophageal position, tracheal secretions cannot be suctioned, but gastric secretions can be eliminated. In the tracheal position, pulmonary secretions can be suctioned, but gastric secretions cannot be assessed.

The role of ETCs in caring for morbidly obese patients is well recognized.[30] They can be used electively for awake intubations or emergently in the cannot-intubate cannot-ventilate scenario.[31] ETCs isolate the respiratory and gastrointestinal tracts, thereby providing superior protection against aspiration, compared to laryngeal mask airways (LMAs);[32,33] but they are not 100% protective from aspiration pneumonia.[34] Although LMAs are twice as likely to be used as rescue devices than ETC,[35] they offer better protection from aspiration than LMAs in morbidly obese patients. Consequently, ETCs have a place in rescue airway management of the morbidly obese.

21.4 Supraglottic airway devices

Historically, morbid obesity has been considered a risk factor for aspiration pneumonia. Supraglottic airway devices do not protect the lower airway from soiling with gastric contents. They do not separate the respiratory and gastrointestinal tracts nor do they block the larynx. Gastric contents reaching the pharynx are free to fall into the trachea. A potential exists for gas delivered to the upper airway, especially under positive pressure, to enter the stomach. A stomach dilated with gas could result in vomiting or regurgitation. Consequently, elective use of supraglottic devices is contraindicated in patients at increased risk for aspiration. However, the emergency situation is different. Supraglottic devices are acceptable alternatives for emergency use in morbidly obese patients.

21.4.1 Face mask ventilation

Obesity is an important independent risk factor for difficult face mask ventilation.[36] Unlike difficult intubation, relatively little has been written about predictors of difficult face mask ventilation. Langeron *et al.* prospectively examined 1502 patients and concluded that DMV occurred in 5% of these patients. Both BMI $> 26\,kg/m^2$ and history of snoring are independent risk factors for DMV and both are associated with obesity. Additional risk factors for DMV included age >55 years, a full beard, and edentulousness. Other factors, such as subjective preoperative evaluation of tongue size, mouth opening and Mallampati class, did not influence the difficulty of face mask ventilation.

Face mask ventilation of morbidly obese patients may be difficult for a number of reasons. The face may be so big that medium size masks do not create an airtight seal at the skin. Large masks are frequently required. The face may be so big that practitioners' hands do not hold the mask securely onto the face. In such cases, two hands on the mask are needed and a second person must compress the reservoir bag. Alternatively, the second person can help by providing jaw thrust. Excess adipose tissues inside the airway tend to fall inward, thereby obstructing the flow of gas. Similarly, relaxed airway dilator muscles allow soft tissues to fall against the posterior pharyngeal wall causing upper airway obstruction. Oropharyngeal and nasal airways can be helpful in such cases. Although nasal airways are tolerated at lighter planes of anesthesia, both require obtunded pharyngeal reflexes. Airways that are too short may not bypass soft tissue obstruction and airways that are too long may create airway obstruction by folding the epiglottis down over the larynx. An improperly positioned oropharyngeal airway could push the tongue posteriorly, thereby creating its own obstruction. Nasal airways sometimes create epistaxis, which can markedly exacerbate the difficulties of mask ventilation. Other recognized complications of airway use include biting, coughing, vomiting, laryngospasm and bronchospasm. Contraindications to nasal airways include coagulopathy, nasal occlusion, nasal fractures, severely deviated nasal septae, prior transphenoidal hypophysectomy, cerebrospinal fluid rhinorrhea and adenoid hypertrophy.

McGee and Vender suggest that face mask ventilation in morbidly obese patients should be undertaken with caution.[37]

21.4.2 Laryngeal mask airway

Classic laryngeal mask airway

Although elective use of LMAs are relatively contraindicated in morbidly obese patients, they are acceptable in emergency situations.[33] The LMA cuff does not create an airtight seal in the pharynx, resulting in frequent gas leaks around the inflated balloon. Consequently, as inspiratory pressures rise, so does the amount of gas escaping around the cuff. This mechanism limits the inspiratory pressures reached when using LMAs. Patients with poor pulmonary compliance, such as the morbidly obese may not receive sufficient tidal volumes. Ideally, LMAs, sit just above the esophagus and surround the laryngeal cartilages (Figure 21.4).

Even when perfectly positioned, the flawed seal between cuff and pharynx permits gastric contents to

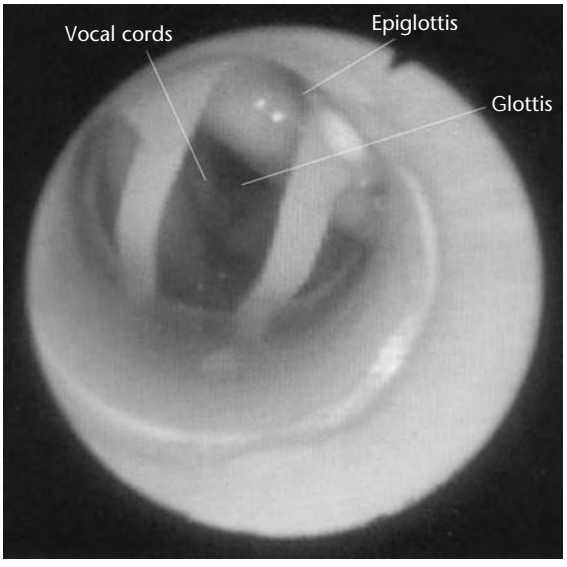

Figure 21.4 Fiberscope view of the glottis as seen through a classic LMA. Vocal cords, epiglottis and glottis are labeled. The two vertical structures on either side of the epiglottis are the arch bars of the LMA. As seen here, arch bars help prevent the epiglottis from falling into the LMA and obstructing the airway.

enter the LMA bowl and slide down the trachea. LMAs provide for gas exchange, despite numerous minor malpositions. Several of these malpositions incorporate the esophagus underneath the cuff. This exposes the esophagus to the LMA bowl, which permits aspiration of gastric contents.

To overcome the aspiration problem, some have attempted to place LMAs while applying Sellick's maneuver. Positioning LMAs during administration of cricoid pressure has met with disappointing results.[38] Nevertheless, 72% of consultant anesthesiologists in the UK favored LMAs as primary airway rescue devices in patients at increased risk for aspiration pneumonia.[39] Once the airway is secured using a classic LMA, it is possible to pass a tracheal tube through the LMA and into the trachea.[38] Ovassapian cautions against blind intubation through the classic LMA, in favor of fiberoptic intubation through the LMA.[40]

ProSeal laryngeal mask airway

A modification of the LMA, the ProSeal LMA,[41] is equipped with an esophageal vent. The vent is intended to collect gastric contents from the esophagus and divert the acidic material away from the larynx. The venting channel also allows for stomach suctioning. ProSeals provide airway patency and protect against aspiration pneumonia better than classic LMAs. There is some evidence to suggest that ProSeal LMAs can prevent aspiration when seated properly.[42,43] They have been suggested as temporary ventilatory devices in morbidly obese patients prior to fiberoptic intubation[44] (Figure 21.5).

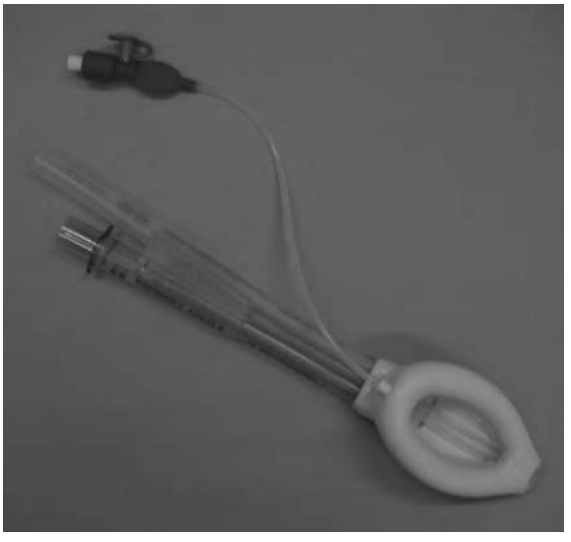

Figure 21.5 ProSeal LMA.

Intubating laryngeal mask airway

Another LMA variation, the ILMA,[45] is applicable to morbidly obese patients as a rescue device and as a primary modality for securing the airway. ILMAs are used in both awake[46,47] and anesthetized patients.[48,49] They boast an overall success rates of 96.5% for blind and 100.0% for fiberoptically guided intubations[49] (Figure 21.6).

Pharyngeal airway

The pharyngeal airway is a supraglottic, disposable device, and is currently available in one adult size. It is manufactured of polyvinylchloride and is latex free. The device features a flexible tip that rests in the hypopharynx; a high-volume, low-pressure cuff that secures itself in the oropharynx and a proximal tube portion, that adapts to any standard anesthetic circuit via a 15 mm connector (Figure 21.7).

It is intended for use in patients who are not at increased risk for aspiration of gastric contents, but like other supraglottic airway devices it can be used in emergency situations, for morbidly obese patients. Pharyngeal airways have been employed in a limited number of obese patients, with good success. Its tip

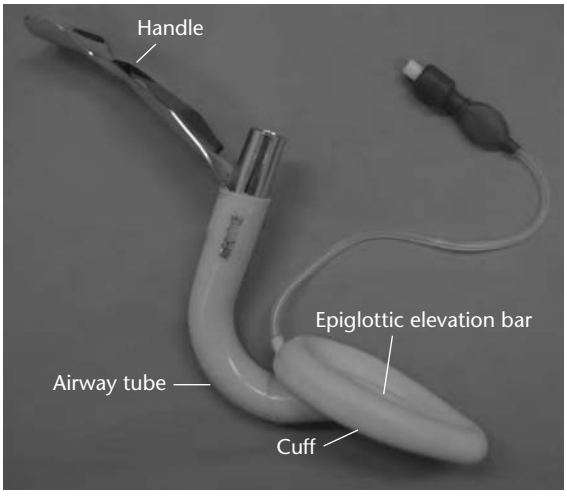

Figure 21.6 ILMA.

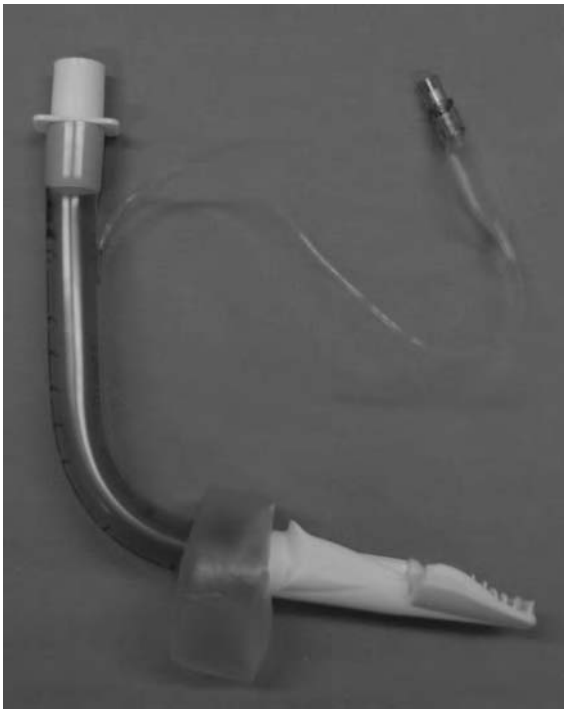

Figure 21.7 Pharyngeal airway.

takes up space in the hypopharynx and serves two functions. First, it is intended to trap gastric contents, thereby reducing the risk of aspiration pneumonia. Second, it is intended to prevent gas entry into the stomach thereby reducing the risk of regurgitation or vomiting. It accommodates a 7.5 mm tracheal tube, which provides the option for tracheal intubation through the device. Pharyngeal airways are easy to place and boast high rates of success.[50]

Pharyngeal airways have been associated with airway trauma, evidenced by blood staining on the tip. In one study, 56% of inserted pharyngeal airways[50] demonstrated staining after insertion. In the same study, 18% showed moderate to severe blood staining.[50] Other authors have discovered trauma from the pharyngeal airway's gilled tip.[51,52] The incidence of trauma associated with pharyngeal airways is higher than that attributed to classic LMAs or ILMAs.[53,54] As of this writing, there are no studies specifically addressing pharyngeal airways in morbidly obese patients.

21.5 Invasive technique

Preoxygenation extends the apnea time, but at some point, if the above techniques do not achieve gas exchange, then invasive airway management may be needed. Invasive techniques differ in their location of entry into the airway and the size of catheter placed. We will discuss small and large catheter techniques at the cricothyroid membrane. The cricothyroid membrane is located between the thyroid cartilage superiorly and the cricoid cartilage inferiorly. It is more easily located in lean patients than in morbidly obese patients. Adipose tissue frequently deposits between membrane and skin, thereby impairing one's ability to identify the cricothyroid membrane. To locate the membrane, first find the superior notch of the thyroid cartilage, the Adam's apple. Run your fingers inferiorly in the midline until a depression and a bump are appreciated. The depression is the cricothyroid membrane and the bump is the cricoid cartilage. These landmarks are oftentimes difficult or impossible to find in the morbidly obese population. Preparation before hand is important. When time is of the essence, none should be lost locating landmarks: inspect the neck and mark the skin overlying the cricothyroid membrane prior to induction of general anesthesia; have needed equipment in the room and readily available. Airway emergencies do not allow time to search for and assemble instrumentation.

21.5.1 Small catheter techniques at the cricothyroid membrane

Among invasive techniques, the fastest way to gain airway access is to place a 14-gauge needle with catheter through the cricothyroid membrane. To do this, attach a saline filled syringe to a 14-gauge needle and catheter set. Insert the needle anterior to the cricothyroid membrane, perpendicular to the skin in all planes, and

apply gentle negative pressure to the syringe. Once the needle enters the inferior larynx, air will bubble up through the saline bath. Advance the needle a bit farther to ensure entry of the catheter into the airway, and push the catheter over the needle. Remove the needle, leaving the catheter in place. Designate one person to hold the catheter immobile. Remove the plunger from a 5 ml syringe, Luer lock the syringe to the catheter, and attach 7.5 mm tracheal tube adapter to the syringe. Any standard airway device will then connect to the tracheal tube adapter. Low-pressure systems, such as resuscitation bags or anesthesia machines, will provide oxygenation for short periods of time, but will ventilate poorly. Injector systems using approximately 50 psi pressure can deliver greater tidal volumes than low-pressure systems. Inspiratory times and rates are generally limited to 1 s and 12 breath/min, using high-pressure injector devices. High-frequency jet ventilation systems generally use lower pressure and higher frequency of breath/min. High-frequency jet ventilation systems approximate 22 psi pressures and 120 breath/min. Jet ventilation systems can provide good oxygenation and ventilation, but chest wall movement and breath sounds will be hard to determine in morbidly obese patients. Regardless of the system selected, in order to prevent gas trapping and pneumothorax, there must be a channel for the egress of expired gas.[55]

These are inherently unstable systems. There is no good way to secure the catheter in the neck, so a designated person must be assigned to hold the catheter and prevent it from moving. Other problems with these systems include catheter kinking and obstruction, lack of protection from aspiration, inability to suction the airway, tendency to produce subcutaneous emphysema, and high incidence of barotrauma. A formal airway should be established as soon as possible.

21.5.2 Large catheter techniques at the cricothyroid membrane

Larger catheters provide better gas flow for oxygenation and ventilation. In the simplest type, a number 11 blade is used to incise the skin and cricothyroid membrane. Tracheal hooks, thin retractors or the scalpel handle can be used to maintain patency while a small tracheal tube is passed through the incision into the airway. Bleeding may occur from laceration of anterior jugular veins or superior cricoid veins. Other complications include failure to cannulate the airway, pneumothorax, perforation of the esophagus, mediastinal emphysema and superior laryngeal nerve damage. Numerous kits are available commercially to serve these functions.

21.6 Conclusion

Airway management remains an inexact science. It is predicated on difficult airway prediction criteria that are fallible. Practitioners find themselves relying on both science and experience to guide patient care. Despite older concerns, most morbidly obese patients undergo rapid sequence induction with cricoid pressure and do well with that technique. The need for awake intubation is infrequent. Nevertheless similar to the lean patient population, some morbidly obese patients will prove to be difficult intubations after induction of anesthesia. Airway managers need to have alternative plans to maintain oxygenation and ventilation.

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INHALATIONAL ANESTHESIA 22

L.H. Hanowell

22.1 Introduction

Any discussion of inhalational general anesthesia for obesity surgery necessarily requires a rudimentary discussion of the pharmacodynamics and pharmacokinetics of inhalational anesthetic agents (see also Chapter 15). This discussion will be of a general nature describing some of the physical principles of the uptake and distribution of general anesthetics, and additionally will be taken into account some of the specifics as they relate to the inhalational agents in current common clinical use. Additionally, the particular effect that the obese physical condition has upon uptake and distribution of these agents will be analyzed. Finally, the specific inhaled agents and their various effects in the obese patient will be explained.

22.2 Definitions of pharmacokinetics and pharmacodynamics

Pharmacokinetics means the effect the body has on a drug with respect to distribution and metabolism. This for an intravenously (i.v.) administered drug generally implies the extent to which it is soluble in the blood and tissues, the extent to which it distributes itself in the body, and the way in which the drug is metabolized (for example, in the liver or bloodstream) or excreted by the kidney. These affect the distribution half-life and elimination half-life of the drug. For inhalational agents there are physical properties that are specific to each inhalational agent, for example their vapor pressure, solubility in tissue and blood, and potency with respect to the effective alveolar concentration. Alveolar concentration will, in turn, determine blood concentration and tissue concentration. Pharmacodynamics implies the effect that the drug has on the body, and for the inhalational agents this is the desired effect of general anesthesia to yield a patient unaware of surgical activities, without pain, and without movement in response to the stimulus (amnesia, analgesia, and relaxation). Effectiveness of anesthetics is generally classified with respect to the minimum alveolar concentration (MAC) of the inhalational agents, which is the alveolar concentration that prevents movement in half of a sample of

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human subjects in response to surgical incision. Also pertaining to pharmacodynamics, there are various unique beneficial or adverse properties or side effects of the various inhalational agents in clinical use.

22.3 Uptake and distribution of gases in the provision of inhalational anesthesia

The rate of blood flow to various tissues has a significant influence on the rate of uptake of a given anesthetic agent. Those tissues with high rates of blood flow include the organs (kidney, liver, heart, brain, and others). They comprise the vessel rich group of body tissues when we discuss the uptake and distribution of the inhaled anesthetic agents. Muscle has blood flow that is intermediate in rate relative to the organs and fat. Fat (adipose tissue) has slower uptake, given less blood flow, but it has a great affinity for inhaled anesthetic agents. Equilibration for anesthetic concentrations will occur in a few minutes for the organs, a few hours for muscle, and after several hours for fat. Other tissues such as bone and tendon have less significant bearing on uptake and distribution of anesthetic since they are less richly perfused with blood. So, the extent to which there is excessive fatty tissue will have an impact on the uptake and distribution, as well as the elimination of inhaled anesthetic. Fat will take up anesthetic relatively more slowly than other tissues; however, fat has great affinity for the inhalational anesthetic agents. When prolonged anesthesia is provided for an obese patient, significant progress toward equilibration of blood and fat concentrations of anesthetics results in prolonged recovery. This occurs since a longer period of time is required for desaturation of fatty tissues with respect to inhaled anesthetic concentration. Some of the inhalational agents undergo metabolism in the body, for example the older agents such as halothane. This effect is less marked in more commonly used inhalational agents in current clinical practice.

22.4 More aspects of pharmacodynamics of the inhalational anesthetics

Inhaled anesthetics result in depression of brain awareness via action on the reticular activating system and have undesirable effects to suppress cardiovascular function by depression of cardiac output. Additionally they may lower systemic vascular resistance. They also produce respiratory depression, which in the obese patient is of major concern.

However, they are known to bronchodilate and this, depending on the agent administered, may be significant in the attenuation of bronchospasm. Bronchospasm may occur in response to airway instrumentation or other peri-operative stimuli.

Some inhalational anesthetic agents can be, themselves, irritating to the airway and contribute to respiratory dysfunction in this manner.

22.5 Obesity alters recovery from inhalational anesthesia

Impaired post-operative ventilation with reduced alveolar ventilation will slow recovery from inhalational anesthesia by delaying the elimination of the anesthetic agent. Due to the restrictive lung defect that is common in the obese, this effect is exaggerated (see also Chapter 4). Impaired alveolar ventilation in the post-operative period contributes to prolonged recovery in the obese. Additionally, the extent to which the individual anesthetic agents vary with respect to their solubilities will also affect elimination of anesthetic from the tissues. Awakening will be delayed as adipose tissue may act as a reservoir for inhalational agent, continuing to contribute anesthetic to sustain blood concentrations, and therefore maintaining a concentration of inhalational agent in the central nervous system that delays recovery. This relationship is complex in that for a procedure in which anesthetic administration is very brief, excessive fatty tissues could conceivably act as a reservoir that, not having yet achieved a substantial concentration of the inhalational agent, will draw anesthetic away from the blood. In this way, the obese condition could potentially enhance recovery speed by making available a tissue group that is a reservoir to more promptly lower effective anesthetic concentration in the central nervous system.

22.6 Solubility of inhalational agents and implications for the obese patient

The various inhalational agents in common clinical use have distinct solubility characteristics that will bear on the rapidity of onset of action, and the speed of recovery after their administration. In clinical practice, for the obese patient, induction of anesthesia is generally achieved after the insertion of an i.v. catheter and administration of one of the i.v. induction agents which render the patient unconscious, after which a muscle relaxant is administered. Sedatives and analgesia may be administered both before and/or

after these drugs to limit the hemodynamic consequences of airway instrumentation to protect the lungs with an endotracheal tube.

Additionally, hemodynamically active drugs may be utilized to control heart rate and blood pressure during induction, and potentially to restore blood pressure or accelerate heart rate if hemodynamics are compromised by the administration of i.v. or inhalational anesthetic drugs during the induction process. The speed of onset of the pharmacodynamic effects and surgical anesthesia imparted by the inhalational agents will be variable dependent upon their blood : gas partition coefficients.

The least to most soluble agents in this regard are (in order of least to most soluble) desflurane (0.42), nitrous oxide (0.47), sevoflurane (0.6), isoflurane (1.4), enflurane (1.9), and halothane (2.3). Enflurane is less commonly used today, so will not be further discussed. Halothane has fallen from favor because of rare but severe hepatic toxicity and its tendency to sensitize the heart to catecholamines. Generally, less soluble agents will have more rapid onset of inhalational anesthesia and will also yield more prompt recovery from inhalational anesthesia because of more prompt elimination from the body after their discontinuance.

22.7 Clinical trials: comparison of inhalational anesthetics for obesity surgery

The goal in provision of inhalational anesthesia as previously mentioned is to provide, in concert with narcotic, sedatives, muscle relaxation, and other ancillary pharmacological agents, a balanced anesthetic that provides the patient with amnesia, analgesia, and relaxation. Additionally, there is a practical matter of utilizing agents that have a relatively prompt onset of action, and importantly, a prompt recovery. Prompt recovery involves return of orientation to person, place, and time. It implies the ability of the patient to follow commands, to protect their airway if they are ready by other parameters for post-operative extubation. In the outpatient setting, anesthetic recovery implies an eventual return to what can be called street readiness such that the patient may return home with customary observation and precautions that they avoid driving, avoid operating dangerous equipment, and refrain from major decision-making until complete recovery from general anesthesia. This generally ensues within 24 h of the discontinuance of general anesthesia. More prompt recovery from anesthesia also has an economic benefit.

If post-operative mechanical ventilation is required because of delayed recovery, additional cost for care will be considerable. Nevertheless, if post-operative ventilation is necessary, inappropriate decisions to prematurely extubate will be even more costly with respect to morbidity for the obese patient and result in additional cost of care for management of complications related to respiratory compromise. There is, therefore, significant impact of prolonged recovery from the inhalational anesthetics, with respect to morbidity and clinical efficiency. Of significance to the anesthetic care of the obese patient has been the more recent introduction of the agents desflurane and sevoflurane into clinical care. Desflurane is distinct from the other inhalational agents in that it has a very low blood : gas partition coefficient (0.42). This is, then a potent inhalational agent with a blood : gas partition coefficient similar to nitrous oxide (0.47). It is more potent than nitrous oxide, and for this reason it can be used in concentrations that provide a complete anesthetic effect without diluting oxygen to the extent that a hypoxic mixture would result. This lack of potency of nitrous oxide, despite its rapid onset and offset of effect, is a limitation to the use of nitrous oxide as a complete anesthetic. The MAC of nitrous oxide to prevent movement of surgical patients in response to incision in the absence of other anesthetic agents exceeds 100%, so it cannot be a complete anesthetic at one atmosphere of barometric pressure. This factor is even more limiting at higher altitudes. However, desflurane with an MAC of no more than 7% can provide prompt onset and offset of anesthetic effect. There are, however (see following discussions) some detractors from its use which are related to adverse respiratory and hemodynamic sequelae that may occasionally occur in the obese patient and others. Sevoflurane, with a relatively low solubility (see above) is also a newer agent that has been more recently introduced into clinical practice. It has relatively prompt onset and offset. In fact, because of its potency, it has even been utilized for single breath induction of general anesthesia. For the morbidly obese patient, and others at risk for aspiration (those with a history of gastric reflux or increased intra-abdominal pressure or with a full stomach), such methods of induction are potentially hazardous as the airway is not protected and the method of i.v. induction and rapid sequence induction with the use of cricoid pressure followed by endotracheal intubation is preferable. Isoflurane, though potent has a blood : gas partition coefficient of 1.4, which makes it suitable for relatively prompt onset and offset of inhalational anesthesia; however, the new agents with lower blood : gas partition coefficients have been popular for their prompt emergences in the anesthesia

care of the obese patient. Arguably, these effects are sometimes subtle; however, in this author's opinion, the newer inhalational agents, with lower tissue solubility, can provide improved recovery experiences in the already higher risk obese patients. Post-operative recovery after desflurane, propofol, or isoflurane anesthesia was compared in morbidly obese patients in a prospective, randomized study by Juvin and colleagues.[1] In this French study, the investigators reported improved recovery characteristics of desflurane relative to either propofol or isoflurane. They assessed the time to extubation, post-operative percutaneously measured oxygen hemoglobin saturation, mobility, and psychometric scores in patients who were all managed with additional agents that included propofol for induction, succinylcholine for relaxation during intubation, and alfentanil narcotic administration. All patients were also administered supplemental nitrous oxide and the study drug (propofol infusion, isoflurane, or desflurane) for maintenance of general anesthesia.

All patients underwent laparoscopic gastroplasties for the management of obesity. The time to extubation in the desflurane group was half that of the propofol or isoflurane groups. Saturation of oxygen was higher and the patients were more mobile in the desflurane group, and sedation was less pronounced in the desflurane group than in the propofol or isoflurane groups. They monitored these improvements demonstrating benefit of desflurane relative to propofol or isoflurane for a period as long as 2 h post-operatively. Whether desflurane is superior to propofol for i.v. anesthesia is not entirely clear. At the same facility, in a separate study of propofol pharmacokinetics, there was no evidence of propofol accumulation in morbidly obese subjects with dosage schemes that provide sufficient clinical anesthetic conditions.[2] An assessment of isoflurane vs. sevoflurane for obese patients was undertaken by Torri and colleagues.[3] They noted that the sevoflurane treated patients were extubated, emerged, and responded more promptly than the isoflurane treated patients. All patients were managed with anesthetics administered to achieve equivalent fractions of the MACs of each inhalational agent. Time to discharge from the recovery room was almost twice as long in the isoflurane treated group than in the sevoflurane treated group. Torri and co-investigators have additionally demonstrated more rapid wash-in and wash-out curves for sevoflurane vs. isoflurane in the obese.[4] Sollazzi and co-workers[5] found that extubation time was shorter and Aldrete scores (a measure of post-operative recovery) were significantly higher (better) in patients managed with sevoflurane vs. isoflurane.

22.8 Metabolism of anesthetics: implications for the obese patient

There is some evidence that obese patients metabolize certain anesthetics to a greater extent than non-obese patients. Bentley and co-workers[6] noted an elevation of ionic fluoride in obese patients anesthetized with halothane in contradistinction to non-obese subjects in whom there were no elevated levels of fluoride. These authors concluded that reductive metabolism of halothane was increased in the obese. This is of some concern in that there may be a link between reductive metabolism and hepatotoxicity. Serum bromide levels in the obese were also elevated relative to non-obese subjects. Serum ionic fluoride concentrations are more significantly elevated in obese subjects vs. non-obese subjects after enflurane anesthesia.[7] This finding was not, however, correlated with any overt evidence of nephrotoxicity attributable to elevation of ionic fluoride concentrations after enflurane. As this agent is less commonly utilized in modern practice, this issue is less of a concern. Nevertheless, for agents that undergo such metabolism, particularly because there is evidence of increased metabolism in the obese, there is need for consideration of this issue in drugs of the future. Drugs of the past, such as methoxyflurane, first used over 50 years ago, are now phased out of clinical usage because of these very concerns. Their tendency to yield elevated levels of fluoride ion was related to their potential to cause renal dysfunction. Young and co-workers[8] found evidence of decrease urinary concentrating ability and elevated fluoride ion in obese patients, prompting limited exposure to methoxyflurane, particularly in obese patients. These concerns contributed to subsequent elimination of this inhaled agent from clinical practice. The more significantly metabolized agents, as noted above, would seem to be less favorable agents in the obese patient, given the increased possibility for renal and hepatic toxicity. Desflurane, because it is not biodegraded in the human body to a great extent, and because of a favorable profile of uptake and distribution with fast onset and prompt recovery, seems a reasonable choice in most obese patients. However hemodynamic lability has been observed (tachycardia and hypertension) associated with high inhaled concentrations of desflurane that suggest the need for cautious administration.[9] Additionally, desflurane does not bronchodilate like other inhalational agents.[10] Particularly in smokers, there can be increased respiratory resistance and potential respiratory compromise in obese patients managed with desflurane. However, in most with patients anesthetized with

desflurane, these pulmonary sequelae do not become overtly manifested. It is perhaps for this reason that some practitioners avoid desflurane in patients with known bronchospatic disorders or reactive airway disease.

Sevoflurane is biodegraded releasing fluoride, however, because of low solubility and rapid elimination, it is less concerning than other more soluble agents in this regard. It is known to degrade on contact with soda lime to yield two compounds identified as compounds A and B. To date, there is minimal evidence to implicate adverse consequences from these metabolites in the course of routine sevoflurane anesthesia. Many practitioners use higher flows of gas than with other inhalational agents when using sevoflurane to purge the breathing apparatus of these metabolites. Bito and Ikeda studied patients who received sevoflurane in low flow circumstances and compared renal and hepatic function with patients managed in a similar fashion with low flow isoflurane.[11] They found no differences in renal and hepatic function between the sevoflurane and isoflurane treated groups. As obese patients may undergo prolonged general anesthetics for laparoscopic gastric surgery, this has implications with respect to cost.

Health hazard from compounds A and B have not been confirmed in the obese or non-obese to date, but are a potential concern at this point in time.

22.9 Nitrous oxide: advantages and disadvantages for the obese patient

Nitrous oxide has been known since the end of the eighteenth century and remains in clinical use today as a carrier for many of the inhalational agents as it is generally well tolerated due to its limited impact on hemodynamics and because its rapid uptake will speed the onset of anesthesia with the second more potent inhalational anesthetic. Due to its lack of potency (MAC 105%), it does dilute administered oxygen and therefore is limited with respect to the concentration that can be administered, generally prohibiting its efficiency as a complete anesthetic unless it is supplemented by i.v. narcotic, i.v. propofol, another i.v. agent, or (more commonly) another inhalational anesthetic agent. As nitrous oxide will expand closed gas spaces including the gut, it may be unfavorable in circumstances wherein the surgeons wishes to avoid bowel distention that could stress anastamosis sites in the bowel. It could impair surgical exposure by yielding bowel overdistention, and must be used with caution in this regard. These circumstances may be encountered in the management of prolonged laparoscopic or open abdominal procedures for the control of obesity. Additionally, prolonged exposure to nitrous oxide can, in those who have subclinical B_{12} deficiency, produce neurological complications of weakness. The inhibition of methionine synthetase by nitrous oxide introduces the hazard of hematological and neurological impairment when exposure occurs over many hours. Termination of nitrous oxide anesthesia requires the administration of 100% oxygen, particularly in the obese patient in whom there is often pre-existing respiratory compromise. This precaution is required because of the phenomenon of diffusion hypoxemia. This occurs as nitrous oxides leaving the body dilutes alveolar oxygen. Diffusion hypoxemia follows if not countered by the prior administration of oxygen during emergence from nitrous oxide anesthesia.

22.10 Rationale for the utilization of inhalational agents with prompt recovery

Surgery for obesity requires a technique of anesthesia that will not further compromise ventilatory function. Patients with morbid obesity may have basically two breathing disorders. They may present with obstructive sleep apnea syndrome or the obesity hypoventilation syndrome. When they present with both syndromes they fit into what is described as the Pickwickian syndrome with severe respiratory compromise and great potential for peri-operative respiratory depression. This syndrome derives its name from the description given one of the characters in the *Pickwick Papers* written by Charles Dickens. In early series of obesity surgery, anesthetic-associated respiratory depression in the post-operative period may well have contributed to a high post-operative mortality rate.[12] Since the inhalational anesthetics impair both minute ventilation/carbon dioxide responsiveness, as well as the hypoxic drive to ventilate, more prompt elimination of anesthetic in the post-operative period could be beneficial in avoiding respiratory depression which leads to hypercapnea. Hypercapnea itself, when profound, can lead to further states of so called "narcosis" with further respiratory depression, and even potential respiratory arrest. The frequent need to administered narcotic analgesia in the post-operative period compounds the post-operative respiratory depression of the inhalational anesthetics.

There is at least one study which refutes the concept that post-operative outcome is affected adversely in

the obese patient by the use of inhalational agents with increased lipid solubility.

Cork and colleagues[13] studied morbidly obese patients prospectively in 1981 to assess whether there was difference in recovery between three groups that received (a) nitrous oxide and fentanyl, (b) nitrous oxide and enflurane, or (c) nitrous oxide and halothane. They found time to eye opening significantly less in the nitrous oxide/fentanyl group. However, time to extubation and recovery room time were not significantly different. This study cannot be extrapolated to refute efficacy of newer inhalational agents such as desflurane and enflurane. The foregoing study may at least be partially explained by the finding that the blood gas partition coefficient of enflurane in the obese is 30% less than in the non-obese.[14]

22.11 Rationale for total intravenous anesthesia vs. inhalational anesthesia for obesity surgery/role of bispectral index monitoring

The utilization of total i.v. anesthesia (TIVA) in this era of cost containment has been a strategy to provide more prompt post-operative recovery (see also Chapter 23). This method has been employed in the care of patients undergoing obesity surgery. Pizzirani *et al.*[15] found that obese patients managed with TIVA utilizing propofol were more alert and awake and able to follow commands earlier than those patients managed with the inhalational anesthetic agent isoflurane. This benefit was subtle and it is not clear presently whether TIVA will demonstrate marked superiority over the less soluble inhalational anesthetics desflurane and sevoflurane. A modality that has been used in conjunction with a variety of anesthetic techniques in an effort to limit exposure to anesthesia and improve post-operative recovery is bispectral index monitoring. This monitors depth of anesthesia via an index derived from the electroencephalogram.[16] Reduction of isoflurane consumption, while still providing a sufficient anesthetic, has been demonstrated utilizing bispectral analysis.

Unfortunately, the study of Guignard and colleagues, which specifically demonstrated this benefit of bispectral index monitoring, excluded obese patients.[17]

22.12 Summary

Inhalational anesthesia will continue for now to be a conventional form of management for the obese patient requiring surgical care. Advances in inhalational anesthetic properties so as to provide greater safety and improved recovery, further development of i.v. anesthesia, and enhanced intra-operative monitoring will all be welcome developments in the progress toward optimal anesthetic management of the obese surgical patient.

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TOTAL INTRAVENOUS ANESTHESIA 23

A.O. Alvarez

23.1 Introduction: anesthetic planning, selection of the anesthetic technique (Why total intravenous anesthesia for the morbidly obese?)

As in every surgical–anesthetic practice, anesthesia for the morbidly obese has to be based upon pathophysiological patient's condition. After knowing how morbidly obese body behaves (and according to this; considering the most frequent risks) anesthetic targets have to be defined. Finally in order to get the best approach to those targets, technique and tactic could be reasonably planned. So the logical line of thoughts should be chronologically developed as follows:

1 Pathophysiological considerations.
2 Frequent risks and complications.
3 Anesthetic targets.
4 Anesthetic planning.

Pathophysiological considerations and frequent risks have been already considered in other chapters (see Chapters 2, 4, 5 and 8). Anyway, it should be remembered that the most frequent and prominent risks are:

1 gastric aspiration;
2 difficult mask ventilation and tracheal intubation;

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3 rapid development of hypoxemia after apnea;
4 pulmonary atelectasis;
5 hemodynamic instability;
6 reduced capability to face stress situations (increments of stress hormones could develop hyperglycemia, hypertension, cardiac failure, arrhythmias and myocardial ischemia);
7 delay in recovery;
8 post-operative respiratory dysfunction;
9 deep venous thrombosis.

Accordingly basic anesthetic targets should be:

1 smooth and quick induction;
2 rapid and secure airway control;
3 prominent hemodynamic stability;
4 high versatility to manage changing levels of surgical stimuli to avoid increments in catecholamine activity;
5 fast and successful recovery, and ambulating capacity.

Hypnosis, analgesia and muscular relaxation have to be provided in the precise level in order to facilitate surgical maneuvers, but maintaining stable physiological performance. Total intravenous anesthesia (TIVA) seems to be a suitable technique for a coherent approach to this particular situation.[1,2]

Currently available drugs (remifentanil, propofol, atracurium, etc.), infusion computerized apparatus (assisted by pharmacokinetical models), and pharmacodynamic monitoring devices allows anesthesiologist to get close to the proposed targets.

TIVA has been employed in the care of patients undergoing bariatric surgery. Pizzirani and co-workers found that obese patients managed with TIVA utilizing propofol were more alert, awake and able to follow commands earlier than those patients managed with the inhalational anesthetic agent isoflurane.[2]

Delay in recovery could happen after inhalational anesthesia, depending on the duration of the procedure, the dose and solubility of the agent and the respiratory impairment of the patient. Adipose tissue has slower uptake than organs and muscle, because of its poorer blood flow, thus equilibration for anesthetic concentrations will take minutes for the organs but hours for fat. On the other hand, it has a great affinity for inhaled anesthetic agents, so the amount of excessive fat tissue will interfere not only on the uptake and distribution, but also on the elimination of the anesthetic. In consequence when the longer the procedure and the higher the inhaled concentration of the agent more chances for accumulation in "adipose compartment" will appear. In addition, the various inhalational agents in common clinical use have distinct solubility characteristics that will bear on the rapidity of onset of action, and the speed of recovery after their administration. The more soluble the anesthetic the slower the induction and the more prolonged the recovery. But the major factor to slow recovery seems to be the reduced capability to remove alveolar gas due to alterations in respiratory function. Air trapping have been demonstrated in obese individuals by obtaining higher values of total lung capacity (TLC) when measured by plethysmography as compared with the value of TLC by the Helium dilution technique.[3] As a conclusion it could be assumed that, morbidly obese patients have excessive amounts of adipose tissue that may act as a reservoir of the volatile agent. This way, once administration is suspended, fat tissue will continue to contribute anesthetic to maintain blood concentrations. This remaining concentration may be sufficient to promote post-operative over-sedation and or respiratory depression which could be of devastating consequences in this particular population. Impaired post-operative ventilation with reduced removal of alveolar gas will contribute to slow recovery from inhalational anesthesia by delaying the elimination of the anesthetic agent. Because of the restrictive lung defect that is common in the obese, this effect is exaggerated.

Possible advantages of TIVA compared with other procedures are summarized below:

1 Fast and stable loss of consciousness (in order to allow a fast airway instrumentation).
2 High versatility to manage different anesthesia compound levels (hypnosis, analgesia and muscular relaxation) to follow step by step the changing situation of any surgical procedure.
3 The elimination of drugs does not depend upon respiratory function (frequently affected in the morbidly obese).
4 Surfactant agent synthesis is not affected as it can be, when inhalational agents are administered (in a population with increased risk of lung atelectasis).
5 No metabolites are produced with the capability to affect renal or hepatic function (in a population with increased risk of renal or hepatic dysfunction).
6 It has not been informed cases of malignant hyperpyrexia.
7 Has lower incidence of shivering (in a population where oxygen consumption is increased and myocardial oxygen balance could be critical so, increments in oxygen consumption should be avoided).[4,5]
8 Fast recovery of consciousness and ambulating capacity (when early ambulation and quick recovery of neurological function are highly desirable in order to protect the airway, achieve sufficient

ventilatory function and prevent deep venous thrombosis).

9 Remarkable hemodynamic stability (in patients that frequently are not capable to face critical perioperative events).

23.2 Pharmacokinetic and pharmacodynamic considerations of the main hypnotic, co-hypnotic and analgesic compound of anesthesia: interactions between them

The objective of providing anesthesia is to titrate the proper dose and delivery rate of a drug to achieve the desirable clinical effect for certain individual undergoing a particular surgical circumstance, while avoiding or at least minimizing the unwanted and toxic side effects.

In addition to the physiological challenges, pharmacological changes associated with obesity might lead to alterations in the distribution, binding and elimination of many drugs. The net pharmacokinetic effect in these patients is often uncertain, making drug titration even more difficult and unpredictable.[6]

Beside kinetics, pharmacodynamic changes have also been observed in morbidly obese patients (see Chapter 15).

Dosing drugs in morbidly obese patients is a difficult and controversial task. Many different weights have been considered. It will be helpful to bring up some clarifying concepts before discussing dosing regimes. For example, dosing remifentanil according to the package insert recommendations may result in a profound overdose. It would be better to scale anesthetic drugs to some other weight instead of considering total body weight (TBW). Lean body mass (LBM) can be calculated from weight in kg, and height in cm as follows:

$$\text{Male: } \text{LBM} = 1.1 \times \text{weight} - 128\left(\frac{\text{weight}}{\text{height}}\right)^2$$

$$\text{Female: } \text{LBM} = 1.07 \times \text{weight} - 148\left(\frac{\text{weight}}{\text{height}}\right)^2.^7$$

Corrected weight can be calculated from this empirical formula as used by Servin and co-workers:

$$\text{corrected weight} = \text{ideal body weight (IBW)} + (0.4 \times \text{excess weight}).^8$$

IBW can be easily calculated in males: height in cm − 100 and in females: height in cm − 105, even for being more accurate it can be extracted from specific tables or more complicated formulas. We have applied this simple formula for calculating doses in our practice with morbidly obese individuals.

So when providing anesthesia in this situation, we will be in front of a patient with significant physiological impairments, prominent changes in body composition, special pharmacokinetic and pharmacodynamic behavior and reduced functional ability to face stress contingencies (such as bleeding, surgical stimuli, etc.). The latter directly related to duration of obesity and body mass index (BMI)[9–13] (see Chapters 5 and 6).

It is clear that surgical–anesthetic planning is essential in order to avoid or at least minimize unwanted reactions during peri-operative period.[14]

In consequence all available resources should be applied to be as accurate as possible when delivering anesthetic drugs to a morbidly obese.

Even it is extremely important to select the drugs that better suits for every clinical situation according to the pharmacological properties of each drug, it is also as much important to take into account the possible interactions between them in order to take advantage of possible synergistic actions. Thus it could be possible to reach the same level of hypnosis not only by increasing the infusion rate of the principal hypnotic, but also by increasing co-hypnotic and or narcotic compound of anesthesia considering the pre-operative level of anxiety, magnitude of surgical stimuli and/or other factors. If we are administrating drugs such as remifentanil with a unique pharmacokinetic behavior, we will be able not only to achieve excellent levels of intra-operative analgesia but also will be able to reduce hypnotic doses which means lower (mainly hemodynamic) adverse effects and faster recovery after long infusions, not only in TIVA but also in inhalational anesthesia.[15,16]

It has been demonstrated that even in high risky patients such as those with obstructive sleep apnea syndrome (OSAS), no significant increase of adverse post-operative events were observed when the levels of wakefulness were carefully maintained.[17]

Finally, obesity is also associated with higher resources utilization according to longer periods of hospitalization and also greater peri-operative morbidity and mortality.[18,19]

Therefore, a reduction of total costs could be expected with a full and secure recovery.

In the following section pharmacological properties of every agent will be analyzed and also their behavior

when administrated in a rational association (co-induction and co-maintenance).

Following the above line of thoughts anesthesiologist would have to be capable to:

1 select the proper drug, or better than that, the best association of drugs according to surgical necessities and patient's condition;
2 define the proper dosing regime;
3 choose the best device to achieve any desired plasma or site effect concentration of the selected drugs at the desired time;
4 select the best monitoring device to follow patient's responses to surgery and anesthesia, thus closing the loop.

23.2.1 Hypnotic (propofol)

The choice of the anesthetic agent for induction and maintenance of general anesthesia in morbidly obese patients remains controversial.

Rapid loss of consciousness (to achieve prompt airway protection), hemodynamic stability and quick recovery (to ensure early efficient coughing minimizing post-operative respiratory complications, and allowing early post-operative ambulation to prevent deep venous thrombosis) are highly desirable.

Propofol is known for its fast onset, offset and lack of hang over compared with barbiturates. It has a favorable pharmacological profile for the induction and maintenance of anesthesia and sedation in normal weight adults.[20]

The pharmacokinetic and pharmacodynamic properties of propofol indicate that this may be an appropriate agent for induction and maintenance of anesthesia in obese patients.

Dosage

Special attention has to be paid to pharmacokinetics and dynamics when administering propofol to morbidly obese individuals. Classically, dosing schemes for propofol are based on patient's weight, but which weight has to be considered?.[21]

Many different dosing regimes have been proposed for the obese patient, but none of them have demonstrated to be the best. After considering advantages and disadvantages of every different scheme, we will try to suggest which one could be the safest and most accurate for these particular population.

Few data are currently available concerning propofol dosages for induction and maintenance of general anesthesia in morbidly obese patients.

Redfern *et al.* found that the total propofol dose required to induce anesthesia did not correlate with the weight of the patient.[22] Kirby *et al.* advised the use of reduced body-related dosages in this cases.[23] Hirota and co-workers found that plasma concentrations of propofol, after a fixed rate infusion were dependent on TBW.[24] This is essential to be understood because if propofol is administered upon total body weight to a morbidly obese patient, this overdose of the drug could lead to significant cardiac depression.

Considering the moderately increased steady-state concentration in heavier patients during propofol constant rate infusions at 3, 6, 9 mg/kg/h, Gepts *et al.* suggested a combination of a fixed dose and body weight-related dose may be preferable.[25]

Servin *et al.* used a specific dosing scheme, based upon an empirical formula: "corrected weight" = IBW + (0.4 × excess weight). They have observed that as a consequence of the simultaneous increase in the VD_{ss} and the clearance, propofol elimination half-life was not prolonged in obese patients, and there were no signs of propofol accumulation, nor of any prolongation of the duration of action. Obese patients opened their eyes when blood propofol concentrations reached 1 mg/l.[8] This propofol concentration when opening eyes on verbal command has already been widely reported in other categories of patients.[26]

A sustained influence of distribution processes governs propofol disposition as it was demonstrated by Hughes *et al.* who emphasized the difference between the elimination half-life of propofol (order of a magnitude 250 min) and the "context sensitive half-time" (time required for the central compartment drug concentration at the end of infusion to decrease 50%) order of magnitude 10–30 min.[27]

For induction and maintenance of anesthesia, propofol dosage can be calculated on IBW.

Drugs with poor or moderate lipophilicity can be dosed on the basis of IBW, or more accurately on LBM. But in the particular situation of a morbidly obese it has to be taken into account that, LBM is frequently higher than expected. Lean mass tissue is often responsible of 20 to 40% of the increased weight of the patient. Muscular mass may be greater in order to move the extra-weighted body. This may be the reason why, when calculating doses upon LBM, it could result clinically insufficient as it was observed by Egan and co-workers when compared remifentanil dosing in lean vs. obese individuals.[28]

Propofol and cardiac performance

Hemodynamic instability has to be taken into account when choosing the hypnotic agent specially in most vulnerable sub-populations such as super-obese or subjects with associated heart disease. It is desirable to ensure a proper hypnotic level to avoid awareness with recall but and overdose of a drug such as propofol with potentially marked hemodynamic effects might lead to severe cardiovascular depression in those patients who are often hemodynamically unstable.

Main hemodynamic effect of propofol is a reduction in arterial, diastolic, systolic and mean blood pressure. It is primarily related to an increment of vascular capacitance even though a decrement in myocardial contraction has also been observed.[29]

Anyway the magnitude of hypotension depends on total dose, and the speed of administration. Roberts and co-workers informed a significant lower reduction of arterial blood pressure, when propofol 1 mg/kg was administered in 20 s followed by an infusion for maintenance, compared with a bolus rapid injection of 2–2.5 mg/kg.[35]

Cardiovascular stability is even higher when propofol is administered with target-controlled infusion (TCI) systems.[34]

Besides hypnotic action, propofol also presents certain properties that makes it suitable for the hemodynamic characteristics of the morbidly obese population. Two aspects should be considered in detail.

Ventricular work conditions

Obese patient has an increased blood volume to satisfy a higher metabolic rate, and a decreased systemic vascular resistance, both factors contributing to produce ventricular over demand. In addition, blood viscosity which is elevated due to an increased hematocrit level, adds to a pressure load on the heart.[36]

These mechanisms are implied in a higher incidence of arterial hypertension and left ventricular dysfunction, not only systolic but diastolic also. In some cases a specific syndrome with biventricular failure (obesity cardiomyopathy) may develop between obese population.[37]

Myocardial oxygen balance

Myocardial oxygenation depends on the relationship between gas offered and consumption. In the morbidly obese, myocardial oxygen consumption is higher than in normal-weighted adults. Ventricular cavity radius is enlarged due to chronic increment of total blood volume (augmented pre-load). An enhanced arterial blood pressure (increased post-load) promotes higher wall tension. In addition, it is also frequent to find ventricular wall hypertrophy.[38–42] Finally due to the higher blood viscosity above mentioned, contractility has to augment and consequently also myocardial oxygen requirements.

On the other hand, oxygen delivery can be lowered in these patients, because chronic hypoxemia is common and also coronary vascular disease.[43–45]

As a conclusion it could be assumed that morbidly obese are at a higher risk of myocardial ischemia (see Chapter 11).

In these subjects, reducing myocardial oxygen consumption and increasing oxygen delivery must be an anesthetic target. Augmented ventricular pre- and afterload have to be also deeply considered.

Possible measures to achieve it, whenever possible, and of course considering every particular clinical situation, could be:

1. To enhance venous capacitance thus reducing ventricular preload.
2. To achieve and maintain low arterial blood pressure values (but physiologically acceptable) specially systolic (systemic vascular resistance) and thus reducing left ventricular postload. Diastolic blood pressure through a rational fluid therapy should be maintained, because left myocardial perfusion is highly dependent on aortic diastolic pressure.
3. To reduce systolic stress (lower quantity of systoles per minute) by achieving and maintaining low cardiac frequencies. Low cardiac frequencies will also increase diastolic period when left ventricular wall is perfused.
4. To avoid interference with normal coronary vascular reactivity (as it could happen when volatile agents are used).
5. To ensure adequate hemoglobin concentration.
6. To achieve and maintain acceptable levels of hemoglobin oxygen saturation.
7. To reduce blood viscosity.

At least in laboratory investigations, it has been proven that propofol reduces arterial blood pressure mainly by increasing systemic vascular capacitance as a result of an inhibition of sympathetic vasoconstrictor activity (reduction of systemic vascular resistance).[29] Total vascular capacitance, which is the relationship between contained volume and distending pressure of systemic vasculature, is a major factor influencing filling of the right heart and therefore has a critical effect on cardiac output. In the same investigation, Hoka and co-workers have observed that propofol also has a tendency to reduce heart rate (or at least not increase it) with low impact on myocardial contraction.[29] The influence of propofol on heart rate is controversial

having been informed increments or decrements. But if propofol is associated with a narcotic such as remifentanil, a reduction in heart rate is expected.[30–32]

In this situation with the enlargement of diastolic period (when left myocardial mass is perfused and oxygenated), ventricular mass would be well protected from ischemia of course if a physiological hemodynamic range is achieved and maintained.

Propofol impact on myocardial contraction can be minimal with proper administration technique (low doses based upon IBW, slow infusion instead of bolus injection).[33] A better respiratory and cardiovascular stability and faster recovery have been observed with propofol TCI compared with manual infusion technique during direct laryngoscopy.[34] Thus with a proper dosage of propofol, left ventricular work condition would improve according to a decrement in ventricular filling pressure and volume, and also a decrement in left ventricular postload. This hemodynamic situation would also be beneficial for myocardial oxygen balance in the morbidly obese.

According to the necessity of achieving hemodynamic stability in the morbidly obese, it is interesting to see what happens in hemodynamically unstable patients such as cardiopathic.

Vermeyen and co-workers in a clinical trial evaluated the possible advantages of a TIVA technique with low doses of propofol and fentanil for elective coronary bypass.[33]

It was considered as a potential benefit for myocardial oxygenation, the myocardial depression induced by propofol, and its effect over the circulatory system, with the consequent reduction in ventricular work and myocardial oxygen consumption. Ventricular function, coronary blood flow and myocardial oxygen consumption were measured in the pre-bypass period. A significant reduction in systolic and diastolic blood pressure, and systemic vascular resistance was observed during induction, while cardiac index remained stable. Left ventricular work index was reduced during all the study period. Median vascular coronary resistance, myocardial oxygen consumption, blood flow in coronary sinus and lactic acid extraction did not suffer significant changes during the study. Authors concluded that low doses of propofol (1.5 mg/kg) for induction, associated with a narcotic (fentanil), was an adequate anesthetic technique for coronary bypass surgery.[33]

In another clinical trial it was observed that TCI propofol (diprifusor) in combination with TCI remifentanil (Minto Model Rugloop software) was very well adapted to variation in surgical stress during cardiac surgery. Only five episodes of hemodynamic instability between 25 surgical procedures required vasoactive therapy, while no recall was observed post-operatively.[46]

In conclusion propofol not only would be an excellent hypnotic drug because of its rapid onset and offset but also because reduces pre- and postload, thus better conditions for improving myocardial function and oxygenation could be achieved.

Other favorable pharmacodynamic effects different from hypnosis

Propofol could be the anesthetic agent of choice when higher *risk of malignant hyperpyrexia* is predicted mainly if used in a TIVA scheme associated with other intravenous (i.v.) drugs.[47,48]

Propofol *reduces pharyngeal and laryngeal reactivity*. This property could allow to manage the airway without the necessity of muscular relaxants as it has been informed by Kallar after the induction with 2.5 mg/kg.[49] This could be a fact of importance in a population in which it has been reported 13% incidence of difficult airway management.[6]

In such a situation, sometimes, quick recovery of spontaneous ventilation could be necessary, mainly if this contingency was not predicted (see Chapter 21).

Propofol markedly *reduces the shivering threshold* and is associated with less post-operative shivering than when thiopental is used as an induction drug.[50] Shivering should be avoided in the morbidly obese in order to prevent dangerous increments in oxygen consumption.

Propofol compared with other induction agents has been associated with a *low incidence of nausea and vomiting* in the post-operative period, beyond that, some authors have reported a direct antiemetic action when used in sub-hypnotic doses (10 mg),[51,52] which is important not only considering patient comfort but also the possible influence of nausea and vomiting as a factor to delay discharge from post-anesthesia care unit (PACU) (see Chapter 25).

Propofol also *reduces anxiety and pruritus* when administered at sub-hypnotic doses (10–15 mg).[53]

Compared with other i.v. induction drugs and inhalational agents different from sevofluorane and desfluorane, propofol shows a *better psychomotor recovery profile*.[54–57]

Metabolism

Morbidly obese are at a higher risk of renal dysfunction because of a higher incidence of nephropathy

secondary to arterial hypertension, diabetes or vascular disease.

Hepatic impairment could also be present since these subjects frequently exhibit liver disease due to fatty infiltration. Consequently, drugs metabolism has to be considered when choosing the anesthetic agents.

The liver remains the main site of metabolism for propofol. Hepatic clearance is heavily dependent on the organ's blood flow. In obese patients, propofol clearance is correlated to body weight, and may reach high values. Increases in blood volume, cardiac output and splanchnic blood flow have been observed related to obesity. In addition, the liver of obese subjects is significantly larger compared to lean ones, because of an increase in the number and size of parenchymal cells.[58] Nevertheless, obesity is associated with a number of pathological conditions, mainly fatty infiltration, which may compromise hepatic function.[59]

The influence of obesity on drug metabolism depends heavily on the metabolic pathway considered. Propofol is primarily biotransformed via hepatic phase 2 conjugation pathway even though extrahepatic metabolism has also been demonstrated. In fact patients with moderated cirrhosis have not presented significant pharmacokinetic differences compared with healthy subjects after bolus propofol administration or continuous infusion.[60,61]

It seems that drugs that undergo phase 1 metabolism are unaffected by obesity, as well as those that undergo acetylation, which is a phase 2 metabolic reaction but most phase 2 reactions of glucuronidation (main metabolic pathway of propofol) and sulfation are enhanced in obesity.[62]

Finally it has also been observed that chronic renal failure does not seems to compromise propofol elimination, anyway administration under this context should be done with precautions.[63]

23.2.2 Co-hypnotic (midazolam)

Midazolam is an excellent agent to achieve anxiolysis, sedation, amnesia and hypnosis with low impact on cardiac function.[64]

Regarding pharmacokinetics, Greenblatt *et al.* demonstrated that volume of distribution (V_d) and elimination half-time increases in line with body weight but they did not find significant change in total metabolic clearance.[111] Thus, following these authors' opinion, midazolam should be administrated in larger absolute doses, but in the same doses per unit body weight. A prolonged sedation can occur from the larger initial dose needed to achieve adequate serum concentrations. The rate of continuous infusion, however, should be adjusted to the ideal (IBW) rather than the total weight (TBW).[64]

But if clinical effect desirable is considered, it is essential to take into account inter-individual variability rather than isolated pharmakokinetic properties. In my own experience, in order to avoid under or overdosing and correspondingly unpredictable clinical effect, the best way of administration is to begin with a titrating bolus dose (0.05 mg/kg) based upon IBW, and evaluate clinical reaction by pharmacodynamic monitoring (bispectral index (BIS), auditory evoked potential (AEP) or other); once the desired index is achieved, an infusion based upon IBW should be started.

23.2.3 Interactions between midazolam and propofol

Rather than considering clinical effects of isolated administration of midazolam, it is more important to evaluate what would happen when this benzodiazepine is associated with propofol in a co-induction scheme. In a study performed by Kenny and colleagues, anesthesia was induced successfully in 40% of patients when the predicted target propofol concentration was 3 μg/ml, in 75% when the target was 4 μg/ml and in 90% when the target was 5 μg/ml.[65] Patients who did not have anesthesia induced successfully with the initial target then received a target of 6 μg/ml and anesthesia was induced successfully in all remaining patients. Therefore, to achieve the identical end point of induction of anesthesia, this group of patients required not one single propofol concentration but a range from 3 to 6 μg/ml. So inter-individual variability is notable when using just propofol for anesthesia induction.[65]

Nevertheless, clear benefits of co-induction to reduce inter-individual variability are emphasized in a clinical study reported by Tzabar and colleagues who administered increasing doses of midazolam before induction with a fixed target propofol concentration of 3 μg/ml. The success of induction increased from 45% when placebo was administered up to 95% when midazolam 4 mg was given before starting TCI propofol.[66]

The pharmacological basis of co-induction has been shown to result from synergistic rather than simply additive effects of various drug combinations. Synergism between propofol and midazolam has been shown to exists in several previous studies, in which 20–55% decrease in the amount of propofol required for induction of anesthesia has been demonstrated, with midazolam doses ranging from 20–70 μg/kg.[67–69]

A propofol-sparing action of midazolam has been clinically proven. Benzodiazepines and propofol are

thought to act at differing sites in the gamma-aminobutyric acid (GABA) A receptor complex. In a clinical investigation, Nel and colleagues compared, using pharmacodynamic monitoring (auditory evoked response, AER) variables, the influence of midazolam on propofol action for induction of anesthesia vs. propofol alone. This study confirmed the propofol-sparing action of midazolam and the AER data suggested that co-induction of anesthesia with midazolam–propofol is achieved via a similar pharmacodynamic action of the two drugs.

In addition, it is notable that there were a significant difference between the two groups in the mean amount of propofol required to achieve loss of consciousness: propofol group 2.4 mg/kg vs. propofol midazolam group 1.3 mg/kg.[70]

It has also been investigated the influence of graded doses of midazolam on propofol infusion requirements, and the quality of recovery, when associated with propofol/alfentanil/oxygen TIVA.[71] Even when this study had to be discontinued because of the appearance of six intra-operative awareness with recall episodes, many important conclusions could be obtained. Induction requirements of propofol were found to be lower, when comparing placebo groups with midazolam groups. Time to awaking and discharge from the recovery room and day care unit, as well as trigger dot test scores were no greater in any midazolam group than in placebo. The lowest incidence of awareness were found in patients receiving midazolam. High incidence of awareness in this study could be explained because infusion rates of propofol and alfentanil were set initially at the lower end of recommended levels for TIVA.[71]

Finally considering inter-individual variability is high with benzodiazepines and because oversedation has to be avoided in these patients, in my own experience I administer BIS-guided midazolam prior to start the narcotic and TCI infusion of propofol. This way midazolam is titrated to reach a BIS score close to 80 (mild sedation with protected reflexes conserved) in the immediate pre-induction period. This pre-induction dose of midazolam would allow a reduction of anxiety, an improvement of amnesia and a reduction on propofol-required dose for induction and decreased time for loss of consciousness.

23.2.4 Analgesic (remifentanil)

Remifentanil seems to be the opioid that would better suit for this population (see Chapter 16). Here it will be analyzed, the possible advantages of a TIVA regime, associating remifentanil as the narcotic compound with propofol as the main hypnotic and midazolam as co-hypnotic and amnesic agent. It has to be emphasized that as any opioid, remifentanil is not just an analgesic, it is an hypno-analgesic, so hypnotic properties of remifentanil could be useful to reduce other hypnotic necessities in a co-induction and co-maintenance scheme.

23.2.5 Interactions between remifentanil and propofol

Influences of narcotics associated with propofol, have been studied by Vuyk *et al.*, demonstrating that by increasing the plasma concentration of alfentanyl from 50 to 150 ng/ml the effective concentration (EC50) of propofol for the regaining of consciousness decreased from 3.8 to 0.8 μg/ml.[72]

In another clinical study, where TCI propofol BIS-guided anesthesia was performed for short surgical procedures, Becx and colleagues have observed that, inter-individual variability increased over time and it might be explained by the use of a bolus of a short-acting opioid at the beginning of the procedure, with no infusion after that. This finding confirms the known interaction between opioids and hypnotics (propofol), which reduces the variability of the hypnotic complement.[73]

Strachan and Edwards observed that increasing infusion of remifentanil resulted in reduction in BIS score in patients sedated with propofol 2 μg/ml TCI. The reduction in sedation score correlated with the reduction in BIS. BIS also demonstrated to be as good a monitor of level of sedation with this combination of infusions as it is with single hypnotic agents.[74]

To test the hypothesis of a dose-dependent interaction of remifentanil with propofol on loss of consciousness, Schraag *et al.* studied the influence of remifentanil on propofol closed-loop anesthesia based on mid-latency auditory evoked potentials (MLAEPs). The results of the study gave evidence of a quantitative interaction between remifentanil and propofol for loss of consciousness. Remifentanil decreased the propofol concentrations necessary for loss of consciousness in a dose-dependent manner.[75]

23.2.6 Interactions between remifentanil and midazolam

Complex interactions between benzodiazepines and opioids have been reported with respect to analgesia, sedation and hypnosis.[76–79]

In laboratory investigations synergistic interactions between midazolam and μ1 agonists opioids have been observed. Jianquiang and co-workers demonstrated that midazolam and alfentanil interact synergistically,

and also that benzodiazepines are effective in mitigating the development of opioid tolerance and dependence.[80]

When comparing remifentanil 1 μg/kg/bolus followed by 0.1 μg/kg/min infusion alone, vs. remifentanil 0.5 μg/kg/bolus followed by 0.05 μg/kg/min associated with bolus doses of midazolam 1 mg for ambulatory surgery during monitored anesthesia care, it has been demonstrated that lower doses of remifentanil combined with 2 mg of midazolam, compared with remifentanil alone resulted in fewer side effects, slightly greater sedation, and less anxiety.[81]

Besides, final mean infusion rates were 0.12 ± 0.05 μg/kg/min in remifentanil patients vs. 0.07 ± 0.03 μg/kg/min for the remifentanil/midazolam group. The use of decreased doses of remifentanil and midazolam is based on the known interaction between opioids and benzodiazepines. The combination of remifentanil and midazolam decreased the incidence of respiratory depression, post-operative nausea and vomiting while still providing effective analgesia, anxiolisys and sedation.[81]

In a similar clinical investigation, Avramov and colleagues concluded that remifentanil alone for monitored anesthesia care did not provide optimal sedation during local anesthesia, however when combining lower doses of remifentanil with midazolam 2 mg provided effective sedation and analgesia.[82] They also noted that sedative doses of midazolam possess antiemetic activity since patients receiving midazolam have lower incidence of post-operative nausea and vomiting compared with remifentanil alone. Early recovery, time to ambulation, home readiness and discharge did not differ among groups. Not surprisingly, midazolam provided significant intra-operative amnesia and a higher degree of patient comfort compared with remifentanil alone.[82]

Finally it could be assumed that multiple association between the three drugs: opioid (remifentanil), hypnotic (propofol) and co-hypnotic (midazolam)) would offer the following advantages:

1. Lower doses of all agents required (hypnotic, co-hypnotic and analgesic) to obtain the same clinical effect.
2. Lower incidence of side effects according to lower drugs doses.
3. Significant reduction of inter-individual variability.
4. Shorter time for loss of consciousness with more stable hemodynamic performance.
5. High versatility to follow step by step the changing situations of any surgical procedure (optimal surgical–anesthetic timing).
6. Quick and predictable recovery.
7. Better amnesia effect, and less anxiety than using only propofol and remifentanil.
8. Lower incidence of awareness with recall.
9. Lower incidence of nausea and vomiting.
10. Lower incidence of post-operative shivering.

23.3 Drugs delivery: pharmacokinetical modeling and target-controlled infusion devices, its application in the morbidly obese

Up to this moment, pharmacological properties of every drug (*main hypnotic*: propofol; *co-hypnotic and amnesic*: midazolam; *hypno-analgesic*: remifentanil) have been deeply considered, and could be assumed that they would be suitable for these patients.

It has also been analyzed in detail, the advantages of a rational association between the three agents, not only for induction but also for maintenance of anesthesia, consequently this association would be suitable too. In addition it also has been commented that dosing has to be based upon IBW or corrected weight.

So having already selected the drugs and doses, now it has to be questioned, which would be the most precise and safe procedure to deliver them.

The i.v. drugs may be delivered through three different patterns: bolus injection, manual infusion or TCI.

Bolus injection produces a rapid peak in plasmatic concentration and site effect, so clinical effect appears quickly. But as the target organ (brain) pharmacokinetically mirrors the myocardial tissue, cardiac function could become dangerously affected mainly in patients such as morbidly obese who frequently are not capable to face hemodynamic stress.[9]

In addition, plasmatic drugs concentration will rapidly decrease and also the clinical effect. Thus this method could be dangerous for induction and inadequate for maintenance of anesthesia.

With manual continuous infusion, time necessary to reach the desired plasma concentration would be excessively long, and after a variable period of application, accumulation may occur. So for induction it is not practical and it would be even dangerous if it is considered that according to a higher risk of gastric aspiration, time for tracheal intubation should be as short as possible. For maintenance, overdosing and or delay in recovery may happen if permanent changes in infusion rhythm are not applied.

Contrary to both previous methods, TCI seems to be suitable not only for induction but also for maintenance of anesthesia. Some drugs such as propofol and remifentanil have a close relationship between blood concentration and clinical effect, consequently the administration of the drug can be improved by basing the dose regimen on the pharmacokinetic of the agent.

TCI systems incorporate real-time pharmacokinetic models which deliver the appropriate dose of the drug to achieve and maintain the requested target concentration. The systems do not sample the blood in real time, but use population kinetics to provide the best estimate of the predicted blood concentration. TCI systems allows the anesthesiologist to facilitate drugs delivery just handling an easy to use dial command. It also gives the possibility to determine the time to reach the requested plasma or site effect concentration. Through a friendly display, different infusion and pharmacokinetical data can be consulted at any time. In addition better respiratory and cardiovascular stability, and faster recovery have been observed with propofol TCI compared with manual infusion technique during direct laryngoscopy.[34]

But how could target-controlled infusion systems be applied in the morbidly obese?

23.3.1 Propofol and pharmacokinetical-guided delivery

The first device commercially available for propofol infusion was "Diprifusor" (Astra Zeneca, London, UK) using the weight adjusted three compartmental model published by Marsh *et al.*[83]

This device has not been developed for morbidly obese. Its limit for weight setting is 150 kg (many morbidly obese are usually heavier than that) and besides there are no recommendations about what weight should be considered for TCI in these cases. Nevertheless, it has been already commented that dosing schemes based on IBW or LBM have been used successfully in morbidly obese population, not only for bolus injection but also for continuous infusion. For manual infusion of propofol in the morbidly obese, Gepts *et al.* recommends the corrected body weight as published previously by Servin *et al.* (IBW = 0.4 × excess weight).[8,25]

In conclusion, even if TCI systems have not been developed for morbidly obese patients, it could be assumed that at least theoretically, they could be used safely if dosing precautions were taken. The same pharmacokinetic principles should be applied for TCI propofol administration (as well as other pharmacokinetically compatible drugs). In my own experience propofol TCI "Diprifusor" (Astra Zeneca, London, UK), remifentanil and midazolam continuous infusion assisted by Rugloop in simulated mode, have been used in 141 morbidly obese patients with similar results than in lean population. The average range of doses and total amount of drugs did not grossly differ from those related to lean population when TCI systems were set upon IBW in morbidly obese patients (see Section 23.6.2).

But even if TCI devices seem to be the most acceptable system available for drugs delivery in this situation, it has to be considered that inter-individual variability still will exist. Beyond that, every surgical procedure is different and dynamic, in which hypnotic, analgesic and muscular relaxants requirements are different at every moment. So it is clear that to determine the precise dose, rhythm and time for drugs administration is a difficult task to manage. Here is where pharmacodynamic monitoring would become extremely helpful in order to follow step by step, the balance between surgical requirements, anesthetic drugs administration and patients responses; in other words, surgical–anesthetic timing. When more accurate the timing more stable will be the course of anesthesia and more predictable will be the recovery.

23.4 Pharmacodynamic monitoring: its importance in surgical–anesthetic timing, hemodynamic stability and recovery

General anesthesia is a dynamic balance between the level of hypnosis, analgesia and muscular relaxation and the effects of stimulation from surgery or instrumentation. Wide variations have been reported in the requirements for induction and maintenance of anesthesia with propofol alone or in combination with different doses of other adjuvant drugs such as benzodiazepines and or opioids. Wide variations in TCI drug requirements have also been shown for sedation and post-operative pain management. These reports demonstrate the greater importance of pharmacodynamic over pharmacokinetic and its effects.

Even if TCI systems may produce the exact target requested, it would not be possible to know if that concentration is satisfactory for each individual patient and for different points during the surgical procedure. The anesthesiologist must be aware of the possible pharmacokinetic variations but also appreciate the pharmacodynamic variations of the agents used.

The teleological objective of any anesthesia procedure is to obtain certain clinical effect in the precise magnitude and moment. Continuous monitoring of clinical effect would help to achieve accuracy in drug delivery and to reduce unwanted reactions due to over- or underdosing. This is a topic of enormous importance in a population in which inter-individual variability may become outstanding (see Chapter 19).

The major requirement of a monitor of anesthetic depth is to distinguish consciousness from unconsciousness, but another desirable feature would be for the signal to provide an estimate of the effect of a given (or calculated) brain concentration of an anesthetic agent to predict movement or awareness.

In the last years many special devices have been developed to evaluate the influence of hypnotics and anesthetic agents over the central nervous system activity. Based on the EEG signal, several parameters like spectral edge frequency (SEF) and median frequency (MF) can be obtained.[84] Nevertheless, up to this moment it is still controversial if their results are unquestionably reliable.[85,86] Another monitor of anesthesia depth is the bispectral index (BIS, Aspect Medical Systems Inc., Newton, MA) which has been tested and validated as a reliable tool for this purpose. It has been informed a sensitivity of 100% and a specificity close to 55% to measure loss of consciousness at indexes below 53 during the curse of propofol anesthesia.[88]

Macquire and colleagues have also observed that in American Society of Anesthesiologist (ASA) physical status III and IV patients undergoing elective cardiac surgery, once BIS below 50 was achieved, the probability of loss of consciousness was 100% when induction was performed with propofol TCI.[89]

MLAEPs have been reported to correlate well with anesthetic depth,[90] and to be able to demonstrate potential awareness.[91,92]

MLAEP are usually obtained intermittently and the waveforms are difficult to use in the clinical situation. More recently, the AEP index, derived from AEPs, has been proposed as a single numerical variable for continuous and practical monitoring depth of anesthesia, allowing to obtain variation of indexes at 3 s intervals.[93–95]

Doi and colleagues have compared four electrophysiological variables as indicators of anesthetic depth, correlation of signals with propofol blood concentration and capability to identify the transition between unconsciousness to consciousness.[96] The systems analyzed were: BIS, 95% SEF, MF, and AEP index. In the study the four variables were examined simultaneously in 10 patients using two methods: first comparing values just before and after eye opening, and before induction of anesthesia; second: the correlation with calculated blood propofol concentrations.

It was observed that mean 95% SEF values just before and after eye opening were not different from each other, but significantly larger than before induction of anesthesia. The 95% SEF values before eye opening also correlated well with calculated blood concentration of propofol. The correlation was best with BIS. BIS values before eye opening correlated well with calculated blood propofol concentrations. Mean BIS values before and after eye opening did not differ from each other, but were significantly smaller than before induction of anesthesia.

On the other hand, AEP indexes values after eye opening and those before induction of anesthesia were clearly distinguished from those before eye opening. There was no difference between values just before induction of anesthesia and those recorded just after eye opening. Mean AEP index before eye opening was significantly smaller than that after eye opening and also significantly smaller than that before induction of anesthesia.

In the study it was observed that AEP index values were low during sleep and increased suddenly just after eye opening, suggesting that AEP index reflected the level of consciousness rather than blood concentration of propofol. The AEP index may therefore be considered a reliable monitor to detect awareness during anesthesia.[96]

Results from different studies suggest that a patient may recover consciousness at BIS index value of 50 to 85, but with an increasing probability at higher values.[97–99]

This suggests that the BIS would not be a reliable monitor to detect the transition from unconsciousness to consciousness. In Doi's study three analyzed variables (BIS, 95% SEF and MF) demonstrated different characteristics from the AEP index. The former three variables were derived from the same two-channel surface EEG signals. They are considered to reflect mainly cerebral cortex activity. Therefore, they correlated with blood (and therefore also site effect) propofol concentrations during emergence from anesthesia. In contrast, the AEP index was calculated from 144 ms of AEP, and it reflects overall responses to auditory stimuli from the brainstem to the cerebral cortex. In fact the overall responses observed throughout the study regarding AEP indexes, demonstrated the transition from unconsciousness to consciousness very sharply, which mirrors the clinical state.

Different characteristics were founded between the four variables for monitoring depth of anesthesia. The variables processed from the surface EEG (BIS, 95% SEF, and MF) generally reflected blood calculated concentrations of propofol. Of the three variables, BIS changed most linearly with propofol concentrations in blood. Therefore, BIS may provide the best prediction of recovery of consciousness during emergence from anesthesia at the end of surgery. MF and 95% SEF changed linearly when patients were unconscious, but lost the linearity during consciousness. BIS was superior to MF and 95% SEF. The AEP index was different from the surface EEG derivatives and was the best variable to distinguish the transition from unconsciousness to consciousness.[96]

In a clinical trial, Gang Ton and co-workers evaluated if monitoring of the EEG response using BIS throughout surgery would allow accurate titration of propofol for each patient, thereby reducing the amount of drug administered and shortening recovery time.[100]

The primary objective of this clinical utility study was to show the efficacy of BIS monitoring as a pharmacodynamic measure of patient response to propofol during general anesthesia. Two groups participate, one BIS guided in which propofol infusion was adjusted in order to achieve a target between 45 and 60 during surgery, and later increasing between 60 and 75 in the last 15 min of surgery. In control group (standard practice, SP), propofol dose adjustments were made based only on standard clinical signs. Results from this clinical utility trial showed that BIS may be used to measure the pharmacodynamic effect of propofol and thereby facilitate its titration to improve recovery from anesthesia. In the group wherein BIS was not used, patients were consistently administered more propofol throughout the anesthetic. This holds true in all study centers and probably reflects current clinical practice in general (it is important to take into account that at higher doses, higher possibilities of adverse effects could appear in susceptible patents, for example, morbidly obese). Most SP patients were maintained at a BIS level below 50 for much of the case, so according to BIS criteria, more propofol was being used than was necessary in this group. BIS group outcomes have also been compared with historical control subjects rather than the SP group; results of this comparison suggested stronger improvements associated with BIS monitoring. On the other hand, titration of propofol based on the BIS resulted in reduced propofol infusion rates, reduced total amount of propofol used, faster wake up, and improved recovery from anesthesia (were extubated sooner, had a higher percentage of patients orientated on arrival to PACU, had better PACU nursing assessments, and became eligible for discharge sooner). No significant increase in the incidence of unwanted reactions such as movement or hypertensive responses occurred, thereby indicating that the benefits of improved recovery times obtained using BIS monitoring were not obtained at the expense of an increase in events associated with inadequate anesthesia. The BIS group also demonstrated greater predictability of rapid emergence. If potential indirect costs savings associated with faster operating room (OR) and PACU turn-over are also considered, it is possible that BIS monitoring may facilitate cost-effective anesthetic delivery. In conclusion this study demonstrated:

1 The safety and efficacy of BIS monitoring as a pharmacodynamic measure of patient response to propofol during propofol–alfentanil–nitrous oxide anesthesia.
2 Addition of routine BIS monitoring to standard anesthetic care resulted in reduced use of propofol and faster recovery compared with standard clinical practice.
3 Routinely BIS monitoring could result in potential economic benefits.[100]

After all these considerations it is clear that pharmacodynamic monitoring would be extremely helpful to titrate anesthetic drugs mainly in a population in which dosing has been historically problematic (the morbidly obese). It would help not only to avoid overdosing and thus hemodynamic depression and delayed recovery but also to prevent episodes of awareness and consequent increase of stress hormones in a patient with reduced physiological capability to respond adequately against and enhancement of catecholamine plasma level. (higher risk of myocardial ischemia, hypertension, arrhythmia, ventricular failure and hyperglycemia).

23.5 Post-anesthetic shivering in the morbidly obese: implications

"Post-operative shivering should be avoided in the morbidly obese, and this is one of the reasons to include this topic in the present chapter." On the other hand, TIVA, especially if propofol is included as hypnotic agent, demonstrated to be better than volatile anesthesia to prevent this complication; this is another reason to be included.

Shivering is often a consequence of accidental perianesthetic central hypothermia, and it is preceded

by peripheral vasoconstriction (presumably according to increases in catecholamine activity). Even if mild hypothermia could be a protective mechanism against tissular ischemia and hypoxia, all other effects are noxious, such as coagulation impairment, higher incidence of wound infections, prolonged pharmacological effect of anesthetic drugs and alteration of post-operative thermal comfort.[101]

Normally, the thermoregulatory system protects body temperature against changes in ambient temperature. The magnitude of the vasoconstriction to shivering range is about 1°C.[102]

Post-anesthetic shivering develops in up to 60% of patients recovering from general anesthesia[103] and approximately 30% of volunteers during epidural anesthesia.[104]

There is a dose-dependent decrease in the thermoregulatory threshold for shivering during general anesthesia, resulting in core hypothermia in unwarmed patients. During the initial recovery from general anesthesia, residual anesthetics suppress thermoregulatory responses. Subsequently, however, hypothermia triggers peripheral vasoconstriction and shivering. Post-anesthetic shivering is thus largely a thermoregulatory compensation for intra-operative hypothermia.[105]

Treatment of visible post-anesthetic shivering may be insufficient because even invisible shivering may significantly increase oxygen consumption.[106] This is a main topic to be considered in morbidly obese population, because increased subcutaneous fat tissue may easily mask clinically evident shivering.

Whether post-anesthetic shivering is attributed to increased spinal reflexes, pain or decreased sympathetic activity, clonidine is likely to be effective.

Recent studies suggest that the incidence of post-anesthetic shivering differs between i.v. and volatile anesthetics. Cheong and Low observed that the incidence of post-anesthetic shivering in patients recovering from propofol/nitrous oxygen anesthesia was significantly lower than in those given isoflurane/nitrous oxygen anesthesia.[107]

Propofol markedly reduces the shivering threshold and is associated with less post-operative shivering than when thiopental is used as an induction drug.[108]

Central adrenergic receptors appear to modulate post-anesthetic shivering. Clonidine, a central α_2-adrenergic agonist, if appropriately administered could protect against post-operative shivering. Horn and co-workers have proven in a clinical trial that the effect of clonidine on post-anesthetic shivering is related to the time, dose and duration of its administration. Sixty patients undergoing elective ear and nose surgery were evaluated comparing shivering incidence, post-operative pain, hemodynamic behavior and recovery performance. Studied groups received either isoflurane/nitrous oxide or propofol/nitrous oxide anesthesia, and each group, with or without 3 μg/kg clonidine bolus dose 5 min before end of surgery. Post-operative shivering was observed in 53% of the patients given isoflurane without clonidine and 13% of the patients given propofol without clonidine. No patient given clonidine shivered. Clonidine administration significantly reduced post-operative pain. There were no clinically important differences in heart rate and mean arterial blood pressure among the groups. When saline was administered, mean arterial blood pressure increased 15 min after extubation and subsequently remained elevated. After clonidine administration, mean arterial blood pressure remained nearly constant. Oxygen saturation exceeded 95% in all patients at all times. There were no significant differences in arousal times.

This suggests that the application mode (bolus application vs. long-term infusion) and time of administration determines the anti-shivering efficacy of clonidine.[109]

In unpublished data we have observed similar results. Ten morbidly obese patients anesthetized with a propofol/remifentanil/midazolam TCI, BIS-guided TIVA, received 3 μg/kg bolus injection of clonidine dosed upon IBW 5 min prior the expected end of surgery. None of the 10 patients shiver during 30 min follow-up, BIS values were lower than in patients from previous experiences in which clonidine was not administered and remain below 90 during the evaluation period. Nevertheless all of them were capable to follow a coherent conversation when verbally stimulated. There were no clinical over sedation, and/or respiratory depression. Hemodynamics remained remarkably stable, in fact we assumed that late intra-operative bolus clonidine, improved immediate post-operative hemodynamic performance, with no incidence of hypotension or bradycardia neither hypertension or tachycardia during transition of intra- to post-operative analgesia. These findings are also consistent with the observation of an improvement in hemodynamic variables during the peri-operative period in patients undergoing coronary bypass surgery.[110]

23.6 Total intravenous anesthesia, target-controlled infusion propofol, midazolam, remifentanil, bispectral index-guided anesthesia in morbidly obese patients: my experience

Due to the heterogeneity observed between our patients (regarding BMI, severity and type of co-existing diseases, chronic consumption of other medications, ASA physical status, and type or duration of every surgical procedure) it is difficult to analyze every factor influencing in post-surgical–anesthetic outcomes. Therefore in order to evaluate the eventual advantages or disadvantages of the anesthetic technique used for the morbidly obese, a retrospective view of my experience with 141 patients have been chosen in which despite of any influencing factor as above mentioned, the same anesthetic technique was applied. Simple end points have been considered accordingly to evaluate how this technique would fit in the unique anesthetic scenario observed when facing a morbidly obese patient. These end points are clearly related to the most frequent complications or misadventures that the anesthesiologist have to deal with, in this particular situation. In the following section, demographic characteristics of the studied population will be shown, anesthetic technique will be described in detail and finally results will be presented in a table format (Table 23.2).

23.6.1 Demographics

All the 141 patients were morbidly obese scheduled for different elective bariatric procedures (laparoscopic adjustable gastric banding, laparoscopic gastric bypass and open Scopinaro technique; obviously some primarily conceived laparoscopic procedures had to be converted to open approach).

Demographic particularities of the studied population are summarized below:

- Gender: males, 45 (31.91%); females, 96 (68.08%).
- Age: range, 17–71 years old (median 43.32).
- BMI: range, 30.1–78.3 (median 47.8).

23.6.2 Anesthesia technique

Taking into account the pathophysiological alterations expected in morbidly obese individuals, and consequently their related risks and complications, I tried to develop a suitable anesthetic technique.

A TIVA propofol TCI, midazolam, remifentanil BIS-guided anesthesia was performed in all cases. Dosing schemes were based upon IBW for all infused drug. No anesthetic adjuvant was administered before surgery. The process begins with a midazolam BIS-titrated sedative pre-induction dose (graded doses of 0.05 mg/kg every 5 min) in order to obtain a BIS value of 80. Considering that it is important to determinate the inter-individual variability with midazolam, empirically, at this point patients are assumed to have high (if one bolus dose is enough to reach the goal) median (if two boluses are needed) or low responses to benzodiazepines (if three or more boluses are required). Subsequently a midazolam infusion starts according to prior responses; high response patients = 0.8 μg/kg/min, median response patients = 1.6 μg/kg/min and low response patients = 2.4 μg/kg/min. Remifentanil infusion at 0.5 μg/kg/min is administered once BIS reached 80 after midazolam. Once remifentanil effect is evident (tendency to a lower heart rate, 3–5 min after starting the infusion), propofol TCI set to reach a concentration of 4 μg/ml (based upon IBW, age and gender) in 15 s (flash mode) is delivered. Once BIS value falls below 60, succinylcholine is given to obtain muscular relaxation for tracheal intubation (this only drug is dosed according to TBW). Atracurium is the relaxant agent for intra-operative period. Propofol TCI is then adjusted to reach values between 40 and 50 until skin incision. Once surgery begins, propofol TCI is adjusted to reach a range of BIS values between 50 and 60. Remifentanil infusion is adjusted according to surgical stimuli by increments of 100% or decrements of 50% every 5 min. At the last 15 min of surgery propofol TCI is adjusted to obtain BIS values between 60 and 80, midazolam infusion stops and remifentanil is reduced at a rate of 0.05 μg/kg/min, starting a transitional analgesic regime according to the type of surgery. Tracheal extubation is performed once full protective reflexes and sufficient ventilatory function are achieved. Patients are then induced to move by themselves from the operating table to the stretcher without any help. Once hemodynamic and respiratory performance are stable, pain is controlled, and are capable to maintain a coherent conversation, patients are sent to their corresponding post-operative destiny (intensive care unit (ICU), intermediate or general care) (Table 23.1).

Results and end points analyzed are in a table format (Table 23.2).

23.7 Conclusions

As it was developed throughout the chapter this approach based upon pathophysiological condition and most frequent risks and complications commonly related to morbid obesity have shown in my experience,

Table 23.1 Anesthesia technique

	Pre-induction		Induction	From tracheal intubation to skin incision	Maintenance	Last 15 min	End of surgery
BIS target	**80**		**40–50**		**50–60**	**70–80**	**Close to 100**
Midazolam	Bolus dose, 0.05 mg/kg every 5 min until reach the goal	Infusion according to bolus response (see text)				End of infusion	
Remifentanil		0.5 μg/kg/min	Infusion according to surgical stimuli (see text)			0.05 μg/kg/min. Starts analgesic transition	
Propofol TCI			2–4 μg/ml	Infusion according to BIS target			End of infusion

Table 23.2 End points analyzed, and results

Range of propofol set concentration required (as appear on diprifusor display)	2–4 μg/ml (based upon IBW set according to age and gender)
Range of midazolam required	0.05–0.15 mg/kg pre-induction bolus dose 0.8–2.4 μg/kg/min maintenance infusion dose
Range of remifentanil required	0.5–2 μg/kg/min infusion dose
Severe immediate peri-operative cardiac complications	One case, ventricular tachycardia with cardiac failure: 0.7% (patient X for future comments)
Severe immediate peri-operative respiratory complications	Deep vein thrombosis, without pulmonary embolism, one case: 0.7%
Necessity of vasoactive therapy (more than one efedrine rescue dose)	One case: 0.7% (patient X)
Necessity of vasodilators according to arterial blood hypertension events not responding to remifentanil increments	None
Necessity of pharmacological hemodynamic support	One case: 0.7% (patient X)
PACU discharge time	41.70 min (excluding patient X for the calculus)
Necessity of assistance to move themselves (when transferring from operating table)	One case: 0.7% (patient X)
Necessity of ICU	Two cases: 1.4% One according to previous co-existing diseases for appropriate special post-operative surveillance (male, 64-year old, central obesity, BMI 60, coronary artery disease, history of cardiac failure, severe arterial hypertension, renal failure (in hemodialysis treatment), type I diabetes mellitus with high insulin requirement, OSAS, chronic obstructive pulmonary disease (COPD)): 0.7% One for post-operative heart failure: 0.7% (patient X)
Necessity of mechanical ventilation	One case: 0.7% (patient X)
Awareness with recall (post-operative questionnaire)	None

acceptable results. Main anesthetic targets could be achieved in most of the patients. Even if it is irrefutable that further investigations should be performed in order to get reliable conclusions, this technique seems to be suitable for the anesthetic management of this population. Summarizing, in my experience TIVA (propofol TCI, midazolam and remifentanil) BIS-guided anesthesia provided:

- Rapid achievement of proper intubating conditions with low hemodynamic variation.
- Fast and successful recovery of respiratory function and consciousness.
- Absence of post-operative over sedation and or respiratory depression.
- Absence of awareness with recall.
- Quick recovery of spontaneous ambulating capacity.
- Easy and quick handling of different levels of analgesia according to changes in nociceptive stimuli (eventually by avoiding increments of plasmatic catecholamine levels that may increase ventricular work and myocardial oxygen consumption).
- High levels of analgesia even at the end of the surgical procedure without delaying recovery.
- Adequate peri-operative hemodynamic stability.
- Addition of routine BIS monitoring to this co-induction and co-maintenance scheme, even if not specially evaluated through a proper clinical trial, showed grossly evident reduction in all drugs doses requirements by simple clinical observation. This latter may result in potential economic benefits.

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ANESTHETIC MANAGEMENT FOR THE OBESE PARTURIENT

24

J.T. Sullivan & C.A. Wong

24.1 Introduction

The management of the obese pregnant patient presents numerous challenges to the anesthesiologist. In addition to the medical co-morbidities associated with obesity, there is an increased incidence of many pregnancy complications and a frequent need for operative management.

The number of case reports describing the management of obese parturients has grown exponentially as the incidence of obesity increases worldwide. These include sensational descriptions of Cesarean deliveries using regional anesthesia on patients with body mass indices (BMI) as great as 88.[1] However, the collection of these anecdotes does little to help the average practitioner make decisions based on sound evidence. There remains a lack of controlled studies to help guide decision-making in this clinical arena.

24.1.1 Gestational weight gain recommendations

There are no definitive recommendations for optimal weight gain during pregnancy. The Institute of Medicine report on nutrition in 1990 offered limited guidelines. The report recommended a 15 lb (6.8 kg) minimum weight gain but made no recommendation for maximal weight gain and no specific recommendations for obese women.[2] Ekblad and Grenman retrospectively reviewed the records of 191 mothers in Finland for the impact of gestational weight gain on labor outcome.[3] Women with abnormal pre-pregnancy weight (≥20% above ideal body weight for height) or excessive weight gain during pregnancy (≥20 kg) were included in the study. These patients were compared with 166 mothers with normal pre-pregnancy weight and normal weight gain during pregnancy. The investigators found that obese women were more likely to

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Table 24.1 Selected outcomes among morbidly obese patients stratified by gestational weight gain

	Weight loss or 0 lb (n = 51)[a]	1–15 lb (n = 153)	16–25 lb (n = 146)[b]	26–35 lb (n = 97)	>35 lb (n = 80)	P
Gestational diabetes	8 (15.7)	23 (15.0)	21 (14.4)	13 (13.4)	10 (12.5)	NS
PIH	6 (11.8)	21 (13.7)	20 (13.7)	12 (12.4)	17 (21.3)	NS
Cesarean delivery	13 (25.5)	41 (26.8)	42 (28.8)	34 (35.0)	27 (33.8)	NS
Mean birth weight[c]	3302 g	3192 g	3337 g	3506 g	3453 g	<0.05
Low birth weight[c]	1 (2.0)	17 (11.1)	12 (8.3)	5 (5.2)	3 (3.8)	[d]
SGA[c]	2 (4.0)	6 (3.9)	8 (5.6)	3 (3.1)	3 (3.8)	[d]
LGA[c]	6 (12)	18 (11.8)	27 (18.8)	25 (25.8)	19 (23.8)	<.01

NS, not significant; PIH, pregnancy-induced hypertension; SGA, small for gestational age; LGA, large for gestational age; Data are presented as n (%); [a]One death *in utero*; [b]Two deaths *in utero*; [c]Live births only; [d]Statistical analysis not meaningful.

require labor induction and emergency Cesarean deliveries compared to non-obese women. Noteworthy was that obese women with low pregnancy weight gain (≤5 kg) did not appear to have increased maternal or obstetric morbidity compared with obese women who had normal gestational weight gain. Edwards *et al*. also evaluated the pregnancy complication rate and neonatal outcomes of obese women relative to gestational weight gain.[4] They retrospectively studied 683 obese and 660 normal-weight women in the US who delivered singleton liveborn neonates. Obese women were significantly more likely to have pregnancy complications than non-obese women, however, the incidence of complications was not associated with gestational weight gain. In order to optimize fetal growth, they recommended that obese women gain between 7 and 11.5 kg (15–25 lb) and normal-weight women gain between 11.5 and 16 kg (25–35 lb). Bianco *et al*. conducted a large retrospective analysis of 613 morbidly obese women (BMI > 35) with singleton pregnancies and compared them with 11,313 non-obese women.[5] They also found an increased incidence of maternal complications including diabetes, hypertension, pre-eclampsia and arrest of labor in the morbidly obese compared with non-obese, and confirmed that the incidence of these complications were not influenced by maternal weight gain during pregnancy (Table 24.1). However, they recommended against gestational weight gain of >25 lb (11.4 kg) in the morbidly obese, as this was strongly associated with large for gestational age (LGA) infants.

24.1.2 Obesity in pregnancy: pathophysiology

Physiologic changes in obese pregnant women

Many of the anatomic and physiologic changes of pregnancy are accentuated by obesity. Oxygen consumption and carbon dioxide production, which normally increase during gestation, are increased further in obese women. Chest wall compliance and lung volumes are further decreased.[6] The supine position may worsen oxygen saturation and the Trendelenburg position may not be tolerated at all. Periods of apnea may rapidly lead to hypoxemia due to the combination of increased oxygen consumption and decreased functional residual capacity. Regional anesthesia, particularly techniques that result in significant thoracic motor blockade, has the potential to adversely affect respiratory mechanics by compromising intercostal muscle activity. During spinal anesthesia, the combination of small doses of neuraxial opioid with local anesthetics allows for the reduction of local anesthetic dose and may help minimize thoracic motor blockade and its adverse impact on respiratory physiology. However, at least one clinical study did not demonstrate a clinically significant worsening of hypoxemia in morbidly obese parturients following spinal anesthesia for Cesarean delivery.[7]

Cardiac output and blood volume are increased in both obesity and pregnancy. Several studies suggest a relationship between cardiomyopathy and obesity in pregnancy.[8,9] Women reported to have died in the peripartum period from cardiomyopathy and myocardial infarction in the UK had a high incidence of morbid obesity.[9]

Some of the physiologic changes at term, including pharyngeal edema and enlarged breasts, are exacerbated by obesity and may combine to make direct laryngoscopy more difficult. Rocke *et al*. conducted a prospective evaluation of the risk factors associated with difficult intubation in the obstetric population in a teaching hospital.[10] Obesity was initially identified as a risk factor for difficult intubation, along with short neck, protruding maxillary incisors and receding mandible. However, multivariate analysis eliminated

Table 24.2 Demographic characteristics among morbidly obese and non-obese women

	Obese (n = 613)	Controls (n = 11,313)	P
Weight (kg, mean ± SD)	104.7 ± 16.2	58.8 ± 7.1	<0.05
Age (mean, years)	27.5	28.7	NS
Non-white	504 (82.3)	4833 (42.7)	<0.01
College education	198 (37.1)	5669 (63.1)	<0.01
Multiparity	409 (66.7)	5068 (44.8)	<0.01
Married	304 (50.1)	8238 (73.4)	<0.01
Clinic service	449 (73.2)	3990 (35.3)	<0.01
Substance abuse	88 (14.4)	1049 (9.9)	<0.01
Pre-existing medical conditions			
Diabetes	45 (7.3)	183 (1.6)	<0.01
Chronic hypertension	33 (5.4)	40 (0.3)	<0.01
Asthma	102 (16.6)	749 (6.6)	<0.01

SD, standard deviation; NS, not significant. Data are presented as n (%).

obesity as an independent risk factor for difficult intubation because of its association with short neck. Hood and Dewan observed in an 11-year case-controlled study of parturients weighing >136.4 kg (300 lbs.) that obese were characterized more frequently as difficult to intubate (6 of 17) than non-obese controls (0 of 8).[11] They recommended that anesthesiology care providers assume that all obese parturients have difficult airways because of the prevalence of difficult tracheal intubation in their investigation.[11]

The risk of aspiration may be increased in an obese pregnant patient. It is unclear whether additional precautions must be taken in an obese pregnant patient to minimize the risk of potential gastroesophageal reflux and aspiration. There are no published studies addressing gastric emptying times in the obese parturient. Whether gastric emptying is prolonged compared with non-obese parturients is not known. Gestational diabetes, a frequent complication of pregnancy in the obese patient, probably does not cause gastroparesis as in chronic diabetes. However, the enlarged uterus exacerbates the anatomical changes (including a higher incidence of hiatal hernia) responsible for gastroesophageal regurgitation already present in obesity. In addition, pregnancy is associated with decreased gastroesophageal sphincter tone because of increased levels of progesterone.[12] Vaughn *et al*. reported that obese non-pregnant patients had increased gastric volume and lower pH. This presumably increases the severity of aspiration pneumonitis should it occur.[13] Whether these data can be extended to the pregnant population, particularly those who have received aspiration prophylaxis, is not known. In the absence of specific data on gastric emptying and risk of aspiration for the obese parturient, many practitioners utilize some form of aspiration prophylaxis (non-particulate antacids, histamine 2 antagonists and/or metoclopramide) and adhere to rigorous fasting guidelines in these patients.

Obesity and pregnancy are known risk factors for deep venous thrombosis.[14,15] Pregnancy alters the balance of anticoagulant and procoagulant activity. Obesity may be associated with a higher incidence of thrombosis because of hemoconcentration, decreased physical activity or more complex interactions of hemostatic mechanisms. The combined risk of obesity and pregnancy for the development of deep venous thrombosis has not been well studied, but it can probably be assumed that obesity further increases the risk in pregnancy.

Maternal co-morbidities

Obesity has been shown to be associated with numerous co-morbid diseases of pregnancy. Obese pregnant women are more likely to be hypertensive, diabetic, asthmatic and pre-eclamptic.[5,11,16] Sleep disordered breathing, including sleep apnea, is more prevalent in obese pregnant patients.[17] Evaluating the impact of obesity alone on labor outcomes is difficult because of the prevalence of associated diseases that also influence labor outcome. In addition, obese pregnant patients differ demographically from non-obese parturients that serve as the control group in many studies including these data from a teaching hospital in New York (Table 24.2).[5] Obese patients are less likely to be married and educated and more likely to suffer from substance abuse. In the US and the UK the incidence of obesity differs among ethnic groups.[5] These demographic factors may influence labor outcomes in

addition to obesity and the co-morbid illnesses associated with obesity. Some, but not all, clinical investigations of obesity have attempted to statistically correct for the impact of some of these variables on labor outcomes.

As in the anesthetic management of obese patients in other clinical environments, the technical and logistical challenges of caring for these patients are complicated by the management of these co-morbidities. Due to the anesthetic challenges presented, the American College of Obstetricians and Gynecologists acknowledges that "marked obesity" is an obstetric risk factor that should prompt an antepartum anesthesia consultation.[18]

24.2 Pregnancy outcomes

24.2.1 Maternal outcomes

The association of obesity with altered maternal outcomes in pregnancy has been well studied. Obesity (BMI > 30) has been associated with an increased incidence of labor induction, arrest of labor, Cesarean delivery, post-partum hemorrhage, infectious morbidity and peripartum maternal death. In addition, many of these adverse outcomes have a higher incidence in overweight women (BMI 25–29) compared with normal-weight women.[19]

Obese pregnant women are more likely to require inductions of labor.[11,16] The common reasons for induction are post-delivery date status, macrosomia, pre-eclampsia and other medical problems complicating pregnancy.[20] In addition, there is evidence that obese women, even if presenting in spontaneous labor, are more likely to have their labor augmented with oxytocin.[21] The duration of labor for morbidly obese primiparous and multiparous women who delivered vaginally has been shown to be comparable with non-obese controls, as was the incidence of instrument vaginal deliveries.[22] A few studies have described a higher incidence placental abruption and post-partum hemorrhage in obese parturients, but did not evaluate the possibility that other variables, such as pre-eclampsia or oxytocin induction of labor, influenced these data.[5,6]

A large number of studies now clearly identify obesity as associated with an increased incidence in Cesarean delivery.[5,11,16,23–26] The relationship has been reported in various clinical environments, including academic and community hospitals, high and low risk patients, and numerous racial and ethnic groups. However, many studies did not control for the high incidence of co-morbidities in this patient population.

Table 24.3 Frequencies of indications for Cesarean delivery

	Obese (n = 192)	Controls (n = 1806)
Arrest disorders	87 (45.3)	698 (38.6)
Fetal distress	28 (14.5)	240 (13.3)
Malpresentation	20 (10.4)	200 (11.1)
Prematurity	4 (2.1)	18 (0.9)
Placenta previa	3 (1.5)	25 (1.4)
Placental abruption	1 (0.5)	20 (1.1)
Cord prolapse	0 (0.0)	15 (0.8)
Failed forceps	1 (0.5)	11 (1.4)
Herpes	3 (1.6)	23 (1.3)
Ammionitis	6 (3.1)	79 (4.4)
Elective	29 (15.1)	303 (16.7)
Other	10 (5.2)	174 (9.6)

Data are presented as n (%).

In addition, most studies evaluating Cesarean deliveries are limited by poorly defined indications for operative delivery. Hood and Dewan prospectively collected data on obese parturients weighing over 136.4 kg (300 lb) between 1978 and 1989.[11] They compared these patients to a contemporary case control group. Of the 117 obese patients, 62% underwent Cesarean delivery compared with 24% of the control group. However, more concerning was that a higher number of obese patients required emergency Cesarean delivery.

The reason(s) for the increased Cesarean delivery rate is not clear but several theories have been proposed. The data suggest that, compared to non-obese control parturients, obese parturients have a higher incidence of "failed induction" or "failure to progress" or "arrest disorders"[5,11] (Table 24.3). It is unclear how obesity affects the physiology of labor, but high rates of macrosomia, oxytocin induction and prevalence of other medical problems probably play a combined role. Hood and Dewan reported a higher Cesarean delivery rate in obese vs. non-obese parturients after correcting for fetal macrosomia.[11] It has been suggested that obesity interferes with effective bearing down during the second stage of labor. However, Buhimschi *et al.* investigated the pushing performance of 52 women with singleton, vertex pregnancies and found that the efficiency by which pushing effort was converted into intrauterine pressure was directly related to BMI.[27]

Obese women have also been reported to have a lower success rate of vaginal birth after Cesarean delivery as compared with non-obese women.[28] Obese women have been shown to suffer from infectious morbidity at

a higher rate than non-obese controls.[5,11,16,24,29] Bianco *et al*. reported in their retrospective review that obese patients had a higher incidence of endometritis than non-obese.[5] Myles *et al*. retrospectively reviewed women who had undergone Cesarean delivery, excluding women with pre-existing chorioamnionitis.[29] Higher BMI was a significant independent risk factor for post-operative infection after both elective and non-elective Cesarean delivery.

Several studies suggest that there is an increased risk of maternal death associated with obesity. Analysis of cases reported in the Confidential Enquiries into Maternal Deaths in the United Kingdom 1994–1996 reveals several associations with obesity. Obesity was identified as a contributing factor in the peripartum period in deaths of women with hypertensive disorders, cardiac disease, pulmonary embolism and epilepsy.[9] Thomas and Cooper reported specifically on anesthetic contributions to maternal deaths in the Confidential Enquiries in the United Kingdom.[30] Of 142 peripartum maternal deaths during a 3-year period from1997 to 1999, anesthetic management was implicated in the cause of death in 20 cases. BMI was not analyzed independently and was noted to be a significant contributing factor in only one of these cases.

Endler *et al*. retrospectively analyzed maternal deaths in the state of Michigan in the US from 1972 to 1984.[31] There were 15 reported maternal deaths in this time period in which anesthetic management was considered the primary cause of death and four cases in which it was considered a contributing factor. Obesity was considered to be a risk factor in 12 of the 15 deaths. Over the 12-year period of the study there appeared to be a trend toward fewer anesthesia deaths related to complications of regional anesthesia and more deaths related to failed tracheal intubation.

In a final retrospective study of maternal mortality in the state of North Carolina in the US spanning a 40-year period, May and Greiss also noted an association between obesity and increased maternal mortality.[32]

24.2.2 Neonatal outcomes

In addition to the adverse impact on maternal outcomes during pregnancy, obesity has also been associated with concerning neonatal outcomes. Infants born to obese mothers have been shown to have a higher incidence of birth defects, macrosomia, and neonatal death.

Maternal obesity has been associated with an increase in offspring with neural tube defects, and is associated with an increased incidence of error in prenatal diagnosis.[33,34] Numerous investigations have demonstrated an independent effect of maternal weight on the occurrence of neonatal macrosomia.[5,24,35,36] Cnattingus *et al*. reported in a large epidemiologic study that obesity is associated with a lower incidence of premature delivery but a higher risk of fetal death at term.[37]

Bianco *et al*. identified retrospectively that morbidly obese patients were more likely to have meconium stained amniotic fluid.[5] This finding can be associated with post-dates status as well as neonatal depression. At least in this retrospective analysis, other measures of neonatal outcome, such as Apgar scores, were comparable to those of babies born to non-obese mothers.

24.3 Labor analgesia

24.3.1 Labor pain

Ranta *et al*. investigated the effects of obesity on labor pain and outcomes in a prospective, non-randomized, observational study in 53 obese parturients (BMI $>$ 30) and 609 non-obese parturient controls spanning a 3-month period in Finland.[22] There were no reported differences in labor pain for either primiparous or multiparous obese parturients compared to non-obese parturients despite the obese parturients having a greater estimated gestational age and larger babies (3865 vs. 3592 g, respectively). Fewer obese parturients complained of poor pain relief (12% of obese patients vs. 23% control).

24.3.2 Systemic opioid analgesia

There are numerous studies on the use of systemic opioids in labor but very few of these studies address the obese population specifically. Ranta *et al*.'s investigation of labor analgesia in obese parturients, although limited by a small number of patients, showed that the quality of pain relief with systemic meperidine was inferior to epidural analgesia and paracervical blockade, but similar to Entonox (50% nitrous oxide and 50% oxygen).[22] There are no data comparing different opioids in obese parturients. Theoretical risks with systemic opioids in the obese parturients include respiratory depression with hypoxemia and hypercapnia.

24.3.3 Paracervical blockade

Paracervical blockade with local anesthetic is an option for first stage labor pain but may be technically challenging in the obese population. Ranta *et al*. reported that paracervical blockade performed by obstetricians had to be repeated more often in obese parturients compared to the control group to maintain analgesia (20% vs. 9%, respectively, $P < 0.05$)

and the quality of analgesia overall was inferior as compared to epidural blockade.[22]

24.3.4 Epidural analgesia

Epidural analgesia in the obese parturients has been shown to be the most effective analgesic option despite the technical difficulties encountered.[22] The risks of neuraxial labor analgesia in obese parturients appear to be minor, but should be weighed against the benefits. Epidural labor analgesia may be preferable to other alternatives because of a higher rate of emergency Cesarean deliveries in obese patients and the higher incidence of difficult airway. Maternal deaths associated with the use of regional anesthesia for Cesarean delivery in the general population appeared to decline during the 1980s while those associated with general anesthesia were stable.[38] Motor blockade from any regional anesthetic technique has the potential to exacerbate existing respiratory compromise in a morbidly obese parturient. For this reason, care should be taken to minimize the degree of motor blockade by titrating the dose to the required sensory level and limiting the local anesthetic concentration to the minimum required concentration for adequate analgesia. Initiation of neuraxial analgesia in the obese parturients is frequently difficult. Hood and Dewan documented a 94% success rate for epidural labor analgesia in their obese population, but the obese parturients required more attempts to identify the epidural space and more commonly required catheter replacement (42% initial failure rate vs. 6%, respectively).[11] Early placement of an epidural catheter may be desirable to allow extra time for the procedure. The sitting position may be a better alternative than the lateral position, as this allows the adipose tissue to fall symmetrically to either side of the spine, and makes the midline easier to identify. The mid lumbar region is typically chosen for epidural catheter placement as it more closely approximates the dermatomes requiring blockade. It also takes advantage of the widest interspaces between spinous processes and minimizes the risk of spinal cord injury. Numerous investigators have documented the distance from the skin to the epidural space. Although the distance from the skin to the epidural space has been shown to be directly related to body weight, only rarely does this necessitate the use of non-standard length epidural needles.[39,40] Epidural needles longer than 9 cm are available from several manufacturers. As false loss-of-resistance is common when initiating epidural analgesia in the obese parturients, some anesthesiologists advocate confirming the correct placement of the epidural needle in the lumbar epidural space by advancing a small spinal needle through the dura, using the epidural needle as an introducer. The presence of cerebral spinal fluid in the spinal needle provides additional confirmation that the epidural needle is in the epidural space.[41]

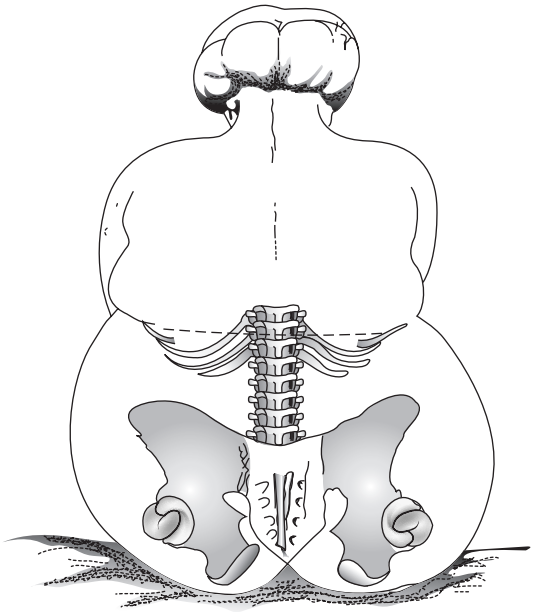

Figure 24.1 *Blass's line*: horizontal line connecting the apices of the bilateral fat pads.

Blass *et al*. elaborated on some of the technical challenges in placing an epidural catheter in the morbidly obese parturients and recommended catheter placement in a low thoracic interspace.[42] They described a cleft in the soft tissue of the morbidly obese parturients typically at the height of the low thoracic vertebral interspaces (Figure 24.1).

This cleft, referred to as Blass's line, represents an area of minimal adipose tissue and potentially the shortest distance from the skin to the epidural space. In their series of 15 morbidly obese patients, placement of a low thoracic epidural was successfully accomplished with minimal difficulty and required a longer needle in only two of their 15 cases. Potential disadvantages of this technique include sparing of sacral nerve roots and the inability to use a spinal needle to confirm epidural needle placement or initiate combined spinal–epidural analgesia (CSEA).

Controversy exists as to the optimal length of epidural catheter that should be advanced into the epidural space. If the catheter is advanced to a short distance (2 cm or less) there is a greater risk of inadvertent migration out of the epidural space. Hamilton *et al*. reported that changes in the position of the epidural catheter are associated with patient movement and that this phenomenon is likely increased in

patients with BMI > 30.[43] However, increasing the distance that a multiorifice catheter is threaded into the epidural space increased the incidence venous puncture and possibly unsatisfactory analgesia.[44] Inadvertent venous puncture may be higher in the obese parturients than in the non-obese (17% vs. 3% in one study).[22] However, this phenomenon is likely dependent on other technical factors, including the approach to the epidural space (midline or paramedian) and catheter type. Flexible, wire-reinforced, uniport epidural catheters have been shown in a randomized controlled trial to have a lower incidence of venous puncture when compared to stiffer, multiport catheters.[45]

Inadvertent dural puncture may occur more frequently in the obese parturients, but the incidence of post-dural puncture headache may be less. Faure *et al*. described a reduced incidence of headache following inadvertent dural puncture with a 17- or 18-gauge epidural needle in those with a BMI > 30.[46] In their retrospective review, the incidence of postural headache following recognized dural puncture was 45% among patients with normal body habitus and 16.4% of all patients required a therapeutic blood patch. Among patients with BMI > 30 only 24% had a postural headache and 12% of all patients required a blood patch. These data are probably limited by non-uniform criteria in the evaluation of post-partum headache. There are no data to suggest that there is a relationship between the efficacy of prophylactic or therapeutic epidural blood patch and BMI.

24.3.5 Combined spinal–epidural analgesia

CSEA has become popular in many institutions for labor analgesia because of its rapid onset and potentially improved analgesia compared with traditional epidural analgesia techniques.[47] There is a greater incidence of pruritus associated with CSEA compared with traditional epidural analgesia techniques although this is rarely a significant clinical problem.[48] Fetal bradycardia has been associated with CSEA. However, in a randomized trial that compared CSEA to traditional epidural analgesia, there was not a significant difference in the incidence of fetal bradycardia between the two techniques.[49] Rare patients experience respiratory depression and this potentially has more profound implications for obese parturients. However, the use of a low intrathecal opioid dose and ensuring adequate time has passed since any systemic opioid administration are both reasonable precautions.

This technique remains controversial in the obese population because of concerns of delay in recognizing a poorly or non-functioning epidural catheter in a population at higher risk for emergency operative delivery and at increased risk of difficult airway. Others argue that the incidence of failed epidural analgesia/anesthesia after initiation of CSEA is acceptably low and feel that these patients can benefit from the faster onset, potentially improved analgesia, and anatomic confirmation of the epidural needle placement in the epidural space inherent in the technique.

As with any neuraxial anesthetic technique, but particularly with spinal techniques where the intrathecal space is intentionally entered, the risk of damaging the spinal cord exists. Anesthesiologists frequently use the iliac crests as anatomical references for initiation of low lumbar neuraxial analgesia to avoid traumatizing the conus medullaris, which ends at or above the L_2 vertebral body in most patients. However, in a study on 100 volunteers comparing clinical examination with radiographic findings, Broadbent *et al*. found that anesthesiologists frequently erred by at least one interspace when estimating lumbar vertebral anatomy, and they typically believe that they are at an interspace than more caudad radiographical confirmed. Obesity further impaired the accuracy of interspace identification and this phenomenon must be recognized to avoid the potential of spinal cord injury.[50]

An intrathecal dose of opioid without local anesthetic as part of CSEA provides excellent early labor analgesia without compromising the ability to ambulate. No well-conducted study has identified significant outcome advantages of walking during neuraxial labor analgesia. Although there are some physiologic advantages of ambulation in the obese patient, the impact on labor outcome has not been studied.

Occasionally an extended length epidural needle is necessary to locate the epidural space in the obese patient. Long pencil-point spinal needles are available to use with a needle-through-needle technique if the anesthesiologist wishes to puncture the dura with a spinal needle, either for anatomic confirmation, or to initiate CSEA.

24.3.6 Continuous spinal analgesia

Another option for neuraxial labor analgesia in the obese parturients is continuous spinal analgesia. Local anesthetics and/or opioids delivered via a spinal catheter provide reliable and very flexible analgesia or anesthesia in a population that may have a lower incidence of post-dural puncture headache (see Section 24.3.4). This option may be particularly attractive following prolonged and difficult attempts at epidural placement that result in inadvertent dural puncture. The catheter can be advanced into the intrathecal space and analgesia can be initiated and maintained

with either intermittent boluses of local anesthetic and/or opioid, or a continuous infusion. However, there is a real risk that the spinal catheter may be mistaken for an epidural catheter. Total spinal anesthesia will rapidly ensue if an epidural dose of local anesthetic is injected into a spinal catheter. This complication would be particularly problematic to manage in an obese patient with a potentially difficult airway. Continuous spinal analgesia, if used in labor, requires explicit communication with colleagues and clear labeling of the catheter as intrathecal.

24.3.7 Inhalational analgesia

Inhalational anesthetics, either nitrous oxide with oxygen, or in combination with a volatile anesthetic such as isoflurane, are used successfully for labor analgesia in many parts of the world. Ranta *et al*. describe the use of Entonox (50% nitrous oxide and 50% oxygen) in an obese pregnant population and described no significant reduction in reported pain scores when used alone.[22] This stands in contrast to their reported significant reductions in pain scores in this obese pregnant population with epidural analgesia or paracervical blockade. The safety of inhalational analgesia is controversial in the non-obese laboring parturients because of the possibility of inducing loss-of-consciousness and depressing airway reflexes in the presence of a full stomach. This risk may be even less justified in the obese parturient population as they may be at even greater risk for pulmonary aspiration, difficult mask ventilation and intubation.

24.4 Cesarean delivery

24.4.1 Spinal anesthesia

Single shot spinal anesthesia has been used successfully for Cesarean delivery in the obese population. Although case duration is very institution and obstetrician dependent, there is evidence to suggest that Cesarean delivery duration is longer in the obese.[11,35,51] One of the limitations of spinal anesthesia is reduced flexibility in responding to longer duration surgery. Intra-operative conversion to general anesthesia in obese patients is potentially associated with more risk than in non-obese patients.

An additional theoretical concern is the predictability of the cephalad spread of sensory and motor blockade in obese patients. High blockade may exacerbate already compromised respiratory function, may adversely affect hemodynamic stability, and in extreme circumstances result in the need to secure a potentially difficult airway. It remains unclear whether a single intrathecal dose of local anesthetic results in higher sensory block in the obese vs. non-obese patient. It has been hypothesized that increased abdominal pressure in obese patients results in decreased spinal canal cerebrospinal fluid volume. This phenomenon has been demonstrated in a magnetic resonance imaging study.[52] Study results in non-pregnant patients after single shot hyperbaric bupivacaine spinal anesthesia are contradictory.[53,54] However, several investigations have demonstrated that the maximal cephalad sensory spread after using hyperbaric bupivacaine in term parturients for Cesarean delivery cannot be predicted based on the patient's height, weight or BMI[55,56] (Figure 24.2).

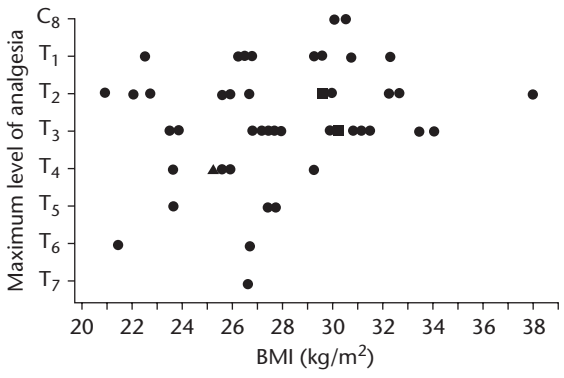

Figure 24.2 Relationship between height and maximum cephalad spread of blockade after 12 mg hyperbaric bupivacaine in 50 term parturients. ●, one patient; ■, two patients; ▲, three patients.

Body habitus was also not predictive of sensory level after hyperbaric lidocaine used for post-partum tubal ligation.[57] Taken together, the results of these studies suggest that alteration of hyperbaric bupivacaine dose based on body habitus is not helpful.

Small gauge spinal needles (25-gauge) commonly chosen because of the lower incidence of post-dural puncture headache lack the directional control of larger gauge needles, particularly after passing through greater amounts of soft tissue on the way to the intrathecal space. Alternative techniques to improve directional control include the use of less flexible larger gauge needles, or using an epidural needle as an introducer for the spinal needle.

24.4.2 Epidural anesthesia

Epidural anesthesia has several advantages compared with spinal anesthesia, including the ability to prolong anesthesia via the indwelling epidural catheter, the ability to titrate the dose, the slower onset of thoracic motor blockade and the ability to provide post-operative epidural analgesia. In addition, it may be easier to

control a large gauge epidural needle than a small gauge spinal needle when multiple readjustments of needle direction are necessary. However, there are no studies that document better outcome for any single neuraxial technique in the obese pregnant population.

Wallace *et al*. recommended the use of ultrasound guidance to facilitate the placement of epidural catheters in obese parturients for Cesarean delivery although this is probably not a commonly used practice.[58]

Regarding epidural dosing, a single study in 250 women undergoing Cesarean delivery with epidural anesthesia (0.75% bupivacaine, 20 ml) found a positive correlation between cephalad sensory spread and BMI.[59] In the absence of time pressure the dose of epidural local anesthetic should be titrated to affect in order to avoid an undesirably high sensory and motor block.

24.4.3 Continuous spinal anesthesia

The successful use of continuous intrathecal catheters for the management of Cesarean delivery has been described in an obese parturient.[60] The obese parturient may be an appropriate target population for this technique because of longer and unpredictable operative times, desire to avoid general anesthesia and the potentially lower post-dural puncture headache rate compared to non-obese parturients. In an urgent situation it may be faster to initiate continuous spinal anesthesia by advancing an epidural needle into the subarachnoid space quickly, rather than attempt to manipulate a small spinal needle. As with continuous spinal labor analgesia, there is a risk that the spinal catheter may be mistaken for an epidural catheter. It is controversial as to whether the incidence of post-dural puncture headache is reduced by the presence of an epidural catheter threaded through the dural puncture.

24.4.4 General anesthesia

Airway management options for the conduct of general anesthesia include intravenous, rapid-sequence induction with direct laryngoscopy; awake, fiberoptic intubation; and awake, direct laryngoscopy. The leading cause of maternal deaths due to complications of anesthesia in the US occur from the inability to intubate following the induction of general anesthesia.[38] Review of retrospective evidence suggests that this risk may be greatly increased by obesity.[11,31]

Rapid-sequence induction of general anesthesia in the obese parturient combines the risks of potentially difficult intubation, increased risk of aspiration and rapid oxygen desaturation with apnea. However, in a carefully selected obese pregnant patient this may be a reasonably safe option.

There are several techniques that can optimize conditions for laryngoscopy in the obese parturients (see also Chapter 21). The patient should be positioned in the sniffing position. This may require several hard pillows or blankets placed under the shoulders and even more under the head. This position with left uterine placement should also be used for patients following placement of neuraxial analgesia, as it improves the mechanics of breathing. Enlarged breasts in obese pregnant women can interfere with direct laryngoscopy. Several solutions are available, including attaching the laryngoscope blade to the handle after it is placed in the mouth, or taping the breasts out of the way. Datta and Briwa described the advantage of using a short-handled laryngoscope to avoid interference with large breasts while intubating obese parturients.[61]

Awake, fiberoptic intubation allows for controlled intubation of the trachea while preserving spontaneous ventilation. In addition to some form of local anesthetic topicalization, most drugs used for sedation in this setting, such as benzodiazepines and opioids, readily cross the placenta. However, many practitioners use sedation with awake, fiberoptic intubation in the pregnant patient as they feel the priority is to secure the airway under the best conditions possible. Opioids and benzodiazepines antagonists are available for the neonate if necessary. Specific techniques for fiberoptic intubation are described in Chapter 21.

There are a variety of creative solutions for airway management in obese parturients when circumstances are extreme or equipment is unavailable. One of the simplest, and potentially safest, is awake direct laryngoscopy following topical anesthesia of the airway. The technique, like all awake techniques, has the goal of preserving spontaneous ventilation. Cohn *et al*. have advocated the use of the Bullard laryngoscope in the management of obese parturients when a fiberoptic laryngoscope is unavailable for awake intubation.[62] Godley and Reddy have described the successful use of an intubating laryngeal mask airway (LMA) to facilitate an awake, fiberoptic intubation of the obese parturient.[63] Although potentially valuable as a conduit for awake fiberoptic intubation or in the emergency airway algorithm, the LMA used alone has limitations in obese patients who are prone to aspiration and may require high inspiratory pressures for ventilation.

Awake, blind nasal intubation has the advantages of preserving spontaneous ventilation in patients. However, nasal intubation has limitations in the

pregnant patient because of nasal mucosal engorgement and an increased risk for epistaxis.

24.4.5 Local infiltration anesthesia

In circumstances of extreme urgency (intravenous access is not immediately available or time must be taken to prepare for an awake fiberoptic intubation) Cesarean delivery anesthesia can be initiated or performed entirely with the infiltration of local anesthetic (lidocaine 0.5% or 1.0%).[64] The technique requires the expertise of the obstetrician, it has significant anesthetic limitations, and if large volumes of local anesthetic are used, a risk of local anesthetic toxicity.

24.5 Post-Cesarean delivery pain management

Options for pain management following Cesarean delivery are similar to those for the non-obese parturients and include systemic opioid, neuraxial opioid, and continuous epidural infusion and non-opioid analgesics techniques (see Chapter 29). Neuraxial opioid analgesia is commonly used following Cesarean delivery and its use in the obese patient population warrants a brief discussion.

24.5.1 Neuraxial opioid analgesia

The use of intrathecal or epidural opioid for post-Cesarean delivery pain relief is an effective form of analgesia. However, there is a theoretical concern about the increased risk of respiratory depression in the obese parturients. Delayed respiratory depression from neuraxial opioid administration remains a poorly understood phenomenon. Abouleish *et al*. identified obesity as a potential risk factor for respiratory depression in a prospective observational study of intrathecal morphine.[65] They studied the 24-h post-operative course of 856 women who received 200 μg of intrathecal morphine as part of a hyperbaric bupivacaine spinal. Respiratory depression, defined as a $SaO_2 < 85\%$ or a respiratory rate of 10/min or less, was observed in eight women, all of whom were "markedly obese". Subsequent to this study, dose response studies of intrathecal morphine after Cesarean delivery have demonstrated satisfactory analgesia at lower morphine doses when the morphine is combined with systemic non-steroidal anti-inflammatory medication. Since the risk of respiratory depression is dose related, this may decrease the risk of respiratory depression. Continuous neuraxial opioid techniques, such as patient controlled epidural analgesia (PCEA) may be inherently safer because the opioid dose is titatrated to affect. This has not been studied for post-Cesarean delivery analgesia. It is unclear whether neuraxial opioid analgesia is safer than alternative analgesia techniques, such as opioid delivered by patient controlled intravenous analgesia (PCIA) pump. At the very least, the use of neuraxial opioid analgesia in the obese post-partum patient should be limited to settings where reliable monitoring exists.

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POST-OPERATIVE CARE

SECTION 8

POST-ANESTHETIC CARE UNIT MANAGEMENT 25

J.C. Flores

25.1 Introduction

When managing the morbidly obese patient in the post-anesthetic care unit, similar procedures to those indicated for any other patient have to be applied, but special attention should be paid to the following factors: tracheal extubation, oxygenation, ventilation, positioning, platelet anti-aggregation and peri-operative pain management.

A preventive monitoring and careful surveillance must be carried out to early detect respiratory dysfunction, hypothermia, hemodynamic instability, thromboembolism and post-operative nausea and vomiting (PONV).[1]

Accordingly, appropriated resources should be available for diagnosis and treatment of these complications. Difficult tracheal intubation has been observed between the obese, and this topic should be considered as a potential factor influencing in dangerous complications.[2]

Even though, this matter remains controversial,[3–7] trained personnel with the same skills and technical resources necessary for tracheal intubation during induction of general anesthesia have to be available when planning or actually performing tracheal extubation, because it may be necessary an emergent tracheal re-intubation during recovery. Obesity is associated with greater peri-operative morbidity and mortality.[8]

The incidence of post-anesthetic desaturation is about three times higher compared to lean population. In addition, these individuals are at higher risk of pulmonary embolism, post-anesthetic nausea and vomiting and eventual gastric aspiration.[9]

These circumstances if not properly managed could lead to life-threatening situations and other complications within which the infections stand out. They may grossly increase the costs and institutional legal risk, prolong hopitalization and constitute a remarkable indicator of low quality medical care.[1,10]

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Obesity, its complications, and treatments have to be considered as the major concern for the anesthesiologist.

25.2 Guide of procedures for the obese patient's post-anesthetic care

Trying to focus on the most important topics for the anesthesiologist who would accept the challenge of dealing with this kind of patients, the authors introduce the items that according to the current knowledge must be part of a recommendation guide, within which it is not advisable to have controversy. In this sense, scientific bibliography offers consensus about the following proposals for the obese patients' post-anesthetic care.

25.2.1 Extubation criteria

Extubation criteria should be systematically used in obese patients. It has to be noticed that especial consideration has to be taken in particular situations such as: obesity hypoventilation syndrome (OHS), obstructive sleep apnea syndrome (OSAS) and the Pickwickian syndrome. Due to the higher risk for post-operative respiratory dysfunction observed between patients with the latter syndromes, the topic will be discussed in a separated section.[9,11]

Recommended extubation criteria are the following:

a Before extubation, patient must be fully awake, alert and able to hold his head up for 5 s.
b Confirmation with neurostimulator of reversion of muscular relaxants effects.[12–19]
c Respiratory rate below 30 breaths per minute.
d Oxygenation and ventilation evaluation:
- arterial blood gases should be equal or better than pre-operative values for a F_iO_2 delivered between 40% and 50%;
- If pre-operative values are not available, acceptable post-operative blood gases should be: pH between 7.35 and 7.45, PaO_2 higher than 80 torr and $PaCO_2$ lower than 45 or 50 torr.[20,21]

e Evaluation of lung mechanics having as reference values:
- maximum inspiratory force between 25 and 30 cmH_2O;
- vital capacity over 10 ml/kg based upon ideal body weight (IBW);
- tidal volume over 5 ml/kg based upon IBW.

f Hemodynamic stability must be confirmed.
- Hemodynamics in the morbidly obese is another outstanding issue to be deeply analyzed (see Chapters 5 and 6). Cardio-respiratory changes usually happen in any kind of patient after general anesthesia especially in upper abdominal or thoracic surgery. In obese patients, position related cardio-respiratory changes are much more pronounced[22–24] (see Chapter 20).

Consequently, once hemodynamic stability is achieved, trachea should be extubated with the upper body elevated between 30° and 45°. This position improves pulmonary compliance and also oxygenation, therefore, it should be maintained when the patient is transferred from the operating room to the post-anesthetic care unit and ideally also during the subsequent post-operative days.[25–27]

If morbidly obese lies in supine position, intra-abdominal viscera cephalic displacement will interfere with diaphragmatic impedance and mobility, thus negatively affecting the respiratory function. In addition and mainly in extremely obese patients or those with co-existing cardiac disease, or after surgeries with significant fluid replacement, supine position could dramatically increase right and left ventricular filling pressure, thus affecting cardiac performance and even sudden death may occur. Finally, also aortic or vena cava compression may happen due to the added weight of abdominal wall and viscera. This situation could significantly decrease right and left ventricular preload.[22,28,29]

Obesity hypoventilation syndrome, obstructive sleep apnea syndrome and Pickwickian syndrome

See also Chapters 2, 4 and 9.

Obstructive sleep apnea syndrome

This is a respiratory disorder characterized by sleep disruption due to increased ventilatory efforts caused by upper airway closure; as a consequence daytime sleepiness appears. For final diagnosis polysomnography is necessary.[30]

Obesity hypoventilation syndrome

Is that characterized by chronic daytime hypoventilation, extreme obesity and *hypercapnia* not related to obstructive pulmonary disease.[31,32]

Pickwickian syndrome

It is the clinical stage, when symptomatic *cor pulmonale* develops as a consequence of severe OHS.[33]

A deep knowledge about these conditions is essential for the anesthesiologist for the following reasons:

- Morbid obesity has a clear correlation with the incidence of these affections.[30,34–38]

- These respiratory disorders are associated with increased morbidity and mortality.[39]
- They may develop chronic daily hypoxemia.
- Co-existence of chronic daily hypoxemia should be known pre-operatively, because if this condition is present there will be increased chances of pulmonary hypertension and cor pulmonale.[40–42]
- Associated difficult mask ventilation and/or tracheal intubation have been observed between these subjects.[43,44]
- Commonly oxygen saturation decreases much faster after apnea.
- Severe respiratory depression related to peri-operative administration of hypnotics and opioids were informed.[45–47]
- Some kind of peri-operative respiratory support measures such as continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) have to be considered ideally since pre-operative period, because they are able to improve pre-operative cardio-respiratory function and may achieve a better post-operative cardio-respiratory performance.[48–53]

25.2.2 Monitoring and prevention of post-anesthetic respiratory dysfunction

a Continuous assessment of respiratory efficiency.
During immediate post-operative period continuous and careful observation must be carried out in order to early detect respiratory dysfunction. All precautions for an emergent tracheal intubation have to be considered (permanent proper positioning, adequate technical resources, trained personnel immediately available).

b Continuous monitoring with pulse oximetry and systematic oxygenation of all obese patients in the post-anesthetic period must be carried out.[54]
Obesity has shown a strong correlation with hypoxemia. Patients with body mass index (BMI) over 25 have increased risk of post-anesthetic hypoxemia. Post-operative hypoxemia is observed (PaO_2 lower than 60 mmHg) in about 75% of obese subjects vs. 25–30% of non-obese population. Supplementary oxygen has to be administered in the first 24 h and in many cases up to 72 h after surgery, with the upper body elevated 30–45°.[26]
If patients are not extremely obese and do not suffer co-existing cardio-respiratory disorders (for example, 35 BMI female with no co-morbidities) strategies to reduce costs should be taken into account.
Downs *et al.* consider that routine oxygen administration would not be necessarily beneficial, since it may develop atelectasis from absorption, and thus increase pulmonary shunt. Additionally it may delay airway obstruction diagnosis.[55]
Dibenedetto *et al.* studied the necessity of post-anesthetic supplementary oxygen administration by pulse oximetry monitoring during post-anesthetic period. He observed that 63% of the patients had acceptable oxygen saturation and did not require supplementary oxygen.[54]
Thus he ratified observations from other studies that have shown that an important percentage of patients have post-anesthetic oxygen desaturation and that supplementary oxygen delivery partially repairs the problem.
In addition a reduction in oxygen expenses of 30,000 dollars over 307 patients has been also demonstrated.[56–59]

c Prevent tracheal tube displacement. There is a higher incidence of tracheal tube misplacement in morbidly obese patients. Correct tracheal tube position has to be carefully controlled mainly when changing surgical-anesthetic position, transferring to post-operative care unit (PACU) or if prolonged intubation is required. It is advisable to confirm proper tracheal tube placement after any of these situations. Since hypoxemia is more frequent during intra- and post-operative periods in these subjects, and many different mechanisms could be involved, inadvertent bronchial intubation has to be permanently present in our minds.[60]

d Confirmation with neurostimulator of effect reversion of NMR.[12–19]

e Assessment of sedation and residual drug effects and exceptional administration of antagonists.

25.2.3 Positioning

Positioning the morbidly obese individual is a topic of enormous importance not only during anesthesia but also during all post-operative period (see Chapter 20). Proper position has to be maintained constantly. The reasons involved for these *strong recommendations* are related to the following factors:

- Prevention of position related injuries (especially in unconscious individuals) and patient discomfort.[61–63]
- Improvement on cardio-respiratory function.[22,25–29]
- Improvement of proper conditions for mask ventilation or eventual emergent tracheal intubation.[64,65]

Conclusion: post-surgical morbidly obese patient has to be constantly positioned with upper body elevated between 30° and 45°.

25.2.4 Recovery of consciousness

Factors eventually involved on the recovery of consciousness in the morbidly obese have to be known in

detail in order to prevent respiratory depression and subsequent complications.

- Temperature management. Hypothermia has to be avoided because it negatively affects time to wakefulness. By using heating systems of forced air, a significant improvement of the Aldrete's score was observed. In unconscious subjects, burn risk has to be considered when treating hypothermia.[66]
  It has been proved that hypothermia prolongs the anesthetic agent effect and delays the conscience recovery. In addition, it decreases the host's defenses, it increases the incidence of coagulopathy and it can affect the myocardial contractility and the hemodynamic stability. In addition, post-operative shivering and consequent increase in oxygen consumption and carbon dioxide production, may be dangerous in cardiovascular compromised patients[67] (see post-operative shivering in Chapter 23).
- The pharmacological properties of each anesthetic agent and/or adjuvant administered at least in the last surgery hour and during the post-anesthetic recovery of these patients have to be taken into consideration (for example, opioids and NMR, but also benzodiazepines and anesthetics in general). Eventual accumulation, impaired hepatic metabolism and/or renal or respiratory elimination may affect recovery of consciousness[29,68–72] (see Chapters 15, 22 and 23).
- Glycemia. Alterations in glucose metabolism is important for the anesthesiologist taking care of the morbidly obese patients (see also Chapters 9 and 10). Diabetes mellitus and insulin resistance are between the most frequent co-morbidities of obesity.[73–75]
  Alterations in plasmatic glucose levels may be one of the mechanisms involved in delayed recovery of consciousness, but further than this only misadventure, also severe complications may develop. In addition, many of these patients are under chronic or at least pre-operative insulin treatment and if this is the case they must continue during immediate post-operative period. Finally, a clear improvement of outcomes has been demonstrated when tight blood glucose control is achieved and maintained especially in those patients requiring post-operative intensive care unit (ICU) admission.[76–78]

25.2.5 Hemodynamic evaluation

Cardiovascular function may be significantly affected in the morbidly obese. Patho-physiological changes have been already deeply analyzed in the book so they will not be further discussed in this chapter (see Chapters 5, 6 and 11).

Nevertheless, careful hemodynamic evaluation is essential during post-anesthetic recovery of these particular individuals for the following reasons.

- Morbid obesity is strongly associated with arterial hypertension,[79,80] coronary artery disease,[81–86] and ventricular dysfunction and/or heart failure.[87–98]
- It is unquestionable that co-existing cardiovascular disease do influence on peri-operative outcomes.[99]
- Duration of obesity, BMI and central distribution of adipose tissue correlates with the severity of cardiovascular diseases.[100–102]
- These situations may lead to significant intolerance to stress situations such as many peri-operative circumstances (pain, hypoxemia, hypercapnia, hypothermia and shivering, large fluid replacement, improper positioning, etc.); thus increasing chances for severe and life-threatening cardiovascular complications.[103]
- Hemodynamic monitoring may result difficulty in the morbidly obese for obvious anatomical reasons. Non-invasive blood pressure would not be reliable since many obese individuals have large circumference and conic shaped arms thus making almost impossible to properly fit the cuff. In these cases arterial non-invasive blood pressure should be monitored at the forearm. Baseline measures have to be registered and peri-operative tendency have to be considered as a useful guide.[104]
- Invasive hemodynamic monitoring and echocardiography could also be more difficult for similar reasons. Invasive monitoring should be indicated according to every individual case since routine invasive monitoring has not demonstrated to be significantly beneficial in the post-operative care of bariatric patients.[105]

Accordingly, recommendations for hemodynamic monitoring are:

- adequate technical resources should be available (for example, extra large cuffs);
- consider non-invasive arterial blood pressure monitoring at the forearm;
- have always a baseline register and do consider the peri-operative tendencies;
- identify those patients that may need invasive monitoring and take into account the extra time that may be necessary to achieve a proper vascular access.

25.2.6 Post-operative nausea and vomiting

Even if the obese patients seem to have higher incidence of post-operative nausea and vomiting (PONV),

this topic remains controversial. Kranke in a recent systematic revision concluded that increased BMI is not a risk factor for PONV.[106]

Nevertheless, many factors associated with a higher incidence of PONV are present in the morbidly obese such as: increased gastric content with decreased pH, higher intra-abdominal pressure, longer time required for gastric emptying, and reduced efficiency of gastro-esophageal anti-reflux system.[107–110]

As commented before, mask ventilation could be difficult in the obese mainly if OSAS co-exists. Thus during mask ventilation prior to tracheal intubation, gastric over-distension may occur due to higher pressures or volumes applied, adding a different mechanism for post-operative vomiting.[111]

In fact these factors could also be involved in a higher incidence of gastric aspiration during induction of general anesthesia or after tracheal extubation in the obese individual. Nevertheless the latter is still controversial (see Chapter 8).

During post-anesthetic period, pharmacokinetic properties of certain drugs (highly lipophilic and/or long off-set) or functional ventilatory alterations (influencing in volatile agents elimination time) may induce a longer exposition to different mechanisms that may also increase PONV.

Anesthetic drugs such as etomidate, ketamine, halogenated agents, opioids and others are associated with increased risk of nausea and vomit, therefore drugs with no effect or even with demonstrated anti-emetic action should be of choice such as propofol, midazolam or thiopentone.[112–115]

Finally according to the comments above, a preventive strategy should be planned taking into account the following:

a Gastric content pH and volume (pre-operative, but not during induction, intra-gastric tubing if necessary, for example, full stomach in not emergent surgery).
b Consider the use of drugs that reduce gastric juice production and acidity (such as ranitidine).
c Consider the use of anti-emetic drugs since the immediate pre-operative period. The following have proved anti-emetic efficiency: anti-histaminics, anti-cholinergics, phenothiazines, butyrophenones, dopamine and serotonine antagonists, and corticoids between others. Nevertheless, the first choice should be those that do not cause central nervous system (CNS) depression such as: metoclopramide, ondasetron, granizetron, and dexamethasone.[116–118]
d Semi-sitting position.
e Avoid excessive volume and/or pressure during mask ventilation.
f Treat anxiety or fear.
g Consider post-operative analgesic strategy, titrating opioids if necessary in order to achieve acceptable pain relief (intense pain may induce nausea and vomiting) but avoiding high doses that could lead to respiratory depression and also increased chances of PONV.
h Finally consider also particular case factors such as gastric blood content due to intra-anesthetic maneuvers (for example, naso-tracheal intubation, naso-gastric tubing).

25.2.7 Post-operative pain management

Acute pain results in several physiologic changes. It is well recognized that in general surgical population, alterations related to untreated or under-treated pain may result in higher incidence of respiratory complications such as atelectasis, pneumonia, and hypoxemia, cardiovascular complications such as arterial hypertension, tachycardia, arrhythmia and myocardial ischemia. In addition alterations in peripheral circulation may increase the incidence of thromboembolic events and also would interfere with wound healing and protective immunologic mechanisms against infection. Digestive, urinary and muscular function are also affected.[119–132]

It is clear that morbidly obese patients may have a reduced tolerance to this kind of physiologic alterations and subsequent complications. Therefore, this could be an important mechanism to be considered as responsible of a higher incidence of these complications and increased mortality observed between them.[8,33,133]

On the contrary, adequate pain management have demonstrated to reduce this alterations and eventual complications.[134]

Rawal *et al*. in a controlled, randomized, double blind and prospective study assessed the pain treatment efficiency in obese patients undergoing gastroplasty surgery. He proved that with the analgesic technique with epidural thoracic morphine (4 mg of morphine/24 h) in t8 vs. intra-muscular morphine (0.1 mg/kg), the patients were more alert and able to stand the respiratory physiotherapy techniques, with less respiratory and thrombo-embolic complications and short hospitalization times.[135]

Many post-operative analgesic regimes are currently used. This topic has been developed in other chapter so will not be discussed here in detail (see Chapter 29).

But anyway it has to be emphasized that a peri-operative analgesic scheme must be carefully planned and organized according with the American Society of Anesthesiologists (ASAs) Guidelines.[136]

Finally the recommendations to improve the treatment of post-operative pain should be:

- assess and record pain systematically and involve the patient whenever possible;
- measure pain intensity not only at rest, but also on cough and movement;
- nominate a staff member to take responsibility for the management of pain relief policy after surgery in each hospital;
- establish an acute pain team;
- use existing and effective pain relief modalities, and introduce new methods when a benefit is proved;
- audit and continuously appraise activity.[137,138]

25.2.8 Scores to assess the post-anesthetic recovery

Since morbidly obese patients do require similar physiological surveillance than any other patient, such as cardiovascular performance, respiratory sufficiency, muscular activity, neurological function, temperature, etc., currently used scores should also be applied in this population to assess post-anesthetic recovery.[139–141]

25.2.9 Delegation of responsibilities

Standards such as those approved by the ASAs have to be implemented. They should specifically include the patient's transport, hospitalization and record, transfer to other professional, continuous care, and discharge.[142]

Summarizing:

- All the patients shall receive appropriate care.
- Patients shall be accompanied and informed about the way the responsibilities shall be delegated.
- Patient's re-evaluation and reports shall be carried out.
- Patient's state or condition shall be continuously assessed while he is in the post-anesthetic care room.
- A physician shall be responsible for the patient's discharge and the criteria shall be approved by the anesthesia department.

25.2.10 Surveillance according to prevent the most frequent complications

Post-operative mortality in obese patients is 2½ times higher than in non-obese.

The most serious post-operative complications are pulmonary dysfunction, surgical wound infection and thrombo-embolism.[29]

Early recovery of ambulating capability is the great objective that may reduce the incidence or severity of all the three potentially life-threatening situations.

Respiratory dysfunction

In Forest's study post-operative respiratory failure was more frequently present in old patients, with previous cardio-respiratory problems who are overweight and undergo urgent major surgery (thoracic and/or abdominal).[143]

As commented before obese patients show higher post-operative pulmonary morbidity than lean population, such as atelectasis, aspiration and ventilatory failure.[33,133]

The following measures are useful to prevent the post-operative atelectasis:

a early ambulating;
b thoracic physical therapy;
c spirometry with incentive;
d effective coughing;
e deep breathing;
f avoid prolonged rest.

The incidence and severity of post-operative respiratory complications are higher in those patients with OSAS, OHS or Pickwickians. It is important to identify these syndromes with their own clinical characteristics (for example, hypoxemia, hypercapnia, cor pulmonale), to distinguish them from other complications that may occur during the post-operative period.

Reasons to be extremely alert when taking care of a morbidly obese with some kind of obstructive breathing disorder during recovery have been already discussed (see OSAS, OHS, and Pickwickian syndrome in *extubation criteria*).

At this point it will be considered what kind of therapy may improve ventilatory and/or cardiovascular performance in these particular situations during post-operative period. It will not be discussed here all possible treatments for these disorders such as surgical or others (see Chapter 26).

During recovery the most important measures to be taken would be: appropriate positioning and ventilatory assistance.

Adequate position and its extraordinary importance in this especial situation have already been commented.

Ventilatory assistance could be applied by two different methods: CPAP and BiPAP.

The objective of both methods is to prevent airway collapse due to decreased pharyngeal muscle tone by splinting upper airway walls through a CPAP system.[144,145,146]

CPAP has shown to be beneficial for both respiratory and cardiovascular dysfunction.[147]

Nevertheless, it has to be taken into account that sometimes CPAP may not be effective, and that patient's adaptation to the system in this sense is of major concern.[148]

This has to be considered during pre-operative evaluation because a training period to achieve the best patient's compliance and to get the highest benefits may improve the post-operative management.

By the use of BiPAP inspiratory and expiratory pressures may be adjusted at different levels. This is important for a better patient compliance because a highest pressure is required during inspiration to prevent airway collapse, but such a high pressure during expiratory time interferes with exhalation and produces patient discomfort and eventually worsens his compliance to the system. In addition, as lower pressures would be applied to the respiratory system, risk of barotrauma would also be reduced.[149,150]

Surgical wound infection

It is important to highlight the role of factors that may be involved in a higher incidence of surgical wound infection such as poor tissue oxygenation and perfusion, co-existance of diabetes mellitus mainly if not well controlled, previous cutaneous infections, surgical factors (such as duration of the procedure), negligent nursing management and others.

Kabon has proven that a 30° head elevation improves tissue oxygenation compared to horizontal and other positions. However, obesity may affect peri-operative tissue oxygenation.[151]

A poor perfused and hypo-oxygenated tissue will affect surgical wound healing and certainly will increase the incidence of infection.

Recommended measures to reduce the incidence of wound infection are as follows:

- Pre-operative antibiotic prophylaxis according to every surgical and clinical case (see Chapter 13).
- Appropriate position.
- Adequate pain management (see Chapter 29).
- Stable and efficient hemodynamic and respiratory function.
- Early recovery of ambulating capability.
- Pre-operative skin care. (cutaneous folds).
- Peri-operative tight control of blood glucose levels (see Chapter 10).
- Meticulous nursing care (see Chapter 28).

Taking into account that the possibility of post-operative wound infection depends on many different factors, it has to be assumed that in order to minimize its incidence, a rational peri-operative planning and implementation is necessary.

If any of the preventive measures are applied in an isolated fashion, the results would be obviously uncertain. On the contrary if *these measures are systematically implemented all together they will provide the patient a reasonable secure assistance.*

Consequently, a multidisciplinary approach, (as in many other aspects involved in the peri-operative care of the morbidly obese surgical patients), seems to be the most appropriate way to obtain better outcomes (see Chapters 1 and 13).

Pulmonary thrombo-embolism

Deep vein thrombosis and pulmonary embolism have been informed to be more frequent between obese individuals.[29] Nevertheless recently observations regarding their incidence in bariatric patients have brought controversy.[152]

It has been observed that most bariatric surgeons affiliated to American Society of Bariatric Surgery (ASBS) consider that these patients have a higher risk for thrombotic events according to previous reports.[153] In fact most of them informed deaths due to pulmonary embolism between their patients.

In Barba and Wu survey it was observed a great difference between the thrombo-prophylaxis applied by different bariatric teams. But the most surprising observation was that the incidence of thrombotic events did not differ from that informed in non-obese population. They hypothesized that this fact may be related to the common practice between bariatric teams of routine thrombo-prophylaxis [152,154,155]

Mantilla and colleagues observed during a study period of 10 years, between 9721 patients undergoing elective hip or knee arthroplasty 116 thrombotic events within 30 days of the primary surgery. These authors observed as independent risk factors for relevant thrombo-embolic events (deep vein thrombosis and pulmonary embolism):

a obesity;
b poor physical condition according to the ASAs status;
c lack of post-operative thrombo-prophylaxis.[156]

As a result, in addition to planning the peri-operative analgesia as it has been mentioned before, the thrombo-prophylaxis has to be specifically planned in obese patients since the lack of thrombo-prophylaxis and obesity are independent predictors of relevant thrombo-embolic events (see Chapter 12).

Pulmonary embolism in these patients already prone to respiratory complications, happens to be a complication that threatens life.

25.3 Recommendations

a Systematic extubation criteria have to be used. Especial care will be necessary for those patients with OSAS, OHS, or Picwickians.

b Monitoring for early diagnosis and treatment of post-anesthetic respiratory depression is essential. All precautions for an emergent tracheal intubation have to be considered (permanent proper positioning, adequate technical resources, trained personnel).

c Adequate positioning is essential for a better cardio-respiratory function, mask ventilation and eventual emergent tracheal intubation.

d Factors that may alter recovery of consciousness have to be carefully considered and accordingly managed (peri-operative drugs pharmacological profile, hypothermia, hypoxemia, hemodynamics and glucose level).

e Consider that hemodynamic monitoring could be problematic. Identify those patients that may need invasive or especial monitoring.

f Prevention of nausea and vomiting must be included in a protocol.

g Peri-operative pain management should be carefully planned and applied. Adequate post-operative pain control will reduce the incidence and severity of the most frequent and dangerous complications in these patients. Especial care has to be taken with those patients with OSAS, OHS and Pickwickians, since they are more prone to respiratory depression induced by hypnotics and/or opioids. It has to be organized in accordance with the ASAs Guidelines.

h Scores to assess post-anesthetic recovery must be always implemented.

i To delegate responsibility, standards such as those approved by the ASAs have to be used.

j Meticulous surveillance has to be oriented to the prevention of the most frequent complications (respiratory dysfunction, pulmonary embolism and surgical wound infection). Early recovery of ambulating capability will be beneficial for their prevention. Systematic care and appropriate pain management are essential issues to reach this goal.

k Multidisciplinary approach and careful peri-operative planning and implementation should be considered a gold standard of medical care for any bariatric team (see Chapter 1).

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RESPIRATORY MANAGEMENT 26

E. Fam & P.E. Marik

26.1 Introduction

Obesity is a major health problem worldwide. The number of overweight men and women in the US has risen steadily since 1960. According to the most recent epidemiological survey, a staggering 64.5% of the adult population in the US are overweight with 4.7% being morbidly obese.[1] Obesity has been linked to increasing morbidity and mortality from numerous medical disorders including non-insulin dependent diabetes mellitus, hypertension, dyslipidemia, cardiovascular and cerebrovascular disease, and many malignancies. It is speculated that morbid obesity increases the incidence of complications in patients requiring hospitalization and this may be associated with an increased hospital length of stay and poorer outcome.[2] As obesity has a major impact on the respiratory system it is likely that the increased morbidity and mortality of hospitalized obese patients is related to an increase in pulmonary complications.[3] This chapter will review the impact of obesity on respiratory function, its associated morbidity and finally the particular clinical management.

26.2 Obesity and the respiratory system

Obese persons are at increase risk of developing respiratory complication such as atelectasis, pneumonia, pulmonary embolism, aspiration pneumonia and acute respiratory failure, particularly in the post-operative period[3] (see Chapter 4). Obesity is the most common factor predisposing to the obstructive sleep apnea (OSA) syndrome.[3,4] A body mass index (BMI) one standard deviation above the mean is associated with a fourfold increased risk of OSA. A subgroup of obese persons develop chronic daytime hypoventilation defined by a sustained increase in arterial carbon dioxide tension >45 mmHg; this syndrome is known as the obesity hypoventilation syndrome (OHS)[5,6] (Table 26.1).

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Table 26.1 Pathological factors involved in OHS

Impaired central drive
Respiratory muscle fatigue
Increased work of breathing
Decreased respiratory compliance
Decreased muscle strength
Abnormal ventilatory load compensation
Coexistent chronic obstructive airway disease or OSA

26.2.1 Obesity and respiratory dynamics

Lung volumes

The degree of obesity, age, body fat distribution (central or peripheral) and smoking history all interact to alter normal pulmonary physiology. In several studies, the expiratory reserve volume (ERV) has been consistently decreased while the forced expiratory volume in 1 s (FEV_1) to forced vital capacity (FVC) ratio is normal or increased.[7–9] The fall in ERV is presumably due to small airway closure.[10] The vital capacity (VC), total lung capacity (TLC) and functional residual volume (FRV) are generally maintained in otherwise normal individuals with mild to moderate obesity but are reduced by up to 30% in morbidly obese patients. These latter changes occur predominantly in patients with central obesity.[11,12]

Pulmonary compliance

Sharp *et al*. reported that in simple obesity, chest wall and total respiratory system compliance were 92% and 80%, respectively, of predicted normal values.[13] These values were substantially lower in patients with OHS whose chest wall and total respiratory compliance were 37% and 44% of normal.[13,14] The lung compliance is decreased by approximately 25% in simple obesity and 40% in OHS.[15,16]

The mechanical effect of obesity causing a decrease in chest wall compliance may not completely explain the altered compliance with obesity. Although excess weight does present an added inspiratory load, it is of the threshold type. The inspiratory threshold load is defined as the load the respiratory muscles most over come before airflow can begin. When the chest wall and respiratory compliance are measured with pulse airflow technique that allow the separation of threshold from other respiratory loads, chest wall compliance is relatively normal in simple obesity.[16]

Airway resistance

No major effect of obesity on airway function would be anticipated and in general, none have been demonstrated in studies confined to non-smokers. An increase in airway resistance measured by plethysmography has been reported, but this is attributed to low functional residual capacity (FRC), as specific airway conductance was normal.[17,18] Some studies have suggested a reduction in maximal expiratory flow at a small lung volume implying narrowing of the small airways, but in most this is probably an effect of smoking.[18–20] In one study in which obese non-smokers were compared with appropriate controls, a small reduction was seen but this was of borderline statistical significance and was found only in men.[17] The FEV_1 divided by the FVC ratio (FEV_1/VC) is normal, which implies that the increased airway resistance is present in the lung tissue and small airways rather than the large airways.

Respiratory muscle function

Reports on the effects of obesity on respiratory muscle function have been conflicting.[15,20] In morbid obesity a reduction of approximately 30% in respiratory muscle pressures have been reported. Muscles biopsy specimens and measurements by computerized tomographical (CT) scan density show fatty infiltration of non-respiratory skeletal muscles in obese individuals.[3] A single report describes fatty infiltration of the diaphragm in a patient with OHS.[21] The extent to which this affects muscle strength is unclear. Newham and co-workers reported an increased density of quadriceps accompanying weight loss after bariatric surgery but there was no corresponding increase in strength of the muscle as assessed by the maximal volumetric contraction.[17] However, a recent report showed increased maximum respiratory pressure (PiMax) 6 months after bariatric surgery.[22,23] Similar improvement in the endurance of non-respiratory muscle function has been reported following weight loss.[24] It seems likely that respiratory muscle function in obesity is compromised both by the increased load which the muscles are required to overcome and by some reduction in their capacity. An adverse load/capacity ratio is likely to contributes to the breathlessness and reduce respiratory reserve.[3] Furthermore, over-stretching of the diaphragm, especially in the supine position, would place this muscle at a mechanical disadvantage leading to decreased inspiratory muscle strength and efficiency.[3,25] Patient with OHS have both increased work and impaired muscle endurance and efficiency. It is, therefore, not surprising to find evidence of respiratory muscle fatigue in these patients.[3]

Metabolism and work of breathing

The basal metabolic rate and consequently the rate of total body oxygen consumption increase as weight

increases.[26] However, since adipose tissue has lower metabolic rate the increase in oxygen consumption is less than the increase in weight. Consequently, if oxygen consumption is standardized by expressing it per kilogram body weight, values lower than normal values are obtained in obese individual. In healthy non-obese persons the oxygen consumed by the work of breathing at rest is 3% or less of the total.[26] The elevated total respiratory resistance and compliance and respiratory threshold load associated with obesity increases the work of breathing. Simple obesity is associated with work of breathing that is 70% higher than normal and oxygen cost that is 28% higher than normal.[27–29] The morbidly obese expend a disproportionately higher percentage of total oxygen consumption on breathing, this relative inefficiency suggests a decrease ventilatory reserve and a predisposition to respiratory failure in the setting of even mild pulmonary or systemic insults.[25]

Obesity and breathlessness

Breathlessness on exertion is a very common symptom, with up to 80% of obese persons reporting dyspnea after climbing two flights of stairs.[25] Sahebjami investigated whether obesity *per se* was the major cause of breathlessness in obese subjects.[30] He recruited 60 patients with BMI >28; 37 had coexisting medical conditions that could cause dyspnea and were excluded from further analysis. Of the remaining 23 patients, 15 reported dyspnea at rest. The dyspneic patients were heavier and more were smokers than those without dyspnea. The only significant differences in respiratory function between the two groups were that dyspneic persons had lower maximum minute ventilation and maximum expiratory pressure. Most importantly the results emphasize the likely synergy between the effect of obesity and even minor degree of airway obstruction, usually related to smoking, in the generation of breathlessness.[2] A recent study in asthma showed that weight reduction improves breathlessness and reduces the need for symptomatic treatment.[31]

In eucapnic morbidly obese, the respiratory rate is approximately 40% higher than normal at rest, while the tidal volume at rest and at maximal exercise is normal.[32]

However, when normalized to body weight or lean body mass, tidal volume is approximately 50% of normal at rest and 33–50% of normal at maximal exercise capacity.[33,34] The tidal volume (ml/kg) is inversely correlated with percent of body fat.[34,35]

26.3 Pulmonary complications of obesity in hospitalized patients

El-Solh and colleagues studied the effects of obesity in a cohort of 117 hospitalized morbidly obese patients.[2] These authors demonstrated that morbid obesity increased the risk of respiratory complications, the duration of mechanical ventilation, length of intensive care unit (ICU) stay and hospital mortality. Goldhaber *et al*. have demonstrated that obesity is the most important risk factor for pulmonary embolism.[36] The increased risk of pulmonary embolism may be related to venous stasis as well as decreased fibrinolytic activity and antithrombin III levels.[37–42] The risk of aspiration pneumonia is increased in morbidly obese patients due to an increase in intra-abdominal pressure, the high incidence of gastro-esophageal reflux, high volume of gastric fluid and low gastric pH[43] (see also Chapter 8).

26.4 Respiratory management of the obese surgical patient

26.4.1 General considerations

Obese patients tend to decompensate after surgery. Abdominal pressure increases after anesthesia particularly with the patient in the supine position[44,45] (see Chapter 20). This is associated with a reduction in end-expiratory lung volume, increased chest wall and respiratory system elastance leading to a decrease in transpulmonary pressure with a consequent reduction in lung volumes and lung collapse.[46] The loss of diaphragmatic tone induced by anesthesia makes the movement of diaphragm dependent on the pressure present in the thoracic and abdominal compartments. Due to the gravitational pressure gradient in the abdomen, the distribution of ventilation is preferentially directed to non-dependent lung regions.[47] With increasing body mass, the gravitational intra-abdominal pressure gradient is likely to increase with cephalic displacement and reduction in the passive movement of the dependent part of the diaphragm. This favors the development of atelectasis in dependent lung regions.[48]

Endotracheal intubation may be exceeding difficult in the morbidly obese patient (see Chapter 21). A plan for airway management should be specifically addressed in all obese patients, even those undergoing regional anesthesia. The use of regional anesthesia may not avoid the need for securing the airway, which may be required urgently if excess sedative agents are administered.[49] It is also important to note that upper airway

topical anesthesia may induce airway obstruction in obese patient with sleep apnea.[50]

Post-operative pulmonary dysfunction is accentuated by the pain associated with thoracic and abdominal incisions. Pain control strategies with minimal respiratory depression, such as continuous epidural analgesia, are recommended (see Chapter 29). Early mobilization and chest physiotherapy, nursing in semi-upright position and deep venous prophylaxis are of utmost importance to avoid respiratory complications[51] (see Chapter 25). Routine supplementary oxygen carries the benefits of decreased pulmonary artery pressures and decreases the incidence of myocardial ischemia, but it may delay the detection of apnea/hypopnea. Pulse oxymetry in a closely monitored environment is therefore required.[52,53] Sleep apnea is an important cause of respiratory failure in obese patient. The diagnosis is often unsuspected and patients with sleep apnea can present for surgical intervention without either a diagnosis or effective ongoing therapy.[49]

26.4.2 Non-invasive positive pressure ventilation

Over the past decade non-invasive positive pressure ventilation (NIPPV) delivered by a nasal or face mask has gained increasingly wide spread acceptance for the support of acute and chronic respiratory failure. Non-invasive ventilation is best suited to alert and cooperative patients. It should be initiated at low pressures and increased gradually as tolerated. NIPPV can be delivered by volume ventilation, a pressure controlled ventilation, bi-level positive airway pressure (BiPAP) or as continuous positive airway pressure (CPAP). Volume cycle non-invasive ventilation delivers a set volume with each breath through a nasal or face mask. Volume cycled non-invasive ventilation has been demonstrated to improve outcome in acute and chronic respiratory failure, however, patient tolerance is often poor.[54,55] Positive pressure non-invasive ventilation, in which the ventilator delivers a set pressure, is commonly given with a BiPAP ventilator or a standard ventilator using the pressure support or pressure control mode.

Nocturnal non-invasive ventilation is useful in patient with heart failure and sleep related breathing disorders where it reduces the frequency of apnea, improves left ventricular function and decrease sympathetic activity. As little as 2 h/day and 4–6 h/night can improve daytime oxygenation and symptoms of dyspnea.[55–61]

26.4.3 Mechanical ventilation

Mechanical ventilation is fraught with complications in obese patients due to airway difficultly, impairment of respiratory dynamics and difficulty with sedation. Likewise weaning these patients from mechanical ventilation is frequently problematic.[55] A tidal volume based on body weight will likely result in high airway pressure, alveolar overdistention, ventilation perfusion mismatch and barotrauma. Initial tidal volume should be calculated according to ideal body mass then adjusted according to airway pressures and blood gases.[55,62] The use of positive end-expiratory pressure (PEEP) is highly recommended and prevents end-expiratory closure of small airways and atelectasis. The prevention of small airway closure and atelectasis improve V/Q mismatch. In addition, PEEP increases lung volume and results in a more even distribution of ventilation. The benefit of PEEP in obese patients is suggested by the upward shift of the pressure–volume (P–V) curve and a decrease of the inflection point with improvement of oxygenation.[63] Interestingly, increasing PEEP to 10 cm/H_2O during anesthesia has been demonstrated to increase arterial oxygen tension and decrease the alveolar–arterial oxygen difference in obese subjects but not in patients of normal body weight.[63] Excessive PEEP, however, will overdistend alveoli and redistribute blood flow with negative effects on V/Q mismatching and oxygenation.[63,64]

26.5 Obesity and sleep-disordered breathing

Apnea is defined as the complete cessation of airflow for at least 10 s while hypopnea is defined as a decrease of 50% in airflow or a decrease of $<$50% lasting at least 10 s with either an oxyhemoglobin desaturation of 3% or arousal from sleep. Sleep apnea disorders are further divided into obstructive, central and mixed. Central sleep apnea is less common and usually result from neurological or muscular causes such as brain stem lesion, bulbar poliomyelitis, myasthenia gravis or myotonic dystrophy.[49] Upper airway resistance syndromes (UARS) are defined by narrowing of the upper airway without apnea/hypopnea, but can fragment sleep and cause daytime sleepiness. Because most healthy subjects hypoventilate to some degree when they fall asleep and during rapid eye movement (REM) sleep, hypoventilation is considered abnormal only if associated with oxyhemoglobin desaturation $<$88% or hypercapnia.[65]

OSA syndrome is characterized by repetitive episodes of complete or partial upper airway obstruction resulting in sleep fragmentation and desaturation. OSA is associated with an increased cardiovascular morbidity and increased mortality. Obesity is the most common predisposing factor to OSA and is present in 60–90% of OSA patients. About 10% of OSA patients, typically

those with morbid obesity, develop chronic daytime hypoventilation defined as a sustained increase in $PaCO_2$ 45 mmHg.[65] The Pickwickian syndrome refers to those morbidly obese patients who are plethoric, cyanotic with both hypoxia and hypercapnia and have significant pulmonary hypertension and right ventricular failure.[66] Though the majority of individuals with OHS have concomitant OSA syndrome, OSA is not an essential feature of OHS.[67] The term obstructive sleep-disordered breathing (OSDB) syndrome encompasses the entire spectrum of obstructive breathing abnormalities. On one end of the continuum of increased upper air resistance is primary asymptomatic snoring, followed by UARS, sleep hypopnea syndrome and finally by OSA syndrome. The OHS is used to describe individuals who have daytime hypoventilation and are typically morbidly obese.[67,68]

26.5.1 Pathogenesis of the obstructive sleep-disordered breathing syndrome

The caliber of the upper airway is determined by the pressure exerted by the pharyngeal dilating muscles, the pharyngeal area and shape, the compliance of the airway, the lamina pressure (which is negative on inspiration), the pressure in the tissue surrounding the pharyngeal wall and the lung volume which independently influences upper airway resistance, caliber and compliance.[69] Obesity influences all of these factors, the most important being the decreased pressure exerted by the pharyngeal dilator muscles and the reduced lung volume.[70] In addition, large neck or para-pharyngeal fat deposits increase tissue pressure resulting in increased upper airway resistance due to a decrease in cross-sectional area and increased collapsibility of the upper airway.[70–72] Obesity affects oxygen consumption and carbon dioxide production as well as lung mechanics and V/Q mismatching (as discussed above) which make the patients with OSA more susceptible to episodes of arterial desaturation and hypercapnia.[73–76]

The precise pathophysiology of OSDB is unclear and likely multifactorial. There is conflicting data on the role of abnormal ventilatory drive in OSDB. Some studies have demonstrated reduced hypercapnic ventilatory response.[67] In contrast, Lopata and Onal demonstrated normal drive and diaphragmatic electromyogram in response to progressive hypercapnia.[77] In addition, some patients with OSDB return to eucapnia after treatment with CPAP or tracheotomy without change in hypercapnic responsiveness, suggesting other factors may play role.[67]

Arousal from sleep that terminates an episode of apnea/hypopnea is usually associated with increasing ventilatory effort rather than oxyhemoglobin desaturation. If this ventilatory effort arousal threshold is exceeded and the respiratory muscles are able to compensate for the increased upper airway resistance and maintain normal airflow, arousal from sleep will occur without a decrease in airflow and no desaturation or hypercapnia. This condition which is associated with daytimes fatigue, tiredness and sleepiness due to sleep fragmentation induced by sleep arousal has been termed the UARS.[67] If ventilatory effort does not exceed its arousal threshold, the respiratory muscle are unable to compensate for the increased upper airway resistance, resulting in a decrease in airflow and tidal volume (hypopnea). If airflow ceases completely prior to arousal from sleep, apnea occurs. Finally if both the ventilatory effort arousal threshold and the ability to compensate for hypoxia, hypercapnia and respiratory loads are sufficiently blunted, hypoventilation alone results without periodic arousal.[67]

Interest in the pathophysiology of obesity has recently intensified with the discovery of leptin. Leptin is a 167-amino acid protein with a structure similar to that of cytokines. The hormone is produced predominantly in white adipose tissue. Leptin levels increase exponentially with increasing fat mass. Leptin acts by binding to specific receptors in the hypothalamus to alter the expression of several neuropeptides that regulate neuroendocrine function, energy intake and expenditure. Most obese subjects have high circulating leptin levels, indicating that in most circumstances obesity is a leptin-resistant state. Much like type II diabetes it is possible that receptor or post-receptor defects could be responsible for leptin resistance in obese subjects. Interestingly, obese subjects with OHS have significantly higher leptin levels when compared to weight matched controls. Mutant obese C57BL/6J-Lepob mice which lack circulating leptin exhibit respiratory depression and elevated $PaCO_2$. An infusion of leptin in these animals markedly increases minute ventilation across all sleep/wake states and improves lung mechanics.[78] These studies suggests that both obesity and OHS may be due to leptin resistence.[78]

26.5.2 Pathophysiological consequence of sleep-disordered breathing

Sleep-disordered breathing has two main primary consequences: arousal from sleep and oxyhemoglobin desaturation and hypercapnia.[79] Daytime sleepiness and motor incoordination are the presumed cause for the increased rate of automobile (sevenfold) and work related accident in patients with OSDB.[79,80] Patients with OSDB characteristically demonstrated marked fluctuation in heart rate with sinus bradycardias and sinus arrest being particularly common. In addition, due to the development of pulmonary hypertension

Table 26.2 Consequences of nocturnal hypoxia/hypercapnia

Chronic hypercapnia
Polycythemia
Pulmonary hypertension
Systemic hypertension
Cor pulmonale
Left side congestive heart failure
Supraventricular and ventricular arrhythmias
Nocturnal angina

with right atrial enlargement supraventricular tachyarrhythmias such as atrial fibrillation and flutter are common.[81,82] Unless there is coexistent coronary artery disease, increased ventricular ectopy and ventricular tachycardia do not typically occur until oxyhemoglobin saturation drops to <60–65%.[83,84] OSDB syndromes are associated with an increased prevalence of hypertension, coronary artery disease and cerebrovascular disease. Indeed, unrecognized OSDB occurs in 20–30% of hypertensive patients[67] (Table 26.2).

26.5.3 Diagnosis of sleep-disordered breathing

Overnight polysomnography remain the most widely accepted diagnostic tool.

The apnea index (AI) is the number of apnea per hour. The respiratory disturbance index (RDI) is the number of apnea and hypopnea per hour of sleep (apnea–hypopnea index, AHI). The oxygen desaturation indexes describes the number of oxygen desaturation episodes per hour.[49] OSDB is defined as AI > 5, RDI > 10 or arousals per hour of sleep > 10 together with clinical sequella such as excessive time sleepiness.[85]

26.5.4 Treatment of sleep-disordered breathing

The optimum therapy depends on the severity of the disease. General measures include weight loss measures, avoidance of alcohol and sedative agents and modification of body position during sleep.[85] Pharmacological approaches to increase respiratory drive such as progestional drugs, acetazolamide and theophylline lack demonstrated usefulness.[86–88] Dental appliances are useful for snoring but second line of therapy for OSA if the patient is intolerant or not a candidate for ventilatory assistance.[89]

Ventilatory assistance

Nasal CPAP is applied using a nasal mask or nasal prongs. CPAP acts predominately by providing a pneumatic splint to the upper airway, preventing narrowing that occur when the dilator muscle activity decreases.[90–92] CPAP has been shown to completely reverse or at least significantly improve all the symptoms including diurnal hypertension, hypercapnia, pulmonary hypertension and corpulmonale.[93] In patients with OHS nasal CPAP may be ineffective, and such cases require either supplemental oxygen or ventilation with a nasal bi-level system or nasal volume ventilation. The major limiting factor is with these devices is patient compliance.[67]

Nasal BiPAP differs from CPAP in that it allows independent adjustment of inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP). Since a higher pressure is required to maintain adequate upper airway patency during inspiration a bi-level system allows to lower EPAP. The lower EPAP reduces problems with exhaling and the sensation of smothering which limits patient compliance as well as reducing the risk of barotrauma.[94,95] In some patients with OHS or without OSDB and chronic obstructive pulmonary disease (COPD) chest wall impedance due to obesity may be so high that BiPAP may not able to generate high peak inspiratory to ventilate the patient in such case nasal volume ventilation may be required.[67,96]

Surgical treatments

Surgical treatments include nasal surgery, adenotonsillectomy, uvulo-palato-pharyngoplasty and maxillofacial surgery.[97] Bariatric surgery may be indicated for significantly obese patients with OSDB or OHS. Results have been quite impressive and include significant weight loss, decrease in RDI of 89–98%, improvement in nocturnal oxygen desaturation, cardiac arrhythmia and daytime somnolence. However, long term follows up on these patients is lacking.[67,98]

26.6 Conclusions

The management of the morbidly obese patients is a challenging and formidable task. A better understanding of the pathophysiological changes that occur with obesity and the complications unique to this group of patients may improve their outcome.

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MANAGEMENT OF THE OBESE CRITICALLY ILL PATIENT IN INTENSIVE CARE UNIT

27

P.E. Marik & F. Brun

27.1 Introduction

Obesity has reached epidemic levels in the US, affecting >30% of adults.[1] The health care costs associated with obesity is estimated to be 4.3% of the total US health care costs. This roughly translates into expenditures over $51.6 billion.[2–4] With the increasing prevalence of obesity in the general population, it is not surprising that many obese patients are treated in intensive care settings. The critically ill obese patient presents the critical care team with many unique problems.

The impact of obesity on outcome in critically ill patients has not been well studied. There are only few comprehensive reviews that detail the management of the obese critically ill patient.[5] Obesity was not included as a co-morbid variable in the development of the APACHE II and III or SAPS prognostic indices for critically ill patients.[6,7] Smith-Choban and colleagues, reported that morbidly obese patients have a 8-fold higher mortality following blunt trauma than non-obese patients.[8] A retrospective review of 117 patients with body mass index (BMI) > 40 admitted to a medical intensive care unit (ICU) over a 6-year span revealed significant increases in ICU stay, mortality and length of mechanical ventilation.[9] In this study the APACHE II scores were not significantly different between obese and non-obese patients. Furthermore, it has been shown that hospitalized obese patients are at an increased risk of developing respiratory and other complications.[10,11] It is therefore likely that obesity increases the incidence of complications of patients admitted to the ICU, and that this is associated with a longer hospital stay and an overall poorer outcome.

27.2 Pulmonary effects

The degree of obesity, age and body fat distribution (central or peripheral) affect normal pulmonary physiology. The changes in pulmonary function have important implications in the management of obese patients (see Chapter 4).

A detailed assessment of the upper airway must be performed in all obese patients, as difficulties with mask ventilation and tracheal intubation may be considerable.[12–14] (see Chapter 21). The incidence of difficult intubation is approximately 13%.[14] Evaluation of the airway must include:

a range of head and neck flexion, extension and lateral rotation,
b jaw mobility and mouth opening,

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c oropharynx and dentition,
d patency of the nostrils,
e history of previous difficulties with intubation,
f features suggestive of obstructive sleep apnea (OSA) syndrome.[14]

A fiberoptic laryngoscope or bronchoscope in addition to equipment for performing percutaneous cricothyrotomy and tracheal ventilation should be readily available.

27.3 Cardiovascular effects

Weight gain increases cardiac output and heart rate in obese patients (see Chapter 5).

The rise in resting heart rate is caused by withdrawal of parasympathetic tone.[15] This is also associated with an increase in total blood volume and resting cardiac output. Both increase in direct proportion to the amount the patient weighs over the ideal body weight (IBW).[16–20] The cardiac and stroke index are normal in otherwise healthy obese patients.[16–20] The increase in cardiac output is accompanied by a decrease of systemic vascular resistance in normotensive patients. De Divitiis and co-workers performed left and right heart catheterization in 10 morbidly obese (mean BMI of 48.8) but otherwise healthy individuals.[17] These authors noted that the mean oxygen consumption (VO_2) was increased (311 ml/min), and that the VO_2 increased linearly with increasing body weight. However, the arterio-venous oxygen difference was normal, suggesting that the cardiac output increases primarily to serve the metabolic requirements of excessive fat.[16–18] The distribution of cardiac output has been reported to be similar in obese and lean individuals.[20]

Although the resting cardiac output is increased, obese patients have been demonstrated to have impaired left ventricular contractility and a depressed ejection fraction, both at rest and after exercise.[17,21–24] This is because excess weight gain increases blood volume and venous return with subsequent increases in preload, cardiac dilation and development of eccentric left ventricular hypertrophy.[15] In addition, decreased myocardial β-adrenergic receptors may contribute to this finding.[24,25] Furthermore, left ventricular mass, left ventricular wall thickness and left ventricular cavity size may increase, resulting in left ventricular dilatation and hypertrophy.[26,27] These changes are related to both the degree and duration of obesity.[26,27]

Systemic arterial hypertension is common in the morbidly obese patient, with superimposed left ventricular hypertrophy (see Chapters 6 and 11). Diastolic dysfunction with a prolonged relaxation phase and early filling abnormalities has been reported to be an early indicator of cardiac involvement in obesity.[26] Electrocardiographic changes with obesity include a leftward shift of the QRS axis and an increase in the PR, QRS and QTc interval (see Chapter 17).

In general, the left ventricular filling pressure is elevated in obese patients due to the combination of increased preload and reduced ventricular distensibility.[16–20] De Divitiis and colleagues reported a mean left ventricular end-diastolic pressure (LVEDP) of 16.6 mmHg in their series of patients.[17] Consequently, fluid loading is poorly tolerated by the obese patient.

27.4 Drug dosing in obese patients

The distribution, metabolism, protein binding and clearance of many drugs are altered by the physiological changes associated with obesity[28–32] (see Chapter 15). Some of these pharmacokinetic changes may, however, negate the consequences of others and the pharmacokinetic alterations may differ in the morbidly obese compared to the mildly or moderately obese.[32] In addition, the patients underlying disease may substantially influence a drug's pharmacokinetic properties.[33] The net pharmacological alteration in any patient is, therefore, often uncertain. Nevertheless, for a number of drugs used in the ICU, most notably digoxin, aminophylline, aminoglycosides and cyclosporin, drug toxicity may occur if the patients are dosed based on their actual body weight (ABW).[28–32,34–36]

The oral absorption of drugs remains essentially unchanged in the obese patient.[29] The volume of distribution (V_d) of drugs in obese patients is largely dependent on the lipophilicity of the drug.[29–31] The V_d of drugs which are weakly lipophilic (aminoglycosides and quinolones) is moderately increased when compared to normal individuals, but the V_d corrected by ABW is significantly smaller. The V_d is increased for many, but not all lipophilic drugs. The clearance of most drugs that are hepatically metabolized is not reduced. For drugs that are renally excreted, elimination will depend on the creatinine clearance. A higher glomerular filtration rate has been reported in obese patients with normal renal function,[37,38] and this will increase the clearance of drugs which are eliminated primarily by glomerular filtration.[39] In obese patients with renal dysfunction, the creatinine clearance, as calculated using standard formulae, correlates very poorly with the measured creatinine clearance.[40] Therefore, in the obese patient with renal dysfunction, the dosing regimen of renally excreted drugs

should be based on the measured creatinine clearance (see Chapter 14).

As a consequence of the complexity of the pharmacokinetic changes that may occur in obese patients and the limited data available for many drugs, there is inconsistency and disagreement in the literature regarding drug dosing in obesity.[28–32] For many drugs it is unclear if weight-related dosage adjustments should be made, and whether these adjustments should be based on the ABW, IBW or a percentage of the ABW. Due to the limited and sometimes conflicting data on drug dosing in obesity monitoring of clinical endpoints, signs of toxicity, clinical response and serum drug levels (when available) is essential. Drugs for which reasonable evidence is available to make dosing recommendations can be seen in Table 27.1. Aminoglycoside dosing should be based on the dosing weight (DW = IBW + 0.4 (total body weight (TBW) − IBW)) and not ABW. Furthermore, once daily dosing is not recommended in these patients and the drug levels should be closely monitored. The dose of beta-lactams should be increased in obesity due to an increase in the V_d and clearance. Forse and colleagues demonstrated a significantly increased risk of wound infection in morbidly obese patients undergoing gastroplasty who received a 1 g dose of cefazolin for surgical prophylaxis as compared to those patients who received a 2 g doses.[41] In obese patients it may be prudent to reduce the dosing interval (that is, give drug more frequently) and to increase the infusion time of beta-lactam antibiotics in order to increase the time the serum concentration remains above the minimal inhibitory concentration (MIC).

Table 27.1 Drug dosing recommendations in obesity

Drug	Loading dose	Maintenance dose	References
Digoxin	IBW	IBW[a]	72
Aminoglycosides	DW	DW[a,b]	73, 74
Quinolones	DW	DW	74, 75
Vancomycin[c]	DW	DW[a]	
Penicillins and cephalosporins[c]	DW	DW	
Macrolides	IBW	IBW	
Heparin	DW	DW[d]	76–78

IBW: for men = 50 kg + 2.3 kg/in of height > 5 ft;[79]
for women = 45.5 kg + 2.3 kg/in of height > 5 ft.

DW = IBW + 0.4(TBW − IBW).

[a] Therapeutic drug monitoring recommended, [b] Dose adjusted according to CrCl, [c] Limited data available, [d] Must monitor activated partial thromboplastin time (aPTT); weight-based dosing nomogram suggested.[76–78]

27.5 Nutritional requirements

Although obese individuals have excess body fat stores and large lean body stores, they are likely to develop protein energy malnutrition in response to metabolic stress, particularly if their nutritional status was poor before injury.[42,43] Nutrition should not be withheld from the obese patients in the mistaken belief that weight reduction is beneficial during critical illness. Traumatized, obese patients mobilize more protein and less fat compared with non-obese subjects.[44] A block in both lipolysis and fat oxidation has been reported in obese patients resulting in a shift to the preferential use of carbohydrates which further accelerates body protein breakdown even further to fuel gluconeogenesis.[44] This increased carbohydrate use for fuel increases the respiratory quotient.

Energy expenditure equations are unreliable in critically ill patients, particularly if they are obese.[45] It is unclear as to whether the IBW or TBW should be used in these equations.[46] The obese patients' energy expenditure should therefore ideally be measured by indirect calorimetry.[47] If indirect calorimetry is not available patients should receive between 20 and 30 kcal/kg/day based on their obesity-adjusted weight (obesity-adjusted weight = IBW + (ABW − IBW) × 0.25).[48,49] Most of the calories should be given as carbohydrates with fats given to prevent essential fatty acid deficiency.[43] It has been suggested that critically ill obese patients receive nutritional support with a hypocaloric high-protein formulation. It has been postulated that if adequate protein is supplied and obligatory glucose requirements are met, endogenous fat stores will be used for energy.[50] This will in turn avoid glucose-related and overfeeding complications as listed in Table 27.2.

A trial involving 40 obese patients in a trauma/surgical ICU revealed hypocaloric enteral nutrition support is at least as effective as eucaloric feeding.[51] In a prospective, double-blind study, Burge and colleagues demonstrated that feeding mildly to moderately stressed obese

Table 27.2 Potential advantages of hypocaloric feeding

1. Reduces incidence of hyperglycemia
2. Decrease in endogenous insulin release
3. Reduces the need for exogenous insulin
4. Decreased CO_2 production
5. Enhanced protein anabolism
6. Enhanced wound healing
7. Improved immune function

patients with a hypocaloric total parenteral nutrition (TPN) solution achieved comparable nitrogen balance to that of patients given conventional TPN formulas.[48] Protein requirements in the obese patient may be difficult to determine because of the increased lean body mass. Current consensus recommends a level of 1.5–2.0 g/kg of IBW to achieve nitrogen equilibrium.[43,48,50] Enteral nutrition is the preferred route of feeding and is only contraindicated in patients with bowel obstruction. Due to the difficulty in obtaining venous access in morbidly obese patients, parenteral nutrition may be associated with an increased risk of catheter associated infection.

The incidence of diabetes mellitus increases with increasing body weight. Furthermore, abdominal obesity is strongly associated with an increased risk of glucose intolerance, hyperinsulinemia and hypertriglyceridemia. Hyperglycemia is therefore common in stressed critically ill obese patients (see Chapter 10). The blood glucose is usually difficult to control with a subcutaneous soluble insulin sliding scale necessitating an insulin infusion. Glucose levels should be aimed to be below 120 mg/dl as tight control has been shown to improve mortality, length of ICU stay and other complications.[52]

27.6 Bariatric surgery patients

Bariatric surgery is on the rise to aid in combating the obesity epidemic because even modest weight loss usually improves co-morbidities seen with severe obesity. The generally accepted indications for bariatric surgery are listed in Table 27.3. Most bariatric surgery patients are triaged to a general ward or telemetry unit post-operatively, however, the ICU team must be aware and ready to deal with this special population of patients. Current bariatric procedures involve the stomach and, to varying degrees, the small intestine.[53,54] There are three types of gastric restrictive operations: stapled vertical banded gastroplasty, adjustable gastric banding and a combination of gastric restrictive and malabsorptive surgery: the gastric bypass (Roux-en-Y procedure)[53,54] (Figures 27.1–27.3).

Table 27.3 Criteria for bariatric surgery

Body weight > 45 kg or 100% above IBW
BMI > 40
BMI > 35 with medical co-morbidities
Absence of endocrine disorders that can cause morbid obesity
Psychological stability:

- Absence of drug abuse
- Understanding of how surgery causes weight loss
- Realization that surgery itself does not guarantee weight loss
- Pre-operative psychological stabilization for selected patients

Patients undergoing bariatric surgery are at great risk of post-operative respiratory complications, particularly following open gastric bypass surgery. A significant fall in vital capacity, peak expiratory flow rates (PEFR), forced expiratory volume in 1 s (FEV_1) with a fall in

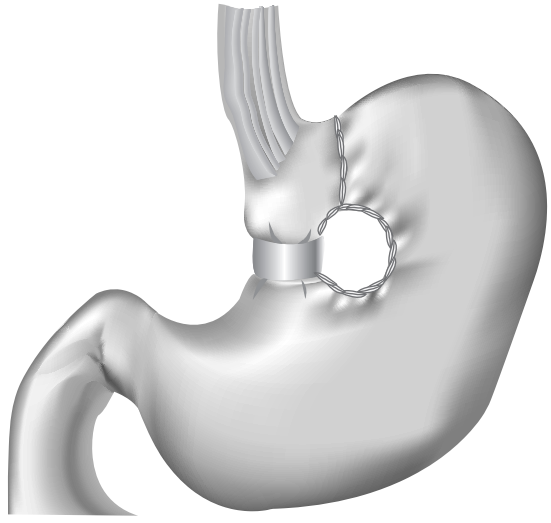

Figure 27.1 Stapled vertical banded gastroplasty.

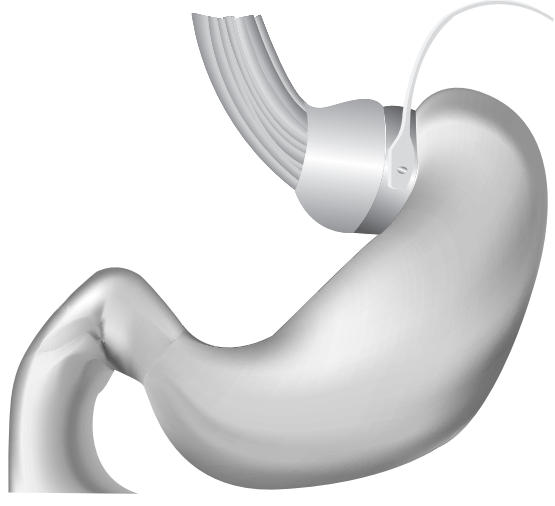

Figure 27.2 Adjustable gastric banding.

arterial saturation has been reported.[55] Ebeo and colleagues demonstrated that these changes in post-operative lung function can be minimized by the use of post-operative bi-level positive airway pressure.[55] In addition these patients are at a great risk of atelectasis, hypostatic pneumonia and thromboembolic disease. Aggressive pulmonary toilet and deep venous thrombosis (DVT) prophylaxis is therefore warranted in all patients undergoing bariatric surgery. Adequate pain control is important to prevent splinting and to facilitate coughing (see Chapter 29). However, the extubated post-operative ICU patient is at high risk for the "resedation" phenomenon. This is related to the redistribution of lipophilic/sedative agents from the fatty tissue back into the bloodstream.[56] The resedation phenomenon is compounded by the very high risk of OSA and upper airway resistance syndrome (UARS) seen in these patients.

Close respiratory monitoring including pulse oximetry is therefore recommended in all patients who have undergone bariatric surgery (see Chapter 18).

Other complications seen following bariatric surgery include anastomotic leaks, wound infection, seromas, hernias, iron and vitamin B_{12} deficiency, dumping syndrome (nausea, bloating, diarrhea and colic) and late-dumping (lightheadedness, palpitations, sweating occurring 1–2 h post-prandially).[54,56]

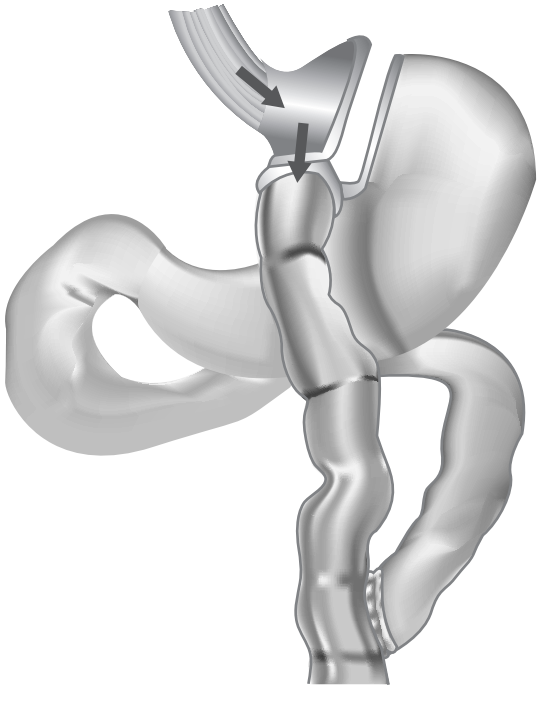

Figure 27.3 Gastric bypass (Roux-en-Y procedure).

27.7 Pregnancy and obesity

Chronic hypertension, diabetes and other chronic health problems are more common in obese pregnant patients than in their lean counterparts (see Chapter 24). One institution observed a 14-fold increase in chronic hypertension in patients who weighed >300 lb at time of delivery.[57] In addition, obesity is an important risk factor for the development of pre-eclampsia and eclampsia.[57–59] The obese patient is at an increased risk for fetal macrosomia and shoulder dystocia. Obesity significantly increases the risk of cephalo-pelvic disproportion and with a resultant increase in the rate of Cesarian section.[58,60]

27.8 Deep venous thrombosis prophylaxis

Goldhaber and co-authors reported that obesity was the single most important risk factor for the development of pulmonary thromboembolism[11] (see Chapter 12). Decreased mobility, venous stasis and an increased thrombotic potential may account for this finding. Diminished levels of antithrombin III and circulating fibrinolytic activity have been demonstrated in obese patients.[61–63] The high risk of thromboembolic disease in obese ICU patients, warrants an aggressive approach to DVT prophylaxis. Low-molecular weight heparin (LMWH), oral anticoagulation or the combination of pneumatic compression and LMWH should be considered in the morbidly obese patient in the ICU. DVT prophylaxis is complicated by the fact that pneumatic compression devices are often poorly tolerated by the morbidly obese patient. Some companies make special boot devices that are limited to the feet and act like standard compression boots.[64] In those patients in whom anticoagulation is contraindicated prophylactic placement of an inferior vena-caval filter should be considered.

27.9 Practical issues

27.9.1 Vascular access

Obtaining adequate venous access is frequently a major problem in the critically ill obese ICU patient. Poor peripheral venous sites in obese patients necessitates more frequent use of central venous access. A short stubby neck, loss of physical landmarks and a greater skin–blood vessel distance make internal-jugular and subclavian vein cannulation technically difficult.[65,66] This results in a higher incidence of catheter mal-positions and local puncture complications. A greater

number of skin punctures during catheter insertion and delayed catheter changes may lead to more catheter-related infections and thromboses.[67] Femoral venous access may not be possible as these patients usually have severe intertrigo. The use of Doppler ultrasound-guided techniques for obtaining central venous access in high risk patients has been demonstrated to reduce the number of needle passes to cannulate the vein, with a reduction in the incidence of complications.[65,68,69] However, the portable vascular-access ultrasound devices currently available can only image structures between 1 and 4 cm deep, and are therefore of limited value in morbidly obese patients. A proactive approach with the early placement of a peripherally inserted peripheral line (PIC) or tunneled central catheter inserted by an interventional radiologist is recommended. Scrupulous attention in maintaining the sterility of the catheter insertion site is essential.

27.9.2 Blood pressure monitoring

The most common cause of inaccurate blood pressure monitoring is the size of the blood pressure cuff in relation to the size of the arm. If the cuff cannot encircle half the arm or the arm is flabby, one should measure 13 cm below the elbow[64] (see Chapter 11).

27.9.3 Radiological procedures

Portable bedside radiographs are usually of a very poor quality in the obese patient, limiting the value of this important diagnostic tool. Abdominal and pelvic ultrasonography is limited by extensive abdominal wall and intra-abdominal fat. Percutaneous aspiration and drainage of intraperitoneal and retroperitoneal collections may be hindered by the obese body habitus. Most computed tomography (CT) and magnetic resonance imaging (MRI) tables have weight restrictions (about 300–350 lb) that prohibit imaging of morbidly obese patient. Many animal hospitals have CT scanners that can accommodate large animals and may be willing to scan morbidly obese patients who exceed the weight limits of the human scanners.

27.9.4 Skin integrity

Skin breakdown is a frequent problem in the morbidly obese. Prevention of pressure ulcers should be tantamount (see Chapter 28). Diligent skin care is therefore required. It is necessary to clean and then dry all areas within skin folds.[64] Nysatin skin powder is frequently used to prevent fungal infections; however, in obese patients the powder may clump requiring more preemptive skin monitoring. Patients requiring bedrest longer than 3 days require specialized bariatric beds to limit the risk of skin breakdown at pressure points. Specialized beds providing kinetic therapy/continuous lateral rotation therapy may be particularly beneficial in morbidly obese patients requiring prolonged ICU care; these beds have been demonstrated to reduce the risk of atelectasis and pneumonia as well as skin breakdown and venous thrombosis.[70]

27.9.5 Maintaining dignity

Caregivers are obliged to be respectful and maintain the dignity of morbidly obese patients who usually have significant psychological problems.[64] The management of morbidly obese patients can be extremely difficult and frustrating and this is often compounded by societal prejudices and bias. A number of bariatric surgery programs have implemented a "buddy system" to assist the patient during their hospital stay. The "buddy" assists with bedside care, ambulation and emotional support.[71] Nurses may find this a welcome concept in regards to physical care needs.

27.10 Conclusions

The complexity frequently observed in the management of the morbidly obese patients especially if a post-surgical subject is considered, requires a particular focus. Multidisciplinary approach and a deep knowledge about patho-physiological alterations and co-morbidities are mandatory in these cases in order to aspire for acceptable outcomes (see Chapter 1).

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NURSING MANAGEMENT 28

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28.1 Introduction

Caring for the morbidly obese patient is a challenge for healthcare providers regardless of the setting. For bariatric patients who require an intensive care unit (ICU) stay, the care provided by the multidisciplinary team, especially nursing, can be quite difficult. At each stage of the patient's recovery, different aspects of care provision require adaptation and creativity since the unique requirements of the morbidly obese patient are not easily delineated by any one-care guideline. Indeed, despite the prevalence of obesity in our critically ill patients, a dearth of information exists on how to best care for them. Regardless, a systematic approach to assuring that care is optimal may achieve good outcomes in this very vulnerable patient population and is the focus of this chapter. The chapter describes some of the most common and trying aspects of nursing care such as skin and wound care, positioning and mobilization, selected aspects of ventilator management, arterial and venous access, nutrition, prevention of complications and psychological issues. It is the authors' hope that the information provided will be useful to the readers of this book on peri-operative management in the morbidly obese individual.

28.2 Skin and wound care

Maintaining the skin integrity of the morbidly obese patient requires the implementation of a proactive approach to avoid skin breakdown. Such an approach may prevent complications and the resultant prolonged duration of hospitalization associated with the complications of obesity. A discussion of some specific preventive strategies follows.

The pressure within skin folds that results from the weight of overlying tissue, in combination with moisture and friction, predisposes the obese patient to tissue excoriation and breakdown. Further compounding the problem is the fact that fatty tissues are poorly perfused and wound healing is delayed. In the critically ill obese patient, the additional factors of immobilization, periodic episodes of hypotension and hyperglycemia all contribute to compromised skin integrity and infection with bacterial and fungal organisms (see Chapter 13).

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The obese patient is especially prone to the development of excoriation between skin folds, under the breasts, in the groin and under the panniculus. Keeping the skin clean and dry, especially in skin folds, is an essential, albeit a daunting task. Key strategies for accomplishing this include frequent turning and repositioning. Patients should be turned every 2 h at a minimum.[1] During turning, skin folds should be inspected for breakdown and drainage tubes repositioned. An absorbent cloth or gauze placed between skin folds can help absorb moisture and reduce friction.[2] Body alignment can be maintained with proper padding in conjunction with positioning of the limbs to prevent pressure between contiguous body parts and against equipment surfaces. While the use of "lift" or "turn" sheets or slings is helpful to assist in turning and positioning, care must be taken to avoid abrading or shearing the skin while using them.

Commonly used equipment may cause or exacerbate skin breakdown. Breakdown can develop beneath inappropriately sized blood pressure cuffs or sequential compression devices, especially if left in place for prolonged time intervals. Blood pressure cuffs that cover at least 75% of the upper arm are available and assure the accuracy of measurements.[3] Drainage tubes easily become entrapped and hidden in skin folds causing skin erosion. The tubes also may be inadvertently pinched or dislodged, resulting in a decrease in measured output, and the potential for erroneous treatment decisions.

If appropriately sized equipment is not available and existing equipment is used, the result can be compression of tissues which come in contact with side rails and other surfaces. Even hospital gowns of an appropriate size are hard to find in many ICUs. Extra large hospital gowns are important to promote the patient's comfort and modesty, as well as to prevent upper arm constriction and circulatory compromise.

The toileting and elimination needs of the morbidly obese patient are especially challenging. With incontinence, undetected urine and stool can quickly lead to skin breakdown. Thus it is essential to keep the perianal region clean and dry. Urinary catheters and rectal bags are useful in helping to protect skin from excessive exposure to waste products and are essential in order to accurately monitor output until the time that the patient is able to assist with self-toileting. If used, urinary catheters must be removed as soon as possible in order to decrease the potential for urinary tract infection. Diarrhea can be effectively contained with a rectal bag and drainage system, and intact skin protected with the use of skin barriers until the etiology of the diarrhea is determined and is controlled.

If the patient is mobile, oversized equipment is essential if self-toileting is to be successful and non-injurious. Oversized portable commodes, raised toilet seats and reinforced wall-mounted toilets with handrails to assist getting on and off the seat are all options. When patients are forced to use toilet seats that are too small or too low, injury to the patient and/or staff (if the patient is unable to rise from the seat independently) is likely to occur. Obese patients can become wedged into small bathroom cubicles or on overly small bedside commodes. Further, if unable to toilet independently, maintaining cleanliness is difficult, and patients are sometimes embarrassed to ask for assistance. Morbidly obese men commonly find the use of a urinal to be very difficult, if not impossible, secondary to their very large abdomens.[2] Standing or sitting on the side of the bed or using the commode may be helpful, when this is possible. The use of pressure reduction mattresses and appropriately sized equipment may contribute to the prevention of pressure sores. The use of such equipment is encouraged. At special risk of skin breakdown are morbidly obese patients who have a decreased mental status or are intubated, since they are often unable to communicate discomfort effectively.

Interventions to prevent skin breakdown such as those discussed above are key elements of care for the morbidly obese patient. If a team of expert wound care consultants is available, contact them for both preventative and therapeutic suggestions.

28.3 Positioning and mobilization

Promoting mobility in the obese patient is important for many reasons. Mobilization helps to prevent associated complications such as skin breakdown, respiratory infections and physical deconditioning. Even a moderate amount of physical activity helps promote endurance and is a good first step in preparing a patient for weaning trials. Further, mobilization improves motivation and emotional well-being. Therefore the patient should be mobilized as soon possible and complete bedrest should be avoided. Active mobilization can begin with trials of sitting on the side of the bed, advancing to standing, walking a few steps and sitting in the chair for short periods of time. Physical therapists can design a program of passive and active exercise that is safe and effective for the bariatric patient. Their consultation is especially necessary when the patient has a history of knee problems or other deficits that are exacerbated by exercise.

Specialized equipment and mobilization techniques promote comfort and dignity and prevent injury to

the patient and the members of the healthcare team. Many healthcare equipment companies offer special equipment that is customized for the special needs of the bariatric population. Healthcare facilities can either rent or buy oversized beds and chairs, commodes, lifts, and scales, obviating the need for more "home-spun" solutions such as strapping two beds or operating tables together to serve as a bed. It is important that the manufacturers recommended weight limit be established for any equipment used for mobilizing the morbidly obese patient so that inadvertent injuries and other accidents are prevented.

Many US hospitals that previously used rental equipment, especially those who offer gastric bypass surgery to bariatric patients, are re-examining past use of rental equipment in favor of buying their own.[4] However, if a facility decides to rent or purchase specialty equipment, it is important to compare the dimensions of the patient room with the specifications of the equipment. If these essential components are not considered, unnecessary delays, cost and frustration will result. Another option is to consider building or remodeling one or more rooms in order to accommodate oversized equipment. This may include reinforcement of weight bearing structures and/or the addition of ceiling-mounted bariatric lifts.[4]

In addition to planning for special equipment needs, healthcare facilities must provide education and staffing strategies to prevent injury to those who provide care to obese patients. Many facilities provide a "lift team", a group of staff members who can be directed to any unit where assistance is needed. In addition, body mechanics training and retraining is essential for all healthcare workers.

Care planning for the mobilization of the morbidly obese patient requires the help of a multidisciplinary team that includes physical and occupational therapists (see Chapter 1). Even simple patient care activities like turning, bathing, changing linen, applying dressings, and inserting a urinary catheter require planning and coordination. Assuring that adequate manpower is available to accomplish mobility goals is both an administrative and clinical task. Scheduling lift team visits to coincide with critical care unit staff availability is essential in order to assure smooth teamwork. It may require a period of trial and error to establish the right number of staff and the most efficient technique to accomplish each task. It is important to document and communicate what works, and to use a similar technique each time the task is performed.

When patients are unable to be actively mobilized, turning and positioning must be assured. However, all positions are not well tolerated in the obese patient. These include the supine, Trendelenburg, lithotomy and prone positions; all which may result in dyspnea, atelectasis and hypoxemia.[5] In contrast, the lateral decubitus position displaces the abdomen and allows greater diaphragmatic excursion.[5] The 30–45° semi-recumbent position has been recommended following gastric surgery[5] (see Chapter 20).

Burns compared positional variations in tidal volume and respiratory rate in patients with large abdomens due to obesity, abdominal distension, and ascites and found that the reverse Trendelenburg at 45° position resulted in significantly larger tidal volumes and lower respiratory rates when compared to head of bed elevation at 90° or supine.[6] These findings have implications for positions used during weaning and exercise, especially if the patient is breathing spontaneously.[6]

Special vigilance is required for activities such as rolling the patient, assisting the patient to sit on the side of the bed or when using a lift device to weigh or to transfer the patient. At these times the patient is at great risk of falling or being dropped, with potential injury to the patient and staff. The alert patient may experience feelings of fear and insecurity during these activities, especially if he or she has experienced pain or a fall with a previous similar activity. By teaching the patient what to expect ahead of time and with gentle coaching and assurance before and throughout the procedure, undue fear of mobilization can be averted. Occasionally a patient may become combative during an activity. This always increases the chance of injury to all involved. Prior forecasting of such a response from a patient is helpful in assuring that proactive preventive interventions, such as the use of sedation, are accomplished as necessary. When repositioning and transferring the patient, the patient's artificial airway, intravascular devices, and other tubes and drains must be scrupulously guarded in order to prevent inadvertent removal.

28.4 Procedures and diagnostic testing

Before transporting patients to diagnostic or procedure areas, it is essential to assure that the diagnostic site and equipment to be used can accommodate the patient's size safely. The technicians in these areas should be consulted beforehand.

Many procedures commonly used for diagnostic purposes have limited applicability in the morbidly obese. Some examples include those to identify intra-abdominal bleeding in surgical patients such as ultrasound and peritoneal lavage. Ultrasound does not

readily penetrate adipose tissue, and diagnostic peritoneal lavage is generally not an option because catheters and trocars are often too short. Computed tomography scans are also not possible with many patients due to weight limits (most scanners accommodate only up to 300 lb) as well as girth circumference limitations.[7] Thus, astute physical assessment must substitute for diagnostic imaging and special procedures in many situations.

28.5 Ventilator management

Other chapters in this book discuss the effects of obesity on respiratory mechanics and mechanical ventilation and therefore are not covered in detail in this chapter (see Chapters 4 and 26). However, some aspects of mechanical ventilation and weaning are unique in the bariatric patient population. To that end, a brief discussion of weaning trials, the application of positive end expiratory pressure (PEEP) and continuous positive airway pressure (CPAP), and the use of speaking valves follow.

The large abdomen of the morbidly obese patient creates an inspiratory workload that may be partially offset with the addition of PEEP, CPAP and inspiratory pressure levels (that is, pressure support). Abdominal pressures, though rarely measured in these patients, may be excessive and impinge on functional residual capacity (FRC) resulting in atelectasis and hypoxemia.[8] In order to offset some of the work of breathing created by the abdominal mass, and restore FRC, PEEP, CPAP and inspiratory pressure levels, must be adjusted appropriately. While no guidelines exist to help us determine what level is high enough to offset the mechanical load imposed by the abdomen, artificial airway and the breathing circuit, it is clear that the selection of arbitrary levels is not appropriate. A common goal for example is to use 5 cmH_2O as the lowest target weaning level for CPAP. In reality the patient may require a much higher level such as 10 cmH_2O. This is especially true if atelectasis is present and the patient is not being mobilized.

Tracheostomy is not necessary for all obese patients but is common, especially since many of the patients also suffer from sleep apnea and may need the tracheostomy until such time that they are fully rehabilitated and have lost weight. In addition, a tracheostomy is often more comfortable for the patient because the patient is able to eat, mobilization can be accomplished more safely, and communication is enhanced with the addition of speaking valves. Speaking valves may also serve another important function as well. Generally, speaking valves utilize a one-way valve to allow air to flow into the trachea on inspiration. With expiration the valve closes so that air is forced past the vocal cords for speaking. During the expiratory phase, backpressure is created; FRC may be restored and atelectasis prevented. Some speaking valves also allow for oxygen to be bled into the trachea. Anecdotal reports suggest that in addition to supporting oxygenation, these valves may also create "backpressure" and restore FRC thus making spontaneous breathing trials more successful. However, caution must be exercised since the speaking valves using oxygen may contribute to dry secretions and occlusion of the airway.

As noted in the sections on mobilization and positioning in this chapter, it is important to assure that the patient is mobilized as early as possible during the course of hospitalization and that positioning is optimized. Positions such as reverse Trendelenburg at 30–45°, and side lining positions when in bed, may go a long way decreasing the work of breathing in morbidly obese patients.[5,6]

28.6 Arterial and venous access

Critically ill patients often require arterial and central venous access for blood pressure monitoring, assessment of acid–base status and for the delivery of essential intravenous medications and continuous infusions. Placement of the lines in the obese patient is difficult and ultrasound guidance is recommended.[9]

In the morbidly obese patient, central line use is double that of normal sized patients and the lines are also maintained for longer.[10] Unfortunately, line infection is also higher putting the patients at high risk of sepsis and death. Though the lines are often essential, removal should be considered as early as is feasible.[10] Additionally, scrupulous line maintenance and vigilant line site monitoring is essential to prevent infection. When the patient is stable and without signs of infection, percutaneous intravenous catheters (PIC) may be placed. The PIC lines are relatively safe to place since they are placed in the veins of the arm vs. intrajugular or subclavian veins. Further they are also stable and flexible allowing for greater mobility of the patient without the risk of dislodgment.

28.7 Nutrition

Nutrition support for the morbidly obese patient is often under appreciated because the patient does not readily appear malnourished. However, adipose tissue stores do not prevent catabolism of lean muscle mass,

Table 28.1 Guides for nutritional management

Adjusted body weight[16,15]	
(Cutts, *et al.*)	(ABW − IBW) × 0.25 + IBW
(Glynn *et al.*)	Average of ABW and IBW.
IBW	
Males:	48.2 kg for the first 1.54 m + 2.7 kg per additional 2.54 cm
Females:	45.4 kg for the first 1.54 m + 2.3 kg per additional 2.54 cm
Resting energy expenditure (REE) (Harris–Benedict Equation)	
Males:	66 + (weight in kg × 13.7) + (height in cm × 5) + (age × 6.8)
Females:	655 + (weight in kg × 9.6) + (height in cm × 1.7) + (age × 4.7)

or slow the development of malnutrition when a patient is unable to eat.[11–13] Traumatized obese patients mobilize relatively more protein compared with normal sized individuals.[14] This shift to preferential use of proteins and carbohydrates in sepsis and trauma require an adequate provision of carbohydrate and protein to prevent wasting of lean muscle mass, for wound healing, and to prevent skin breakdown.[11–14]

Calculating the calorie expenditure of morbidly obese patients is a challenge. Use of actual body weight (ABW) with standard prediction equations will overestimate energy expenditure yet if ideal body weight (IBW) is used, energy expenditure will be underestimated.[15,16] While indirect calorimetry is the preferred method in obese patients, modified equations may be useful when this option is not available[15,16] (Table 28.1).

Another point to keep in mind related to nutrition in obese patients is that they are able to utilize endogenous lipid stores to meet part of their calorie requirements.[15–19] Several studies have looked at the use of hypocaloric, protein-sparing feeding in the obese patient. These study regimens provided approximately 22 kcal/kg of IBW or 14 kcal/kg ABW and 2 g protein/kg of IBW.[17–19] The results indicate that obese patients, fed a hypocaloric, high protein regimen, maintained similar nitrogen balance and had comparable outcomes to those patients fed higher calorie levels.[15–19] These hypocaloric feedings may allow for adequate nutrition support in the critically ill obese patient without the complications associated with overfeeding. However, before this assumption is accepted for widespread application, other questions require exploration. One recent study found results similar to those above in younger patients, but raised questions about the optimal calorie and protein recommendations for patients over the age of 60.[20] In addition, this type of regimen has not been studied in patients with renal or hepatic disease. As noted previously, obese patients are at high risk for skin breakdown and infection. Appropriate and early nutrition are essential to assure good outcomes. If a nutrition service is available, early consultation with these experts is recommended.

28.8 Prevention of complications

28.8.1 Pneumonia

Several factors predispose the obese patient to nosocomial pneumonia, especially in the post-operative period and during periods of immobilization. The obese patient has a larger gastric volume with a lower than normal pH, which can contribute to the development of aspiration pneumonitis or pneumonia[21] (see Chapter 8). In addition, increased abdominal fat can result in high intra-abdominal pressures, increasing the risk of gastric reflux in the obese patient.[22] Lower FRC due to diaphragmatic elevation by abdominal fat predisposes to atelectasis, especially when the obese patient is in the supine position or when breathing shallowly due to pain or sedation.[23] The risk of aspiration also increases when the patient is in the supine position.[24] Strategies to decrease the potential development of nosocomial pneumonia in the obese patient include avoiding the supine position once hemodynamic stability is assured and use of the reverse-Trendelenburg position for pneumonia prevention. The reverse-Trendelenburg position may also result in improved oxygenation.[6,25]

Early mobilization and ambulation are imperative. Deep breathing and coughing exercises and the use of incentive spirometry can be taught and practiced preoperatively and aggressively pursued in all immobilized and post-operative obese patients. If an abdominal binder is used in the obese patient who has had abdominal surgery, close monitoring should be done to ensure

that the binder does not constrict the lower costal margin and foster splinting and atelectasis.[26]

Control of pain, especially in obese patients who have had chest or abdominal procedures is essential to prevent incision splinting and the development of further atelectasis (see Chapter 29). Patient-controlled analgesia and epidural analgesia may offer the advantage of less sedation and respiratory depression.[5,21,25]

28.8.2 Venous thromboembolism

Venous thromboembolism (VTE) affects approximately 2 million Americans annually; 600,000 develop a pulmonary embolism (PE) and one-third die.[27,28] Obesity has long been recognized as a risk factor for VTE[27,29] (see Chapter 12). In a study by Blaszyk *et al.*, morbid obesity was identified as an independent risk factor in cases of sudden death due to PE.[30] Obese patients with surgical or medical conditions are especially at risk for VTE and PE due to the prevalence of Virchow's triad of factors including venous stasis, hypercoagulability (prothrombotic abnormalities) and endothelial damage (proinflammatory states, etc.).[29,31]

Diagnosis of VTE in the obese patient is problematic. Common tests used for diagnosis include Doppler ultrasonography, real-time B-mode compression ultrasonography, impedance plethysmography, magnetic resonance imaging (MRI) and D-dimer. Unfortunately, many of the tests are not useful in obese patients since their size prevents adequate evaluation. Details related to advantages or disadvantages of the different VTE diagnostic testing methods are listed in a table (Table 28.2).

The early initiation of VTE prophylaxis in medically and surgically ill obese patients is an essential part of good nursing care. Subcutaneously (SQ) administered unfractionated heparin is routinely used for deep venous thrombosis (DVT) prophylaxis. However, there are few studies of the efficacy of unfractionated SQ heparin in the prevention of PE and DVT in individuals greater than 100 kg. Since adipose tissue has less vascular supply, unfractionated heparin administered by the SQ route may not be sufficient to protect against DVT.[32] The American College of Chest Physicians recommends that 3500 U of SQ unfractionated heparin be administered every 8 h and that activated partial thromboplastin time (aPTT) levels be maintained at high normal levels for high risk patients.[33]

Anticoagulation with warfarin, low molecular weight heparin (LMWH) or intravenous heparin are also options for VTE prophylaxis. With each option however, different planning and monitoring is required. Intravenous heparin and warfarin require frequent measurement of laboratory tests of coagulation as well

Table 28.2 VTE diagnostic tests (adapted from Enders)

Test and mode	Advantages	Disadvantages
Doppler ultrasonograhy (uses imaging and measurement of low velocity)	Non-invasive, performed at the bedside, most commonly performed	Requires experienced operator; due to large amount of SQ tissue in the obese, compressibility of veins may be unreliable; low sensitivity in asymptomatic DVT
Real-time B-mode compression ultrasonography (produces two-dimensional image)	Non-invasive, performed at bedside	Requires subjective assessment by the examiner; due to large amount of SQ tissue, imaging of veins may be unreliable, low sensitivity in asymptomatic DVT
Impedance plethysmography (pneumatic thigh cuff detect change in impedance)	Non-invasive, best suited for symptomatic proximal vein thrombi	Insensitive to calf-vein, occlusive proximal DVT and small thrombi. Need X-large thigh cuff for the obese, may be unavailable. Low sensitivity in asymptomatic DVT
MRI (imaging of thrombus and decreased flow)	Highly reliable	Expensive, due to weight limit of MRI table, may not be available to obese patient
D-Dimer (enzyme-linked immunoabsorbent assay, (ELISA), sample of fibrin degradation products)	Rapid, can rule out DVT	High percentage of false positives (low specificity), especially in the elderly

as frequent dosage adjustment. LMWH must be adjusted for renal insufficiency. Dosage adjustment may be accomplished by monitoring anti-Xa assay.[34]

Most published reports of immobilization and associated VTE define 3–7 days of immobilization as a risk factor.[27] The avoidance of prolonged immobility may be the single most important non-pharmacologic VTE and PE prophylaxis modality available. While widely used, pneumatic compression stockings are poorly studied in the obese population and problems with assuring an adequate fit are common.

28.8.3 Hyperglycemia

Obesity is a risk factor for the development of insulin resistance and subsequent development of type 2 diabetes mellitus[35,36] (see Chapter 10). Hyperglycemia is associated with increased infections, delayed wound healing, decreased utilization of nutrients and fluid imbalance. Neutrophil function involving bactericidal ability, phagocytosis and chemotaxis is also affected by hyperglycemia.[37] The importance of normalizing blood glucose in all patients was illustrated by a recent study that demonstrated that intensive insulin therapy and tight glucose control (maintenance of blood glucose at a level between 80 and 110 mg/dl) reduced mortality and morbidity among critically ill patient in a surgical ICU.[38] Another study by Umpierrez revealed that in hospital hyperglycemia is a common finding among all patients and is a marker of poor outcomes and higher mortality.[39] It is therefore important to carefully monitor hyperglycemia in the high risk obese patient and institute aggressive glucose control strategies. Insulin infusions and sliding scale protocols are generally necessary for critically ill patients while oral hypoglycemics and/or combination insulins may be used for more stable patients.

28.9 Psychological considerations

The obese patient lives with a level of discrimination and prejudice that can only be appreciated by the affected individuals and their families. In the US obese individuals attend less school, are less likely to be married, and have lower household incomes. Because of the social stigmatization that occurs with obesity from an early age, obese individuals are at risk for mood disorders. Multiple studies have identified a history of major depressive disorders among women with extreme obesity. Studies also reveal that obese women are more likely to have suffered adult and childhood rape, molestation, crime victimization and post-traumatic stress disorder.[40]

Research has shown that the obese patient is often a target for negative social attitudes by healthcare professions. Hebl conducted a study to determine whether the care a patient receives from their physician is influenced by weight.[41] The study revealed that physicians play an influential role in the decreased quality of health care that overweight and obese patients receive. An examination of nurses' attitudes toward obese patients found similar prevailing negative attitudes. A quarter of the nurses surveyed agreed with the statement: "caring for an obese patient usually repulses me".[2]

To complicate matters, obese patients are less likely to seek out preventative healthcare services.[42] It is important for the obese patient to be treated with compassion and respect. As with all patients, an individual with obesity must be treated as the center of the team. He/she must be included in goal setting. Periodic family and patient meetings should be scheduled to discuss progress, obstacles and goals. Physicians, nurses and other staff need to be educated regarding the prevalence of discrimination and prejudice that occurs with the obese patient and how this has been shown to interfere with positive patient outcomes.

28.10 Summary

Nursing care of the morbidly obese patient requires unique skills and knowledge if the patients are to be cared for optimally. Unfortunately, despite the prevalence of obesity in technologically advanced societies, little specific attention has been paid to bariatric medical care. Diagnostic and therapeutic equipment to manage the obese patient population are scarce and rarely considered by hospitals to be essential purchases. As a result, equipment such as hydraulic lifts and oversized beds are not available. Further, the psychological needs of the patients are often ignored; negative perceptions of healthcare workers magnify the problem. These factors often result in morbidly obese patients' languishing in beds, incurring increased complications, and ultimately sustaining poor clinical and financial outcomes. Critical care nursing focuses on stabilization and restoration of baseline or near baseline status. In the case of the morbidly obese, early interventions such as mobility, nutrition and weaning in addition to the prevention of common complications such as skin breakdown and pneumonia are essential if good outcomes are to be realized.

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POST-OPERATIVE ANALGESIA 29

A.G. Haidbauer

29.1 Introduction

As defined by the International Association for the Study of Pain (IASP),[1] pain is recognized not only as a sensory experience but also as a phenomenon with affective and cognitive responses. An important aspect of pain is nociception, a complex series of electrochemical events that involves activation of specialized neural pathways in response to (potentially) tissue-damaging stimuli. Clinically, the degree of nociception is manifested as signs of tissue damage. Pain, in contrast to nociception, is a subjective experience that may involve stimulus-induced activation of afferent neural pathways or other components, such as somatosensory processing or psychosocial factors. Reflex responses to nociceptive stimulation can be described as suprasegmental or cortical and spinal or segmental. Spinal reflexes are generated by nociceptive signals being transmitted through the dorsal horn to somatomotor or autonomic neurons at various spinal levels, resulting in responses such as paralytic ileus, vasoconstriction, tachycardia, or muscle spasm.[2] Suprasegmental reflexes are propagated via the ascending pathways to the brain stem, hypothalamus, and cortex, where withdrawal reflexes and autonomic responses are generated.

Acute pain results in various physiologic changes, such as the general stress response, that have significant effects on the respiratory, cardiovascular, gastrointestinal, genitourinary, and musculoskeletal systems.[2,3]

29.2 Consequences of acute post-operative pain

29.2.1 General stress response

The stress response to surgical and other trauma results in endocrine and metabolic changes, such as

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increased secretion of catabolic hormones (for example, adrenocorticotropic hormone, antidiuretic hormone (ADH), and catecholamines) and decreased secretion of anabolic hormones (for example, insulin and testosterone). These changes can cause nausea, intestinal stasis, alterations in blood flow, coagulation, and fibrinolysis, and can increase demands on the cardiovascular and respiratory systems.[2,4,5]

The stress response may be divided into two phases: an initial acute "ebb phase," characterized by a hypodynamic state, followed by a hyperdynamic "flow phase," which may last for days or weeks, depending on the magnitude of the injury or on the occurrence of complications. Nociceptive impulses are believed to play an important role in the ebb phase and in the initial part of the flow phase, but many other factors, including anxiety, hemorrhage, infection, and local tissue factors (inflammation), are also involved.[4,5]

The general stress response also affects water and electrolyte flux. Increased production of hormones such as catecholamines, cortisol, adrenocorticotrophine, ADH, results in retention of water and sodium ions and increased excretion of potassium ions.[2] Thus, unrelieved pain is likely to cause adverse effects in more than one body system, particularly in high-risk surgical patients, as the obese patients are.

29.2.2 Respiratory effects

Acute pain can result in high-inspiratory and expiratory pressures and reductions in tidal volume, vital capacity, functional residual capacity (FRC), and alveolar ventilation.[5,6] Reduced FRC can contribute to regional lung collapse (atelectasis) and ventilation/perfusion (V/Q) mismatch. The resultant hypoxemia is associated with considerable impairment of pulmonary gas exchange. Elderly patients, smokers, obese subjects, and those with respiratory diseases are particularly at a higher risk. Another deleterious effect of acute pain, especially in such high-risk patients, is reduced mobility, which may lead to hypostatic pneumonia.[6] In the surgical setting, involuntary spinal reflex responses to noxious stimuli from the injured site, result in reflex muscle spasm in the area of tissue injury and in muscle groups surrounding the injury site.[5,6] The patient's perceived pain may cause voluntary reduction of muscular movement in the thorax and abdominal regions, a phenomenon often described as "muscle splinting." This splinting can be associated with partial closure of the glottis, producing a "grunting" sound during breathing. Muscle splinting interferes with the patient's ability to cough and clear secretions, possibly progressing to lobular or lobar collapse and hypoxemia.[6] Infections and pneumonia may result. Inability to participate in chest physiotherapy prolongs the course of pulmonary complications, such as infections or pneumonia, which in turn may increase duration of hospitalization.[6]

On the other hand, anesthesia normally leads to significant pulmonary changes. These changes are more pronounced in obese patients, who often have preexisting respiratory derangements.[7]

29.2.3 Cardiovascular effects

A major component of segmental and suprasegmental reflex responses is enhanced general sympathetic tone.[2] This results in increased peripheral resistance, stroke volume, and heart rate, which lead to an increase in cardiac output (CO). High-blood pressure results in increased myocardial work and myocardial oxygen consumption.[5]

The raise in heart rate causes decreased diastolic filling time, possibly resulting in reduced oxygen delivery to the myocardium, with the risk of ischemia.[5,8] The effects of post-operative pain on various cardiovascular variables has been examined by Sjögren and Wright.[8] They found that pain was associated with increases in total peripheral resistance, mean arterial blood pressure, heart rate, and CO. They also noted increases in left ventricular minute work and left ventricular stroke work. Alpha receptors in the coronary vasculature may respond to sympathetic stimulation by producing coronary vasoconstriction.[9] This pathophysiologic process may lead to ischemia, angina, and myocardial infarction. Anginal pain has been associated with increased anxiety and increased release of catecholamines, with further potential for coronary arterial constriction.[5] All of these alterations could develop devastating complications in labile individuals such as morbidly obese, who commonly are at a higher risk of myocardial ischemia and ventricular dysfunction or heart failure even at minimal increases in stress hormones levels.

29.2.4 Gastrointestinal and urinary effects

Acute pain and the resultant sympathetic hyperactivity can result in increases in intestinal secretions and smooth muscle tone, and decreased intestinal motility.[5] These effects may lead to gastric stasis or paralytic ileus. Importantly, opioid analgesics may also contribute to such gastrointestinal effects.[5,10] Sympathetic hyperactivity also results in increased tone of the urinary sphincter, possibly causing urinary retention. Again, opioids may play *per se* a significant role in the development of urinary retention.[5]

29.2.5 Musculoskeletal effects

Segmental and suprasegmental motor activity in response to pain results in muscle spasm, which further increase the pain. This cycle may also activate sharp increases in sympathetic activity and further raise the sensitivity of peripheral nociceptors.[5] Persistent post-operative pain and limited mobility may be associated with impaired muscle metabolism, muscular atrophy, and marked delays in return to normal muscular function.[11] These effects are the result of pain and reflex responses, such as vasoconstriction, that may be partly reversed by effective pain relief.

29.2.6 Effects on peripheral circulation

In the peripheral circulation, acute pain is associated with decreased blood flow to the limbs, which can be particularly serious in patients undergoing vascular grafting procedures.[5] In addition, severe surgical pain and the levels of sympathetic hyperactivity may cause reductions in arterial inflow and venous emptying.[12] Further, a hypercoagulable state, particularly in immobilized patients, can lead to deep venous thrombosis (DVT) and pulmonary embolism (PE).[13]

Acute pain has been associated with decreased peripheral blood flow, which may result in reduced tissue perfusion. This can have consequences on wound repair. Several studies that examined the role of oxygen in wound repair have demonstrated that reduced levels of arterial and tissue oxygen may retard tissue repair.[14,15] This could develop improper conditions for the desired evolution of a digestive suture or grapping and at least hypothetically should be taking into account, since many bariatric procedures involve digestive sutures, and also digestive leak between the most severe surgical peri-operative complications. Changes in immunocompetence and acute- phase proteins after surgical trauma have been documented. Certain analgesic methods, such as neural blockade, may mildly influence various aspects of such immunocompetence. Although the mechanisms involved have not been clearly elucidated, concomitant inhibition of various endocrine metabolic responses may play a role.[5] Jorgensen *et al.*,[16] have found that alterations in coagulation and fibrinolysis that are associated with surgical procedures may be partly modified by analgesic neural blockade. Thus, it appears that acute surgical pain may be associated with a hypercoagulable state and fibrinolysis. This situation is of major concern in morbid obesity due to the high incidence of deep venous thrombosis with or without PE reported between them. However, interpretation of these results is complex, because various factors different than pain may be involved in these processes.[5]

29.2.7 Psychologic effects

Anxiety and fear are major emotional effects of unrelieved severe acute pain and can exacerbate it, contributing to delirium in patients in the intensive care setting.[5,17] In addition, patients with acute pain can exhibit various behavioral changes, including depression, withdrawal from personal contact, and hypersensitivity to external stimuli, such as light and sound. Sleeplessness compounds the problem, leading to a vicious cycle of acute pain, anxiety, and further sleep deprivation.[5,17]

29.2.8 Effects on pain-signaling systems

Certain types of acute pain, such as post-operative pain, are partly the result of inflammatory conditions caused by peripheral tissue damage. Noxious stimuli and the resulting inflammatory response elicit peripheral changes as well as alterations in the central nervous system. Peripheral nociceptors become sensitized to noxious stimuli and release chemical mediators, which further increase the sensitivity of the nociceptors.[5,18] The pain threshold is lowered, resulting in hyperalgesia, that is, enhanced pain in response to suprathreshold stimuli. Peripheral sensitization also can result in allodynia (pain provoked by non-noxious stimuli). Hypersensitivity of the central nervous system also occurs and may outlast the duration of the initiating noxious stimulus. Thus, acute pain that serves as a warning mechanism to signal tissue injury may become pathologic in nature when it is prolonged, possibly leading to chronic or neuropathic pain.[18,19]

29.2.9 Consequences conclusions

Most of the major obesity-related health risks increase disproportionately with increasing weight. Diabetes, hypertension, hyperlipidemia, heart diseases, infertility, hepatobilary diseases, cerebrovascular disease, degenerative joint disease, chronic back pain, gallstones, increased rates of colon and breast cancer and asthma are also linked to rising levels of obesity. A body mass index (BMI) $>29\,kg/m^2$ increases the prevalence of PE. Risk of coronary artery diseases is doubled if BMI is $>25\,kg/m^2$. A BMI of $35\,kg/m^2$ leads to a 40-fold increase in developing diabetes, respiratory diseases, sleep apnea and osteoarthritis. Risk of death increases with body weight. Mortality raises exponentially with increasing body weight.

Hence, aggressive and effective pain control is essential to minimize post-operative complications and

to facilitate a rapid recovery in this group of patients. All those potential consequences of poor pain control are a problem with morbidly obese patients undergoing surgery.

29.3 Analgesia: general considerations

Despite the increased interest in pain pathophysiology, most patients with surgical pain do not receive adequate pain relief.[20] This undertreatment of acute pain may be attributed to several factors, such as a lack of formal education in pain management; mistaken beliefs regarding potential opioid addiction and drug tolerance; inadequate pain assessment; misinterpretation of orders; and the traditional emphasis on "Pro re nata" (PRN) dosing.[21] As well as lack of prospective, randomized, double-blinded studies in the obese population, which could contribute to the type I evidence material.

All patients have the right to pain relief, including post-operative pain, and this right should be respected and supported by the healthcare professionals caring for the patient, as well as to relief from other side-effects such nausea, vomiting, pruritus, sedation, constipation, etc. Failure to relieve pain is not only clinically, but also morally unaccepted. Therefore, effective post-operative analgesia is mandatory for all surgical patients. In spite of this, a limited number of studies have been published on post-operative analgesia in the obese patient. Healthcare practitioners frequently experience difficulty in controlling the pain of morbidly obese due to difficulties associated with determining dosages of opioids in accordance with the body surface area, and the tendency of the patients to develop sedation and respiratory depression.[22] This situation could become particularly dangerous in those subjects with obstructive sleep apnea syndrome (OSAS) or obesity hypoventilation syndrome (OHS), common co-morbidities of obesity.

Unrelieved pain can have profound adverse physiologic, behavioral, and psychologic effects on patients, which have the potential to inhibit recovery (see above). Thus, pain requires attentive management. To address this issue, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) worked with an advisory panel of pain experts from various healthcare settings, such as ambulatory care, hospitals, and healthcare networks, to write new and revised standards for appropriate pain assessment and treatment.[23] According to the JCAHO and American Pain Society (APS) recommendations, pain should be considered the *fifth vital sign*, that is, patients should be assessed for pain every time their pulse, blood pressure, core temperature, and respiration are measured.[23,24] JCAHO recommends the use of individualized interdisciplinary team assessments,[23,25] including designating a place in the patient's medical records to document pain assessment (that is, pain would be recorded as the fifth vital sign).

Self-reports are the most reliable indicators of pain intensity. The three scoring systems most commonly used in adults are as follows:[26]

- Visual analog scale (VAS): this employs a 10-cm horizontal line rated from "no pain" at the left to "worst pain possible" on the right. The patient marks their pain intensity on this continuum. The VAS score is the distance from "no pain" point to the patient's estimate. Being a continuous scale, it has the advantage of being infinitely sensible. Therefore, is the imposed scale in pain research setting, especially in post-operative pain.
- Verbal numerical rating score (VNRS): this also asks the patient to rate their pain from "no pain" (0) to "worst pain" (10). It's a very simple and useful scale, and probably the most frequently used in the clinical post-operative setting.
- Categorical rating scale (CRS): in this one, different descriptors can be used to rate the patient's pain. It usually consists of a set of words or short phrases that are ranked for magnitude of pain intensity (for example, none, mild, moderate, and severe).

Pain should be assessed and documented preoperatively; at regular intervals post-operatively, as determined by the procedure and pain intensity; with each new report of pain; and at suitable intervals after each analgesic intervention. In addition, the patient's assessment of pain relief should be documented at regular intervals (fifth vital sign).[27] The optimal efficacy of analgesia is frequently measured by the ability to cough and move without pain or discomfort, and not only by the absence of pain at rest, enabling that an earlier mobilization, taking in mind how important could that be, for these high-risk patients.

Using one or more of these tools, healthcare providers must recognize that reported unrelieved pain may serve as a "red flag," an indication of potential morbidity. The JCAHO standards,[23] emphasize the importance of patient involvement in all aspects of their care, including pain management.

29.3.1 Benefits of patient preparation

Early literature reviews indicate that preparing patients for stressful medical procedures may offer advantages, but later studies do not clearly identify whether the increased availability of information or enhanced

cognitive skills are responsible for the benefits.[28] This issue was examined in patients who were provided disease-related information and assistance in learning behavioral changes and different pain control techniques.[29,30] Several advantages of patient education, albeit relatively minor, were noted: the patients showed increased knowledge of their painful conditions and demonstrated increased functional ability. These patients also experienced less pain and depression. Patient preparation also may reduce pre-operative anxiety, a condition that can affect outcome, especially in patients with trait anxiety. Boeke *et al.*,[31] found that pre-operative anxiety did not predict post-operative pain, but did predict length of hospitalization. Thus, a cognitive approach to pain management, which involves patient preparation and motivation, is becoming an increasingly important tool in pain therapy.

29.3.2 Recommendations to improve the treatment of post-operative pain[23,26]

- Assess and record pain systematically and involve the patient whenever possible.
- Measure pain intensity not only at rest, but also on cough and movement.
- Nominate a staff member to take responsibility for the management of pain relief policy after surgery in each hospital.
- Establish an acute pain team.
- Use existing and effective pain relief modalities, and introduce new methods when a benefit is proved.
- Audit and continuously appraise activity.

29.3.3 Analgesic options

In 1986, The World Health Organization (WHO) proposed guidelines for the selection of appropriate drug regimens. These guidelines primarily were applied to the management of cancer pain, but also may be applied for management of acute and chronic non-malignant pain. According to the WHO guidelines, pain intensity should serve as the principal subjective measure that necessitates intervention. Non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and aspirin should be used for mild to moderate pain. For moderate to severe pain intensities, NSAIDs alone would not be effective, therefore opioids should be used along with non-opioid analgesics. With such combinations, a low-potency opioid should be used to treat moderate pain intensities, and a high-potency opioid should be prescribed for severe pain.[32]

Several analgesic options exist for the treatment of acute pain: opioids, and non-opioid agents, such as acetaminophen or anti-inflammatory drugs, ketamine, corticosteroids, α_2 agonist; combination formulations, in which opioid and non-opioid agents may be combined; local anesthetics, and other adjuvants.

The effects of opioid analgesics are based on the interaction with receptors for endogenous opioids and several receptor types have been identified, namely, OP3 (μ), OP1 (δ), and OP2 (κ) receptors.[33] Opioids are currently among the most effective agents available for the relief of moderate to severe pain. Most of the commercially available opioids act at the OP3 receptor, which has several subreceptors, and differ mainly in their potency, speed of onset, duration of action, and optimal route of administration.[34] The considerable variability in patient responses to the opioids may be partially the result of differences in these receptors and subreceptors. Changes at the receptor level also may account for tolerance, a characteristic feature of opioids, in which progressively higher doses of the drug must be used to produce the same analgesic effect. Opioids play a prominent role in the management of post-operative pain, but the doses required to relieve pain associated with movement or coughing often cause deleterious side-effects, such as depression of the central nervous system, which results in sedation and confusion; respiratory depression; prolongation of post-operative ileus; and increased urinary retention.[35] Although most of these side-effects can be reversed by the opioid antagonist naloxone, sedation is particularly problematic in situations involving outpatient, reduced hospitalization settings, or in cases in which an early ambulation is mandatory, as with morbidly obese patients. Moreover, increased urinary retention and delayed return of bowel function can prolong hospitalization. The incidence of clinically important respiratory depression requiring intervention after opioid use is approximately 1% in general population.[36] Other side-effects of opioid use include nausea, which has been reported to occur in approximately 30–48% of patients;[36,37] vomiting (30% of patients);[36,37] constipation;[38] and pruritus.[38]

Unfortunately, use of opioids in morbidly obese patients (especially with long-lasting infusions of large doses) is limited due to the tendency to accumulate in the corporal tissues, mainly the adipose. The latter redistribution could result in variable adverse effects, such as sedation, respiratory depression, nausea and vomiting, etc.[39] Thus, although opioids have been effective for the management of post-operative pain, development of other analgesic agents raises the possibility that opioid-reduced or opioid-free analgesia may be optimal in some situations, like the peri-operative management of obese patients. There

is growing interest for less demanding modes of peri-operative analgesia such as wound infiltration with local anesthetic combined with systemic medications to achieve multimodal analgesia.[40]

As pain from surgery has three major components (tissue injury, nociceptor stimulation, and activation of central pathways),[41] a multimodal approach to analgesia based upon simple, low-tech interventions, such as pre-incisional infiltration with local anesthetic, supplemented by repeat incisional infiltration at the end of the operation, as a component of a multimodal peri-operative analgesic strategy for obese patients undergoing open gastric bypass surgery, can be effective.[40] The development of local anesthetics like levobupivacaine,[42] that permit larger total doses to be given safely, extends opportunities for infiltration analgesia and suggests that such approaches could play an increasing role in peri-operative regional anesthesia. This technique improves post-operative pain relief and decreases the total opioid requirement, thus reducing post-operative nausea and vomiting.[43]

29.3.4 Multimodal analgesia

The rapid advances in the understanding of pain pathophysiology have not been matched by similar advances in providing optimal post-operative pain relief. Kehlet *et al*.[44] have suggested that an important reason for this discrepancy is that most post-operative treatment programs focus on unimodal therapies. Kehlet and colleagues prefer a multimodal approach, which involves the use of combined analgesic regimens integrated with effective rehabilitation programs. It is hoped that such strategies would lead to more effective pain relief and faster return of patient mobility. The rationale for such an approach is the achievement of sufficient analgesia (a result of the additive or synergistic effects of the different analgesics used) combined with a reduction in the dose-related severity of side-effects (because of the use of lower doses of each analgesic and the differences in the side-effects profiles). Optimal management of post-operative pain can only be achieved by multimodal regimens (balanced analgesia).[44]

Multimodal analgesia involves the use of combined formulations of various analgesic agents, such as opioids, anti-inflammatory agents, or acetaminophen, local anesthetics, α_2 agonist, *N*-methyl-D-Aspartate (NMDA) antagonist; with different yet complementary mechanisms of action. Local anesthetic agents combined with opioids epidurally/intrathecally may act synergistically, thus reducing the total dose of each drug.[45,46] Similarly, the different sites of analgesic action found with NSAIDs and opioids suggest additive, or possibly even synergistic effects and in clinical practice they are often used in combination.[47] The opioid sparing effect of NSAIDs may lead to a reduction in opioid-induced side-effects.[48,49] In particular, nausea, vomiting, ileus, pruritus, and respiratory depression have been reported as being more effectively controlled when NSAIDs are added to a conventional opioid regimen.[47,50,51]

29.3.5 Pharmacological considerations[52]

Drug pharmacokinetics differ in obese compared with non-obese patients, depending on factors related to both obesity and the drug used[53,54] (see Chapter 15). Changes in volume of distribution and protein binding properties, increased renal clearance and changes in liver clearance have been reported.[52]

Volume of distribution

The distribution of drugs changes in obese patients. The etiology of this change is multi-factorial[54] and includes: smaller than normal fraction of total body water; greater adipose tissue content; increased lean body mass and changed tissue protein binding; increased blood volume and CO; increased concentrations of blood constituents such as free fatty acids, triglycerides, cholesterol and α_1 acid glycoprotein; organomegalies, etc.[53,55,56]

The volume of the central compartment (where drugs are first distributed) is not significantly altered by obesity. However, absolute body water content and lean body and adipose tissue mass are increased, affecting lipophilic and polar drug redistribution, and may lead to mistakes in the given doses.[54]

Many drugs are administered on the basis of dose per body weight unit, assuming that clearance is proportional to body weight, and that volume of distribution per weight unit does not differ with large variations in body mass. These assumptions are not valid in obesity because of the changes in body composition, volume of distribution, and possible change in renal and hepatic function.

Plasma protein binding

Plasma protein binding and plasma albumin concentrations are not changed significantly by obesity.[53,54] However, increased plasma concentration of α_1 acid glycoprotein, even though not a consistent finding[53,54] and hyperlipidaemia, which is a common counterpart of obesity,[53] may affect protein binding, thus reducing free drug concentration. Lipophilic drugs may be adsorbed to lipoproteins, but the influence of

hyperlipoproteinemia on free drug concentration is not known.[54]

Drug clearance

Kidneys

Renal clearance in obesity is raised because of increased renal blood flow, glomerular filtration rate (GFR) and tubular secretion[55] (see Chapter 14). The greater than normal GFR increases clearance of drugs that are not biotransformed before renal excretion and are filtered by the glomeruli.[53]

Liver

Drug metabolism in the liver is changed only partially by obesity.[53,54] As hepatic blood flow is changed moderately in obesity, clearance of rapidly cleared drugs such as lidocaine and midazolam remains unaltered.[53,54] However, congestive heart failure can affect clearance of rapidly cleared drugs, as a result of decreased hepatic blood flow.[53,55]

Specific drugs used in analgesia

Benzodiazepines

There are no clear recommendations for the dose of benzodiazepines in obesity. Their extensive distribution into fat and their prolonged elimination half-life, even in non-obese patients, explain their effects, persisting long after discontinuation of therapy. Central compartment volume for midazolam is similar in obese and non-obese patients when corrected for body weight. Thus midazolam should be administered in larger absolute doses, but in the same doses per body weight unit.[57] The same recommendation also pertains for diazepam.

Opioids

Little is known about the pharmacokinetic changes of opioids in obese patients, and there is no evidence that the more lipophilic opioids, such as fentanyl, have longer-lasting effects on them.

- *Fentanyl*: As well as with other lipophilic drugs, will have a greater volume of distribution.[58] Serum concentrations decline at a similar rate in both obese and non-obese patients after administration of 10 μg/kg absolute body weight, intravenous (i.v.) fentanyl suggesting that it should be administered in usual doses on the basis of total body weight.[59]
- *Alfentanil*: It was suggested that loading and maintenance doses of alfentanil should be calculated according to lean body weight in obese patients, because of its prolonged elimination half-life in them.[60]

However, similar loading and maintenance doses in both populations (obese and non-obese), calculated according to total body weight, have also been suggested.[61]

It has to be considered anyway, that if opioids different than remifentanil are delivered in long-lasting infusions, or high doses in order to achieve prominent intra-operative analgesic effect, since context-sensitive half-life basically depends on the opioid selected and duration of infusion, delayed recovery or post-operative respiratory depression should be expected (see Chapter 16).

Local anesthetics

The absolute volume of distribution of lidocaine is increased in obesity, but is not changed when corrected for body weight. Therefore, i.v. administered lidocaine should be given according to total body weight.[55,62] The pharmacokinetics and pharmacodynamics of extradurally administered local anesthetics and opioids are complicated and not fully understood,[63,64] especially in obese patients.[65,66] It is conceivable that the greater extradural fat content in these patients necessitates greater initial doses. Fat absorption, however, could prolong drug effects[67] and raise the level of anesthesia–analgesia attained.[66,68] Moreover, the engorged extradural veins and the large amount of extradural fat constrict the potential extradural space, thereby increasing segmental drug distribution. Thus dose requirements of local anesthetics for intrathecal and extradural anesthesia–analgesia in obese populations, calculated for total body weight, are reduced by 20–25%.[66,68–71]

29.4 Analgesia techniques

Few clinical trials have evaluated different types of post-operative analgesia in morbidly obese patients.

29.4.1 Oral route

Oral is the post-operative analgesic route of choice in surgeries with low nociceptive impact, in the ambulatory surgery setting, and in those cases in which due to the normal evolution of the post-operative period the systemic or regional routes are no longer necessary.

Oral absorption of drugs remains essentially unchanged in the obese patient.[72]

The most common drugs used by this route are NSAIDs and opioids. Remember that NSAIDs alone are efficacious only to treat mild and only some cases of moderate pain. But are not suitable to treat severe

pain intensities. In cases of moderate or severe pain intensity, opioids would be the gold standard.

29.4.2 Intramuscular route

Intramuscular (i.m.) injection of analgesic drugs *is not recommended*, because of their unpredictable effects, and has been shown to provide poorer analgesia than other routes.[73,74]

29.4.3 Intravenous route

Intermittent i.v. bolus injections of opioids is a possible therapeutic method in obese patients, although the changed pharmacokinetics of these drugs should be taken into account. Despite no prospective, studies have been carried out to prove the safety of this method. Sprigge and colleagues found that continuous i.v. administration of pethidine was safe for post-operative analgesia in morbidly obese patients.[75] In spite of this, great care is required when parenteral opioids are administered peri-operatively, particularly to the morbidly obese.[76]

In order to perform a multimodal analgesia with combined route of administration, i.v. NSAIDs (for example, tenoxicam 20 mg i.v. as rescue medication or every 8 h, with H_2-receptor antagonists) could be associated with a background spinal analgesia with local anesthetics and opiods.[77]

But, if the i.v. route is to be used, then a patient-controlled analgesia (PCA) system is probably the best option for this kind of patients.[78]

29.4.4 Patient-controlled analgesia

PCA has been developed to allow i.v. administration of analgesics in an incremental fashion, so that respiratory depression and profound sedation may be avoided. The concept of demand analgesia was based on the premise that patients are best able to determine the timing of analgesic administration to obtain the optimal analgesia for their pain.[79–81]

It has been shown that PCA:

1. minimizes the time delay between the perception of pain and the administration of analgesic medication;
2. decreases anxiety associated with waiting for pain relief medication;
3. decreases post-operative complications;
4. facilitates early ambulation and more efficient respiration;
5. decreases the length of hospitalization after surgery.[82,83]

In addition, PCA affords the physician the opportunity to individualize pain management therapy.[22]

It is essential to identify patients who may benefit most from PCA, namely:

- those who have had major surgery;
- those who have pain associated with physiotherapy or dressing changes;
- those with a contraindication to other pain management strategies.

Historically, PCA use in morbidly obese patients has been discouraged due to the potential of side-effects, mainly respiratory depression. In spite of published data, there still exist a paucity of literature on the efficacy and safety of PCA for post-operative pain management in morbidly obese patients, but there are case reports describing respiratory complications after the initiation of PCA post-operatively, especially in patients with OHS or obstructive sleep apnea (OSA).[84]

The risk factors for OSA are male gender, middle age, and night sedation, as well as evening alcohol consumption. Other features which can help identify OSA are BMI $> 30\,kg/m^2$, hypertension, observed episodes of apnea during sleep, hypoxemia, hypercapnia, changes in electrocardiogram (ECG), and Echo. Final diagnosis is made by polysomnography in sleep laboratory. Such patients pose a great challenge to surgery, anesthesia and peri-operative care.

These conditions are currently considered relative contraindications for the use of PCA in morbidly obese populations. And when the PCA is the technique of choice in such a patient, obviously, it is strongly recommended to perform a very close monitoring of all the related parameters. In spite of this, we have to recognize that the optimal use of PCA in patients with OSA or OHS, remains undefined.

PCA is effective in relieving pain in obese patients.[78,81] Opioid doses administered this way are not weight- or body surface area-dependent.[78,81] Dosing rate should be based on ideal, rather than absolute body weight. In their study, Choi and colleagues[22] recommend, as other authors do,[52] to base PCA dosages on the patients ideal weight, such as morphine 20 μg/kg, with a lockout interval initially setting at 10 min, and a 4-h limit at 80% of the total calculated dosage. They found a wide variation in the post-operative analgesic requirements following abdominal surgery, ranging from 12 to 180 mg/daily of i.v. morphine. This wide dosage range suggests that an individual dosage plan is needed for morbidly obese patients.

Something important to recognize, as Choi and colleagues did, is the patients education in PCA device

management as well as what we expect from him/her, since approximately 10% of patients are not able to understand easily the explanations given pre-operatively. And therefore it is logic to suspect an unsuccessful rate of around 10% in achieving the best results in terms of analgesia, due to this type of errors.

29.4.5 Regional analgesia

For the morbidly obese patient undergoing upper abdominal or thoracic surgery or any other procedure with great nociceptive impact, regional analgesia may be the technique of choice,[52] due to the ability to provide a better analgesic efficacy, diminishing the several deleterious effects of uncontrolled post-operative pain, especially in such high-risk patients.

The particular anatomical landmarks in obese patients, however, may make the procedure technically difficult, and often larger needles are needed, at the sacrifice of tactile cues.[69,85] Epidural and spinal anesthesia–analgesia may be made easier by sitting the patient upright, and some authors suggest the concomitant use of ultrasound guidance in order to identify the epidural space and to guide the Tuohy needle into correct position.[86] Even after successful placement, inadequate epidural function requiring catheter replacement is more common in obese than non-obese patients,[40,85] possibly because of increased mobility of overlying excess soft tissue. In the same way, peripheral nerve blockade may be made easier and safer by the use of insulated needles and a nerve stimulator.

In spite of these problems most authors strongly recommend the use of regional anesthesia–analgesia whenever possible. It has to be remembered that most data published according to these techniques (and also many others), were extracted from experiences performed in non-obese patients, and several concepts have to be cautiously extrapolated to this very special population.

Local anesthetic requirements for epidural and spinal analgesia are reduced to 75–80% of normal in the morbidly obese, since fatty infiltration and the increased blood volume caused by increased intra-abdominal pressure reduce the volume of the epidural space.[58,68,69] This can lead to an unpredictable spread of local anesthetic and variability in block level.[87] Blocks extending above T5 risk respiratory compromise, and cardiovascular collapse secondary to autonomic blockade.[76] Be prepared to treat hypotension with fluid and vasopressors (i.v. ephedrine 5–10 mg, or i.v. phenylephrine 50–100 μg).

The epidural/spinal route for opioid administration is preferred over other routes because they produce less drowsiness, nausea and respiratory depression, earlier normalization of bowel motility, improved pulmonary function and reduced hospital stay.

Local anesthetic agents combined with opioids epidurally/intrathecally may act synergistically, thus reducing the total dose of each drug, achieving the best analgesic efficacy due to different mechanisms of action (multimodal regional analgesia).[45,46]

Regional analgesia side-effects

Respiratory depression is a well-recognized side-effect of spinal opioids.[88] Lipid-soluble opioids are theoretically more suitable for intrathecal use. The early of respiratory depression reported after intrathecal or epidural fentanyl or sufentanil, may develop rapidly within minutes till 2 h.[89,90] This danger may be prevented by appropriate monitoring. Factors increasing respiratory depression risk after epidural or intrathecal administration, have been reported previously,[88] including: high doses of opioids, repeated doses of opioids, intrathecal administration, hydrophilic drugs such morphine, other systemically administered sedatives, advanced age, co-existing diseases, lack of opioid tolerance, thoracic epidural administration, increased intra-abdominal pressure, and OSA, which is a very common co-morbidity in grossly obese patients. Benumof[91] recommend that if opioids are used for the extubated post-operative patient, then one must keep in mind an increased risk of pharyngeal collapse and consider the need for continuous visual and electronic monitoring.

Other clinically-relevant undesirable side-effects of intrathecal administration of opioids are the well-known problems of drowsiness, pruritus, nausea, vomiting, and urinary retention. Drowsiness is a very common side-effect and occur more frequently on the first post-operative day.[77] Pruritus is usually mild or moderate and generally need no treatment. In those cases reporting severe pruritus, ondansetron,[92] tenoxicam,[93] propofol, nalbuphine or naloxone could be useful.[94] Nausea and vomiting should be prevented. Ondansetron 4 mg i.v. followed by a 4 mg infusion,[77] or by 4 mg every 6 or 8 h, could generally be a reasonable measure. But in several cases the addition of metoclopramide 10 mg i.v. every 6 h, offer a better symptom control.

Epidural analgesia

Post-operative epidural analgesia, by using either local anesthetics or opioids, may be the route of choice for post-operative analgesia in obese patients. It permits more vigorous cough and chest physiotherapy, vigorous

leg exercise and earlier ambulation and discharge from hospital.[73,74,95] These advantages lead to a more benign post-operative course, as manifested by earlier interest in reading, earlier walking and feeding and a lower incidence of pulmonary alveolar collapse and thrombo-embolic complications.[73,74,95] The epidural route is preferred over other parenteral routes for opioid administration also because of a reduced incidence of opioid side-effects such as drowsiness, respiratory depression, and nausea.[73,74] Moreover, when epidural morphine analgesia was applied in obese patients, supplementary requirements were seven to eight times less compared with i.m. morphine.[73,74] Post-operative extradural bupivacaine analgesia was more efficient than i.v. morphine with regard to cardiac protection.[96]

Spinal analgesia

Continuous spinal analgesia (CSA) could be a good choice alone or in combination with a general anesthesia for the surgery of obese patients, and may also be extended into the post-operative period as a natural progression from its intra-operative use.[77,97–100.]

The possibility of accomplishing excellent analgesia with the presence of an intrathecal catheter perioperatively makes the continuous spinal technique very attractive.

All the benefits described for the epidural technique in terms of reduced post-operative complications may also apply to CSA. However, there are distinct advantages of the CSA over a continuous epidural technique. These are: technically easier catheter insertion in obese patients, maximal analgesic effect with a minimum amount of drug, faster onset, and more predictable and controllable level of anesthesia–analgesia.[77,101]

Michaloudis and colleagues[77] believe that the CSA technique combined all the advantages and benefits during the intra-operative period, and provide satisfactory pain relief during the post-operative period, enabling this high-risk surgical population to go through the post-operative stressful and dangerous period safely, ameliorating most of the problems, and preventing the complications to which these patients are prone.[69,95,102] Furthermore, using low dose of local anesthetics, aids the physician in the diagnosis of a rare but disastrous subdural hematoma, since it does not produce dense motor or sensory block, allowing the symptoms and signs to become apparent.[77]

Patient-Controlled Intrathecal Analgesia

An important factor to achieve the better results of this high-technology technique, is the proper patient education in the use of the Patient-Controlled Intrathecal Analgesia (PCIA) facilities. In a recent study, Michaloudis and colleagues[77] performed a PCIA based on bupivacaine 0.05% plus fentanyl 10 μg/ml. A bolus of 1 ml of the solution was initially injected and then a continuous infusion was commenced at a rate of 1 ml/h. The PCIA settings were: bolus dose 0.5 ml (5 μg fentanyl + 0.25 mg bupivacaine), lock out interval 15 min, maximum total dose limits over 4 h 120 μg fentanyl + 6 mg bupivacaine. Obviously, all these regimens must be adapted to the patient's requirements. It's very common the necessity to increase or decrease the flow rate as well as the rescue doses or lock out interval, depending on pain intensity or patient's sedation–depression, respectively. Nevertheless it has to be noticed that these authors reported in their study an elevated rate of motor block, ranging from Bromage scale degree 1–3.

Other concomitant measures to apply with spinal/epidural analgesia

Caution is generally advised when parenteral opioids are administered to morbidly obese compared to non-obese patients, since they are thought to be more sensitive to the side-effects of this drugs.[52,69,102]

Monitoring

Respiratory rate, sedation score, sensory level of anesthesia, motor response (or motor block) and intensity of pain (remember the JCAHO recommendations)[23] must be monitored.

Oxygen therapy

Michaloudis and colleagues,[77] recommend the use of oxygen therapy, beginning at the end of surgery, continuing for the first 48 h and then for all the nights that patients are receiving CSA with local anesthetics and opioids. And we extrapolate the same measure to all the patients receiving epidural analgesia, with local anesthetics or opioids, alone or in combination.

29.5 Analgesic considerations for bariatric surgery

The pain from an open bariatric surgical procedure can be quite significant. Epidural local anesthetics and/or opioids via the thoracic route are a safe and effective technique to achieve sufficient post-operative analgesia in the obese population.[103] Potential advantages of thoracic epidural analgesia in the setting of bariatric surgery include prevention of DVT, improved analgesia, and earlier recovery of intestinal motility. Investigators have been unable to document

a difference in the incidence of thrombophlebitis and PE with continuous epidural analgesia.[95,74]

Less oxygen consumption and decreased left ventricular stroke work have, however, been documented as benefits of local anesthetic epidural analgesia.[96]

A recent abstract,[104] looked at patient-controlled thoracic epidural analgesia after gastric bypass surgery and found that it provided adequate post-operative pain control with few side-effects and no serious complications. Most of the patients were able to start oral intake on the second post-operative day and were discharged home by the fourth post-operative day. Another study on thoracic epidural analgesia,[105] found distinct advantages over PCA with morphine in providing a superior quality of analgesia and shortening the duration of post-operative ileus.

A recent meta-analysis reported a reduced overall mortality in patients receiving neuraxial blockade for major surgery further justifying the neurological risk and increased preparation time, which may be associated with a regional approach.[106]

Charghi and colleagues,[107] were surprised to find that patients receiving epidural analgesia had a four times greater risk of wound infection than subjects in the i.v. analgesia group. This difference was still valid when potentially confounding variables such as choice of antibiotics, patient demographics and co-morbidity are taken into account. This result was highly unexpected because it is commonly believed that, compared to i.v. opioid-based analgesia, peri-operative epidural blockade better preserves the cellular and humoral immune competence secondary to direct cytoprotective and anti-inflammatory effects and/or a more profound inhibition of neuroendocrine stress responses.[108]

Furthermore, i.v. opioids *per se* have been reported to produce immunosuppressive effects in surgical patients.[109] It also contrasts with the assumption that local anesthetics, as used in the bupivacaine/fentanyl epidural group, can favorably influence wound healing through a suppression of the neutrophil release of toxic products, thereby limiting the extent of surgical tissue damage.[110,111] They can only speculate about the factors responsible for the greater incidence of wound infections in patients receiving epidural analgesia. One explanation could be that better pain control enabled patients to move earlier and more extensively leading to less guarding and micro-dehiscence of the wound. It is tempting to hypothesize that a certain amount of pain during movement is "protective" after surgery, especially in the morbidly obese patient who is prone to poor wound healing. Intrathecal opioids are also a viable option. CSA has been used for post-operative analgesia after open vertical banded gastroplasty with demonstrated safety, efficacy, and a small incidence of morbidity.[77]

Laparoscopic bariatric surgery induces less post-operative pain and is less likely to interfere with pulmonary mechanics.[112] Most laparoscopic bariatric patients do well with local anesthetic wound infiltration and basic parenteral opioids, such as PCA. In a study of 200 patients who underwent vertical banded gastroplasty,[113] effective post-operative analgesia sufficient to allow mobilization was achieved by i.v. infusion of opioids or PCA. Choi *et al.*[22] also prospectively investigated the efficacy of PCA with morphine in morbidly obese patients undergoing Roux-en-Y gastric bypass surgery and found that it provided satisfactory analgesia without deleterious effects on oxygen saturation, blood pressure, heart rate, or respiratory function. Patients can be switched to liquid oral opioids on the first post-operative day after contrast (Gastrografin) swallow has eliminated anastomotic leaks, or as soon as they can tolerate them. Supplementation with oral or rectal non-opioid analgesics may be considered, but chronic NSAIDs drugs should be discouraged because of concern about gastric ulcers after bariatric procedures.

Feld and colleagues[114] found that with a pre- and intra-operative non-opioid drug combination (ketorolac, clonidine, lidocaine, ketamine, magnesium sulfate, and methylprednisolone), obese patients in the post-operative care unit (PACU) were less sedated, required less morphine by PCA and had similar pain scores compared to those fentanyl anesthetized patients, during gastric bypass surgery. The hypothesis of their study was that anesthetic adjuvants that decrease pain by mechanisms separate from opioids could produce analgesia in lower doses when given together, producing less side-effects and more rapid recovery compared to fentanyl. This is an advantage for gastric bypass surgery in patients that are at higher risk for respiratory depression. Although the non-opioid combination decreased sedation during recovery from anesthesia and reduced morphine requirements in the PACU, it is unclear how each one of the treatment compounds contributed to this effect.

29.6 Conclusions

All the potential consequences of poor pain control are a problem with morbidly obese patients undergoing surgery; and most of the major obesity-related health risks increase disproportionately with increasing weight; and in spite of this, most obese

patients with surgical pain do not receive adequate pain relief.[20]

According to the JCAHO and APS recommendations, pain should be considered the "fifth vital sign".[23,24]

The optimal efficacy of analgesia is frequently measured by the ability to cough and move without pain or discomfort, and not only by the absence of pain at rest. Early mobilization without discomfort should be considered an anesthetic target in this population due to the fact that DVT and PE are one of the most frequent causes of mortality during the first 30 post-operative days.

Few clinical trials have evaluated different techniques of post-operative analgesia in morbidly obese patients, but we can affirm that optimal management of post-operative pain can only be achieved by multimodal regimens (balanced analgesia).[44]

Drug pharmacokinetics differ in obese compared with non-obese patients, depending on factors related both to obesity and the drug used.[53,54] If the i.v. route is to be used, then a PCA is probably the best option for this kind of patients,[78] but there are case reports describing respiratory complications after the initiation of PCA post-operatively, especially in patients with OHS or OSA.[84] Opioid doses administered this way are not weight- or body surface area-dependent.[78,81]

For the morbidly obese patient undergoing upper abdominal or thoracic surgery or any other procedure with prominent nociceptive impact, regional analgesia may be the technique of choice.[52]

Local anesthetic requirements for epidural and spinal analgesia are reduced to 75–80% of normal in the morbidly obese. The epidural/spinal route for opioid administration is preferred over other routes because they produce less drowsiness, nausea and respiratory depression, earlier normalization of bowel motility, improved pulmonary function, and reduced hospital stay. Both agents combined epidurally/intrathecally may act synergistically, thus reducing the total dose of each drug, achieving the best analgesic efficacy due to different mechanisms of action (multimodal regional analgesia).[45,46]

All the benefits described for the epidural technique in terms of reduced post-operative complications may also apply to CSA. However, there are distinct advantages of the CSA over a continuous epidural technique. These are: technically easier catheter insertion in obese patients, maximal analgesic effect with a minimum amount of drug, faster onset, and more predictable and controllable level of anesthesia–analgesia.[77,101]

Up today, there is no enough supporting data resulting from prospective, randomized, double blind, controlled protocols, about the best analgesia technique for morbidly obese patients in each post-operative setting. Therefore, further studies are essential to improve post-operative pain management of this high-risk population.

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CONCLUSIONS

SECTION 9

ANESTHESIA AND MORBID OBESITY: PRESENT AND FUTURE

30

A.O. Alvarez

30.1 Obesity a growing medical problem

30.1.1 Conclusions regarding the disease: morbid obesity

Obesity is a major healthcare problem, and the prevalence is increasing. Recently it has been informed that its prevalence has grown dramatically from 1996 to 2000,[1] and is expected that it will rise to 40% by 2025. Actually 20% of patients have a body mass index (BMI) over 30, 2% over 40 and 0.25% over 50. Morbid obesity is a life-threatening situation in the long term and BMI over 40 if not treated, significantly shortens the individual's life expectancy.

The World Health Report for 2002 estimated that there were more than 2.5 million annual deaths due to weight-related problems, with 220,000 of those deaths in Europe and more than 300,000 obesity-related deaths in the US.

Deaths between the obese population are principally caused by coronary heart disease, stroke and diabetes mellitus, although sudden unexplained death, malignancies and fatal accidents are also more prevalent when compared with lean people. It has been shown that there is a 12-fold excess mortality in men in the age group 25–34 years and a 6-fold in those aged 35–44 years. In addition, the prevalence and severity of co-existing diseases has shown a clear correlation with the duration of obesity, therefore, it is advisable to provide a successful weight reduction treatment as early in the patient's life as possible.[2,3]

30.1.2 Conclusions regarding treatments for the morbidly obese

In 1990 it was estimated that 46 billion dollars, or 6.7% of all healthcare costs, were spent on obesity-related health problems in the US. It is assumed that actually, those costs are much higher. It has been

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noticed that obesity is associated with higher resource utilization.[4]

It would be advisable to evaluate the cost/benefit rate of every possible therapy, and accordingly design strategies in order to reduce costs and yet providing high quality health care.

Non-surgical therapy

Medically supervised weight-control programs have been ineffective in morbid obesity, because patients cannot maintain pronounced long-term weight loss.[5]

Bariatric surgery

In contrast, current operative methods have been proved to be effective in helping patients achieve and maintain permanent weight reduction. For optimal results, *patients must be carefully selected and treated by a multidisciplinary group*.[5]

The National Institutes of Health Consensus Conference in 1991 recommended that obesity surgery is an appropriate treatment for patients with BMI greater than 40 who had failed in attempts at medical treatment and for patients with a BMI greater than 35 with severe complications of obesity. Bariatric surgery remains the most reasonable treatment option for most morbidly obese patients. Vertically banded gastroplasty and Roux-en-Y gastric bypass were the two operations recommended because of their relative safety and effectiveness.[6] Both techniques induce an impressive loss of weight, and are surprisingly well tolerated, even by severely obese persons. The usual 50–75% reduction of initial weight excess, is followed by a clear-cut reduction, or even disappearance of, obesity-related co-morbidity, such as hypertension, diabetes mellitus or obstructive sleep apnea syndrome (OSAS).[7]

30.1.3 Conclusions regarding anesthetic management

The number of bariatric surgery procedures per year is significantly increasing; having been estimated that just in USA nearly 200,000 bariatric surgical procedures will be performed in 2004. Similar trends are observed in other countries. If this fact is combined with the permanent growth of the prevalence of obesity observed since more than five decades (with many of the patients at the range of morbid obesity), means that inevitably everyday, every anesthesiologist will have to deal with higher percentage of morbidly obese surgical patients scheduled for bariatric procedures. But since obesity is present in such a high percentage of the general population, and is also associated with a higher incidence of different surgical co-morbidities (such as gallbladder disease, several types of cancer and arthritis on weight bearing joints, coronary artery disease and others) anesthesiologist will also be frequently in front of a morbidly obese patient for non-bariatric surgical procedures.

As Dr. Brodsky mentioned in the preface, considering his practice at a major university medical center, he estimates that at least 25% of their routine surgical patients are obese and at least 10% of all patients are morbidly obese.

In addition technological and medical improvements achieved during the last decades, and a better knowledge about pathophysiology of obesity resulted in better outcomes in surgical therapies. This means that today patients who would not have been considered for any type of operation 20 years ago are being included for surgical treatment. Finally, some studies have shown efficacy in older obese patients.[8,9] Consequently patients with a higher number and also more severe co-morbidities are actually scheduled for elective bariatric surgery.

Unfortunately, the risks associated with anesthesia and surgery are believed to be higher for the obese patients than for normal weight patients. Greater perioperative morbidity and mortality have been observed in this population, specially related to derangements of the cardiopulmonary system.[10–14]

It is surprising, for example, that facing this situation, to date no specific cardiac risk index has been proposed for obese patients.

Deep vein thrombosis with pulmonary embolism is a dramatic complication associated with the morbidly obese patient, and is considered as the most frequent cause of death during the first 30 post-operative days, after bariatric surgery, therefore all efforts have to be done in order to diminish its incidence.[15–21] Early recovery of consciousness, ambulating capacity, pharmacological prevention and mechanical devices may reduce its occurrence.[22]

Pathophysiological changes induced by overweight (cardiac, respiratory, metabolic and digestive functions between others) and frequent co-morbidities (diabetes, arterial hypertension, sleep apnea, etc.) are involved in the increased risks and complications.[23–33]

Finally, fatal accidents are also more common between these subjects, and anesthesiologist should be the best skilled for initial treatment of trauma patient.

So it is clear why everyday is more frequent for every anesthesiologist to find these patients not only in the

operating room but also in emergency room and consequently why they should know in detail how to manage properly the obese individual.

30.2 Evolution of bariatric surgery

30.2.1 Scientific organizations

Bariatric surgery has gone already through a long history, but it has got a significant development in the last two decades.

Bariatric surgeons early recognized that if they got together and share experiences and information, surgical development would be faster and better.

Every medical society has born from the necessity of facing a new and different challenge between a group of professionals interested in a novel or particular procedure or situation. Motivations have always been the same: sharing experiences and information and to explore the possibility of development and improvement, but also to establish guidelines of procedures that have shown satisfactory results in the experience of the majority.

At present we have a new example, new procedures (for example, bariatric surgery) and new pathophysiological situation (morbid obesity). Surgeons have noticed this situation earlier. This has been the initial stone to build their societies.

Scientific Bariatric Societies have been created in order to search for improvements, through an organized process of investigation, data collection, guidelines of procedures, registration of complications and results. A pioneer organization is the American Society of Bariatric Surgery (ASBS) founded in 1983 (21 years ago). Since this very first experience, many other national bariatric societies appeared. To date dozens of national bariatric societies exists in the world.

These organizations have born as a different branch of general surgery because patient's characteristics are so particular that surgical procedures needed special surgical skills.

An International Federation for the Surgery of Obesity (IFSO) has been created many years ago and actually has a membership that includes over 30 national bariatric surgical organizations and members from 53 countries. IFSO members (most of them surgeons) have realized that a multidisciplinary approach, and a better and more profound knowledge about pathophysiology involved in these treatments have contribute to improve the outcomes.

Accordingly, in the lasts IFSO World Meetings, an increasingly allied health participation was noted. In fact, during Sao Paulo IFSO Annual Meeting 2001 a special conference about anesthesia and analgesia for the morbidly obese was included in the general program by Dr. Arthur Garrido (IFSO's 2000 Congress President) who is deeply persuaded about the importance of the combined work between surgeons and anesthesiologists. For the very first time, anesthesiologists (A.O. Alvarez, Buenos Aires, Argentina), bariatric surgeons (Alan Wittgrove, California, USA) and nutritionists (Tracy Owens, California, USA) got together in an international multidisciplinary experts round table to discuss about the complexity regarding the peri-operative management of the bariatric patient.

30.2.2 Investigation, data collection and communication

A National Bariatric Surgery Registry (NBSR) was created during 1980 decade in USA, encouraged by Dr. Edward Mason. Considering that surgeons have always learned from review of their personal experience and by comparisons with the experience of others, special computer programs were developed to provide surgeons with the proper tools to make these studies on a recurring basis. With the help of those programs all participating bariatric surgeons have the opportunity to review and compare their experience in a way that requires insertion of the information about each patient's encounter into the NBSR data base only once. This capability, together with the opportunity to exchange information rapidly with others who have similar interests, helps in the provision of optimum care for extremely heavy patients. It is the nature of clinical research to look for partial answers or trends and then to use that information to design specific prospective randomized studies to confirm or further test the hypothesis. The NBSR provides a better basis for designing such studies. Summarizing the NBSR has been developed to facilitate the gathering, analysis and dissemination of information about the care of morbidly obese patients. The basis for its creation is the belief that in the experience of hundreds of surgeons, with many thousands of patients, there are answers to questions about unusual situations that arise and that there is also information about selection of patients, operations, operative techniques, peri-operative care, quality of life and longevity that will further improve the management of extreme obesity.[34]

More recently an *International Bariatric Surgery Registry* (IBSR) has been created with similar purposes.

30.2.3 Technological issues

Laparoscopic approach, mechanical suture devices, adjustable gastric bands and robotic assistance have contribute to reduce time of surgery and body aggression, which have reduce morbidity and mortality, and eventually also healthcare costs. With the help of this technological development, special procedures have been designed, tested and finally performed successfully in morbidly obese subjects such as adjustable gastric banding and laparoscopic gastric bypass as described by Wittgrove and Clark.

In addition, during the last years, special equipment for heavy individuals such as beds, operating tables and transferring devices have been developed in order to improve patient's comfort, reduce position-related complications and facilitate many peri-operative practices.

30.2.4 Education (updating resources, training centers)

Many *books* dedicated solely to the surgical aspects of the morbidly obese individual are available for bariatric surgeons these days.

An official *journal* (*obesity surgery*) of the IFSO monthly publishes actualized information since more than 13 years ago. Every year an IFSO *Annual Meeting* takes place, in which bariatric surgeons from all over the world are able and encouraged to communicate each ones experience. National scientific events also take place in many countries with similar purposes (for example, ASBS Annual Meeting, Sociedad Española de Cirugia de Obesidad, SECO, and many others).

A web site "obesity-online" has been created by Dr. Karl Miller from Austria, encouraged by IFSO, as a multidisciplinary forum for research and treatment of massive obesity, including mostly information for bariatric surgeons but also plastics, psychiatry, endocrinology, nutrition, nursing, dietetics and other allied health. In addition useful links gives one the possibility to search for books, articles, ASBS Guidelines and mounts of other information. *Unfortunately anesthesia is not included yet*. In this web site it is emphasized once again the importance of the multidisciplinary approach to the morbidly obese surgical patient (see Chapter 1).

Finally information for patients is also available.

International training centers have been created to give surgeons the possibility to develop special skills and knowledge for the safety care of this population like the Salzburg Obesity Academy Foundation (recommended training center of IFSO). Also training programs like the *Laparoscopic Morbid Obesity Surgery Workshop* at Mount Sinai Hospital in New York are available for the bariatric surgeons to learn or improve their skills under the guidance of recognized experts.

30.3 Anesthesia for the morbidly obese: present situation

Why anesthesia have not grown together with surgical improvement regarding the morbidly obese individual? I am not capable to give a satisfactory answer.

30.3.1 Scientific organizations

Up to this moment anesthesiologists have not got any organization dedicated solely to the care of morbidly obese patients. Anesthesiologists nowadays have our possibility, just following the natural history of facts, to do the same and build our own organizations.

30.3.2 Investigation, data collection and communication

Investigation

There is an impressive paucity of randomized-controlled trials performed specifically for the morbidly obese population, even regarding basic anesthetic topics such as pre-operative evaluation, pharmacokinetics and dynamics, airway management, mechanical ventilation, post-operative pain management and many others. This seems to be inadmissible considering the prevalence of obesity and morbid obesity observed all over the world, and the fact that everyday more bariatric and non-bariatric procedures are performed in these patients. In fact the majority of the randomized-controlled trials exclude almost always the obese patients.

Data collection

In addition, there is not any national or international registry from which anesthetic outcomes of morbidly obese patients could be analyzed.

Communication

Communications about anesthetic procedures in this individuals are spread all over different kind of publications. In fact those that faced the challenge of writing this book had to deal with this undesirable situation.

30.3.3 Technological and pharmacological issues

It is clear that anesthetic technology has grown fast in Western civilization during the last two decades. Infusion devices assisted by pharmacokinetic models,

warming devices, anesthesia depth monitors and so, are now available for the anesthesiologist, making easier to follow closely the intra-operative evolution of his patients. Closed loop anesthesia is an extremely promising field, and quite suitable for this population. Unfortunately none of them have been validated yet in the morbidly obese and beyond that, many of them have to improve their results to be absolutely reliable even in lean population.

Some intravenous (remifentanil, propofol, atracurium and rocuronium) and inhalational (sevoflurane and desflurane) agents have demonstrated to be quite suitable for the obese patients.[35–42]

Nevertheless, controversy still exists regarding dosing schemes for most of them. Finally no randomized-controlled trials were performed to get reliable information about the outcomes with different drugs, dosing schemes or anesthetic techniques.

30.3.4 Education (updating resources, training centers)

It is unquestionable that it would be extremely helpful to count with bibliographic resources, in which all actualized information regarding peri-operative management of these subjects would be available for every anesthesiologist that has to face this contingency.

Updating resources

It is surprising and frustrating that there is an impressive paucity in scientific literature regarding this specific issue. In the last 30 years the only book written solely dedicated to the anesthetic management of obesity is a small monograph: *Anesthesia and the Obese Patient* in the *Contemporary Anesthesia Practice Series*, edited by Brown and Vaughan, and published over 20 years ago. Obviously, the techniques of anesthesia and surgery (laparoscopy, epidural opioids, total intravenous anesthesia, patient-controlled analgesia, target-controlled infusion, pharmacokinetic modeling, closed loop anesthesia, pharmacodynamic monitoring, etc.) have changed markedly over the past two decades. To date, unfortunately, information about this topic is usually incomplete, not actualized, controversial, poorly reliable and spread out wildly in different types of journals, being very difficult for the anesthesiologist to find easy and fast information. Up to this moment there is no other book, journal or web site exclusively dedicated to the peri-operative management of the morbidly obese.

Training centers

No specialized *training center or educational program* exists currently for anesthesiologists interested in providing anesthesia to these individuals.

30.4 Future of anesthesia for the morbidly obese: suggested actions to be taken

Facing the actual situation, it is more than licit to propone or at least hypothesize what actions should be taken to aspire for a possible and permanent improvement in the peri-operative care of the morbidly obese. Surgeons experience could be used as a guide for anesthesiologists.

30.4.1 Scientific organizations

Scientific anesthesiological organizations should be created with similar purposes than surgical ones.

In fact during last IFSO Annual Meeting held in Salamanca (2003), it has been discussed the feasibility of creating an international committee, for the study and development of anesthesia for the morbidly obese. All bariatric National Societies affiliated to IFSO have been encouraged to collaborate with the project. Many of the authors of the present book have already accepted to face this challenge.

The teleological objective is to develop an organization through which, anesthetic management (an in extension, also peri-operative care) be able to follow surgical development as a rational mechanism to improve the outcomes, quality of health care and peri-operative comfort of the morbidly obese individual. In addition, to stimulate the investigation and data collection in this field in a multidisciplinary fashion.

Why these scientific organizations should be created? Many reasons support this belief:

- Morbidly obese population is consistently increasing.
- Consequently, bariatric procedures are also increasing.
- Other type of operations in obese patients are also more frequently performed.
- Morbidly obese is more prone to suffer fatal or nearly fatal accidents.
- Therefore everyday higher chances for every anesthesiologist exist to be in front of a morbidly obese patient not only in the operating room but also in the emergency room.
- But these patients have severe pathophysiological alterations.
- And they suffer often severe co-morbidities.
- Thus morbidity and mortality is higher between them.
- Surprisingly there is a frustrating paucity of randomized-controlled trials especially performed for this population.

- As a final result, no guidelines for safety and efficient anesthesiological practice have been developed.

To reverse this situation it sounds rational to create scientific *ad hoc* organizations with clear objectives such as:

- review current data;
- design proper studies (randomized-controlled trials) to obtain reliable information;
- supervise and analyze the results;
- on the basis of results, suggest guidelines for anesthetic and peri-operative practice or design new studies in controversial or not explored fields;
- stimulate lines of investigation;
- design a data base;
- propone educational programs.

IFSO is the only surgical international organization dedicated solely to the morbidly obese patient. Anesthesiologists who work in a bariatric team will be frequently or may be absolutely devoted to the care of the obese surgical patient. Consequently this arena in which all patients will be morbidly obese, is the ideal place for this organization to be born.

IFSO has already gone through a long history, and actually accounts adequate resources to better diffuse any scientific development regarding surgery. It is obvious that these resources applied to anesthetic issues would be more than helpful for a faster communication of knowledge.

30.4.2 Investigation, data collection and communication

Investigation

In the era of evidence-based medicine, a rational systematic approach of all medical practices is the norm. We are therefore called upon to measure the success or the merit of any anesthetic practice on the basis of outcomes. Due to the above-mentioned paucity of reliable studies in morbidly obese individuals, many randomized-controlled trials should be designed and performed.

Data collection and communication

A special registry about anesthesia outcomes should be created, ideally encouraged, orientated and supervised by a related *ad hoc* scientific organization, which also would help in the diffusion and communication of the obtained results.

30.4.3 Technological and pharmacological issues

As it could be noticed through a careful reading of the book, it is obvious that anatomical physiological and pharmacological characteristics of these patients make the peri-operative care particularly problematic. Positioning and mobilization, monitoring, vascular and epidural access, drugs dosing and delivering, airway management and mechanical ventilation are between the most outstanding difficulties.

Accordingly investigation in all of this topics should be strongly encouraged.

30.4.4 Education (updating resources, training centers)

Updating resources

The first step has already been taken. A *book* considering peri-operative management of the morbidly obese is now available. But obviously even if re-editions already have been considered, the speed of scientific and technological development make it impossible to keep actualized information just through a book. This book should be considered as the first global approach to the topic. In fact, it is necessary to count at least with a *monthly publication* where not only anesthesiologists that work in this field, but also anesthesiologists working in other fields, have the opportunity to find easily, actualized, organized and complete information.

But further than a monthly publication, it is possible today to be daily actualized since we can count with Internet resources. *A web site* with forum discussions coordinated by experts in this field would be invaluable for permanent actualization. Further, it would be also possible to ask for counseling in different topics such as peri-operative assessment in particular individual situations or even any intra-operative query could be replied online by a 24 h available team of specialists. This latter could be helpful not only considering the anesthetic practice but also as a protective legal tool.

In my opinion, these days, every operating room should count with a computer permanently connected to the net. In fact necessary technology to provide a total intravenous anesthesia through Internet is already available in developed world (computerized infusion pumps, computerized perfusors and multiparametric and anesthetic monitors from which a feed back is possible from any computer in the world). In fact taking advantage of robotics virtual reality and Internet resources, trans-continental laparoscopic surgeries have already been performed. For anesthesiologists this kind of technology could be useful for training purposes, and scientific professional support.

Today we have the appropriate tools to aspire for significant development in our science. The long history

of medical evolution supports this belief. It is my deepest hope that in the near future we can witness the necessary improvement in the peri-operative care of the morbidly obese patient.

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AFTERWORD

In recent years, there has been, literally, a field change in bariatric surgery. In a compound word, it has become "well-developed". And, this development has manifested itself in the many different ways that this book has sought to convey.

However, further development lies particularly in the sustained productivity of those who support the surgeon and his/her patients, including *you*, "The Reader". For example, there is, as of yet, *no* bariatric surgical cardiologist, pulmonologist, infectious disease or those of other relevant specialties who have taken sufficient interest in bariatric surgery so as to unify as a group to "push the envelope" further in improving the quality of their knowledge and services for the morbidly obese patient. The only exception, apart from the International Federation for the Surgery of Obesity (IFSO) Allied Health Sciences Section, has been the anesthesiologists, who have recently organized under the rubric of the IFSO.

In time, we expect that, with hundreds of thousands of bariatric surgeries performed annually, professional necessity alone will eventually cause each bariatric, surgically relevant specialty to join together just as the anesthesiologists have done.

And, this will arrive none too soon. The current "mysteries" of the excessive appearance of post-operative acute respiratory distress syndrome (ARDS), systemic inflammatory response syndrome (SIRS), multi-system organ failure, infections, depression and other distressing complications following bariatric surgery demand better scientific explanation. And, even more important, they need better therapy and, hopefully, means of anticipating and preventing them in the first instance. Hopefully, many of these will arrive sufficiently soon so that we can include them in the next edition of this book.

The "cure" of morbid obesity and lesser forms of excessive body weight appear to be as elusive as are cancer and the common cold. Since it will be at least two or more decades until a "cure" for certain forms of obesity are developed, refined and approved, bariatric surgery will remain the sole resort for those morbidly obese, who seek long-term relief from their massive, excessive weight and its punishing co-morbidities. Therefore, there is no excuse from any sub-specialists who work with the morbidly obese, or the bariatric surgeons themselves, from strongly encouraging, nay, demanding that each of the specialties involved unite in support of "Our People", the morbidly obese. We will be watching, and waiting, to report your welcome contributions.

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