Minimally Invasive Cardiac Surgery

CONTEMPORARY CARDIOLOGY

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SPRINGER SCIENCE+BUSINESS MEDIA, LLC

Originally published by Humana Press Inc. in 1999
Softcover reprint of the hardcover 1st edition 1999

This publication is printed on acid-free paper. ∞
ANSI Z39.48-1984 (American National Standards Institute)
Permanence of Paper for Printed Library Materials.

Cover design by Patricia F. Cleary and Karen Schulz.

10 9 8 7 6 5 4 3 2 1
Minimally invasive cardiac surgery / edited by Mehmet C. Oz, Daniel J. Goldstein.
p. cm. -- (Contemporary cardiology ; 2)
Includes index.
ISBN 978-1-61737-108-0 ISBN 978-1-4757-3036-4 (eBook)
DOI 10.1007/978-1-4757-3036-4

1. Heart--Surgery--Miscellanea. 2. Coronary artery bypass--Miscellanea. 3. Operations, Surgical--Miscellanea. I. Oz, Mehmet C., 1960– . II. Goldstein, Daniel J., MD. III. Series: Contemporary cardiology (Totowa, NJ) ; 2.
[DNLM: 1. Heart Diseases--surgery. 2. Surgical Procedures, Minimally Invasive--methods. 3. Cardiac Surgical Procedures--methods. 4. Vascular Surgical Procedures--methods. WG 169M665 1999]
RD598.M525 1999
617.4'12--dc21
DNLM/DLC
for Library of Congress 98-30788
CIP

PREFACE

The purpose of *Minimally Invasive Cardiac Surgery* is to introduce the reader to the exciting developments in the field of "minimally invasive" or "minimal access" cardiac surgery. All the chapters have been written by investigators actively involved in their respective fields. We are appreciative of the concerted effort made by our collaborators to provide us with the most up-to-date material possible, thus making the book both timely and useful for those working in this rapidly evolving field. More than highlighting specific experiences and surgical procedures, we hope this text will outline an optimal approach to a rapidly developing new field of cardiac surgery, one that will substantially benefit future investigators and practitioners, as well as their patients.

Minimally Invasive Cardiac Surgery is organized into three major sections. The first part, Physiology of Injury, consists of a basic science review of the pathophysiological mechanisms underlying cardiopulmonary bypass and endothelial injury. To understand the benefits of avoiding cardiopulmonary bypass, Dr. Ron H. Speekenbrink and his colleagues examine the effect of extracorporeal circulation on the stimulation of coagulation pathways, the generation of interleukins and cytokines, the expression of adhesion molecules, and the regulation of vascular tone by the endothelium. Potential approaches to the attenuation of these effects are also discussed.

Vascular endothelium has emerged as a crucial player in the genesis of the diverse biological events that occur during the perioperative course of patients undergoing cardiac surgery. Indeed, surgical manipulation, shear stress, vasospasm, and ischemia/reperfusion injury are just a few of the important mediators of endothelial cell injury. This topic is reviewed in detail by Drs. Talia Spanier and Ann Marie Schmidt, prominent researchers in the field of vascular biology.

The second theme, Less Invasive Approaches to Coronary Bypass Grafting, is the most extensive section in the book, owing to the burgeoning interest in less invasive approaches to myocardial revascularization. Dr. LeRoy Rabbani and associates present the interventional cardiologist's perspective on minimally invasive approaches to coronary revascularization. A comprehensive review of the data derived from the randomized trials comparing angioplasty and stent therapy with surgical revascularization is presented and the benefits, disadvantages, and indications for each therapy are discussed.

Optimal visualization, careful and meticulous harvest of the internal mammary artery, and reduction of cardiac motion are the three key factors underlying the success of beating heart coronary bypass grafting through limited incisions. In the following three chapters, renowned authors discuss these topics. Dr. Michael J. Mack dissects the elements that presently comprise videoscopic systems in his chapter on visualization techniques. A glimpse into the state-of-the-art in videoscopic surgery, including the use of head-mounted displays and "virtual" surgery, is presented.

Controversy persists on the vessel length and incision necessary to achieve an optimal internal mammary artery conduit. Based on the various techniques of less invasive

revascularization currently practiced, Dr. Patrick Nataf presents an overview of the different approaches to the harvest of the internal thoracic artery. Particular attention is focused on the advantages of the thoracoscopic approach.

A factor critical to the success of beating heart bypass grafting is immobilization of the surgical field. Dr. M. Clive Robinson from the University of Kentucky has pioneered the use of pharmacological techniques to achieve myocardial wall stabilization. In the chapter entitled "Myocardial Stabilization Techniques During Off-Pump Coronary Grafting," the author presents the rationale and clinical experience with adenosine-induced transient asystole for the creation of coronary anastomosis and reviews the different mechanical stabilizers that are currently available to achieve optimal surgical conditions for beating heart surgery.

The ensuing two chapters encompass the clinical experience of pioneering groups of investigators who have advanced our knowledge of beating heart coronary grafting through their extensive clinical experience. Drs. Antonio M. Calafiore and Valavanur A. Subramanian are largely responsible for the introduction and dissemination of coronary grafting on the beating heart through limited incisions in Europe and the United States, respectively.

Port-access coronary bypass grafting, a major alternative to off-pump revascularization, was in part developed by the New York University group who discuss in detail the technique and excellent results that can be obtained. Unlike off-pump techniques, the port-access method relies on the conventional use of cardiopulmonary bypass and myocardial protection, achieved through endovascular access and tiny incisions.

The final five chapters of this section deal with aspects peripherally related to less invasive bypass grafting. Dr. Nader Moazami discusses the different systems available for endoscopic saphenous vein harvest and reviews the clinical experience in the literature. Though the hand-sewn technique remains the preferred method for creation of a vascular anastomosis, many investigators in the field believe that broader applicability of beating heart bypass grafting is contingent upon the development of facilitated methods for creation of coronary anastomosis. Dr. Paul M. N. Werker, from the Hospital of Utrecht, presents a comprehensive historical perspective on alternative methods of anastomosis, including the use of mechanical devices, laser welding, glues, and automated staplers.

The use of miniature axial flow pumps instead of cardiopulmonary bypass to unload the left ventricle and to reduce ventricular motion while maintaining coronary and systemic perfusion is currently being investigated. Dr. Robert K. Jarvik who pioneered and developed one such device collaborates with Dr. Joseph J. DeRose to describe the current state of the art in cardiac support using these innovative pumps.

Increasingly, the success of innovative ideas hinges on the cost-effectiveness associated with their application. To this effect, Dr. Gerald M. Lemole and colleagues examine the economic impact associated with the use of off-pump coronary grafting procedures at one institution, and dissect the New York State Database to identify the predictors for length of stay. In the last chapter in this section our group reviews the generally neglected yet very important quality-of-life issues that are associated with the use of less invasive cardiac procedures.

The third and final section in this book addresses growing areas of less invasive cardiac surgery, including valvular and congenital heart operations. Drs. W. Randall Chitwood and Steven R. Gundry, pioneers in the less invasive revolution describe their extensive experiences with "mini" approaches to mitral and aortic valve pathology. Finally, Dr. Gregory P. Fontana delineates the advances made in both extracardiac and intracardiac repairs via less invasive approaches and hints at the roadblocks that must be overcome and the advances that are likely to take place to achieve less invasive correction of complex congenital cardiac repairs.

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CONTENTS

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1 Introduction

What is Minimally Invasive Cardiac Surgery?

Daniel J. Goldstein, MD
and Mehmet C. Oz, MD

CONTENTS

INTRODUCTION

The excitement that began with the introduction of laparoscopic cholecystectomy in the late-1980s has grown to encompass every surgical field. Fueled by commercial interests, patients' expectations, and surgeons' fascination with new technologies, minimally invasive surgery has, within a short decade, forever revolutionized the practice of surgery. The unwavering enthusiasm with which minimal invasive surgery has been adopted is reflected by recent predictions that within 5–7 yr, 70% of operative interventions in this country will involve minimal access techniques *(1)*.

The major benefit of minimal access surgery lies in reducing the trauma associated with gaining exposure without compromising the operative field. Inherent to this approach is the maintenance of a closed physiologic environment, the reliance on two-dimensional visual input, and the use of small instruments to expose, dissect, and divide tissues *(2)*. Some of the theoretical advantages of these approaches—decreased postoperative pain, rapid convalescence, and early return to work—have been confirmed in the clinical arena. Other purported benefits such as decreased cost, decreased postoperative complications, and less adhesion formation remain to be proven. Moreover, unforeseen and unresolved issues such as access port neoplastic recurrence *(3–5)* and potential immunologic benefits *(6)* are likely to impact the widespread acceptance of minimally invasive approaches.

Initially limited by a lack of technology and frank skepticism, minimally invasive cardiac surgery has now become technically feasible and widely accepted. Although the

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

most significant developments and clinical experience have been realized with coronary bypass surgery, efforts are increasingly being directed toward implementation of these techniques in valvular repairs and replacements and in congenital heart surgery.

CORONARY BYPASS SURGERY: WHAT IS MINIMALLY INVASIVE?

Although arising for a variety of motivations and rationales, the "mini" movement in heart surgery is really a call for more attention to the quality of life rather than just the mortality rates provided by procedures. A review of the cardiac surgical literature to date demonstrates a remarkable paucity of studies on how well our procedures restore patients to a "normal" life. Rather, we have been deluged with mortality and major morbidity data on perhaps the best and most widely studied operation in history. These large multicenter and multinational studies appropriately needed to demonstrate that these major operations could be done with some degree of safety and reproducibility. However, over the past decade, surgeons and their patients have become comfortable with the low mortality rates that are often quoted in major databases. Both groups desired to move to the next level of service—the same operation with fewer side effects, especially in the short run. This fertile soil for procedural growth awaited the innovative approaches that were developed in part by many of the authors in this book.

Especially for minimally invasive coronary artery bypass grafting (CABG), the current increase in interest has also, in part, been stimulated by a recognition of the importance of a patent graft to the left anterior descending (LAD) to long-term survival after CABG *(7)*. Indeed, the inability of percutaneous procedures to address many LAD lesions, as well as concerns about durability and costs associated with these interventions, has created a demand for a surgical procedure that avoids cardiopulmonary bypass (CPB), allows rapid recovery, and provides results equivalent to those attained with conventional surgical techniques. However, the definition of what is minimally invasive remains clouded. The argument over terminology centers on the size and location of the incisions and whether CPB is avoided.

At least six different approaches to myocardial revascularization have been popularized (Table 1). The different modalities vary with regard to whether the heart is arrested or not, the type of access employed, and the method and extent of internal mammary artery (IMA) harvest. Moreover, for beating heart revascularization, mechanical, pharmacologic, or neural stabilization methods have been used (Table 2).

The current terminology used to describe these techniques is confusing. The terms "MIDCAB," "keyhole," "port access," "LAST" and "video-assisted" have all been used to denote minimally invasive techniques in the literature. Unlike the tenets used by general surgeons, we would argue that the surgical approach for patients undergoing cardiac operations is less important in defining minimally invasive techniques than is the avoidance of CPB. And indeed, this was the sentiment expressed by the majority of cardiac surgeons polled at a recent national meeting.

We propose, therefore, that the terminology for nonconventional open heart surgery be modified to reflect the change in incisions ("minimal access") or the avoidance of CPB

Table 1
Features of the Different Approaches Currently or Soon to Be Available for Surgical Myocardial Revascularization

	"Incision invasiveness"	*Sternotomy*	*Ease of IMA harvest*	*CPB*	*Ease of anastomoses*	*Appropriate for multivessel disease*	*Short-term results*	*Long-term results*	*Comment*
Conventional CAB	Most invasive	Yes	Very easy	Yes	Very easy	Yes	Excellent	Excellent	Most tested, safe, and reliable approach
"Off-pump" CAB	Very invasive	Yes	Very easy	No	Difficult	Not for posterior heart	Good	NA	Expanding experience
MIDCAB[a] ± VA[b]	Minimally invasive	No	Moderate	No	Difficult	No	Good	NA	Limited experience
MIDCAB + HFA[c]	Less invasive	No	Easy	Yes	Easy	Not for posterior heart	NA[d]	NA	Very limited experience
Port access	Less invasive	No	Easy	Yes	Easy	Yes	Good	NA	Limited experience
Device-supported CAB	Very invasive	Yes	Easy	No	Easy	Yes	NA	NA	Is device support better than CPB?
Complete thoracoscopic CAB	Least invasive	No	Moderate	No	Very difficult	No	NA	NA	Minimal clinical experience

[a]Minimally invasive direct coronary artery bypass.
[b]Videoscopic assistance.
[c]Hypothermic fibrillatory arrest.
[d]Not available.

Table 2
Variable Techniques That Have Been Clinically Used for "Globally Arrested" and "Beating Heart" Myocardial Revascularization

- Access
  - Median sternotomy with full skin incision
  - Median sternotomy with limited skin incision
  - Hemi- or partial sternotomy
  - Limited thoracotomy
  - Port
- IMA harvest
  - Method
    - Direct
    - Video assisted
  - Extent
    - Complete
    - Partial
- CPB
  - Atrio-aortic (standard)
  - Femoro-femoral
  - None
- Cardiac arrest
  - Cardioplegia: warm vs cold, anterograde vs retrograde, blood vs crytalloid
  - Hypothermic fibrillatory arrest with continuous coronary perfusion
  - None
- Stabilization
  - Mechanical
    - Epicardial traction sutures
    - Coronary artery stabilizer
  - Pharmacologic
    - β-blockers
    - Adenosine
    - Calcium-channel blockers
  - Neural
    - Vagal stimulation
- Anastomoses
  - Hand sewn
  - Clipped: automated

("beating heart"). Some operations, such as the limited anterior small thoracotomy advocated by Calafiore, would be termed "minimal access beating heart." A HeartPort approach would be categorized as "minimal access" whereas a sternotomy incision for an off-CPB procedure would be termed "beating heart." The connotation is that the ideal procedure would offer the smallest, least painful incision and the avoidance of CPB.

With regard to valvular surgery, the terminology is more straightforward. At present, all approaches to valvular repair and replacement rely on the use of CPB and cardioplegic arrest. Hence, the term "minimal access" or "minimally invasive" valvular surgery evoke the same image. To maintain consistency with the previous

definition of "invasive," these operations would be best categorized as minimal access valvular surgery because they all rely on extracorporeal circulation.

Part of the goal of this book is to provide answers to these challenging questions. Which incisions fulfill the presented criteria and what alternatives exist to CPB? Are the small gains worth the effort? The experts spotlighted in this book will present their perspectives on these complex issues and will help lay the foundation on which current investigators can stand as they clarify what "minimally invasive" really means.

REFERENCES

1. Lawrence K. Minimal access surgery: harnessing the revolution. Lancet 1994;343:308,309.
2. Cuschieri A. Minimal access surgery and the future of interventional laparoscopy. Am J Surg 1991;161:404–407.
3. Drouard F, Delamarre J, Capron JP. Cutaneous seeding of gallbladder cancer after laparoscopic cholecystectomy. N Engl J Med 1991;325:1316.
4. Dobronte Z, Wittman T, Karacsony G. Rapid development of malignant metastasis in the abdominal wall after laparoscopy. Endoscopy 1978;10:127–130.
5. Alexandre RJ, Jaques BC, Mitchell KG. Laparoscopically assisted colectomy and wound recurrence. Lancet 1993;341:355–358.
6. Allendorf JD, Bessler M, Whelan RL, et al. Postoperative immune unction varies inversely with the degree of surgical trauma in a murine model. Surg Endosc 1997;11:427–430.
7. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal mammary artery graft on 10 year survival and other cardiac events. N Engl J Med 1986;314:1–6.

I Physiology of Injury

2 Pathophysiology of Cardiopulmonary Bypass

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Contents

INTRODUCTION

From the earliest clinical experiences with cardiopulmonary bypass (CPB) for cardiac operations, it was apparent that significant morbidity and mortality were associated with the CPB procedure itself *(1)*. Often, only the contact of blood with the foreign material of the extracorporeal circuit was held responsible. However, CPB implies more than just connecting the circulation of the patient to an extracorporeal circuit, resulting in the material *dependent* activation of blood. With CPB a number of other nonphysiological events are introduced, including hemodilution, hypothermia, nonpulsatile blood flow, retransfusion of shed blood, and exclusion of the metabolic function of the lung, resulting in material *independent* activation. Together, these events cause the massive and systemic activation of the patients' defense systems with repercussions on nearly every organ system. Signs of this "whole body inflammatory reaction" can be observed in every postoperative patient. In a number of patients, especially neonates, the elderly, and those undergoing large procedures or with severe comorbidity, this phenomenon can escalate into the so-called postperfusion syndrome, which is characterized by elevated cardiac

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
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output with decreased vascular resistance, capillary leak, and renal dysfunction, and is associated with increased mortality *(2)*.

The impressive clinical recovery that is achieved with so-called minimally invasive cardiac procedures without CPB further illustrates the deleterious effects of CPB. Recently, a biochemical evaluation in patients in whom coronary artery bypass grafting (CABG) was accomplished using minimally invasive off-pump techniques was performed. We found no activation of complement, leukocytes, or platelets. This freedom of side effects on a biochemical level was supplemented by a 50% reduction in postoperative blood loss, no need for transfusion of donor red blood cells, and a 40% reduction in ventilatory support time and hospital stay *(3)*. Although these figures certainly support further expansion of minimally invasive procedures, the use of CPB for more complex and intracardiac repairs at present, cannot be obviated. The favorable results with minimally invasive procedures should act as a stimulus to improve the procedure of CPB.

In this chapter, we discuss the various biochemical mechanisms that underlie the deleterious effects of CPB, methods to mitigate these effects, and guidelines for future developments.

MATERIAL-DEPENDENT ACTIVATION

In the past, activation of the contact system by the nonbiocompatible surface of the extracorporeal circuit was considered to be the initiating factor in blood activation in CPB, and to be responsible for most of the detrimental effects of CPB. Because the contact system is linked to the other humoral defense systems, its activation would result in activation of the kallikrein, fibrinolytic, and coagulation systems. The active products of these systems would cause, directly or indirectly, via activation of leukocytes, platelets, and endothelium, part of the detrimental effects of CPB *(4)*. This concept is supported by studies in simulated bypass models showing activation of the contact system by the extracorporeal circuit *(5)*. However, clinical observations from patients with a deficiency in contact system proteins have undermined this concept. Indeed, patients with a severe deficiency of the primary factor of contact activation, factor XII, were shown to have similar patterns of thrombin generation as in healthy patients *(6,7)*. Moreover, data from recent clinical investigations have shown no change in the marker for contact activation, kallikrein-C1 esterase inhibitor complex between prebypass and bypass levels, and no increase of factor XIIa levels during CPB *(8,9)*. Furthermore, the levels of a second marker for contact activation factor XIIa-C1 esterase inhibitor complex during CPB remained below the detection limit in the majority of patients *(8)*. Coagulation studies have shown that factor X activation and thrombin generation precede factor IX activation during CPB, which indicates activation through the extrinsic (tissue factor) pathway and not through the intrinsic (contact phase) pathway *(9,10)*. From these data it appears justified to conclude that the role of the contact system in CPB needs to be redefined.

It is undisputed that the contact of blood with foreign materials results in the activation of the complement system. Complement is activated through one of two pathways: the "classical" or the "alternative" pathway. The latter is predominantly involved in complement activation by biomaterials since it can be activated in the absence of specific antibodies *(11)*. Both pathways form complexes named "C3 convertases" that cleave the third component of complement, C3, generating the anaphylatoxin C3a and a major cleavage fragment, C3b. Accumulation of C3b molecules onto the surface in the vicinity of C3 convertases changes the specificity of the C3-cleaving enzyme into a C5 convertase, resulting in the cleavage of C5, generation of the leukocyte-activating C5a, and recruitment of the terminal complement complex (TCC) C5-C9 *(12)*. During CPB, C3a appears in the circulation after 10–20 min, followed by C5a and TCC *(13)*.

Although the composition of the artificial surfaces plays a predominant role in complement activation during CPB, complement can also be activated by nonbiomaterial–dependent triggers. Contact of air with blood as it occurs in bubble oxygenators and in the cardiotomy suction line activates complement *(14)*. This advantage of the membrane oxygenator, having no direct blood-air contact, may be nullified by its larger surface *(15)*. Dextran 70 and, to a lesser extent, polygeline induce complement activation *(16)*. Classical pathway activation is also initiated by the interaction of C1 with antigen–antibody complexes and, in some instances, with other activators, including some bacterial and viral surfaces and bacterial endo- or exotoxins *(17,18)*. Furthermore, activation of the classical pathway occurs after administration of protamine through formation of heparin–protamine complexes *(19,20)*.

The effects of complement activation are mediated by the products C3a, C5a, and TCC. TCC, also called the membrane attack complex, deposits on erythrocytes and leukocytes to augment cell lysis and cell activation *(21)*. Recently we found that TCC concentrations formed during pediatric CPB correlated with postoperative fever and gain in body weight *(22)*. C3a and C5a are also called the anaphylatoxins. These molecules have chemotactic activity for neutrophils and monocytes *(23)* and induce cytokine release. Binding of C5a and C5a desArg to specific receptors on neutrophils induces:

1. Aggregation of the cells and their adherence to endothelial cells *(24,25)*;
2. Release of reactive oxygen species that may damage the endothelium to which activated neutrophils have bound *(26,27)*;
3. Release of lysosomal enzymes *(28)*; and
4. Neosynthesis and release of leukotrienes *(29,30)*.

Special attention has been paid to the lysosomal enzyme elastase, which affects the endothelial junctions *(31)* and enhances vascular permeability for blood proteins *(32)*. The appearance of proteins, including elastase in the alveolar space, may be an important cause for surfactant dysfunction and decreased lung compliance, resulting in pulmonary dysfunction and possibly in the adult respiratory distress syndrome *(33)*.

Cytokines are released by monocytes, macrophages, endothelium, and other cells upon stimulation with the anaphylatoxins or the lipopolysaccharide endotoxin, a constituent of the cell wall of Gram-negative bacteria. A number of acute and chronic adverse

consequences, such as hypotension and an increased body temperature after extracorporeal circulation, may be attributed to the cytokine interleukin-1 (IL-1) *(34)*. IL-1 is an essential component of the inflammatory reaction and the immune response by its ability to stimulate neutrophil degranulation *(35)* and to activate T- and B-cells *(36,37)*. The cytokine tumor necrosis factor (TNF), a mediator of the host response in sepsis, is derived from monocytes and macrophages *(38)*. It has some common properties with IL-1 such as induction of fever *(39)*. TNF induces procoagulant activity *(40)* and IL-1 release *(39,41)* from endothelial cells by interaction with specific receptors. TNF generation has been measured in CPB patients and was assumed to be associated with endotoxin release *(42,43)*. Interleukin-6 (IL-6) is produced by activated monocytes, endothelial cells, fibroblasts, and T- and B-cells. It is therefore a general marker of blood and tissue damage, observed in a variety of surgical interventions and diseases. In CPB, IL-6 is of interest by its correlation with the ischemic time during cross-clamping *(44)*: four hours after CPB, peak levels of IL-6 are observed *(45)*. Next to its function as a marker for inflammation, IL-6 generated in the ischemic myocardium appeared to induce intercellular adhesion molecule-1 (ICAM-1) on the myocyte surface, which could be held responsible for granulocyte adhesion in the myocardial tissue after reperfusion of the ischemic heart *(46)*. IL-8, similar to IL-6, is produced in several cell types, including alveolar macrophages, fibroblasts, lymphocytes, and endothelial cells. IL-8 plays an important role in leukocyte activation and contributes to myocyte reperfusion injury. Its responses have been reported to be at maximum during or 2 h after CPB *(44,47)*, which is faster than other proinflammatory cytokines. IL-8 release is thought to be dependent on C5a generation *(48)*. IL-10 was recently reported as an anti-inflammatory cytokine that deactivates monocytes and macrophages and thus likely reduces release of IL-6, IL-8, and TNF. Its rapid release within 1 h after CPB may offer important negative feedback to further TNF production *(44)*.

Adhesion molecules play a major role in the recruitment of neutrophils to the site of inflammation. Multiple steps are involved in this process. In each step, a different family of adhesion molecules takes part. The rolling phase of neutrophils over the endothelial layer is mediated by the selectin family, the E-, L-, and P-selectins and their ligands. The next step, the activation and adhesion of the neutrophils to the endothelium, is regulated by the integrin family and their ligands. The final step of transendothelial migration is mediated by these two families of adhesion molecules, the selectins, and integrins. It was found that soluble isoforms of these adhesion molecules can be found in circulation. In addition, these soluble isoforms appeared useful as markers of disease activity and they have physiologic effects *(49)*.

E-selectin is a specific marker for endothelial activation. The soluble form is biologically active in its capacity to bind to neutrophils. High concentrations of (recombinant) E-selectin can inhibit neutrophil adhesion. L-selectin is produced by leukocytes after stimulation with chemotactic peptides, IL-8, or endotoxin, and enhances the binding of leukocytes to (inflammed) endothelium. P-selectin is produced by platelets and endothelium and mediates the interaction with neutrophils and some lymphocyte subsets. It has

been suggested that P-selectin has anti-inflammatory effects, shown by reduced oxygen radical production by neutrophils and by the inhibition of integrin-mediated adhesion of neutrophils *(49)*. The most extensively studied integrin in the field of CPB surgery is CD11b/CD18, previously called Mac-1 or CR3 *(50,51)*. The increased adhesiveness of neutrophils following incubation with C5a and C5a desArg is dependent on the enhancement of membrane expression of the adhesion-promoting glycoprotein Mac-1 on the cells *(52)*. The integrins bind to the ECAM-1, ICAM-1, and VCAM-1, which are constitutionally expressed ligands on endothelium *(53)*.

The expression of CD11b/CD18 and L-selectin have been used as markers for neutrophil activation during CPB *(54)*. CD18 expression increased immediately at the start of CPB, whereas L-selectin was shed from the neutrophil surface, shown by a gradual loss during 60 min of CPB. Similarly, instant activation of platelets, reflected by a decreased expression of the adhesive receptor Gp1b after initiation of CPB has been reported *(55)*. Markers for activation of the complement, coagulation or fibrinolytic systems do not show such rapid increases at the onset of CPB but rather increase slowly during the procedure. Therefore, the stimulus for this rapid activation of platelets and neutrophils is unclear. It is possible that direct activation by the foreign surface is involved. Another explanation could be the production of trace amounts of activators, not distinguishable systemically, on the surface of the extracorporeal circuit *(56)*. Based on the observations of fast cellular responses to extracorporeal circulation, the generally used activation scheme—contact activation leads to activation of humoral defense systems, which leads to activation of cells—probably needs to be revised. Most likely, the activated cell membranes and the cell constituents form major triggers for activation of the hemostatic and inflammatory reactions to CPB.

The endothelium plays an important role in the regulation of vascular tone. Two systems are involved in this regulation: the nitric oxide (NO)/endothelin and the prostacyclin/thromboxane systems. Both systems are affected by the inflammatory response after CPB. NO was formerly known as endothelium-derived relaxing factor. It is formed by two synthases, a constitutive form, which produces NO in picomolar quantities, and an inducible form, which produces nanomolar amounts of NO *(57)*. The activity of the inducible form is increased by endotoxin, TNF, and IL-1. Increased NO concentrations are found during and after CPB, and might have a role in the vasoplegic syndrome affecting some patients after cardiac procedures *(57)*. The cardiodepressive effect of IL-6 and TNF was shown to result from increased NO production through inducible synthase activation *(58)*. Moreover, NO in high concentrations has been implicated in vascular, lung, and bowel injury *(59)*. The counterpart of NO is endothelin, a small peptide with potent vasoconstrictive capacities that is produced by endothelium, macrophages, and the hypothalamus *(60,61)*. Institution of CPB results in a rapid increase of endothelin, which is likely the result of a neurohumoral response to decreased blood pressure. During CPB, a slow increase of endothelin concentrations can be observed that correlates with endotoxin concentrations *(62)*. Inappropriate endothelin concentrations can cause pulmonary hypertension, myocardial ischemia, and might have a role in perioperative gut ischemia *(62–64)*.

Prostacyclin and thromboxane are products of the cyclooxygenase pathway located in platelets and endothelium. Prostacyclin (PGI_2) is produced by endothelial cyclooxygenase. It is a potent vasodilator and inhibits platelet adhesion to endothelium in synergy with NO. Thromboxane B_2 (TXB_2) is produced by activated platelets and results in irreversible platelet aggregation and vasoconstriction. The balance between prostacyclin and TBX_2 can be modified with acetylsalicylic acid, which irreversibly inhibits platelet cyclooxygenase. This is a common therapy in patients with coronary heart disease. During CPB, prostacyclin levels are increased owing to the presence of heparin. Following platelet activation, TBX_2 levels are increased during and after CPB *(65)*. This results in a disturbed balance between prostacyclin and TBX_2 in the immediate postoperative period, which might have an influence on graft patency. It has been advocated to continue acetylsalicylic acid therapy in the perioperative period, but fear of increased postoperative bleeding has discouraged many centers to adopt this policy. Since treatment with aprotinin effectively inhibits the increased bleeding in acetylsalicylic acid–treated patients but maintains the effect of acetylsalicylic acid on platelets, this policy is no longer warranted *(66)*.

METHODS TO ATTENUATE MATERIAL-DEPENDENT ACTIVATION

Heparin Coating

A large improvement in the biocompatibility of the extracorporeal circuit was expected with the development of heparin-coated extracorporeal circuits. The concept behind heparin coating is to mimic the endothelial surface that contains heparan-sulphate. Currently two types of heparin coating are commercially available for extracorporeal circuits. In the first, heparin is ionically bound to the polymeric surface of the extracorporeal circuit (Duraflo II, Baxter, Irvine, CA). The second type of coating uses covalently bound heparin (Carmeda, Medtronic, Minneapolis, MN; Bioline, Jostra, Hirrlingen, Germany). Both coatings have been extensively studied during the past decade. The most striking effect of heparin-coated circuits is the reduction of complement activation, which has been estimated at 45% *(67)*. Another study comparing Duraflo II with Carmeda coatings demonstrated a 25% reduction with both coatings *(68)*. The reductions are most prominent in C5a and TCC levels, probably owing to their slower clearance. Secondary to the reduced complement activation, the inflammatory responses of leukocytes, platelets and endothelium are attenuated, resulting in reduced lactoferin and myeloperoxidase levels *(69,70)*, IL-6, IL-8, and E-selectin *(71,72)*, oxygen-free radical production *(73)*, integrin and selectin response of platelets *(74)*, and platelet β-thromboglobulin release *(75)*.

Although heparin coating is effective in reducing complement activation through the alternative pathway, classical pathway activation after protamine infusion was also shown to be reduced *(76)*. This might indicate that a key component of the complement system is either inactivated or bound by the coating *(77)*.

Levels of kallikrein-C1 esterase inhibitor complex, a marker for contact activation, were shown to be reduced during CPB with heparin-coated circuits, but remained

unchanged when uncoated circuits were used *(8)*. Binding of factor XII to the coating could be responsible for this observation *(78)*.

Contrary to initial expectations, thrombin generation and the activity of the fibrinolytic system are not reduced with heparin coating *(79,80)*. Improved hemostasis, reflected by a decrease in perioperative blood loss and transfusions, with the use of coated circuits has been reported only anecdotally. These results were obtained when heparin coating was combined with a lower dose of systemic heparin *(81,82)*. However, the use of a decreased dose of heparin in conjunction with heparin-coated circuitry is not considered to be safe and is indicated only in special circumstances *(83)*.

Although substantial reductions in blood activation can be obtained with heparin-coated circuits, it has been proven difficult to translate these into an improved clinical performance. In one study, a decreased intrapulmonary shunt with improved respiratory index was found after CPB with heparin-coated circuits. However, intubation time and intensive care unit (ICU) stay were not affected *(84)*. A composite score, consisting of intubation time, the central-peripheral temperature difference, and postoperative fluid balance was significantly reduced with heparin-coated circuits *(85)*. Similarly, a composite score of adverse events after coronary surgery was improved by using heparin-coated circuits *(86,87)*. In a multicenter European trial, a significantly better postoperative recovery was found in females and in patients with cross-clamp times exceeding 60 min when heparin-coated circuits were used *(88)*.

Aprotinin

Aprotinin is a polypeptide processed from bovine lung that acts as an inhibitor of serine proteases such as plasmin, trypsin, and kallikrein *(89)*. It was first introduced into cardiac surgery in an attempt to reduce complement activation during CPB. Although this attempt failed, "bone-dry" operative fields with significantly reduced postoperative blood loss and perioperative homologous blood product use were noted *(90)*. Since these initial reports, use of aprotinin has become widespread as an adjunct in blood-saving programs in cardiac surgery. Two dosage regimens with aprotinin have evolved, the low "Groningen" and the high "Hammersmith" dosages, which have a similar efficacy in reducing blood loss and transfusion requirements *(91–93)*. More recently, encouraging results were obtained with aprotinin administered topically to the pericardial sac *(94)*.

Owing to its nonspecific mode of action, aprotinin has several effects. Most notably aprotinin preserves platelet function by preventing the acute loss of the Gp1b adhesive receptor expression on platelets that occurs at the onset of CPB *(55)*. The mechanism underlying this protective effect has not been elucidated. Possibly, aprotinin inhibits the activity or production of trace amounts of agonists on the surface of the extracorporeal circuit, or interferes with the interaction between the platelet and the foreign surface. Inhibition of hyperfibrinolysis is a second mechanism by which aprotinin reduces bleeding in CPB, and probably explains the efficacy of topically administered aprotinin and other antifibrinolytic agents *(95,96)*. Aprotinin has also been shown to protect platelets against the inhibitory effect of heparin, a phenomenon present in 30% of the patients that is not clarified *(97)*.

A number of anti-inflammatory effects of aprotinin have been demonstrated. In simulated bypass, aprotinin inhibited contact, complement, and neutrophil activation *(98)*. During CPB, aprotinin and high-dose methylprednisolone equally inhibited upregulation of neutrophil CD11b expression and TNF levels *(99)*. Bronchoalveolar lavage fluid obtained from patients after CPB contained fewer neutrophils and less IL-8 when aprotinin was used during CPB *(100)*. In vitro, aprotinin inhibits expression of the cytokine inducible form of nitric oxide synthase *(101)*, resulting in decreased airway NO levels *(102)*.

Many clinicians have cautioned against the liberal use of aprotinin, arguing that the inhibition of fibrinolysis might increase thrombo-embolic complications, and especially, occlusion of the thrombogenic de-endothelialized vein grafts *(103–105)*. Others have implicated inhibition of activated protein C, a pivotal factor in the regulation of coagulation, by aprotinin as a cause for thromboembolic complications *(106)*. Although thrombo-embolic complications after aprotinin treatment have been reported only incidentally, it appears to be safer to use the lowest effective dose of aprotinin during CPB. Currently, the low-dosage regimen and topical aprotinin meet this criterion. As for the inhibition of activated protein C, we recently demonstrated that aprotinin treatment, with either low- or high-dose, does not change the pattern of activation of the protein C system *(107)*.

Corticosteroids

Administration of high-dose corticosteroids has been shown to attenuate the inflammatory response induced by CPB and to improve the postoperative course *(42)*. Although inhibition of the alternative pathway by methylprednisolone has been demonstrated *(108)*, C3a and elastase levels during CPB were not influenced by high-dose corticosteroids *(109,110)*. The cytokine response during CPB is markedly modulated by high-dose corticosteroids. Increase of the inflammatory cytokines IL-6, IL-8, and TNF is prevented whereas concentrations of the anti-inflammatory IL-10 increase 10-fold *(111–114)*. Reduced cytokine-mediated activation of neutrophils results in reduced CD11b expression and leukotriene B_4 release *(110,115)*. Moreover, leukocyte adhesion to endothelium is reduced because glucocorticoids inhibit the expression of ICAM-1 to which CD11b adheres *(116)*. The attenuated inflammatory response with high-dose corticosteroids has been associated with enhanced myocardial recovery, reduced pulmonary damage, and overall better clinical recovery after CPB *(108,117,118)*.

MATERIAL-INDEPENDENT ACTIVATION

Cardiotomy Suction

Blood collected in the pericardium is highly activated by tissue factor and t-PA, and is rich in the highly procoagulant microparticles derived from damaged platelets and erythrocytes *(119,120)*. Tissue factor is not expressed by pericardium, but enters the pericardium from the surgical wounds *(121)*. Being a mesothelial surface, pericardium

is rich in t-PA *(122)*. In vitro experiments have indicated that the activation of pericardial blood is triggered by the extrinsic (tissue factor) coagulation system and that the activation of fibrinolysis is secondary *(119)*. Retransfusion of the activated blood introduces fibrin(ogen) degradation products into the circulation that interfere with platelet receptors, fibrinogen binding to platelets, and clot formation *(123,124)*. Moreover, activators are retransfused, which can result in further systemic activation and impaired hemostasis *(125)*. Similarly, retransfusion of mediastinally shed blood after operation was shown to result in a dose-dependent inflammatory response, impaired hemostasis, and increased bleeding *(126)*. Nevertheless, with a limited amount of retransfusion, reductions in blood use could be achieved *(127)*.

There are several ways to reduce the activation of pericardial blood. Use of a controlled suction device, which incorporates a level sensor that is activated when blood accumulates in the pericardium, minimizes superfluous suctioning and air entering the suction line and, thus, the formation of activating air-blood interfaces *(128)*. Reduction of the contact time between blood and pericardium might have additional effects.

Topical administration of aprotinin into the surgical wound and the pericardium can inhibit the hyperfibrinolysis that occurs in the pericardial blood and improve hemostasis *(94)*. Since heparin levels in pericardial blood were shown to be lower than systemic levels, topical administration of heparin might also reduce the activation of pericardial blood, by reducing thrombin activity *(119)*.

Ischemia and Reperfusion

The negative effect of ischemia on the heart after cross-clamping of the aorta is attenuated by reducing the metabolic demand of the myocardium with cooling and cardioplegia. Nevertheless, ischemia either will occur or is already present owing to the disease process that is being treated. This ischemia will reduce high energy phosphate content of cells and may cause a degree of reversible and irreversible myocardial damage. Proposed mediators of reperfusion injury following ischemia involve the generation of oxygen-free radicals that are produced via the xanthine oxidase reaction *(129)* and by activated neutrophils *(130)*. Exposure of the ischemic endothelium to oxygen-free radicals induces a rapid upregulation of P-selectin and integrin expression *(131)*. At reperfusion, this process results in the accumulation of more activated neutrophils, which shed their cytotoxic enzymes, cytokines, and oxygen-free radicals on the endothelium, leading to tissue injury. Damage to receptors involved in the activation of constitutive NO synthase will reduce NO production, and, as a consequence, coronary spasm and the no-reflow phenomenon can occur *(132)*. Possible ways to reduce reperfusion damage include the use of oxygen radical scavengers *(133)*, inhibition of xanthine oxidase by allopurinol *(134)*, or prevention of ischemia by using continuous blood cardioplegia techniques *(135)*.

Respiratory dysfunction is a well-recognized side effect of cardiac operations. One-quarter of uncomplicated CPB patients still have a significant respiratory impairment 1 wk after operation *(136)*. A proportion of these impairments can be attributed to deteriorated breathing mechanics as a result of surgical factors (e.g., wound pain, drains, effusions).

The effects of CPB primarily involve gas flow and gas exchange owing to parenchymal damage *(137)*.

Bronchial circulation will protect the lung parenchyma from ischemia during aortic cross-clamping. However, low or absent flow in the pulmonary circulation during aortic cross-clamping does occur and will result in similar reperfusion phenomena as in the myocardium. This is supported by the positive role of inhaled NO or intravenous NO donors in the treatment of postperfusion pulmonary dysfunction *(138,139)*. Apart from reperfusion injury, other factors unique to the lung render it more susceptible to damage by CPB. First, the lung filters the venous circulation, and hence, all active or activating substances and cells generated during CPB transit the pulmonary circulation. Second, the lung capillaries are smaller in diameter than the average systemic capillaries, resulting in preferential trapping of aggregates in the lung. Third, a considerable pool of neutrophils is present in the lungs *(140)*. The importance of neutrophils in inducing lung damage is illustrated by the correlation of post-operative shunt fraction and respiratory index with elastase levels *(141)*. Animal experiments demonstrated that leukocyte depletion by filtration reduced heart and lung reperfusion injury *(142)*. Clinically, the use of leukocyte filters transiently improved the pulmonary shunt fraction and the mean arterial pressure *(143)*. In another study, postbypass filtration of 2 L of heart-lung machine blood significantly improved the postoperative lung function *(144)*. Maintenance of some pulmonary flow during aortic cross-clamping, as is achieved with the use of two-stage venous cannulas, was shown to prevent the increase in extravascular lung water content and preserve endothelin clearance *(145,146)*. This concept is expanded by using the Drew perfusion technique, in which no oxygenator is used but the patient's lungs provide oxygenation through separate perfusion of the systemic and pulmonary circulations *(147)*. Use of this technique resulted in reduced pulmonary leukocyte sequestration and complement activation *(148)*.

Hemodilution

At the initiation of CPB, mixing the patient's blood with the relatively large asanguineous pump prime results in a sudden hemodilution. Although moderate hemodilution is considered beneficial in the setting of CPB, unwanted side effects do occur. More specifically, hemodilution can reduce the plasma colloid oncotic pressure to borderline values, resulting in transcapillary oncotic imbalance. Consequently, important fluid shifts toward the interstitial tissue take place, contributing to edema formation, hypovolemia, and impaired oxygen delivery to vital organs such as the digestive tract *(149,150)*. Reduction of the priming volume of the extracorporeal circuit was demonstrated to attenuate the hyperdynamic response to CPB, as measured by fluid load, arterial pressure, cardiac index, vascular resistance, and oxygen delivery *(151)*. Furthermore, endotoxin levels, probably derived from ischemic intestines, were reduced in these patients. Increasing the colloid oncotic pressure of the priming solution by replacing crystalloids with colloids similarly improved the postoperative course and resulted in reduced hospital stay *(152)*. Reduction of priming volumes also results in important savings in the use

of donor blood by two mechanisms *(151)*. First, the reduction of hemodilution will allow for predonation of relatively large volumes of blood in the majority of patients while maintaining a sufficiently high hematocrit during perfusion. Retransfusion of predonated blood after perfusion has been shown to improve hemostasis *(153)*. Second, the attenuated hyperdynamic response will reduce the need for fluid administration and thus further hemodilution during and after perfusion *(152)*. Other methods to prevent or treat excessive hemodilution during extracorporeal circulation, such as the use of blood cardioplegia or perioperative hemofiltration, were shown to further reduce the need for blood transfusions in coronary surgery *(154)*.

Hypothermia

Hypothermic perfusion has, for a long time, been a standard procedure during CPB. In addition to its effect on cell metabolism, a reduction of the inflammatory reaction can be anticipated. Indeed, during normothermic perfusion, compared to hypothermic conditions, IL-1, IL-6, TNF, and elastase levels were higher *(155,156)*. Also the production of E-selectin was reduced, and CD11b upregulation was delayed at low temperature, which could account for reduced leukocyte adherence to the vasculature after reperfusion *(157,158)*. Other researchers have found a similar release of cytokines at normothermia (>36.5°C) compared to hypothermia *(159)*.

Although normothermic CPB appears to induce a more severe inflammatory reaction on a biochemical level, this is not reflected in clinical parameters. No difference in adverse events such as perioperative infarctions, use of an intra-aortic balloon pump, length of ICU stay, or mortality were observed *(160)*. However, vasopressors are used more frequently in normothermic perfusion, probably as a result of reduced endothelin-1 release *(160,161)*. Other studies reported improved pulmonary function with shorter intubation times after normothermic CPB *(162,163)*.

When considering normothermic CPB, neuroprotection is of special interest. Cognitive impairment can be identified in up to 45% of patients who undergo CPB, and focal deficits in 1–3% *(164,165)*. The cerebral damage is mainly caused by emboli. Focal defects are the result of large emboli that originate from surgical manipulation of the heart and aorta. Microemboli are thought to be responsible for the more subtle neurologic defects detected in neuropsychological testing *(166)*. With the use of a particle counter, it was found that a bubble oxygenator produced more microemboli of 15–80 μm than a membrane oxygenator, but that 80% of all particles were produced in the blood circulation owing to cardiotomy suction *(167)*. The small capillary and arteriolar dilatations, caused by diffuse depositions of acellular fatty materials found postmortem in the brains of patients who have recently undergone CPB might be the result of these microemboli *(168)*.

Several studies have addressed the issue of perfusion temperature and cerebral protection, often with the use of an impressive battery of neuropsychological tests *(169–174)*. The results of these studies are contradictory and current opinion is far from conclusive. In many centers, an intermediate course with temperatures between 32 and 35°C is followed. Recently specific markers for cerebral damage such as the S-100 protein and

neuron-specific enolase have become available *(175)*. A correlation of CPB time with levels of S-100 could be explained by intensified suction in these patients *(176)*. Similarly, intracardiac operations appeared to be associated with higher S-100 levels than CABG operations and the use of an arterial filter with reduced S-100 levels in CABG operations *(177,178)*. These assays will aid the development of improved neuroprotective strategies in CPB.

Heparin

Since blood will clot in an extracorporeal circuit, strict anticoagulation is necessary. Traditionally, heparin is used for this purpose because of its easy dosage, control of efficacy and the availability of an antidote. However, heparin does have side effects. Despite adequate heparin levels, thrombin generation can be detected during CPB. Moreover, heparin administration results in a rapid release of t-PA from its body sources, which may induce fibrinolysis *(42,179,180)*. Recently in vitro inhibition of platelet function by heparin was reported *(181)*. This inhibition, which was present in more than 30% of the study population, was associated with an increased postoperative blood loss. Heparin also has activating properties on granulocytes and platelets *(182,183)*. With the neutralization of heparin with protamine, complexes are formed that activate the complement system through the classical pathway. This classical pathway activation correlates with postoperative pulmonary shunt fraction *(184)*. The recombinant form of platelet factor 4, a polypeptide present in platelets that binds and inhibits heparin, could become an attractive alternative to protamine *(185,186)*.

The disadvantages related to heparin and protamine have prompted a search for better anticoagulants. Hirudin, a selective thrombin inhibitor derived from leeches, is frequently named as an attractive alternative. Animal studies comparing recombinant hirudin with heparin demonstrated good clinical results without increased bleeding tendency *(187)*. Unlike heparin, however, hirudin only inhibits thrombin; it does not prevent its formation. This could result in the escape of small amounts of thrombin, as was demonstrated in vitro *(188)*. The absence of an inhibitory effect of hirudin on components higher in the coagulation cascade will not prevent an ongoing activation at this level and might result in depletion of these factors *(189)*. Finally, an antidote to hirudin is not available. Based on these considerations, replacement of heparin with hirudin is not to be advised. Perhaps there is a role for hirudin as an adjunct to heparin.

FUTURE DEVELOPMENTS

From the previous sections, it is clear that a multitude of factors are involved in the detrimental effects of CPB. Therefore, substantial improvements in the procedure of CPB can be obtained only when a multifactorial approach is followed, directed at both material-dependent and -independent factors. Thus, biocompatibility of material surfaces has to be improved, and material-independent sources of blood activation should be controlled by adaptation of perfusion techniques and, when necessary, pharmacological intervention.

Based on current insights and available technologies, we propose a novel system for CPB aimed at minimal disturbance of the patient's homeostasis. Primary in this system is a newly designed low-prime, closed volume, and hemocompatible extracorporeal circuit. The basic principle of this circuit is to abandon the use of gravity drainage and to use a veno-arterial blood pump instead. This allows placement of the device close to the patient. Together with a low-prime oxygenator with an integrated arterial filter, a drastic reduction of the prime-volume will be achieved. Handling of air in such a system is more complicated and will require an advanced air-trapping mechanism. The cardiotomy reservoir will be connected to a controlled suction or a cell-saving device. All components of the circuit will be coated with heparin and primed with aprotinin.

The described system is expected to provide a more physiological perfusion. The reduced prime-volumes will avoid hemodilution, hypo-oncotic pressures, and fluid shifts, ensuring improved preservation of the patient's autoregulatory mechanisms and better hemodynamic stability and organ perfusion. The use of controlled suction will minimize the contact time between blood and nonendothelialized tissues, thus avoiding activation of the coagulation and fibrinolytic systems. Addition of heparin, hirudin, or aprotinin to the pericardial sac can be of further aid to achieve this goal. An alternative to controlled suction might be the use of a cell-saving device, which separates red cells from the fluid in the pericardial sac. In the proposed system, heparin coating is used. However, it should be emphasized that this coating results in only a 25–45% reduction in complement activation and, to a lesser extent, inhibits contact activation. Although contact activation can be inhibited by the addition of aprotinin to the pump-prime, the problem of complement activation will persist. Since the mechanism of heparin coating is probably the result of absorption of an essential factor of the complement system, it does not seem pragmatic to improve the efficacy of the heparin coating. Instead, research should be focused at the development of biologically active coatings that actually prevent the activation of the humoral and cellular components of blood.

REFERENCES

1. Kirklin JW. Open-heart surgery at the Mayo Clinic: the 25th anniversary. Mayo Clin Proc 1980;55:339–341.
2. Westaby S. Organ dysfunction after cardiopulmonary bypass: a systemic inflammatory reaction initiated by the extracorporeal circuit. Intensive Care Med 1987;13:89–95.
3. Gu YJ, Massimo AN, van Oeveren W, Grandjean J, Boonstra PW. Reduction in inflammatory response in patients having minimally invasive coronary artery bypass surgery. Ann Thorac Surg (in press).
4. Edmunds LH, Jr. Blood–surface interactions during cardiopulmonary bypass. J Cardiac Surg 1998;65:420–424.
5. Wachtfogel YT, Harpel PC, Edmunds LH Jr, Colman RW. Formation of C1s-C1-inhibitor, kallikrein-C1-inhibitor and plasmin-alpha 2-plasmin-inhibitor complexes during cardiopulmonary bypass. Blood 1989;73:468–471.
6. Burman JF, Chung HI, Lane DA, Philippou H, Adami A, Lincoln JC. Role of factor XII in thrombin generation and fibrinolysis during cardiopulmonary bypass. Lancet 1994;344:1192–1193.
7. Moorman RM, Reynolds DS, Communale ME. Management of cardiopulmonary bypass in a patient with congenital factor XII deficiency. J Cardiothorac Vasc Anesth 1993;7:452–454.
8. te Velthuis H, Baufreton C, Jansen PG, et al. Heparin coating of extracorporeal circuits inhibits contact activation during cardiac operations. J Thorac Cardiovasc Surg 1997;114:117–122.

9. Boisclair MD, Lane DA, Philippou H, et al. Mechanisms of thrombin generation during cardiopulmonary bypass. Blood 1993;82:3350–3357.
10. Philippou H, Adami A, Boisclair MD, Lane DA. An ELISA for factor X activation peptide: application to the investigation of thrombogenesis in cardiopulmonary bypass. Br J Haematol 1995;90:432–437.
11. Kazatchkine MD, Nydegger UE. The human alternative pathway: biology and immunopathology of activation and regulation. Prog Allergy 1982;30:193–234.
12. Müller-Eberhard HJ. Complement: chemistry and pathways. In: Gallin JI, Goldstein IM, Snyderman R, ed. Inflammation: Basic Principles and Clinical Correlates. Raven, New York; 1988;pp. 21–54.
13. Chenoweth DE, Cooper SW, Hugli TE, Stewart RW, Blackstone EH, Kirklin JW. Complement activation during cardiopulmonary bypass. N Engl J Med 1981;304:497–503.
14. Parker DJ, Cantrell JW, Karp RB, Stroud RM, Digerness SB. Changes in serum complement and immunoglobins following cardiopulmonary bypass. Surgery 1972;71:824–827.
15. Videm V, Fosse E, Mollnes TE, Garred P, Svennevig JL. Complement activation with bubble and membrane oxygenators in aortocoronary bypass grafting. Ann Thorac Surg 1990;50:387–391.
16. Videm V, Mollnes TE. Human complement activation by polygeline and dextran 70. Scand J Immunol 1994;39:314–320.
17. Cooper NR. The classical complement pathway: activation and regulation of the first complement component. Adv Immunol 1985;37:151–216.
18. Loos M, Wellek B, Thesen R, Opferkuch W. Antibody-independent interaction of the first component of complement with gram-negative bacteria. Infect Immun 1978;22:5–9.
19. Fehr J, Rohr H. In vivo complement activation by polyanion-polycation complexes: evidence that C5a is generated intravascularly during heparin-protamine interaction. Clin Immunol 1983;29:7–14.
20. Kirklin JK, Chenoweth DE, Naftel DC, et al. Effects of protamine administration after cardiopulmonary bypass on complement, blood elements, and the hemodynamic state. Ann Thorac Surg 1986;41:193–199.
21. Salama A, Hugo F, Heinrich D, et al. Deposition of terminal C5b-9 complement complexes on erythrocytes and leukocytes during cardiopulmonary bypass. New Engl J Med 1988;318:408–414.
22. Schreurs HH, Wijers MJ, Gu YJ, et al. Heparin coated bypass circuits: effects on inflammatory response in paediatric cardiac surgery. Ann Thorac Surg (in press).
23. Hugli TE, Müller-Eberhard HJ. Anaphylatoxins C3a and C5a. Adv Immunol 1978;26:1–53.
24. Charo IF, Yuen C, Perez HD, Goldstein IM. Chemotactic peptides modulate adherence of human polymorphonuclear leukocytes to monolayers of cultured endothelial cells. J Immunol 1986;136:3412–3419.
25. Tonnesen MG, Smedly LA, Henson PM. Neutrophil–endothelial cell interactions. J Clin Invest 1984;74:1581–1592.
26. Bender JG, van Epps DE. Stimulus interactions in release of superoxide anion (O_2^-) from human neutrophils. Inflammation 1985;9:67–86.
27. Bender JG, Mc Phail LC, van Epps DE. Exposure of human neutrophils to chemotactic factors potentiates activation of the respiratory burst enzyme. J Immunol 1983;130:2316–2323.
28. Henson PM, Zanolari B, Schwartzman NA, Hong SR. Intracellular control of human neutrophil secretion. I. C5a-induced stimulus-specific desensitisation and the effects of cytochalasin Br. J Immunol 1978;121:851–855.
29. Clancy RM, Dahinden CA, Hugli TE. Arachidonate metabolism by human polymorphonuclear leukocytes stimulated by N-formyl-Met-Leu-Phe or complement component C5a is independent of phospholipase activation. Proc Natl Acad Sci USA 1983;80:7200–7204.
30. Palmer RMJ, Salmon JA. Release of leukotriene B4 from human neutrophils and its relationship to degranulation induced by n-formyl-methionyl-leucyl-phenylalanine, serum-treated zymosan and the ionophore A23187. Immunology 1983;50:65–73.
31. Cochrane CG, Spragg RG, Revak SD. Studies on the pathogenesis of the adult respiratory distress syndrome: evidence of oxidants in the broncheoalveolar lavage fluid. J Clin Invest 1983;71:754–761.
32. Royston D, Minty BD, Higenbottam TW, Wallwork J, Jones GJ. The effect of surgery with cardiopulmonary bypass on alveolar-capillary barrier function in human beings. Ann Thorac Surg 1985;40:139–143.

33. Rinaldo JE, Rogers RM. Adult respiratory distress syndrome: changing concepts of lung injury and repair. N Engl J Med 1982;306:900–909.
34. Dinarello CA. Interleukin-1. Rev Infect Dis 1984;6:51–95.
35. Smith RJ, Speziale SC, Bowman BJ. Properties of interleukin-1 as a complete secretagogue for human neutrophils. Biochem Biophys Res Commun 1982;130:1233–1240.
36. Mizel SB. Interleukin 1 and T cell activation. Immunol Rev 1982;63:51–72.
37. Falkoff RJM, Muraguchi A, Hong JX, Buttler JL, Dinarello CA, Fanci AS. The effects of interleukin 1 on human B cell activation and proliferation. J Immunol 1983;131:801–805.
38. Old LJ. Tumor necrosis factor (TNF). Science 1985;230:630–632.
39. Dinarello CA, Cannon JG, Wolff SM, et al. Tumor necrosis factor (cachectin) is an endogenous pyrogen and induces production of interleukin 1. J Exp Med 1986;163:1433–1450.
40. Nawroth PP, Stern D. Modulation of endothelial cell hemostatic properties by tumor necrosis factor. J Exp Med 1986;164:740–745.
41. Nawroth PP, Bank I, Handley D, Cassimeris J, Chess L, Stern D. Tumor necrosis factor/cachectin interacts with endothelial cell receptors to induce release of interleukin 1. J Exp Med 1986;163:1363–1375.
42. Jansen NJ, van Oeveren W, van de Broek L, et al. Inhibition by dexamethasone of the reperfusion phenomena in cardiopulmonary bypass. J Thorac Cardiovasc Surg 1991;102:515–525.
43. Jansen NJ, van Oeveren W, Gu YJ, van Vliet MH, Eijsman L, Wildevuur CR. Endotoxin release and tumor necrosis factor formation during cardiopulmonary bypass. Ann Thorac Surg 1992;54:744–748.
44. Wan S, Marchant A, DeSmet JM, et al. Human cytokine responses to cardiac transplantation and coronary artery bypass grafting. J Thorac Cardiovasc Surg 1996;111:469–477.
45. Butler J, Chong GL, Baigrie RJ, Pillai R, Westaby S, Rocker GM. Cytokine responses to cardiopulmonary bypass with membrane and bubble oxygenation. Ann Thorac Surg 1992;53:833–838.
46. Kukielka GL, Smith CW, Manning AM, Youker KA, Michael LH, Entman ML. Induction of interleukin-6 synthesis in the myocardium: potential role in postreperfusion inflammatory injury. Circulation 1995;92:1866–1875.
47. Jorens PG, Jongh R de, Backer W de, et al. Interleukin-8 production in patients undergoing cardiopulmonary bypass. The influence of pre-treatment with methylprednisolone. Am Rev Respir Dis 1993;148:890–895.
48. Ivey CL, Williams FW, Collins PD, Jose PJ, Williams TJ. Neutrophil chemoattractants generated in two phases during reperfusion of ischemic myocardium in the rabbit. Evidence for a role for C5a and interleukin-8. J Clin Invest 1995;95:2720–2728.
49. Gearing AJH, Newman W. Circulating adhesion molecules in disease. Immunol Today 1993;14:506–512.
50. Gu YJ, van Oeveren W, Boonstra PW, de Haan J, Wildevuur CR. Leukocyte activation with increased membrane expression of CR3 receptors induced by cardiopulmonary bypass. Ann Thorac Surg 1992;53:839–844.
51. Gillinov AM, Bator JM, Zehr KJ, et al. Neutrophil adhesion molecule expression during cardiopulmonary bypass with bubble and membrane oxygenators. Ann Thorac Surg 1993;56:847–853.
52. Arnaout MA, Hakim RM, Todd RF III, Dana N, Colten HR. Increased expression of an adhesion-promoting surface glycoprotein in the granulocytopenia of hemodialysis. N Engl J Med 1985;312:457–462.
53. Etzioni A. Adhesion molecules—their role in health and disease. Pediatr Res 1996;39:191–198.
54. Dreyer WJ, Michael LH, Millman EE, Berens KL. Neutrophil activation and adhesion molecule expression in a canine model of open heart surgery with cardiopulmonary bypass. Cardiovasc Res 1995;29:775–781.
55. van Oeveren W, Eijsman L, Roozendaal KJ, Wildevuur CR. Platelet preservation by aprotinin during cardiopulmonary bypass. Lancet 1988;19:644.
56. Moncada S, Higgs A. The L-arginine-nitric oxide pathway. N Engl J Med 1993;329:2002–2012.
57. Speziale G, Ruvolo G, Marino B. A role for nitric oxide in the vasoplegic syndrome. J Cardiovasc Surg (Torino) 1996;37:301–303.
58. Finkel MS, Oddis CV, Jacob TD, et al. Negative inotropic effects of cytokines on the heart mediated by nitric oxide. Science 1992;257:387–389.

59. Alican I, Kubes P. A critical role for nitric oxide in intestinal barrier function and dysfunction. Am J Physiol 1996;270:G225–G237.
60. Yanagisawa M, Kurihara H, Kimura S, et al. A novel potent vasoconstrictor peptide produced by vascular endothelial cells. Nature 1988;332:411–415.
61. Yoshizawa T, Osamu S, Giaid A, et al. Endothelin, a novel peptide in the posterior pituitary system. Science 1989;247:462–464.
62. te Velthuis H, Jansen PG, Oudemans-van Straaten HM, et al. Circulating endothelin in cardiac operations: influence of blood pressure and endotoxin. Ann Thorac Surg 1996;61:904–908.
63. Kirshbom PM, Tsui SS, Di Bernardo LR, et al. Blockade of endothelin-converting enzyme reduces pulmonary hypertension after cardiopulmonary bypass and circulatory arrest. Surgery 1995;118:440–444.
64. Matheis G, Haak T, Beyersdorf F, Baretti R, Polywka C, Winkelmann BR. Circulating endothelin in patients undergoing coronary artery bypass grafting. Eur J Cardiothorac Surg 1995;9:269–274.
65. Nakamura H, Kim DK, Philbin DM, et al. Heparin-enhanced plasma phospholipase A2 activity and prostacyclin synthesis in patients undergoing cardiac surgery. J Clin Invest 1995;95:1062–1070.
66. Tabuchi N, Gallandat Huet RC, Sturk A, Eijsman L, Wildevuur CR. Aprotinin effects on aspirin treated platelets and hemostasis during cardiopulmonary bypass. Ann Thorac Surg 1994;58: 1036–1039.
67. Videm V, Svennevig JL, Fosse E, Semb G, Osterud A, Mollnes TE. Reduced complement activation with heparin-coated oxygenator and tubings in coronary bypass operations. J Thorac Cardiovasc Surg 1992;103:806–813.
68. Ovrum E, Mollnes TE, Fosse E, et al. Complement and granulocyte activation in two different types of heparinized extracorporeal circuits. J Thorac Cardiovasc Surg 1995;110:1623–1632.
69. Lundblad R, Moen O, Fosse E. Endothelin-1 and neutrophil activation during heparin-coated cardiopulmonary bypass. Ann Thorac Surg 1997;63:1361–1367.
70. Moen O, Fosse E, Brockmeier V, et al. Disparity in blood activation by two different heparin-coated cardiopulmonary bypass systems. Ann Thorac Surg 1995;60:1317–23.
71. Steinberg BM, Grossi EA, Schwartz DS, et al. Heparin bonding of bypass circuits reduces cytokine release during cardiopulmonary bypass. Ann Thorac Surg 1995;60:525–529.
72. Weerwind PW, Maessen JG, van Tits LJ, et al. Influence of Duraflo II heparin-treated extracorporeal circuits on the systemic inflammatory response in patients having coronary bypass. J Thorac Cardiovasc Surg 1995;110:1633–1641.
73. Bozdayi M, Borowiec J, Nilsson L, Venge P, Thelin S, Hansson HE. Effects of heparin-coating of cardiopulmonary bypass circuits on in vitro oxygen free radical production during coronary bypass surgery. Artif Organs 1996;20:1008–1016.
74. Moen O, Hogasen K, Fosse E, et al. Attenuation of changes in leukocyte surface markers and complement activation with heparin-coated cardiopulmonary bypass. Ann Thorac Surg 1997;63:105–111.
75. Fukutomi M, Kobayashi S, Niwaya K, Hamada Y, Kitamura S. Changes in platelet, granulocyte and complement activation during cardiopulmonary bypass using heparin-coated equipment. Artif Organs 1996;20:767–776.
76. Gu YJ, van Oeveren W, Akkerman C, Boonstra PW, Huyzen RJ, Wildevuur CR. Heparin-coated circuits reduce the inflammatory response to cardiopulmonary bypass. Ann Thorac Surg 1993;55:917–922.
77. te Velthuis H, Jansen PGM, Hack CE, Eijsman L, Wildevuur CR. Specific complement inhibition by heparin-coated extracorporeal circuits. Ann Thorac Surg 1996;61:1153–1157.
78. van der Kamp KW, van Oeveren W. Contact, coagulation and platelet interaction with heparin treated equipment during heart surgery. Int J Artif Organs 1993;16:836–842.
79. Gorman RC, Ziats N, Rao AK, et al. Surface-bound heparin fails to reduce thrombin formation during clinical cardiopulmonary bypass. J Thorac Cardiovasc Surg 1996;111:1–12.
80. Ovrum E, Brosstad F, Am Holen E, Tangen G, Abdelnoor M. Effects on coagulation and fibrinolysis with reduced versus full heparinization and heparin coated cardiopulmonary bypass. Circulation 1995;92:2579–2584.
81. von Segesser LK, Weiss BM, Garcia E, von Felten A, Turina MI. Reduction and elimination of systemic heparinization during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1992;103:790–799.

82. Ovrum E, Holen EA, Tangen G, et al. Completely heparinized cardiopulmonary bypass and reduced systemic heparin: clinical and hemostatic effects. Ann Thorac Surg 1995;60:365–371.
83. Edmunds LH Jr. Surface-bound heparin: panacea or peril? Ann Thorac Surg 94;85:2855–2860.
84. Ranucci M, Cirri S, Conti D, et al. Beneficial effects of Duraflo II heparin-coated circuits on post-perfusion lung dysfunction. Ann Thorac Surg 1996;61:76–81.
85. Jansen PG, te Velthuis H, Huybrechts RA, et al. Reduced complement activation and improved post-operative performance after cardiopulmonary bypass with heparin-coated circuits. J Thorac Cardiovasc Surg 1995;110:829–834.
86. Jansen PG, Baufreton C, Le Besnerais P, Loisance DY, Wildevuur ChRH. Heparin-coated circuits and aprotinin prime for coronary artery bypass grafting. Ann Thorac Surg 1996;61:1363–1366.
87. Baufreton C, Le Besnerais P, Jansen P, et al. Clinical outcome after coronary surgery with heparin-coated extracorporeal circuits for cardiopulmonary bypass. Perfusion 1996;11:437–443.
88. Wildevuur CR, Jansen PG, Bezemer PD, et al. Clinical evaluation of Duraflo II treated extracorporeal Circuits (2nd version): The European Working Group on heparin coated extracorporeal circulation circuits. Eur J Cardiothorac Surg 1997;11:616–623.
89. Verstraete M. Clinical application of inhibitors of fibrinolysis. Drugs 1985;29:236–261.
90. van Oeveren W, Jansen NJ, Bidstrup BP, et al. Effects of aprotinin on hemostatic mechanisms during cardiopulmonary bypass. Ann Thor Surg 1987;44:640–645.
91. Wildevuur CR, Eijsman L, Roozendaal KJ, Harder MP, Chang MP, van Oeveren W. Platelet preservation during cardiopulmonary bypass with aprotinin. Eur J Cardiothorac Surg 1989;3:533–538.
92. van Oeveren W, Harder MP, Roozendaal KJ, Eijsman L, Wildevuur CR. Aprotinin protects platelets against the initial effect of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1990;99:788–797.
93. Speekenbrink RG, Wildevuur CR, Sturk A, Eijsman L. Low-dose and high-dose aprotinin improve hemostasis in coronary surgery. J Thorac Cardiovasc Surg 1996;112:523–530.
94. Tatar H, Cicek S, Demirkilic U, et al. Topical use of aprotinin in open heart operations. Ann Thor Surg 1993;55:659–661.
95. Speekenbrink RG, Vonk AB, Wildevuur CR, Eijsman L. Hemostatic efficacy of dipyridamole, tranexamic acid and aprotinin in coronary bypass grafting. Ann Thorac Surg 1995;59:438–42.
96. Horrow JC, Hlavacek J, Strong MD, et al. Prophylactic tranexamic acid decreases bleeding after cardiac operations. J Thorac Cardiovasc Surg 1990;99:70–74.
97. John LC, Rees GM, Kovacs IB. Reduction of heparin binding to and inhibition of platelets by aprotinin. Ann Thorac Surg 1993;55:1175–1179.
98. Wachtfogel YT, Kucich U, Hack CE, et al. Aprotinin inhibits the contact, neutrophil, and platelet activation systems during simulated extracorporeal perfusion. J Thorac Cardiovasc Surg 1993;106:1–10.
99. Hill GE, Alonso A, Spurzem JR, Stammers AH, Robbins RA. Aprotinin and methylprednisolone equally blunt cardiopulmonary bypass-induced inflammation in humans. J Thorac Cardiovasc Surg 1995;110:1658–1662.
100. Hill GE, Pohorecki R, Alonso A, Rennard SI, Robbins RA. Aprotinin reduces interleukin-8 production and neutrophil accumulation after cardiopulmonary bypass. Anesth Analg 1996;83:696–700.
101. Hill GE, Taylor JA, Robbins RA. Differing effects of aprotinin and e-aminocaproic acid on cytokine-induced inducible nitric oxide synthase expression. Ann Thorac Surg 1997;63:74–77.
102. Hill GE, Springal DR, Robbins RA. Aprotinin is associated with a decrease in nitric oxide production during cardiopulmonary bypass. Surgery 1997;121:449–455.
103. van Oeveren W, van Oeveren B, Wildevuur CR. Anticoagulation policy during use of aprotinin in cardiopulmonary bypass. J Thorac Cardiovasc Surg 1992;104:210–211.
104. Feindt P, Seyfert U, Volkmar I, Huwer H, Kalweit G, Gams E. Is there a phase of hypercoagulability when aprotinin is used in cardiac surgery? Eur J Cardiothor Surg 1994;8:308–314.
105. Bidstrup BP, Underwood SR, Sapsford RN. Effect of aprotinin (Trasylol) on aorta-coronary bypass graft patency. J Thorac Cardiovasc Surg 1993;105:147–153.
106. Westaby S. Aprotinin in perspective. Ann Thorac Surg 1993;55:1033–1041.
107. Speekenbrink RG, Bertina RM, España F, Wildevuur CR, Eijsman L. Activation of the protein C system during cardiopulmonary bypass with and without adrotinin. Ann Thor Surg (in press).

108. Weiler JM, Packard B. Methylprednisolone inhibits the alternative and amplification pathways of complement. Infect Immun 1982;38:122–126.
109. Boscoe MJ, Yewdall VM, Thompson MA, Cameron JS. Complement activation during cardiopulmonary bypass: quantitative study of effects of methylprednisolone and pulsatile flow. Br Med J (Clin Res Ed) 1983;287:1747–1750.
110. Jansen NJ, van Oeveren W, van Vliet M, Stoutenbeek CP, Eijsman L, Wildevuur CR. The role of different types of corticosteroids on the inflammatory mediators in cardiopulmonary bypass. Eur J Cardiothorac Surg 1991;5:211–217.
111. Hill GE, Snider S, Galbraith TA, Forst S, Robbins RA. Glucocorticoid reduction of bronchial epithelial inflammation during cardiopulmonary bypass. Am J Respir Crit Care Med 1995;152:1791–1795.
112. Kawamura T, Inada K, Okada H, Okada K, Wakusawa R. Methylprednisolone inhibits increase of interleukin 8 and 6 during open heart surgery. Can J Anaesth 1995;42:399–403.
113. Teoh KH, Bradley CA, Gauldie J, Burrows H. Steroid inhibition of cytokine-mediated vasodilation after warm heart surgery. Circulation 1995;92:347–353.
114. Tabardel Y, Duchateau J, Schmartz D, et al. Corticosteroids increase blood interleukin-10 levels during cardiopulmonary bypass in men. Surgery 1996;119:76–80.
115. Hill GE, Alonso A, Thiele GM, Robbins RA. Glucocorticoids blunt neutrophil CD11b surface glycoprotein upregulation during cardiopulmonary bypass in humans. Anesth Analg 1994;79:23–27.
116. Cronstein BN, Kimmel SC, Levin RI, Martiniuk F, Weissman G. A mechanism for the anti-inflammatory effects of corticosteroids: the glucocorticoid receptor regulates leukocyte adhesion to endothelial cells and expression of endothelial-leukocyte adhesion molecule 1 and intercellular adhesion molecule 1. Proc Natl Acad Sci USA 1992;89:9991–9995.
117. Busuttil RW. George WJ. Hewitt RL. Protective effect of methylprednisolone on the heart during ischemic arrest. J Thorac Cardiovasc Surg 1975;70:955–965.
118. Hill DG, Aguilar MJ, Kosek JC, Hill JD. Corticosteroids and prevention of pulmonary damage following cardiopulmonary bypass in puppies. Ann Thorac Surg 1976;22:36–40.
119. Tabuchi N, de Haan J, Boonstra PW, van Oeveren W. Activation of fibrinolysis in the pericardial cavity during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1993;106:828–833.
120. Nieuwland R, Berckmans RJ, Rotteveel-Eijkman RC, et al. Cell-derived microparticles generated in patients during cardiopulmonary bypass are highly procoagulant. Circulation 1997;96:3534–3541.
121. Chung JH, Gikakis N, Rao AK, Drake TA, Colman RW, Edmunds LH Jr. Pericardial blood activates the extrinsic coagulation pathway during clinical cardiopulmonary bypass. Circulation 1996;93:2014–2018.
122. van Hinsbergh VW, Kooistra T, Scheffer MA, van Bockel JH, van Muijen GN. Characterization and fibrinolytic properties of human omental tissue mesothelial cells: comparison with endothelial cells. Blood 1990;75:1490–1497.
123. Adelman B, Michelson AD, Loscalzo J, Greenberg J, Handin RI. Plasmin effect on platelet glycoprotein Ib–von Willebrand's factor interaction. Blood 1985;65:32–40.
124. Coller BS. Platelet and thrombolytic therapy. N Engl J Med 1990;99:518–527.
125. de Haan J, Boonstra PW, Monnink SH, Ebels T, van Oeveren W. Retransfusion of suctioned blood during cardiopulmonary bypass impairs hemostasis. Ann Thorac Surg 1995;59:901–907.
126. Schönberger JP, van Oeveren W, Bredee JJ, Everts PA, de Haan J, Wildevuur CR. Systemic blood activation during and after autotransfusion. Ann Thorac Surg 1994;57:1256–1262.
127. Schönberger JP, Bredee JJ, Speekenbrink RG, Everts PA, Wildevuur CR. Autotransfusion of shed blood contributes additionally to blood saving in patients receiving aprotinin (2 million KIU). Eur J Cardiothorac Surg 1993;7:474–477.
128. Boonstra PW, van Imhoff GW, Eijsman L, et al. Reduced platelet activation and improved hemostasis after controlled cardiotomy suction during clinical membrane oxygenator perfusions. J Thorac Cardiovasc Surg 1985;89:900–906.
129. Menasché P, Piwnica A. Free radicals and myocardial protection: a surgical viewpoint. Ann Thorac Surg 1989;47:939–945.
130. Royston D, Fleming JS, Desar JB, Westaby S, Taylor KM. Increased production of peroxidation products associated with cardiac operations. J Thorac Cardiovasc Surg 1986;91:759–766.

131. Lefer AM. Role of selectins in myocardial ischemia-reperfusion injury. Ann Thorac Surg 1995;60:773–777.
132. Seccombe JF, Schaff HV. Coronary artery endothelial function after myocardial ischemia and reperfusion. Ann Thorac Surg 1995;60:778–788.
133. Menasché P, Grousset C, Gauduel Y, Piwnica A. A comparative study of free radical scavengers in cardioplegic solutions: improved protection with peroxidase. J Thorac Cardiovasc Surg 1986;92:264–271.
134. Bochenek A, Religa Z, Spyt TJ, et al. Protective influence of pretreatment with allopurinol on myocardial function in patients undergoing coronary artery surgery. Eur J Cardiothorac Surg 1990; 4:538–542.
135. Lichtenstein SV, Kassam AA, El Dalati H, Cusimano RJ, Panos A, Slutsky AS. Warm heart surgery. J Thorac Cardiovasc Surg 1991;101:269–274.
136. Taggart DP, El-Fiky MM, Carter R, Bowman A, Wheatley DJ. Respiratory dysfunction after uncomplicated cardiopulmonary bypass. Ann Thorac Surg 1993;56:1123–1128.
137. Ratcliff NB, Young WG Jr, Hackel DB, et al. Pulmonary injury secondary to extracorporeal circulation: An ultrastructural study. J Thorac Cardiovasc Surg 1973;65:425–432.
138. Hillman ND, Cheifetz IM, Craig DM, Smith PK, Ungerleider RM, Meliones JN. Inhaled nitric oxide, right ventricular efficiency, and pulmonary vascular mechanics: selective vasodilation of small pulmonary vessels during hypoxic pulmonary vasoconstriction. J Thorac Cardiovasc Surg 1997;113:1006–1013.
139. King RC, Binns OA, Kanithanon RC, et al. Low-dose sodium nitroprusside reduces pulmonary reperfusion injury. Ann Thorac Surg 1997;63:1398–1404.
140. MacNee W, Selby C. Neutrophil kinetics in the lungs. Clin Science 1990;79:97–107.
141. Tönz M, Mihaljevic T, von Segesser LK, Fehr J, Schmid ER, Turina MI. Acute lung injury during cardiopulmonary bypass: are the neutrophils responsible? Chest 1995;108:1551–1556.
142. Bando K, Pillai R, Cameron DE, et al. Leukocyte depletion ameliorates free radical–mediated lung injury after cardiopulmonary bypass. J Thorac Cardiovasc Surg 1990;99:873–877.
143. Johnson D, Thomson D, Mycyk T, Burbridge B, Mayers I. Depletion of leucocytes transiently improves postoperative cardiorespiratory status. Chest 1995;107:1253–1259.
144. Gu YJ, de Vries AJ, Boonstra PW, van Oeveren W. Leukocyte depletion results in improved lung function and reduced inflammatory response after cardiac surgery. J Thorac Cardiovasc Surg 1996;112:494–500.
145. Boldt J, Zickmann B, Dapper F, Hempelmann G. Does the technique of cardiopulmonary bypass affect lung water content? Eur J Cardiothorac Surg 1991;5:22–26.
146. Matheis G, Haak T, Beyersdorf F, Baretti R, Polywka C, Winkelmann BR. Circulating endothelin in patients undergoing coronary artery bypass grafting. Eur J Cardiothorac Surg 1995;9:269–274.
147. Dobell AR, Bailey JS. Charles Drew and the origins of deep hypothermic circulatory arrest. Ann Thorac Surg 1997;63:1193–1199.
148. Bochenek A, Religa Z, Kokot F, et al. Biocompatibility of extracorporeal circulation with autooxygenation. Eur J Cardiothorac Surg 1992;6:397–402.
149. Beattie HW, Evans G, Garnett ES, Webber CE. Sustained hypovolemia and extracellular fluid volume expansion following cardiopulmonary bypass. Surgery 1972;71:891–897.
150. Utley JR, Wachtel C, Cain RB, Spaw AE, Collins JC, Stephens DB. Effects of hypothermia, hemodilution, and pump oxygenation on organ water content, blood flow, and oxygen delivery, and renal function. Ann Thorac Surg 1981;31:121–133.
151. Jansen PG, te Velthuis H, Bulder ER, et al. Reduction in prime volume attenuates the hyperdynamic response after cardiopulmonary bypass. Ann Thorac Surg 1995;60:544–550.
152. Jansen PG, te Velthuis H, Wildevuur WR, et al. Cardiopulmonary bypass with modified fluid gelatin and heparin-coated circuits. Br J Anaesth 1996;6:13–19.
153. Schönberger JP, Bredee JJ, Tjian D, Everts PA, Wildevuur CR. Intraoperative predonation contributes to blood saving. Ann Thorac Surg 1993;56:893–898.
154. Schönberger JP, Woolley S, Tavilla G, et al. Efficacy and safety of a blood conservation program including low-dose aprotinin in routine myocardial revascularization. J Cardiovasc Surg (Torino) 1996;37:35–44.

155. Menasché P, Haydar S, Peynet J, et al. A potential mechanism of vasodilation after warm heart surgery. J Thorac Cardiovasc Surg 1994;107:293–299.
156. Menasché P, Peynet J, Lariviere J, et al. Does normothermia during cardiopulmonary bypass increase neutrophil-endothelium interactions? Circulation 1994;90:II275–II279.
157. Haddix TL, Pohlman TH, Noel RF, Sato TT, Boyle EM Jr, Verrier ED. Hypothermia inhibits human E-selectin transcription. J Surg Res 1996;64:176–183.
158. Menasché P, Peynet J, Haeffner-Cavaillon N, et al. Influence of temperature on neutrophil trafficking during clinical cardiopulmonary bypass. Circulation 1995;92(Suppl II):334–340.
159. Frering B, Philip I, Dehoux M, Rolland C, Langlois JM, Desmonts JM. Circulating cytokines in patients undergoing normothermic cardiopulmonary bypass. J Thorac Cardiovasc Surg 1994;108:636–641.
160. Birdi I, Regragui I, Izzat MB, Bryan AJ, Angelini GD. Influence of normothermic systemic perfusion during coronary artery bypass operations: a randomized prospective study. J Thorac Cardiovasc Surg 1997;114:475–481.
161. Tonz M, Mihaljevic T, von Segesser LK, Shaw S, Luscher TF, Turina M. Postoperative hemodynamics depend on cardiopulmonary bypass temperature: the potential role of endothelin-1. Eur J Cardiothorac Surg 1997;11:157–161.
162. Ranucci M, Soro G, Frigiola A, et al. Normothermic perfusion and lung function after cardiopulmonary bypass: effects in pulmonary risk patients. Perfusion 1997;12:309–315.
163. Ohata T, Sawa Y, Kadoba K, Masai T, Ichikawa H, Matsuda H. Effect of cardiopulmonary bypass under tepid temperature on inflammatory reactions. Ann Thorac Surg 1997;64:124–128.
164. Vingerhoets G, Van Nooten G, Vermassen F, De Soete G, Jannes C. Short-term and long-term neuropsychological consequences of cardiac surgery with extracorporeal circulation. Eur J Cardiothorac Surg 1997;11:424–431.
165. Sotaniemi KA. Long-term neurologic outcome after cardiac operation. Ann Thorac Surg 1995;59:1336–1339.
166. Blauth CI. Macroemboli and microemboli during cardiopulmonary bypass. Ann Thorac Surg 1995;59:1300–1303.
167. Liu JF, Su ZK, Ding WX. Quantitation of particulate microemboli during cardiopulmonary bypass: experimental and clinical studies. Ann Thorac Surg 1992;54:1196–1202.
168. Moody DM, Brown WR, Challa VR, Stump DA, Reboussin DM, Legault C. Brain microemboli associated with cardiopulmonary bypass: a histologic and magnetic resonance imaging study. Ann Thorac Surg 1995;59:1304–1307.
169. Plourde G, Leduc AS, Morin JE, et al. Temperature during cardiopulmonary bypass for coronary artery operations does not influence postoperative cognitive function: a prospective, randomized trial. J Thorac Cardiovasc Surg 1997;114:123–128.
170. Engelman RM, Pleet AB, Rousou JA, et al. What is the best perfusion temperature for coronary revascularization? J Thorac Cardiovasc Surg 1996;112:1622–1632.
171. Regragui I, Birdi I, Izzat MB, et al. The effects of cardiopulmonary bypass temperature on neuropsychologic outcome after coronary artery operations: a prospective randomized trial. J Thorac Cardiovasc Surg 1996;112:1036–1045.
172. Mora CT, Henson MB, Weintraub WS, et al. The effect of temperature management during cardiopulmonary bypass on neurologic and neuropsychologic outcomes in patients undergoing coronary revascularization. J Thorac Cardiovasc Surg 1996;112:514–522.
173. McLean RF, Wong BI, Naylor CD, et al. Cardiopulmonary bypass, temperature, and central nervous system dysfunction. Circulation 1994;90:II250–II255.
174. Martin TD, Craver JM, Gott JP, et al. Prospective, randomized trial of retrograde warm blood cardioplegia: myocardial benefit and neurological threat. Ann Thorac Surg 1994;57:298–304.
175. Johnsson P, Lundqvist C, Lindgren A, Ferencz I, Alling C, Stahl E. Cerebral complications after cardiac surgery assessed by S-100 and NSE levels in blood. J Cardiothorac Vasc Anesth 1995;9:694–699.
176. Westaby S, Johnsson P, Parry A, et al. Serum S100 protein: a potential marker for cerebral events during cardiopulmonary bypass. Ann Thorac Surg 1996;61:88–92.
177. Taggart DP, Mazel JW, Bhattacharya K, et al. Comparison of serum S-100β levels during CABG and intracardiac operations. Ann Thorac Surg 1997;63:492–496.

178. Taggart DP, Bhattacharya K, Meston N, et al. Serum S-100 protein concentration after cardiac surgery: a randomized trial of arterial line filtration. Eur J Cardiothorac Surg 1997;11:645–649.
179. Khuri SF, Valeri CR, Loscalzo J. Heparin causes platelet dysfunction and induces fibrinolysis before cardiopulmonary bypass. Ann Thorac Surg 1995;60:1008–1014.
180. Upchurch GR, Valeri CR, Khuri SF, et al. Effect of heparin on fibrinolytic activity and platelet function in vivo. Am J Physiol 1996;271:528–534.
181. John LCH, Rees GM, Kovacs IB. Inhibition of platelet function by heparin. J Thorac Cardiovasc Surg 1993;105:816–822.
182. Wahba A, Black G, Koksch M, et al. Cardiopulmonary bypass leads to a preferential loss of activated platelets: a flow cytometric assay of platelet surface antigens. Eur J Cardiothorac Surg 1996;10:768–773.
183. Videm V. Heparin in clinical doses "primes" granulocytes to subsequent activation as measured by myeloperoxidase release. Scand J Immunol 1996;43:385–390.
184. Shastri KA, Logue GL, Stern MP, Rehman S, Raza S. Complement activation by heparin-protamine complexes during cardiopulmonary bypass: effect of C4a null allele. J Thorac Cardiovasc Surg 1997;114:482–488.
185. Levy JH, Cormack JG, Morales A. Heparin neutralization by recombinant platelet factor 4 and protamine. Anesth Analg 1995;81:35–37.
186. Dehmer GJ, Fisher M, Tate DA, Teo S, Bonnem EM. Reversal of heparin anticoagulation by recombinant platelet factor 4 in humans. Circulation 1995;91:2188–2194.
187. Riess FC, Potsch B, Behr I, et al. Recombinant hirudin as an anticoagulant during cardiac operations: experiments in a pig model. Eur J Cardiothorac Surg 1997;11:739–745.
188. Bernabei A, Rao AK, Niewiarowski S, Colman RW, Sun L, Edmunds LH Jr. Recombinant desulphatohirudin as a substitute for heparin during cardiopulmonary bypass. J Thorac Cardiovasc Surg 1994;108:381,382.
189. Edmunds LH Jr. HIT, HITT and desulphatohirudin: look before you leap. J Thorac Cardiovasc Surg 1995;110:1–3.

3 Endothelial Cell Injury

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CONTENTS

INTRODUCTION

In conventional cardiac surgery, use of cardiopulmonary bypass (CPB) initiates a series of events best-characterized as a "whole body inflammatory response," with activation of coagulation, fibrinolysis, and inflammatory cascades *(1–3)*. Perturbation and activation of the endothelium are central in this response *(4–6)*. However, with the emergence of minimally invasive techniques that allow coronary artery bypass grafts to be performed on a beating heart without CPB, it is likely that diminished acute systemic endothelial activation will result.

Despite the absence of CPB, minimally invasive cardiac procedures may still be associated with local endothelial perturbation. Specifically, mechanical trauma from manipulation of the target vessels, the force of air and desiccation directly on the endothelial surface from the blower required to maintain operative field visibility, trauma from traction tapes placed on either side of the target vessel, and warm temperature ischemia/reperfusion injury all represent circumstances in which endothelial injury may ensue. Acutely, endothelial cell injury is likely to stimulate procoagulant mechanisms, thereby presenting unique challenges in perioperative anticoagulation strategies. In the chronic setting, local endothelial cell injury may contribute to the development of intimal

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Edited by: M. C. Oz and D. J. Goldstein

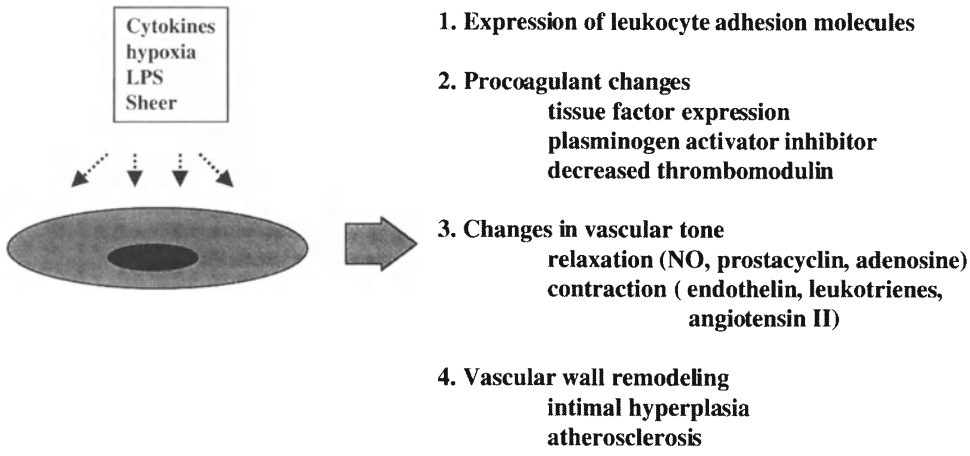

Fig. 1. Endothelial cell response to injury. Acute and chronic endothelial cell injury results in endothelial cell activation, a response that results in expression of leukocyte adhesion molecules, promotion of transendothelial cell migration, coagulation, changes in vascular tone, and a smooth muscle fibroproliferative response that contributes to vascular wall remodeling. NO, nitric oxide.

hyperplasia at the anastomotic site, as well as to the progression of atherosclerosis, *(7,8)* both of which will influence the long-term outcome of these grafts. Therefore, delineation of endothelial cell injury and activation in minimally invasive cardiac surgery will be critical in assessing overall efficacy and safety.

ACUTE ENDOTHELIAL INJURY AT THE ANASTOMOSIS

Endothelial cells are extremely sensitive to injurious stimuli, such as hypoxia, exposure to cytokines, endotoxin, or physical injury, in the form of surgical manipulation or shear stress. All of these may initiate changes that mediate endothelial cell participation in the inflammatory response *(9–13)*. In this setting, endothelial cell activation causes endothelial-derived factors to enhance vasoconstriction, coagulation, leukocyte adherence, and proliferation of smooth muscle cells (Fig. 1). Although these proinflammatory, procoagulant, and proliferative changes likely exist as protective mechanisms, an exaggerated response may portend suboptimal immediate and long-term outcome in cardiovascular surgery.

VASOMOTOR DYSFUNCTION AT THE ANASTOMOSIS

Endothelial-mediated vasomotor dysfunction may profoundly affect the immediate anastomotic outcome because endothelial cells produce factors that act both locally and remotely to influence vascular tone *(14)*. For example, constitutively expressed relaxant factors such as nitric oxide (NO), prostacyclin, and adenosine act to promote vascular patency by dilating vessels and preventing thrombosis *(15)* whereas endothelin, leukotrienes, and angiotensin II promote increased vascular tone.

Most patients with end-stage coronary artery disease complicated by advancing age, diabetes mellitus, hypertension, hypercholesterolemia, and arteriosclerosis have preexisting impairment of vasomotor control with a decreased capacity to produce relaxant factors *(16)*. Also, the intraoperative and postoperative milieu in cardiovascular surgery may contribute additionally to vasomotor dysfunction. In response to injury such as ischemia-reperfusion injury or direct manipulation, endothelial cells not only lose their ability to promote vasodilation, but also produce potent vasoconstrictive agents such as endothelin, thromboxane A_2 (TXA_2), and angiotensin II *(17)*. Endothelial cell injury in response to hypoxia and exposure to cytokines further causes the production of superoxide-free radicals, which increase vascular tone by quenching NO *(18)*. Such increased vascular reactivity may predispose to coronary spasm or spasm of the internal mammary artery conduit. Although not yet specifically defined in the setting of off-pump bypass grafting, preliminary experience with these procedures has suggested that vascular reactivity will emerge as a major factor contributing to the immediate and long-term success of this procedure. Increased understanding of endothelial cell injury will allow therapeutic interventions that may maximize the acute and long-term graft patency and outcome of these procedures.

PROCOAGULANT ALTERATIONS AT THE ANASTOMOSIS

The vascular endothelium plays a central role in the regulation of coagulation through the constitutive expression and release of anticoagulant factors, and the inducible expression of procoagulant substances *(19)*. Activation of endothelial cells may lead to significant dysregulation of these normally homeostatic properties, ultimately promoting both bleeding and thrombosis *(20)*.

The central role of the endothelial cell in maintaining blood fluidity has been well defined *(20,21)*. In the resting state, blood is maintained in a fluid form by endothelial cells and circulating plasma protein inhibitors such as antithrombin III (ATIII) and antitrypsin, which act by scavenging circulating thrombin. Furthermore, endothelial cells are coated with proteoglycans that form a repellent surface for plasma coagulation proteins. Heparin is incorporated into this proteoglycan surface, geometrically potentiating the action of circulating ATIII. Endothelial cells also normally express the surface protein thrombomodulin, which actively prevents the promotion of the coagulation cascade by binding with proteins C and S, thereby also resulting in the inhibition of thrombin *(22,23)*. Proteins C and S contribute to the anticoagulant response by inhibiting the cofactors of factors Va and VIIIa (Fig. 2) *(24)*. The endothelium also constitutively releases tissue factor pathway inhibitor, which inhibits the extrinsic system after VIIa is generated. Furthermore, coagulation is prevented by endothelial-derived substances such as NO, which is released into the local environment and acts not only as a potent vasodilator but also as a potent localized platelet and neutrophil inhibitor *(15,18)*. In addition, endothelial-derived prostaglandins and adenosine inhibit platelet aggregation *(13)*.

In response to endothelial injury, therefore, a loss of many of the natural anticoagulant mechanisms and a generalized procoagulant phenotype emerges that is characterized by

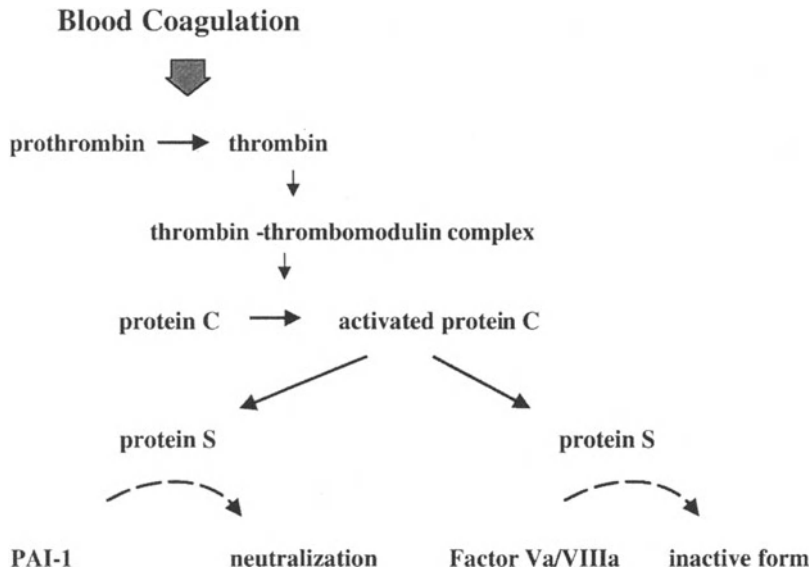

Fig. 2. Protein C-thrombomodulin anticoagulant pathway. Dotted lines indicate neutralization or inactivation.

three principal mechanisms that function to minimize blood loss *(20)*. First, there is the vascular response to injury that promotes vasoconstriction. Second, platelets adhere to sites of injury and become activated, releasing von Willebrand factor and other molecules that increase platelet adhesiveness and accelerate coagulation. Third, a series of reactions are triggered that result in activation of the coagulation cascade and the ultimate formation of insoluble fibrin, which binds avidly to platelet surfaces, forming a solid clot (Fig. 3).

In homeostasis, there is a delicate balance between clot formation and clot dissolution. In response to local and systemic injury, however, the balance may tip toward systemic breakdown, or the formation of clots may result *(25–27)*. The extent of the ensuing procoagulant phenotype is also greatly affected by the degree of plasminogen activation and fibrinolysis. The fibrinolytic system is a complex cascade of serine proteases and their inhibitors that regulates the conversion of plasminogen to the protease plasmin *(27)*. Plasmin controls the reaction of clot acceleration by degrading fibrinogen and fibrin (Fig. 4). The degree of plasmin formation is regulated by the balance between plasminogen activators such as t-PA and serum urokinase plasminogen activator, and plasminogen activator inhibitors such as PAI-1 *(28)*, which prevent fibrinolysis by binding with and deactivating t-PA. PAI-1 is upregulated when endothelial cells are activated by substances such as cytokines. When procoagulant surface alterations are enhanced, therefore, many of the anticoagulant mechanisms are concurrently downregulated (e.g., thrombomodulin, proteins C and S), promoting an overall procoagulant surface. In states of generalized inflammation, such as that seen after CPB, endothelial cells initially promote fibrinolysis by releasing t-PA stores, and then thrombosis by the loss of constitutive antithrombin mechanisms, the inducible expression of tissue factor and the release of PAI-1 *(28–30)*.

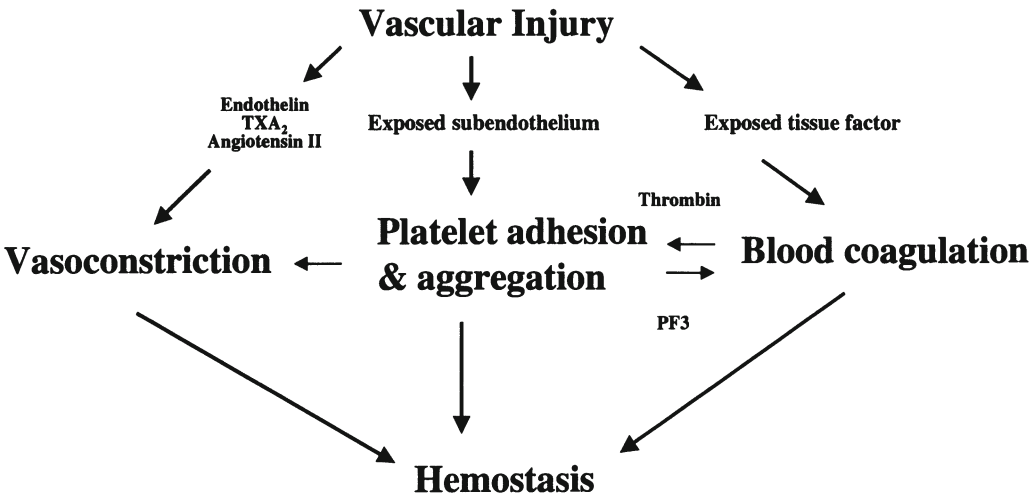

Fig. 3. Overview of the hemostatic mechanism. Endothelial injury results in changes that promote vasoconstriction, platelet adhesion and aggregation, as well as the acceleration of coagulation, all of which together promote solid clot formation, resulting in hemostasis. TXA_2, thromboxane A_2; PF3, platelet factor 3.

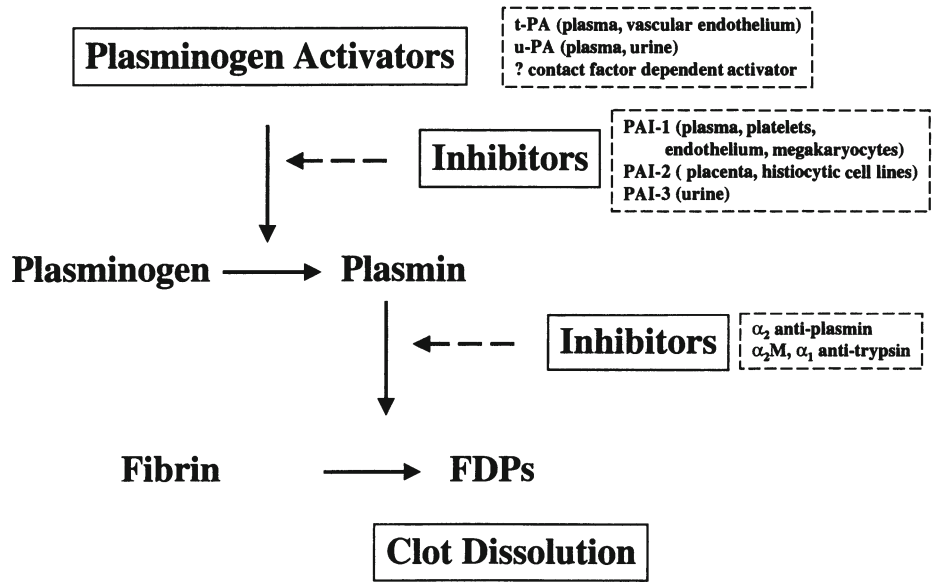

Fig. 4. Fibrinolytic enzyme system. Fibrin deposits, both intravascular and extravascular, are removed in healthy individuals via the fibrinolytic enzyme system. Abnormally increased activity in this system may result in premature or excessive fibrin removal from wounds, with consequent hemorrhage. t-PA, tissue plasminogen activator; u-PA, urinary plasminogen activator (urokinase); PAI; plasminogen activator inhibitor; α_2M, α_1 anti-trypsin; FDP, fibrin-degradation product.

In minimally invasive coronary artery bypass grafting (MICABG), however, fibrinolytic responses are less likely, thereby favoring overall a procoagulant, rather than an antithrombotic, response at the anastomosis. Factors that may contribute to local endo-

thelial cell injury and activation include direct mechanical trauma to the endothelial surface on manipulation of the target vessels, traction tapes placed on either side of the vessel, and air blown onto the anastomosis to create a dry operative field, which may also directly damage the endothelial surface by desiccation. Finally, warm temperature ischemic injury during the anastomosis with subsequent reperfusion will likely activate the endothelium as well.

All these factors, then, favor a procoagulant phenotype, thereby mandating careful attention to anticoagulation strategies. This situation appears most analogous to that observed in coronary stent placement, in which acute platelet-endothelial interactions have emerged as the critical determinants of both the acute perioperative and long-term outcomes at the anastomotic site.

PLATELET–ENDOTHELIAL INTERACTIONS AT THE ANASTOMOSIS

Platelet–endothelial interactions are of central importance in the overall schema of endothelial-derived injurious stimuli in cardiac surgery, especially in MICABG *(31,32)*. Platelet activation is closely regulated by endothelial cell activation in response to inflammation and injury. Thrombin is also an extremely potent stimulus for platelet activation, resulting in the release of the contents of platelet and endothelial cell storage vesicles, known as Weibel-Palade bodies, which contain von Willebrand factor (which increases platelet adhesive function), P-selectin (an endothelial cell adherence molecule that mediates leukocyte interaction with the vascular endothelium), and thromboplastin (which participates in plasminogen activation) *(33)*.

Once activated by thrombin, platelets express glycoprotein binding sites that facilitate platelet–platelet adhesion as well as platelet incorporation into the fibrin clot. Glycoprotein IA, the binding site for von Willebrand factor, mediates the initial adhesiveness of platelets *(34)*. Fibrin has six binding sites of a specific amino acid sequence for platelets (glycoprotein IIB/IIIA), and, therefore, each molecule can link a number of platelets into the cement-like solid clot.

When endothelial cells are activated by injury, platelets become activated and adhere to fibrin and neutrophils, as well as the activated endothelium. Platelet activation and adherence to the injured endothelium at the site of surgical anastomosis will therefore play a major role in acute graft patency.

In this context, the role of platelet–endothelial cell interactions in intracoronary stents has been well defined; indeed directed protective interventions have emerged from this understanding *(35–37)*. Based on the thrombogenic nature of the stents as well as the potential endothelial damage induced by placement of the stent, the potential for thrombosis and/or restenosis of the coronary artery at the site of stent placement has been recognized. Therefore, aggressive use of anticoagulant therapy has been actively investigated in many prospective, randomized trials *(38–41)*. Since full anticoagulant therapy introduces additional risks of increased bleeding and vascular complications, thereby requiring more intensive monitoring, specific antiplatelet therapies have been tested

(42,43). The rationale for the different antiplatelet strategies stems from the distinct mechanisms underlying the potential role of the platelet in thrombus formation. Platelet adhesion, the first phase of thrombus formation, is affected by two factors: nonspecific contact of the platelet with the damaged endothelial surface, and exposure of collagen fibers, causing platelets to become more firmly attached and spread across the damaged surface. During the second phase of thrombus formation, platelets adhere to one another, resulting in platelet mass expansion. Platelet aggregation also seems to be mediated by at least two processes: the release of platelet intracytoplasmic granule constituents such as adenosine diphosphate (ADP), and the synthesis of TXA_2.

Aspirin inhibits only one of these pathways of platelet aggregation by irreversible inhibition of cyclooxygenase, preventing the conversion of arachidonic acid to TXA_2 *(42–44)*. The final common pathway of platelet aggregation, however, is ADP-mediated platelet activation whereby ADP induces exposure of the fibrinogen binding site of the platelet glycoprotein IIB/IIIA receptor complex *(45)*. Aspirin has little or no effect on ADP-mediated platelet aggregation, whereas specific inhibitors of the fibrinogen binding site for the glycoprotein IIB/IIIA receptor complex, such as ticlopidine (Roche Pharmaceutical, Nutley, NJ) or specific inhibitors of the receptor such as abciximab (Eli Lilly, Indianapolis, IN), have targeted effect. Although increased bleeding complications associated with the use of these anticoagulant strategies in the surgical setting are possible, lessons learned about the importance of platelet–endothelial cell interactions at the anastomosis must be considered in the evolving management of MICABG patients.

VASCULAR ANASTOMOSIS AND ITS CHRONIC ADAPTIVE RESPONSE

The importance of the endothelium and the vessel wall in anastomotic outcome is seen in all coronary artery bypass grafts whether performed in the presence or absence of CPB. The vessel wall is composed of three layers, each of which contributes uniquely to the success of the anastomosis. The adventitia and the media compose the structural background of the vessel wall and are essential in vascular wall remodeling. The endothelial-lined intima situated on a basement membrane and subendothelial matrix is in a unique position to regulate both intravascular and extravascular events.

The endothelium therefore plays a critical role in the structural evolution of the vascular wall in response to injury *(46,47)*. Growth factors as well as growth inhibitors that regulate vascular wall structure are manufactured and secreted by endothelial cells. These regulatory molecules, which include platelet-derived growth factor (PDGF), insulin-like growth factor, and interleukin-1, allow endothelial cells to actively participate in the production and maintenance of the basement membrane collagen and the proteoglycans on which they rest. Removal of the endothelium has been shown to lead to a proliferative response by the underlying smooth muscle, suggesting that factors released by the homeostatic endothelium are usually responsible for inhibiting

smooth muscle cell proliferation—a process clearly gone awry in certain diseased and postoperative states.

THE INTIMAL HYPERPLASTIC RESPONSE

The long-term success of CABG is limited by the development of intimal hyperplasia at the sites of vessel injury *(48)*. All forms of arterial reconstruction result in some form of endothelial injury *(49)*. Graft harvest and handling as well as the construction of the anastomosis are common causes of graft damage in cardiac patients. The intimal response to injury is characterized by a subendothelial proliferation and the formation of a neointima *(48,50)*. This intimal hyperplastic response is part of the reparative process that takes place in all the vessels after injury. This response is important because neointimal formation occurs in all arteries secondary to a variety of insults including direct trauma, construction of an anastomosis, dilation, or transplant arteriosclerosis. In some cases, however, the response is exaggerated with proliferation of the neointima and loss of the natural anticoagulant phenotype, resulting in luminal narrowing, restricted blood flow, and a tendency toward thrombosis.

Three phases of the intimal response to injury have been described. The first begins within 24 h of injury and is characterized by smooth muscle proliferation. Once the endothelium is stripped away, platelets adhere to the vessel wall, spread, and degranulate. Mitogens released from activated adherent platelets such as PDGFs, stimulate smooth muscle cells to migrate into the intima *(49)*. After 3–14 d of proliferation in the media, migration of smooth muscle from the media to the intima begins, which forms the neointima. Once the neointima has formed, these smooth muscle cells rapidly proliferate to form a thick layer, which ultimately can obstruct the lumen.

Experimental data in a porcine model of coronary stenting emphasizes the importance of acute vascular injury and events occurring in the perioperative period at the site of the anastomosis in the eventual anastomotic outcome. Specifically, a reduced incidence of acute thrombus formation, as accomplished by aggressive perioperative antithrombin therapy, has been associated with a significantly reduced neointimal fibroproliferative response at 4 wk *(51)*. This emphasizes the critical role of anticoagulant management of the activated endothelium in the immediate perioperative period.

CHRONIC ENDOTHELIAL INJURY AND ATHEROSCLEROSIS

The progression of atherosclerosis involves inflammatory infiltration of the vessel wall, cellular proliferation, fibrous plaque formation, and, ultimately, plaque rupture and occlusive thrombus; chronic injury of the vascular endothelium has also been implicated *(52–55)*. Endothelial injury from pathophysiologic states common to most cardiovascular patients such as hypertension, diabetes, hyperlipidemia, fluctuating shear stress, or smoking disrupts normal endothelial cell functions, leading to the loss of protective

mechanisms and an increase in inflammatory, procoagulant, vasoactive, and fibroproliferative responses. All these changes promote vasospasm, intimal proliferation, and thrombus formation, which will play a role in the initiation, progression, and clinical manifestations of atherosclerosis *(56,57)*.

The specific role of endothelial cell injury in the pathogenesis of atherosclerosis has been implicated in the "endothelial cell injury hypothesis," which proposes that endothelial cell injury is largely responsible for the localization of cellular elements that drive the development of atherosclerosis *(58)*. Changes in the endothelium with injury permit pathologic interactions between the elements of the vascular wall and the circulating blood with the subsequent production of biochemical signals that downregulate protective mechanisms and upregulate the synthesis of proteins that recruit platelets, monocytes, and lymphocyte. Overall, this results in excessive inflammatory and fibroproliferative responses.

CONCLUSION

In this chapter, the critical role of the endothelial cell in the development of vasomotor dysfunction, bleeding and thrombosis, neutrophil and platelet–endothelial cell interactions, and obstructive arteriopathy in the setting of MICABG has been explored. Many forms of endothelial cell injury occur during the course of cardiovascular procedures that have a significant impact on the cardiovascular surgical patient both acutely and chronically, and locally and systemically. An improved understanding of endothelial cell biology in response to local injury is therefore essential to improve outcomes in cardiac surgery. Recent discoveries in the field of endothelial biology have certainly altered the present outlook on the perioperative management of the cardiovascular surgical patient, especially in the setting of CPB. The development of new, minimally invasive techniques to perform cardiac surgery that eliminate extracorporeal circulation, thereby decreasing foreign surface–blood interactions as well as shear stress response, are likely to attenuate the spectrum of endothelial activation.

In conclusion, then, this chapter emphasizes the unique aspects of endothelial cell activation at the anastomotic site in MICABG procedure. An acute change in the resting, quiescent anticoagulant state of the endothelial cell with the varied injurious forces applied to the anastomosis promotes a procoagulant phenotype. Anticoagulation issues, therefore, become paramount in ensuring perioperative graft patency. Strategies such as systemic anticoagulation with heparin without subsequent reversal with protamine are already being pursued. Moreover, perioperative antiplatelet therapy with aspirin is included in many perioperative protocols. Future strategies may include more specific local antiplatelet factors directed against platelet adhesion molecules as well as platelet receptors. Furthermore, novel new anticoagulant strategies directed specifically at intravascular anticoagulation with the preservation of extravascular hemostasis may come to play an important role in the perioperative management of patients and the ultimate success and applicability of this procedure.

REFERENCES

1. Colman RW. Hemostatic complications of cardiopulmonary bypass. Am J Hematol 1995;48:267–272.
2. Edmunds HL. Why cardiopulmonary bypass makes patients sick: strategies to control the blood synthetic surface interaction. Adv Cardiac Surg 1996;6:131–167.
3. Boyle EM Jr, Pohlman TH, Johnson MC, Verrier ED. The systemic inflammatory response. Ann Thorac Surg 1997;64:S31–S37.
4. Verrier ED, Boyle EM Jr. Endothelial injury in cardiovascular surgery: an overview. Ann Thorac Surg 1997;64:S2–S8.
5. Davies MG, Hagen PO. The vascular endothelium: a new horizon. Ann Surg 1993;218:593–609.
6. Vane JR, Anggard EE, Botting RM. Regulatory functions of the vascular endothelium. N Engl J Med 1990;323:27–36.
7. Ross R. Cell biology of atherosclerosis. Annu Rev Physiol 1995;57:791–804.
8. Luscher TF. Vascular biology of coronary artery bypass grafts. Coronary Artery Dis 1992;3:157–65.
9. Harlan J. Leukocyte-endothelial interactions. Blood 1985:65:513–525.
10. Pober JS, Cotran RS. Cytokines and endothelial cell biology. Physiol Rev 1990;70:427–451.
11. Bevilacqua MP, Pober JS, Wheeler ME, Cotran RS, Gimbrone MA Jr. Interleukin-1 activation of vascular endothelium: effects on procoagulant activity and leukocyte adhesion. Am J Pathol 1985;121:394– 403.
12. Bevilacqua MP, Pober JS, Majeau GR, Fiers W, Cotran RS, Gimbrone MA Jr. Recombinant tumor necrosis factor induces procoagulant activity in cultured human vascular endothelium: characterization and comparisons with the actions of interleukin 1. Proc Natl Acad Sci USA 1986;83:4533–4537.
13. Kourembanas S, Marsden PA, McQuillan LP, Faller DV. Hypoxia induces endothelial cell gene expression and secretion in cultured human endothelium. J Clin Invest 1991;88:1054–1057.
14. Selke FW, Boyle EM Jr, Verrier ED. The pathophysiology of vasomotor dysfunction. Ann Thorac Surg 1997;64:S9–S15.
15. Billar TR. Nitric oxide: novel biology with clinical relevance. Ann Surg 1995;221:339–349.
16. Luscher TF, Tanner FC, Tschundi MR, Noll G. Endothelial dysfunction in coronary artery disease. Annu Rev Med 1993;44:395–418.
17. Boyle EM Jr, Pohlman TH, Cornejo CJ, Verrier ED. Ischemia-reperfusion injury. Ann Thorac Surg 1997;64:S24–S30.
18. Kubes P, Suzuki M, Granger DN. Nitric oxide, and endogenous modulator of leukocyte adhesion. Proc Natl Acad Sci USA 1991;88:4651–4655.
19. Davie EW, Fumikawa K, Kisiel W. The coagulation cascade: initiation, maintenance, and regulation. Biochemistry 1991;30:10,363–10,370.
20 Stern DM, Espisito C, Gerlach H, et al. Endothelium and regulation of coagulation. Diabetes Care 1991;14:160–166.
21. Boyle EM Jr, Verrier ED, Spiess BD. The procoagulant response to injury. Ann Thorac Surg 1997;64:S16–S23.
22. Esmon CT. The role of protein C and thrombomodulin in the regulation of blood coagulation. J Biol Chem 1989;264:4743–4746.
23. Esmon NL. Thrombomodulin. Prog Hemost Thromb 1989;9:29–55.
24. Sakata Y, Curriden S, Lawrence D, et al. Activated protein C stimulates fibrinolytic activity of cultured endothelial cells and decreases antiactivator activity. Proc Natl Acad Sci USA 1985;82:1121–1125.
25. Lucore C. Regulation of fibrinolysis by vascular endothelium. Coronary Artery Dis 1991;2:157–166.

26. Emeis JJ, Kooistra T. Interleukin-1 and lipopolysaccharide induces and inhibitor of tissue type plasminogen activator in vivo and in cultured endothelial cells. J Exp Med 1986;163:1260–1266.
27. Nachman RL, Hajjar KA, Silverstein RL, Dinarello CA. Interleukin 1 induces endothelial synthesis of plasminogen activator inhibitor. J Exp Med 1988;163:1595–1600.
28. Hanss M, Collen D. Secretion of tissue type plasminogen activator and plasminogen activator inhibitor by cultured human endothelial cells : modulation by thrombin, endotoxin, and histamine. J Lab Clin Med 1987;109:97–104.
29. Tanaka K, Takao M, Yaka I, et al. Alterations in coagulation and fibrinolysis associated with cardiopulmonary bypass during open heart surgery. J Cardiothorac Anesth 1989;3:181–188.
30. Chandler WL, Fitch JC, Wall MH, et al. Individual variations in the fibrinolytic response during and after cardiopulmonary bypass. Thromb Hemost 1995;74:1293–1297.
31. Santos MT, Valles J, Marcu-AJ, et al. Enhancement of platelet reactivity and modulation of eicosanoid production by intact erythrocytes. J Clin Invest 1991;87:571–580.
32. Rinder CS, Bohnert J, Rinder HM, et al. Platelet activation and aggregation during cardiopulmonary bypass. Anesthesiology 1991;75:388–393.
33. Weyrich AS, Ma XY, Lefer DJ et al. In vivo neutralization of p-selectin protects feline hearts and endothelium in myocardial ischemia and reperfusion injury. J Clin Invest 1993;991:2620–2629.
34. McEver RP, Beckstead JH, Moore KL, et al. GMP 140, a platelet alpha granule membrane protein, is also synthesized by vascular endothelial cells and is localized in Wiebel Palade bodies. J Clin Invest 1989;84:92–99.
35. Marzocchi A, Piovaccari G, Marrozzini C, Ortolanii P, Palmerini T, Branzi A, Magnani B. Results of coronary stenting for unstable vs. stable angina pectoris. Am J Cardiol 1997;79:1314–1318.
36. Chambers CE, Kozak M, Ettinger SM, Gilchrist IC. Interventional cardiology: present and future. J Cardiothorac Vasc Anesth 1997;11(2):211–219.
37. Van der Giessen WJ, Serruys PW, Visser WJ, et al. Endothelialization of intravascular stents. J Int Cardiol 1988;1:109–120.
38. Zubaid M, Penn IM, Buller CE, Moscovich MD, Ricci DR, Chauhan A. Antiplatelet therapy alone is safe and effective after coronary stenting: observations of a transition in practice. Can J Cardiol 1997;13(4):335–340.
39. Berger PB, Holmes DR Jr, Ohman EM, et al. Restenosis, reocclusion and adverse cardiovascular events after successful balloon angioplasty of occluded versus non occluded coronary arteries: results from the multicenter American research trial with cilazapril after angioplasty to prevent transluminal coronary obstruction and restenosis (MARCATOR). J Am Coll Cardiol 1996;27:1–7.
40. The RESTORE Investigators. Effects of platelet glycoprotein IIb/IIIa blockade with Tirofiban on adverse cardiac events in patients with unstable angina or acute myocardial infarction undergoing coronary angioplasty. Circulation 1997;96:1445–1453.
41. Kleiman NS. Primary and secondary safety endpoints from IMPACT II. Am J Cardiol 1997;80(4A):29B–33B.
42. Schror K. Antiplatelet drugs. Drugs 1995;50:7–28.
43. Hobson AG, Sowinski KM. Ticlodipine and aspirin following implantation of coronary stents. Ann Pharmacol 1997;31:770–772.
44. Coller BS. Platelets and thrombolytic therapy. N Engl J Med 1990;322:33–42.
45. Lefkovits J, Plow EF, Topol EJ. Platelet glycoprotein IIb/IIIa receptors in cardiovascular medicine. N Engl J Med 1995;332:1553–1559.
46. Simons M, Leclerc G, Safian RD, et al. Relation between activated smooth muscle cells in coronary artery lesions and restenosis after atherectomy. N Engl J Med 1993;328:608–613.
47. Raines EW, Dover SK, Ross R. Interleukin-1 mitogenic activity for fibroblasts and smooth muscle cells is due to PDGF-AA. Science 1989;243:393–396.

48. Allaire E, Clowes AW. The intimal hyperplastic response. Ann Thorac Surg 1997;64:S38–S46.
49. Schwartz SM, deBlois D, Obrian ER. The intima: soil for atherosclerosis and restenosis. Circ Res 1995;77:445–465.
50. Gay CG, Winkles JA. Interleukin-1 regulates heparin-binding growth factor 2 gene expression in vascular smooth muscle cells. Proc Natl Acad Sci USA 1991;88:296–300.
51. Clowes AW. Prevention and management of recurrent disease after arterial reconstruction: new prospects of pharmacologic control. Thromb Hemost 1991;66:2–66.
52. Unterburg C, Sandrock D, Nebendahl K, Buchwald AB. Reduced acute thrombus formation results in decreased neointimal proliferation after coronary angioplasty. J Am Coll Cardiol 1995;26:1747–1754.
53. Boyle EM, Lille ST, Allaire E, Clowes AW, Verrier ED. Atherosclerosis. Ann Thorac Surg 1997;64:S47–S56.
54. Cybulsky MI, Gimbrone MA Jr. Endothelial cell expression of a mononuclear leukocyte adhesion molecule during atherogenesis. Science 1991;251:788–791.
55. Galis ZS, Sukhova GK, Kranzhofer R, et al. Macrophage foam cells from experimental atheroma constitutively produce matrix-degrading proteinases. Proc Natl Acad Sci USA 1994;94:402–406.
56. Velican D, Velican C. Intimal thickening in developing coronary arteries and its relevance to atherosclerotic involvement. Atherosclerosis 1976;23:345–355.
57. Corson MA, Berk BC. Growth factors and the vessel wall. Heart Dis Stroke 1993;2(2):166–170.
58. Ross R. The pathogenesis of atherosclerosis—an update. N Engl J Med 1986;314:488–500.

II Less Invasive Approaches to Coronary Bypass Grafting

4 Minimally Invasive Coronary Bypass Grafting vs Percutaneous Coronary Interventions

The Cardiologist's Perspective

LeRoy E. Rabbani, MD, Alan D. Simon, MD, and Allan Schwartz, MD

CONTENTS

INTRODUCTION

At present, percutaneous coronary intervention procedures as well as minimally invasive coronary artery bypass grafting (MICABG) surgery are procedures in evolution. This chapter examines the rationale, indications, and results of both approaches for the treatment of single-vessel coronary artery disease (CAD), as well as the role of MICABG in patients with multivessel CAD.

SINGLE-VESSEL CAD

There are two major modes of revascularization for single-vessel CAD: catheter-based and surgical. Catheter-based revascularization consists of percutaneous coronary interventions that include percutaneous transluminal coronary angioplasty (PTCA) and coronary artery stenting. In addition, there are debulking devices such as the directional coronary atherectomy, the transluminal extraction catheter, and several ablative devices of which rotational atherectomy has received the most attention. The vast majority of percutaneous procedures presently carried out include PTCA and/or coronary artery stenting. In fact, coronary artery stenting now accounts for over half of all percutaneous coronary interventions in the United States.

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

By contrast, there are two modes of surgical revascularization for single-vessel CAD: conventional CABG and MICABG. The former utilizes a median sternotomy, cardiopulmonary bypass (CPB), and cardioplegic arrest. MICABG comprises a spectrum of operative procedures ranging from the absence of CPB, a limited incision, and the surgeon sewing into a beating heart, to full CPB via the groin, cardioplegic arrest, and balloon occlusion of the aorta. For the purposes of this chapter, we deal with the former technique as the "mini-operation" most suitable for single-vessel disease.

Studies evaluating the natural history of patients with single-vessel CAD reveal that medical therapy alone is associated with good long-term prognosis, except in patients with severe proximal left anterior descending (LAD) stenoses *(1)*. An observational study from the Duke University Medical Center suggests that PTCA may offer a slight advantage in long-term survival over CABG for patients with single-vessel CAD, except for those patients with at least 95% proximal LAD stenoses *(2)*. PTCA for single-vessel CAD has been shown to be superior to medical therapy in terms of improving exercise capacity and reducing provocable ischemia, as demonstrated by the Veterans Administration study *(3)*. The limitations of PTCA include a 30–50% angiographic restenosis rate within 3–6 mo of the procedure *(4,5)*; moreover, restenosis can present as a recurrent ischemic syndrome in approx 20% of patients, manifesting as a positive stress test or a crescendo anginal pattern. It is uncommon however, for restenosis to present as a myocardial infarction. A major liability of restenosis is that it prompts the need for early repeat revascularization, thereby resulting in significant costs. Indeed, it is estimated that restenosis costs $2 billion per year *(6)*. In addition, more than 400,000 Americans and 800,000 patients worldwide undergo a percutaneous coronary intervention each year *(6)*. Although the advent of coronary artery stenting has decreased the need for target vessel revascularization within 6 mo of stent placement, stent restenosis remains a formidable problem.

Coronary artery stenting has revolutionized percutaneous coronary interventions. The two seminal studies documenting the benefit of coronary artery stenting are the Belgium Netherlands Stent (BENESTENT) trial *(7)* and the Stent Restenosis Study (STRESS) *(8)*. In the former, a total of 520 patients were randomized to undergo either coronary artery stenting with the Palmaz-Schatz stent or PTCA. After coronary interventions, the patients receiving a stent had a significantly larger acute gain in minimum lumen diameter. However, late loss in luminal diameter was also increased in this group. The rate of restenosis at 7 mo, using the binary definition of 50% or greater diameter stenosis, was 22% for the stent placement group compared with 32% in the PTCA group ($p = 0.02$). In addition to this reduction in restenosis, there was a 42% reduction in the need for repeat percutaneous interventions in the stent group. There were also fewer primary clinical end points of death, stroke, myocardial infarction, or target vessel revascularization in the stent group. These clinical benefits, however, occurred at the expense of an increased hospital stay and a four-fold increase in the risk of vascular complications.

In the STRESS trial, patients were also randomized to receive either the Palmaz-Schatz stent or PTCA *(8)*. At 6-mo follow-up, there was a lower rate of angiographic stenosis in the stent group compared to the PTCA group (32% vs 42%, $p = 0.046$). Clinical

follow-up revealed a trend toward a decrease in target lesion revascularization procedures in the stent group. However, as in the BENESTENT trial, these benefits were obtained at the expense of increased hemorrhagic complications in the stent group. More recently, based on the landmark study of Nakamura and colleagues *(9)*, it has been demonstrated that if the stent struts are adequately apposed to the vessel wall with high-pressure balloon inflations after stent deployment, aggressive anticoagulation is not required. Indeed, an anticoagulation regimen consisting of aspirin daily and Ticlopidine twice daily (Syntex Labs, Palo Alto, CA) for 2–4 wk is sufficient to decrease the subacute thrombosis rate to <1%.

In general, coronary artery stenting is most suitable for patients with discrete lesions with lengths <15 mm and proximal lesions of similar morphology in large-diameter (>3 mm) vessels. Table 1 depicts the incidence of clinical end-points (death, myocardial infarction, need for coronary reintervention, and angina-free rate) among patients undergoing PTCA or coronary artery stenting in both trials.

The proximal LAD artery has been shown to be the coronary artery site of greatest restenosis with an angiographic rate of 40–50% after PTCA. A number of trials have evaluated the results of PTCA vs conventional CABG for proximal LAD stenosis. Goy et al. *(10)* compared PTCA to CABG with left internal mammary artery (LIMA) graft to the LAD among 134 patients with isolated LAD disease and preserved left ventricular function. There was a 2% incidence of periprocedural myocardial infarction in the LIMA CABG group, and a 3% incidence of abrupt vessel closure with myocardial infarction and the need for emergency CABG in the PTCA group. After 2 yr, the rate of myocardial infarction continued to be higher in the PTCA group (12% vs 3%), although this difference did not attain statistical significance. No deaths occurred in the PTCA group, and one death occurred in the CABG group. However, the need for repeat revascularization was substantially higher in the PTCA group (25% vs 3%, $p < 0.01$). Therefore, the composite of primary end points including repeat revascularization, deaths, and myocardial infarction was higher for the PTCA group (37% vs 8%, $p < 0.01$). Moreover, at 2-yr follow-up, a significantly larger number of patients with PTCA were on antianginal drugs. Therefore, although PTCA and LIMA CABG improved clinical status with a similar risk of death and myocardial infarction in patients with single-vessel proximal LAD disease, PTCA is limited by a higher rate of repeat interventions.

Cameron et al. *(11)* retrospectively compared outcome and quality of life (QOL) in patients undergoing revascularization with CABG or PTCA for significant narrowing of the LAD. Two hundred and fifty-four patients underwent PTCA and 104 patients received conventional CABG. Of the patients in the surgical group, 88% underwent grafting using the LIMA graft. Rates of freedom from death were similar, but CABG patients had greater rates of freedom from repeat angina, myocardial infarction, and the need for repeat revascularization. Therefore, as with Goy et al.'s study, both PTCA and CABG result in excellent survival, functional ability, and QOL, but patients undergoing PTCA required more procedures to attain this end point.

In the Medicine, Angioplasty, or Surgery Study, 214 patients with single-vessel proximal LAD stenosis were prospectively randomized to medical therapy, PTCA, or CABG

Table 1
Comparison of Incidence of Death, Myocardial Infarction, Repeat Coronary Intervention and Angina-Free Rate Among Patients Undergoing PTCA or PTCA and Coronary Artery Stenting in the BENESTENT and STRESS Trials[a]

	BENESTENT[b]			*STRESS*[c]		
Clinical endpoints	*PTCA*[d]	*CAS*[e]	*p-value*	*PTCA*	*CAS*	*p-value*
Death (%)	0.4	0.8	NS[f]	1.5	1.5	NS
Myocardial infarction (%)	4.6	4.2	NS	6.9	6.3	NS
Repeat PTCA (%)	23	13	0.005	12.4	11.2	NS
Coronary bypass surgery	4.2	6.2	NS	8.4	4.9	NS
Angina-free rate (%)	66	73	NR[g]	71	79	0.08

[a]Adapted from refs. *7* and *8*.
[b]Belgium Netherlands Stent trial; includes up to 7 mo of follow-up.
[c]Stent Restenosis Study; includes up to 240 d of follow-up.
[d]Percutaneous transluminal coronary angioplasty.
[e]Coronary artery stent.
[f]Not significant.
[g]Not recorded.

(12). Patients who received a LIMA graft to the LAD had a significantly lower incidence of cardiac events over the next 3 yr than patients assigned to either medical therapy or PTCA, but as with the previously cited studies, the rate of death and myocardial infarction was similar across treatment groups. More recently, a study comparing coronary artery stenting to PTCA for symptomatic isolated proximal LAD stenosis revealed that stenting results in a lower rate of restenosis (19% vs 40%, $p = 0.02$) and a better clinical outcome (87% event-free survival at 12 mo for stenting compared with 70% after PTCA, $p = 0.04$) *(13)*.

Although prospective studies evaluating the merits of PTCA vs MICABG have not appeared, existing reports of MICABG for single-vessel disease describe excellent patency rates, low perioperative morbidity and mortality, and early discharge *(14–16)*. Based on this early data and the prospective studies described previously, certain subsets of patients with single-vessel disease are more likely to benefit from initial MICABG rather than percutaneous coronary intervention. These include patients who:

1. Are at high risk for abrupt closure during PTCA (e.g., those patients undergoing dilation of long, eccentric, or curved stenotic segments);
2. Are at high risk should abrupt closure occur;
3. Are at high risk of other acute complications of PTCA (e.g., patients with aortoiliac occlusive disease);
4. Are at high risk of restenosis (e.g., patients with diabetes); or
5. Have a low probability of success with PTCA.

Factors that would favor percutaneous coronary interventions over MICABG include discrete proximal lesions in large coronary arteries, small distal target vessels, stenosis or occlusion of the left subclavian artery, and patient's desire to avoid bypass surgery.

MULTIVESSEL CAD

In view of the advances in minimally invasive techniques for myocardial revascularization, one can foresee that MICABG may also play a role in the therapeutic management of patients with multivessel coronary disease. In comparing multivessel PTCA to multivessel CABG, complete revascularization is more frequently achieved by CABG compared to PTCA. Indeed, in the BARI study *(17)*, only 57% of patients in the PTCA group attained complete revascularization compared to 91% of patients in the CABG group. Other considerations in the management of patients with multivessel CAD include the presence or absence of large targets, identification of potential culprit lesion(s), and involvement of the LAD.

In this regard, the LIMA graft to the LAD has proven to be a superior conduit to the LAD compared to the saphenous vein graft *(18)*. In a study of over 5000 patients undergoing CABG followed for over 10 yr, patients who received saphenous vein grafts only had 1.41 times the risk of late myocardial infarction, 1.25 times the risk of hospitalization for cardiac events, twice the risk of reoperation, and 1.27 times the risk of all late cardiac events when compared to patients who received LIMA grafts to the LAD *(19)*. Therefore, the MICABG hypothesis is predicated on the notion that the survival value of a CABG procedure is based on the presence of a patent conduit to the LAD. In particular, if the LIMA to the LAD is successful in 99% of patients, can the remaining lesions in the patient with multivessel CAD disease be managed medically or with PTCA/coronary stenting, and is this the patient's optimal choice?

In the European Coronary Surgery Study *(20–22)*, patients with double-vessel coronary disease who had >75% stenosis in the proximal LAD had a better survival rate than patients with double-vessel coronary disease that did not include the proximal LAD. The incidence of Q-wave myocardial infarction was similar in the overall surgical group. Freedom from angina at 5 yr was reported in 46% of patients in the CABG group compared with 28% of patients in the medical group ($p < 0.001$). In patients who had at least a 75% stenosis in the proximal segment of the LAD, there was a 90% 8-yr survival rate in the CABG group compared with a 79% survival rate in the medical therapy group ($p = 0.013$). In patients without involvement of the proximal LAD, there was a survival rate of approx 89% in the CABG group and an 86% survival rate in the medical group at 8 yr (p = ns).

Several randomized trials conducted during this decade have compared CABG to PTCA for patients with multivessel CAD. These include the RITA *(23)*, the BARI *(17)*, the ERACI *(24)*, the CABRI *(25)*, the GABI *(26)*, and the EAST studies *(27)*. All these studies have shown similar survival rates between multivessel PTCA and multivessel CABG; however, patients randomized initially to multivessel PTCA had a much higher incidence of repeat revascularization procedures and ultimately bypass surgery. Of particular importance, the BARI trial demonstrated that the subgroup of patients with diabetes mellitus, whether insulin dependent or noninsulin dependent, had a significantly lower mortality rate with CABG than with PTCA at 5-yr follow-up (19.4% mortality with CABG compared 34.5% with PTCA, $p = 0.003$) *(17)*. By contrast, the 5-yr mortality rate

in nondiabetics and diabetics not taking drug treatment was 9% for both CABG and PTCA patients. Note that only a small percentage of patients with multivessel CAD screened for BARI were ultimately randomized to either treatment arm. Of 25,000 patients who underwent coronary angiography and who were found to have multivessel CAD, half were excluded for clinical or angiographic reasons (usually a totally occluded vessel), and ultimately only 4110 patients were thought to be clinically and angiographically eligible for the study. Only 1829 patients (7%) originally screened were randomly assigned to undergo CABG or PTCA in this trial.

Although randomized evaluation of conventional CABG vs MICABG vs PTCA for multivessel coronary disease has not been performed, advantages and disadvantages to the three revascularization approaches can be outlined. The benefits of multivessel CABG include the following:

1. Proven survival benefit of CABG vs medical therapy in subgroups of patients;
2. Complete revascularization;
3. Excellent relief of angina;
4. Fewer subsequent procedures;
5. Possible long-term survival benefit of CABG vs percutaneous coronary interventions; and
6. The most intraoperative control in patients with hemodynamic/ischemic instability *(28)*.

By contrast, the potential disadvantages of multivessel CABG include:

1. Increased magnitude of surgery and longer in-hospital recovery period;
2. The use of CPB and its attendant problems (in particular neurologic complications); and
3. A questionable increased risk of periprocedural Q-wave myocardial infarction *(28)*.

The primary potential benefits of MICABG include the avoidance of CPB and less magnitude of surgery, resulting in less postoperative pain, earlier hospital discharge, and earlier return to work. However, several questions remain unanswered regarding minimally invasive approaches to surgical revascularization: For patients with multivessel CAD, does MICABG provide equivalent survival benefit to conventional multivessel CABG? For patients with single-vessel proximal LAD, is MICABG safer and more effective than coronary artery stenting? The potential drawbacks of MICABG in multivessel CAD include the following:

1. Incomplete revascularization;
2. Unproven survival benefit;
3. More technical demands than multivessel CABG;
4. Lack of long-term follow-up; and
5. Suboptimal management of intraoperative hemodynamic/ischemic instability compared to traditional CABG.

The advantages of percutaneous coronary interventions include:

1. Avoidance of surgery in 70% of patients over 5 yr;
2. Overnight or same-day discharge with shorter hospitalizations than with MICABG or CABG;

Table 2
Advantages and Disadvantages of MICABG and Percutaneous Coronary Interventions[a]

Technique	*Advantages*	*Disadvantages*
MICABG	Avoidance of CPB Less extensive surgery	Unknown survival benefit Unproven safety and efficacy Incomplete revascularization for multivessel CAD
Percutaneous coronary interventions	Avoidance of surgery in 70% of patients Overnight or same-day discharge Fewer periprocedural Q-wave infarctions Five-year survival roughly comparable to CABG in nondiabetics Proven efficacy vs medical therapy for single-vessel CAD	Higher incidence of repeat interventions Less angina relief compared with CABG Possibly lower 5-yr survival compared with CABG in diabetics

[a]Adapted from ref. *28*.

3. Fewer periprocedural Q-wave myocardial infarctions;
4. Proven efficacy for angina and ischemia relief vs medical therapy for single-vessel CAD; and
5. Survival rate comparable to CABG at 5 yr *(28)*.

The deficiencies of multivessel percutaneous coronary interventions for multivessel CAD include:

1. A higher incidence of repeat interventional procedures;
2. Incomplete revascularization;
3. Less angina relief compared to multivessel CABG;
4. Decreased survival in the diabetes subgroup at 5 yr, as evidenced by the BARI trial *(17)*; and
5. Lesion-specific risk factors *(28)*.

Table 2 summarizes the advantages and disadvantages of MICABG vs percutaneous coronary interventions.

One preliminary study *(29)* has examined coronary stenting vs MICABG vs CABG in 498 consecutive patients with isolated LAD disease. Patients were referred for surgery if their anatomy was deemed not suitable for PTCA. There were no differences with respect to gender, risk factors, or prior PTCA. In this study, MICABG patients were older with a higher incidence of diminished left ventricular ejection fraction (<30%) and had a higher incidence of prior CABG.

A total of 353 patients (71%) received stents, 92 patients (18%) underwent conventional CABG, and 53 patients (11%) underwent MICABG *(29)*. The mortality rate was 0.8% in the stent group compared with 3.3% in both the CABG and MICABG groups, and the incidence of myocardial infarction was 0.8% in the stent group compared with

3.3% in both the CABG and miniCABG groups. Cerebrovascular accidents occurred in 1.8% of the MICABG group but not in the other two groups. The only statistically significant differences observed were a reduced length of stay in the stent group of 4 d compared with 8.4 d for the CABG and 7.7 d for the MICABG ($p < 0.05$), and reduced hospital charges of $20.190 for the stent group compared with $31.703 for the CABG and $28.260 for the MICABG ($p < 0.05$).

Most recently, the value of PTCA compared to MICABG for the treatment of isolated type C stenosis of the LAD associated with angina was investigated *(30)*. In-hospital and 1-yr follow-up results were reported on 181 consecutive patients who underwent one of the two procedures on an elective basis. The study was not randomized because patients had the final choice of treatment. The incidence of in-hospital death, periprocedural myocardial infarction, emergency reoperative CABG, use of intra-aortic balloon pump, and cerebrovascular accidents was not significantly different between the two groups. At 1-yr follow-up, survival was not significantly different (95.7 ± 0.2% for MICABG vs 95.3 ± 0.2% for PTCA, $p = 0.89$). Freedom from repeat revascularization was significantly more common in the MICABG cohort than in the PTCA group (96.9 ± 0.2% vs 67.6 ± 0.5%, $p < 0.001$).

In conclusion, both MICABG and percutaneous coronary interventions, particularly coronary artery stenting, are procedures in rapid evolution. Randomized comparison of MICABG to coronary stenting for single-vessel CAD, particularly proximal LAD disease, is warranted. Furthermore, the potential role of MICABG as part of a multitiered strategy or "hybrid therapy" (in combination with medical and percutaneous therapies *[31]*) for patients with multivessel CAD is an attractive option and deserves future investigation.

REFERENCES

1. Hartz RS. Minimally invasive heart surgery. Executive Committee of the Council on Cardio-Thoracic and Vascular Surgery. Circulation 1996;94:2669–2670.
2. Jones RH, Kesler K, Phillips HRD, et al. Long-term survival benefits of coronary artery bypass grafting and percutaneous transluminal angioplasty in patients with coronary artery disease. J Thorac Cardiovasc Surg 1996;111:1013–1025.
3. Parisi AF, Folland ED, Hartigan P. A comparison of angioplasty with medical therapy in the treatment of single-vessel coronary artery disease. Veterans Affairs ACME Investigators. New Engl J Med 1992;326:10–16 (see comments).
4. Nobuyoshi M, Kimura T, Nosaka H, et al. Restenosis after successful percutaneous transluminal coronary angioplasty: serial angiographic follow-up of 229 patients. J Am Coll Cardiol 1988;12:616–623.
5. Liu MW, Roubin GS, King SB. Restenosis after coronary angioplasty: potential biologic determinants and role of intimal hyperplasia. Circulation 1989;79:1374–1387.
6. Pepine CJ, Holmes DR Jr. Coronary artery stents. American College of Cardiology. J Am Coll Cardiol 1996;28:782–794.
7. Serruys PW, de Jaegere P, Kiemeneij F, et al. A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coronary artery disease. Benestent Study Group. New Engl J Med 1994;331:489–495.

8. Fischman DL, Leon MB, Baim DS, et al. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. Stent Restenosis Study Investigators. New Engl J Med 1994;331:496–501.
9. Nakamura S, Hall P, Gaglione A, et al. High pressure assisted coronary stent implantation accomplished without intravascular ultrasound guidance and subsequent anticoagulation. J Am Coll Cardiol 1997;29:21–27.
10. Goy JJ, Eeckhout E, Burnand B, et al. Coronary angioplasty versus left internal mammary artery grafting for isolated proximal left anterior descending artery stenosis. Lancet 1994;343:1449–1453.
11. Cameron J, Mahanonda N, Aroney C, et al. Outcome five years after percutaneous transluminal coronary angioplasty or coronary artery bypass grafting for significant narrowing limited to the left anterior descending coronary artery. Am J Cardiol 1994;74:544–549.
12. Hueb WA, Bellotti G, de Oliveira SA, et al. The Medicine, Angioplasty or Surgery Study (MASS): a prospective, randomized trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending artery stenoses. J Am Coll Cardiol 1995;26:1600–1605.
13. Versaci F, Gaspardone A, Tomai F, Crea F, Chiariello L, Gioffre PA. A comparison of coronary-artery stenting with angioplasty for isolated stenosis of the proximal left anterior descending coronary artery. New Engl J Med 1997;336:817–822.
14. Calafiore AM, Teodori G, Di Giammarco G, Vitolla G, Contini M. Minimally invasive coronary artery surgery: the LAST operation. Semin Thorac Cardiovasc Surg 1997;9:305–311.
15. Subramanian V, Stelzer P. Clinical experience with minimally invasive coronary artery bypass grafting (CABG). Eur J Thorac Cardiovasc Surg 1996;10:1058–1063.
16. Robinson MC, Gross DR, Zeman W, Stedje-Larsen E. Minimally invasive coronary artery bypass grafting. A new method using an anterior mediastinotomy. J Cardiothorac Surg 1995; 10:529–536.
17. The BARI Investigators. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. The Bypass Angioplasty Revascularization Investigation (BARI) Investigators. New Engl J Med 1996;335:217–225.
18. Zeff RH, Kongtahworn C, Iannone LA, et al. Internal mammary artery versus saphenous vein graft to the left anterior descending coronary artery: prospective randomized study with 10-year follow-up. Ann Thorac Surg 1988;45:533–536.
19. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the intemal-mammary-artery graft on 10-year survival and other cardiac events. New Engl J Med 1986;314:1–6.
20. Varnauskas E. European coronary surgery study. Zeitschrift fur Kardiologie 1985;74:73–78.
21. Varnauskas E. Survival, myocardial infarction, and employment status in a prospective, randomized study of coronary bypass surgery. Circulation 1985;72:V90–V101.
22. Varnauskas E. Twelve-year follow-up of survival in the randomized European Coronary Surgery Study. New Engl J Med 1988;319:332–337.
23. RITA Trial Participants. Coronary angioplasty versus coronary artery bypass surgery: the Randomized Intervention Treatment of Angina (RITA) trial. Lancet 1993;341:573–580.
24. Rodriguez A, Boullon F, Perez-Balino N, Paviotti C, Liprandi MI, Palacios IF. Argentine randomized trial of percutaneous transluminal coronary angioplasty versus coronary artery bypass surgery in multivessel disease (ERACI): in-hospital results and 1-year follow-up. ERACI Group. J Am Coll Cardiol 1993;22:1060–1067.
25. CABRI Trial Participants. First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularisation Investigation). CABRI Trial Participants. Lancet 1995;346:1179–1184.
26. Hamm CW, Reimers J, Ischinger T, Rupprecht HJ, Berger J, Bleifeld W. A randomized study of coronary angioplasty compared with bypass surgery in patients with symptomatic multivessel coronary disease. German Angioplasty Bypass Surgery Investigation (GABI). New Engl J Med 1994;331:1037–1043.

27. King SBR, Lembo NJ, Weintraub WS, et al. A randomized trial comparing coronary angioplasty with coronary bypass surgery. Emory Angioplasty versus Surgery Trial (EAST). New Engl J Med 1994;331:1044–1050.
28. Simoons ML. Myocardial revascularization—bypass surgery or angioplasty? New Engl J Med 1996;335:275–277 (see editorial; comment).
29. Fry ETA, Hermiller JB, Lips DL, et al. Comparison of stents, bypass surgery (CABG), and minimally invasive bypass (MICAB) for isolated LAD revascularization: patient selection, outcomes, and cost. Circulation 1996;94:I–324.
30. Mariani MA, Boonstra PW, Grandjean JG, et al. Minimally invasive coronary artery bypass grafting versus coronary angioplasty for isolated type C stenosis of the left anterior descending artery. J Thorac Cardiovasc Surg 1997;114:434–439.
31. Friedrich GJ, Bonatti J, Dapunt OK. Preliminary experience with minimally invasive coronary artery bypass surgery combined with coronary angioplasty. N Engl J Med 1997;336(20): 1454,1455 (letter).

5 Visualization Techniques for Minimally Invasive Cardiac Surgery

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CONTENTS

INTRODUCTION

The last decade has witnessed a paradigm shift in the practice of surgery with the application of minimally invasive techniques to everyday clinical practice. With the use of these techniques in general surgery, gynecology, orthopedics, and thoracic surgery, "minimally invasive" became synonymous with "minimal access." Naturally the parallel development of visual-imaging technology to replace direct vision was necessary to overcome the limitations of small incisions. But rather than technology filling a void, video imaging actually created and catalyzed the field of minimally invasive surgery.

An integral element of video imaging technology is the charged-coupled device (CCD) chip, a tool that allows image digitization. The CCD was developed and first introduced to the home video camera market. Application of this technology allowed miniaturization of video cameras. Further adaptation of this technology to the operating room allowed visualization of body cavities that, in some instances, exceeded direct visualization through open incisions. The combination of this technology with lens magnification and xenon or halogen light sources in close proximity to the target organ resulted in excellent image quality, display, and resolution. The more recent addition of three-chip technology and digitally enhanced imaging provided even higher definition of the operative field.

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

Problematic, however, was the necessity for trained surgeons to adapt their standard surgical procedures to the new techniques. The shift of vision from an operative field in proximity to the surgeon's hands to an eye level video monitor, and the loss of the ability to see the instrument directly, as well as the fulcrum effect of the abdominal wall causing the instrument tip to move in the opposite direction from the hand movement, all required relearning standard procedures. Fortunately, cholecystectomy allowed general surgeons to surmount the new learning curve fairly expeditiously by providing a high-volume, technically straightforward operation to develop their new skills. Within a 2-yr period, more than 90% of cholecystectomies performed in the United States were converted from an open to a closed videoscopic technique *(1)*.

Gradually, as instrumentation improved, video techniques were adopted for more complex general surgical procedures (Nissen fundoplication and inguinal herniorrhaphy) and for other surgical specialties (thoracic and spine surgery). However, whereas excisional, simple, high-volume procedures could be readily adapted to minimally invasive techniques, the learning curve was and remains much steeper for complex reconstructive procedures, including cardiac surgery. Indeed, although a number of centers embarked on determining the feasibility of the totally endoscopic coronary artery bypass in the animal model, the challenges imposed by the conversion of the complex procedure to a totally thoracoscopic approach proved to be prohibitive.

Cardiac Surgery

Whereas most surgical subspecialties present only one opportunity to make the surgical procedure less invasive by minimizing access trauma with the use of ports rather than large incisions, cardiac surgery presents additional opportunities to decrease the invasiveness of its conventional operations. The major morbidities of conventional cardiac operations, and coronary bypass grafting in particular, arise from the need for a median sternotomy, cardiopulmonary bypass, and manipulation of the aorta. Efforts to abolish all these potential sources of morbidity heralded the introduction of the minimally invasive direct coronary artery bypass (MIDCAB) grafting, a procedure that reduces the trauma of access, avoids extracorporeal circulation, and does not require aortic manipulation.

In addition to reducing incision size, the use of a limited anterior thoracotomy obviated a major obstacle of an endoscopic coronary artery bypass by allowing the technically difficult anastomosis to be performed under direct vision. Thus, the technical challenges of the endoscopic suturing were overcome and, although the procedure was not performed totally endoscopically, it was still "less invasive." However, the necessity of video assistance for the harvest of the internal mammary artery (IMA) still required the surgeon previously not conversant with video endoscopic techniques to "struggle with the scope."

This barrier was eventually overcome by the development of offset rib retractors, which create a tunnel of direct vision that facilitates harvest of the IMA without video assistance. In fact, this is currently the technique by which most MIDCAB and port access procedures are performed today *(2,3)* (Fig. 1).

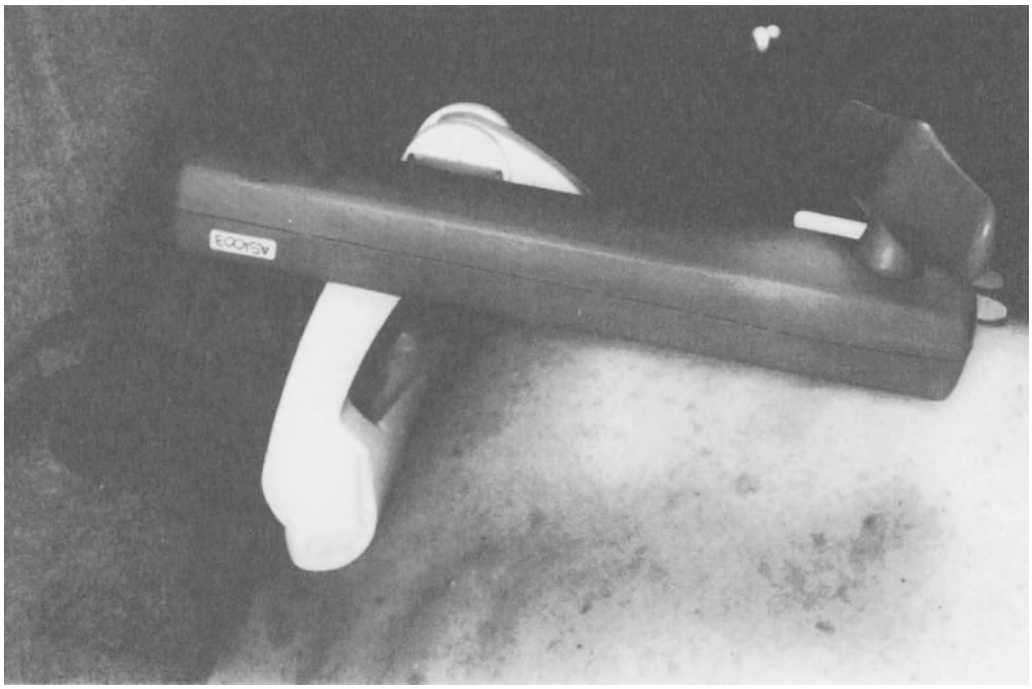

Fig. 1. Offset rib retractors for IMA harvest.

Is there a need to further "enhance" these procedures to render them even less invasive? Significant morbidity is still caused by chest wall retraction, rib spreading, and costal or cartilage resection. Therefore, in an attempt to minimize further the access trauma to the chest wall, the pursuit of a totally endoscopic coronary bypass approach continues. Video imaging is an intricate and necessary part of such an approach. The following discussion focuses on the basics of video imaging and the current uses of video assistance in cardiac surgery.

A PRIMER ON IMAGING SYSTEMS

The components of imaging systems required for any endoscopic surgery are a telescope, a source of illumination, a video camera, and a video projection system. Technological developments are occurring at breakneck speed, and often systems are obsolete almost as soon as they become commercially available. Imaging systems that are 4 or 5 yr old, although not considered state-of-the-art, are still sufficient for most purposes.

Telescopes

The standard telescope for endoscopic procedures is a 10-mm rigid scope of a Hopkins lens system that transmits an image from the distal end of the telescope to a video camera attached to the opposite end (Table 1). The shaft of the telescope contains both illuminat-

Table 1
Equipment Options for Video Assistance

Telescopes
Rigid
Diameter: 2, 5, 10 mm
Angle: 0°, 30°, 45°
Flexible
Fiberoptic
"Chip on a tip"
Cameras
Single chip
Digital enhancement single chip
Three chip
Light Sources
Xenon
Halogen
Monitors
Two-dimensional
Three-dimensional

ing and viewing optics. The imaging system consists of an objective lens, a relay lens and an eyepiece lens. The illumination system is actually a fiberoptic system. The objective lens or distal lens is most susceptible to damage from instruments or abrasion. The Hopkins lens system offers superior optics and accurate transmission of image. The standard scope is a 0° end-viewing scope in which the field of vision is limited to the area directly ahead of the scope. For complex procedures including IMA harvest, the 30° scope offers superior ability to broaden the viewed operative field. Although there is a greater degree of difficulty for the novice using such angled scopes, the advantages quickly become obvious by allowing the surgeon to "see around the corner." Although scopes are available in smaller versions down to 5 or even 2 mm, the illumination quality is reduced and the field of vision is narrowed.

As well as standard rigid scopes, two types of flexible scopes are available. The earlier generation flexible scope transmitted the image to the camera through fiberoptic bundles. Unfortunately, considerable loss of illumination and resolution results. In addition, significant distortion of the image by a "fish eye" effect occurs. Newer generation scopes employ "chip on the tip" technology in which a CCD chip that digitizes the image is contained within the distal end of the scope lying within the body cavity. A superb image is then transmitted digitally over a wire rather than through an optical lens or fiberoptic system. Systems exist in which two chips are placed on the tip slightly offset, allowing flexible three-dimensional (3D) vision.

Cameras

As alluded to earlier, the key component of endoscopic cameras is the CCD, a silicone chip with a surface composed of thousands of light-sensitive pixels. When a series of

photons strike the CCD, an electronic signal is generated and sent to a processor and reassembled to form a television picture. A color image can be produced by several methods, the simplest of which is to place a finely divided color grid in front of the standard CCD chip, which makes each pixel sense red, green, or blue light. A color picture results from recombining the three colors into a final signal. Resolution, however, is reduced in this single-chip approach. Another method is to pass the incoming white light through a prism, thus dividing the light into component red, green, and blue colors and to use a separate CCD chip positioned to detect each color. Although three-chip cameras have better resolution than the single-chip models, the cost rises exponentially.

A third method uses a digitized single chip and a red, green, and blue (RGB) strobe light operating at a rate of 30 Hz as a light source. The CCD chip detects each of the three colors sequentially for 1/30th of a second. The images are stored in digital memory and recombined to form a picture. This digitized single-chip method offers image quality approximating the three-chip model, but at a lower cost. The digital system increases resolution and creates a sharper image by digitally enhancing desired image lines.

Light Sources

Modern light sources use either halogen or xenon lamps for illumination. These bulbs, which are usually in the 300-W range, generate considerable heat, so proper light source placement is important. Most light sources have both an automatic iris and a manual control, features that modulate light intensity as it changes with distance and color.

Video Output

Video output is composed of three basic signals:

1. Synchronizing signals (S), which cause the television monitor to paint video lines on the screen;
2. Illuminate signals (Y), which contain information on brightness and fine picture detail; and
3. Chroma signals (C), which contain color information.

These signals are sent to video monitors and recording devices in three standard modes:

1. Composite video, which is a one-channel signal that contains Y and C components;
2. Y/C or S video, which involves two separate signals; and
3. RGB, which provides the best reproduction because each color has its own bandwidth.

Video Monitor

The quality of image generated is only as good as the video monitor on which it is displayed. Sharpness of image depends on the number of lines of resolution on the monitor. Larger monitors do not necessarily create sharper images. To convey the ever-increasing resolution of CCDs, the introduction of high-definition television monitors appears inevitable.

Table 2
Accessories for Enhancing Video Assistance

Telescope holders
Fixed
Activated by voice, motion or pedal control
Zoom Lenses
Defogging systems
Recording devices

Image Recording

Most video systems have the ability to record procedures on either VHS tapes or video printers. Most videotapes are either VHS format, which contains 240 lines of horizontal resolution or S-VHS format, which has 400 lines of resolution.

Accessories for Video Assistance

When a scope is used, there are multiple accoutrements that enhance video assistance and facilitate the procedure (Table 2). Although, in most video-assisted procedures a surgical assistant holds and directs the telescope, holders can be used. These work particularly well for IMA harvest. Numerous activation stimuli including voice activation, head motion sensors, eye motion sensors, as well as pedals that allow the surgeon to direct the scope to the proper operative field are currently undergoing clinical evaluation.

Zoom lenses also allow enhanced magnification of the operative field. Fogging of the lens is a problem with all available scope systems, and several defogging devices are available.

CURRENT USES OF VIDEO ASSISTANCE IN MINIMALLY INVASIVE CARDIAC SURGERY

As mentioned previously, for numerous reasons, most minimally invasive cardiac surgeries do not use video assistance. However, there are many areas in which videoscopic techniques can enhance the surgical procedure. Perhaps the most common operations in which video enhancement has been used are ligation of patent ductus arteriosus *(4)*, harvest of the IMA *(5)*, and mitral valve procedures *(6)*.

IMA Harvest

Numerous chest wall retraction devices allow harvest of the IMA under direct vision (Fig. 2). Unfortunately, all cause considerable chest wall trauma by the upward traction on the cephalad portion of the exerted chest wall. To minimize this trauma, video assistance can be used, particularly if the IMA dissection is carried to the apex of the chest (Table 3). A scope placed laterally in the fourth intercostal space (Fig. 3) allows the

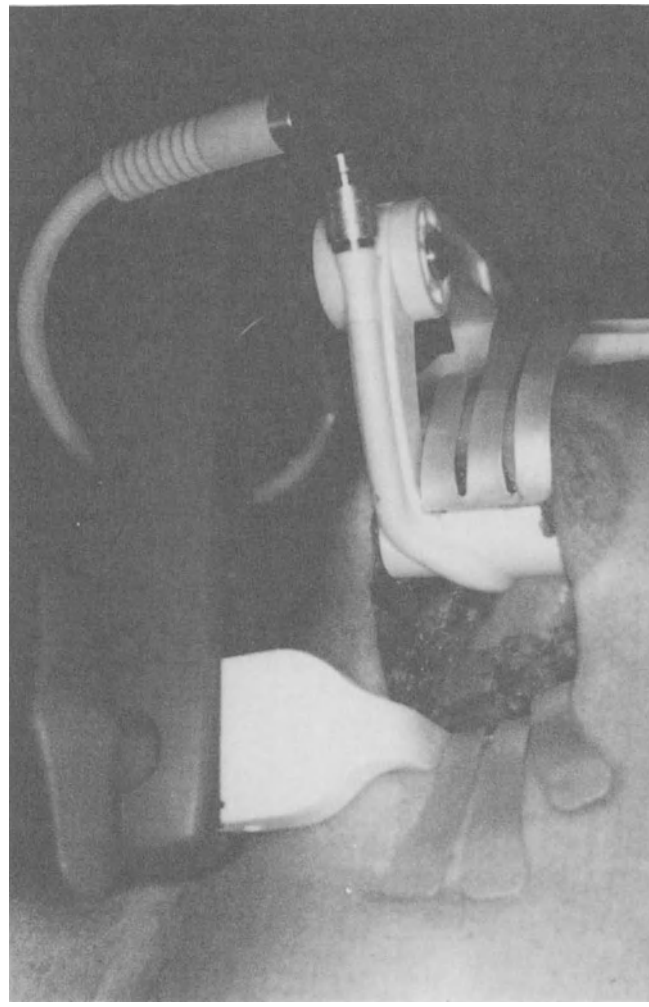

Fig. 2. Chest wall retraction device for harvesting of IMA under direct vision.

Table 3
Visualization Techniques for Mimimally Invasive Cardiac Surgery

Direct vision
Video assited
Endoscopic
Two-dimensional
Video
Three-dimensional
Head-mounted display
Monitor with glasses

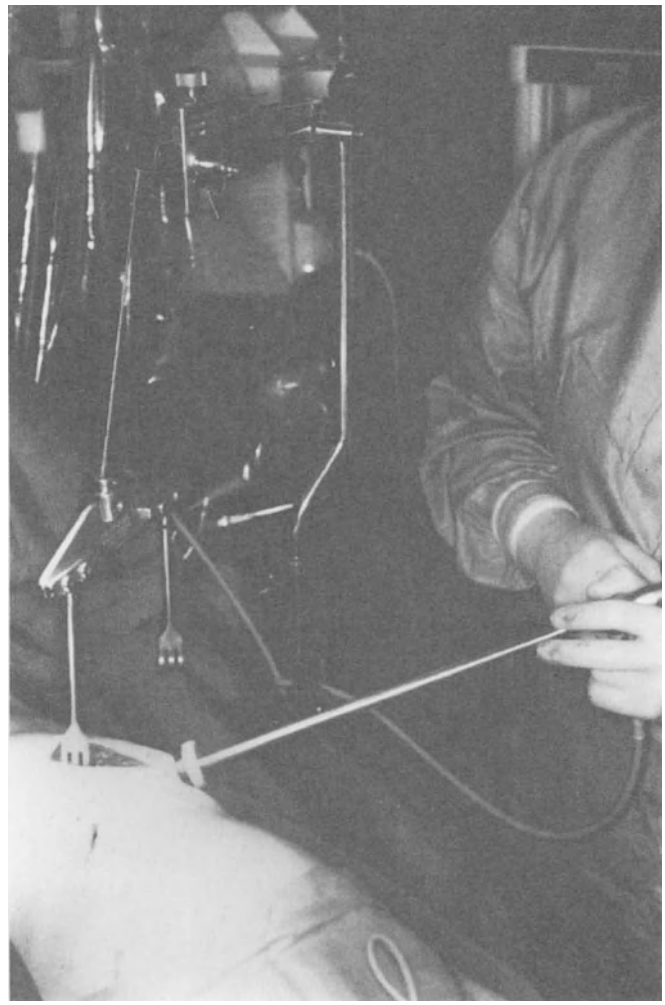

Fig. 3. A telescope is placed laterally in the fourth intercostal space to aid the harvest of the IMA.

surgeon to visualize the IMA as the instruments are placed directly through the incision (Fig. 4). This hybrid approach obviates some of the difficulties of a totally endoscopic video approach by allowing the instruments to go through incisions, albeit small, providing more instrument maneuverability than the access afforded by the use of ports. An added benefit of this approach is that it allows the surgeon to gain experience with video procedures more easily.

A further extension of the video-assisted technique involves the complete thoracoscopic harvest of the IMA. In this approach, three ports are placed in the lateral chest wall (Fig. 5) and both the video camera and instruments are manipulated through the access ports without any additional incisions. The advantage of this approach lies in its reduced chest wall trauma; its disadvantages are those inherent to endoscopic procedures in general. This latter approach has been most enthusiastically advocated by Nataf et al. *(5)*

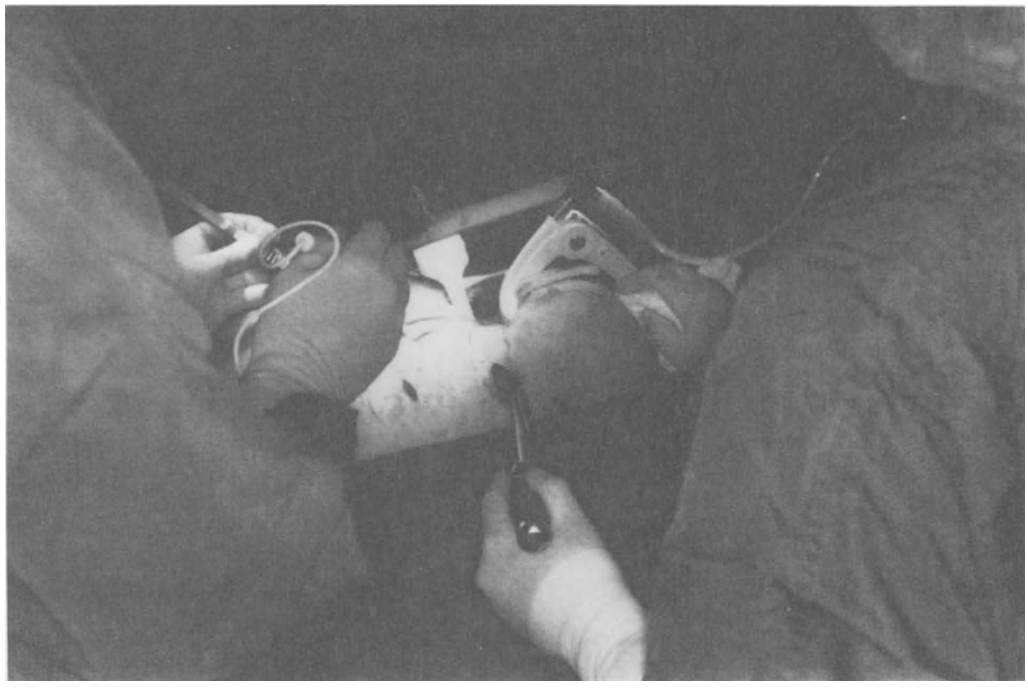

Fig. 4. "Hybrid" technique for IMA harvest: the open incision allows passage of instruments while the telescope provides an expanded visual field.

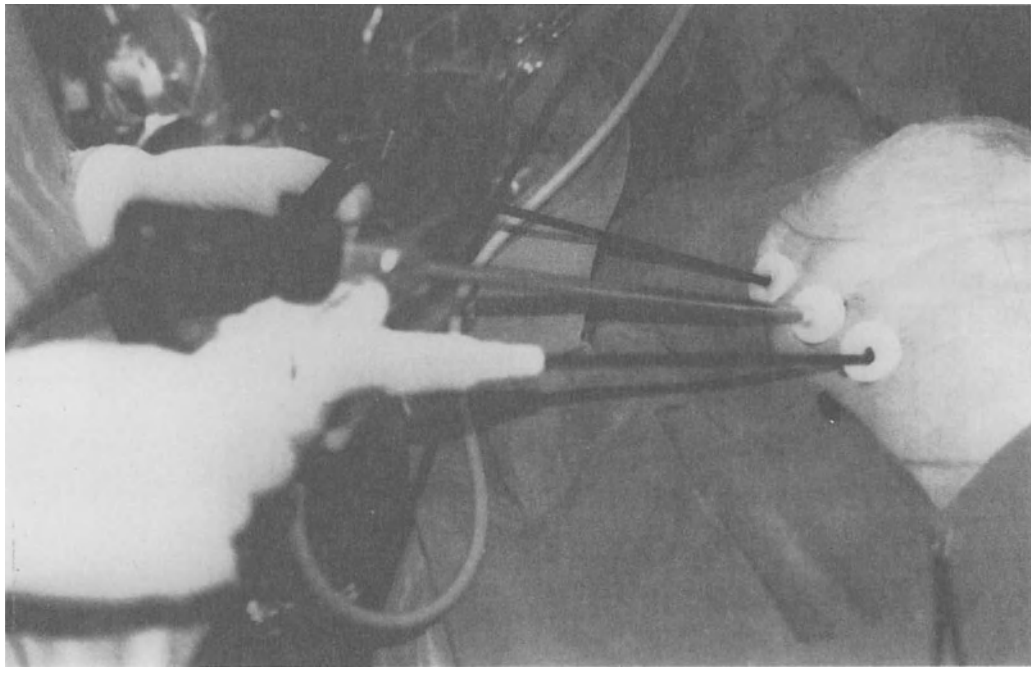

Fig. 5. Complete thoracoscopic harvest of the IMA. Three thoracoports are placed as shown. The telescope is passed through the middle port while thoracoscopic dissectors, scissors, and electrocautery are manipulated under direct thoracoscopic vision through the other two ports.

(*see* Chapter 6). The use of an ultrasonic scalpel and a 30° scope as advanced by Ohtsuka et al. *(7)* seems to facilitate the endoscopic procedure by minimizing the exchange of instruments. The most difficult aspect of this thoracoscopic approach is the inferior dissection of the IMA, where the pericardium lies in close proximity. This obstacle can be overcome by using carbon dioxide insufflation at a pressure of 10–15 cm H_2O to depress the pericardium away from the anterior chest wall. Alternatively, the dissection can be started through a limited anterior thoracotomy incision, and when the IMA is identified, the inferior portion can then be performed more easily.

Mitral Valve Procedures

Minimally invasive mitral valve procedures are now most commonly performed through a limited right anterior or anterolateral thoracotomy *(6,8)*. Most of this experience has been gained by application of the HeartPort technology, and by the methods of Chitwood et al. *(6)*, as described elsewhere in this book (*see* Chapter 16). Video assistance allows a magnified and lighted view of the mitral valve, which is particularly useful when reconstruction of the subvalvular apparatus is entertained.

Ligation of the Patent Ductus Arteriosus

Ligation of the patent ductus arteriosus was one of the first procedures investigated with thoracoscopic approaches (Fig. 6). The experiences of Laborde *(4)* and Burke *(9)* with several hundred cases of patent ductus arteriosus ligation with the aid of video assistance have established these techniques as standard therapy. Indeed, with the use of 3-mm scopes and endoscopic instrumentation, these procedures can be carried out routinely with minimal morbidity. Efforts are under way to extend these approaches to other pediatric cardiac procedures including the ligation of vascular rings and the construction of extracardiac shunts *(10)*. Furthermore, Burke and others have now employed the videoscopic equipment for cardioscopic examination of intracardiac structures, including delineation of left ventricular thrombus and evaluation of the adequacy of ventricular septal and mitral valve repairs *(11,12)*.

FUTURE APPLICATIONS OF VIDEO IMAGING IN MINIMALLY INVASIVE CARDIAC SURGERY

The quest for performance of a totally endoscopic coronary artery bypass procedure continues. Developments that may facilitate reaching this goal include the implementation of a 3D head-mounted displays (HMDs) and robotic suturing systems (Fig. 7). These HMDs are an application of virtual reality systems to endoscopic surgery. At present, HMDs are too cumbersome and isolate the members of the operating team from each other. A promising innovation in this field involves the use of head-up displays (HUDs), which project the image beneath eye level, enabling the surgeon to retain visual contact with the operating field *(13)*.

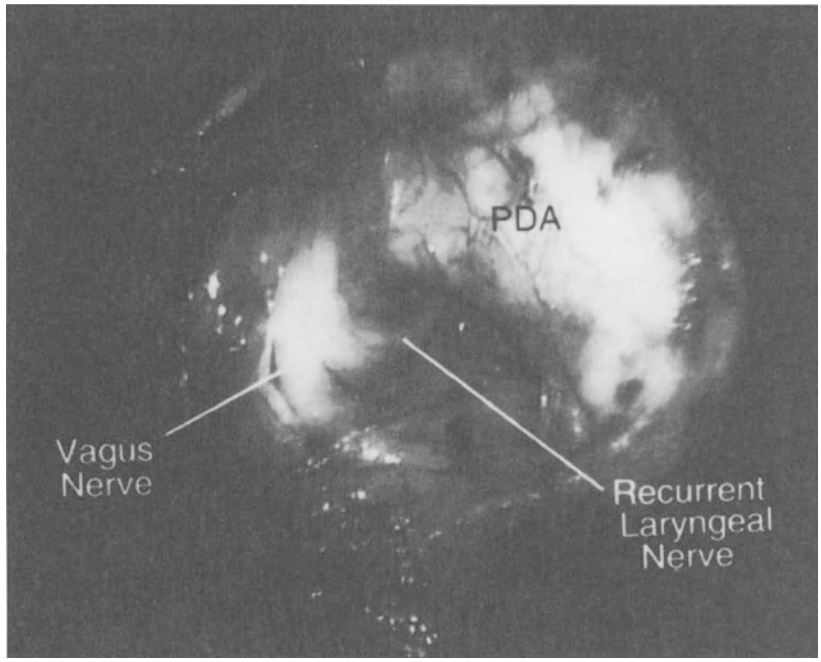

Fig. 6. Intraoperative thoracoscopic view of a patent ductus arteriosus. The vagus nerve and recurrent laryngeal nerve crossing under the ductus are clearly visualized.

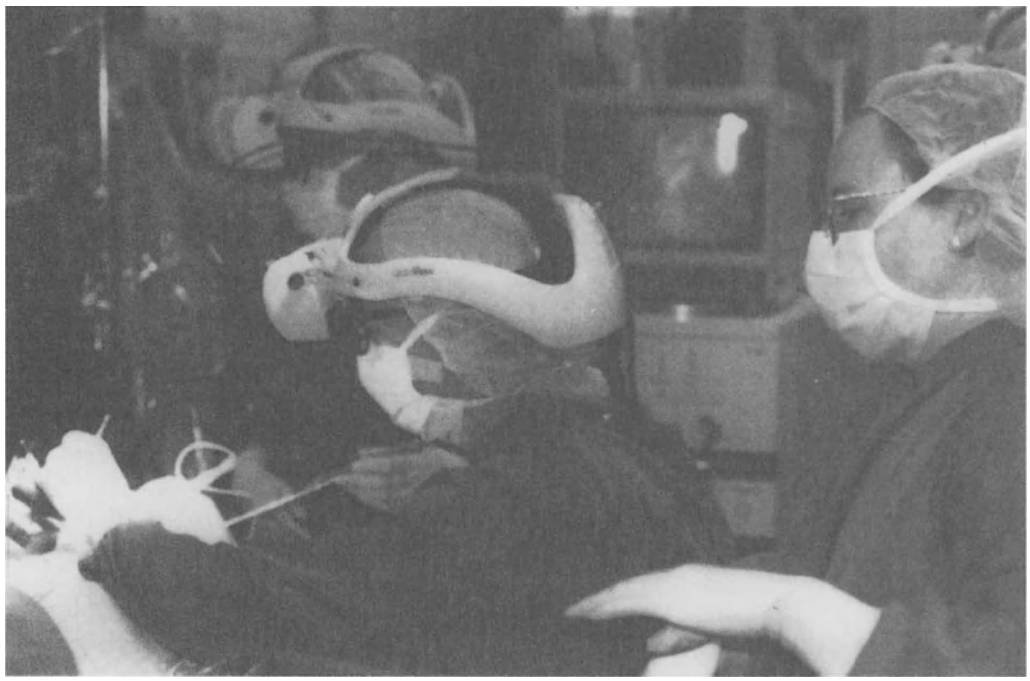

Fig. 7. HMD allows three-dimensional visualization.

Another potential application to the field of minimally invasive surgery relies on the use of human-systems interface technology to create a camera holder that automatically alters its position according to the surgeon's needs. This technology depends on remote tracking that responds to head or eyeball movements of the surgeon. The signals generated by these trackers is relayed to a computer that translates this information into desired camera movements such as zooming and horizontal and vertical motions.

The principal barrier to total endoscopic coronary bypass grafting is the creation of an optimal anastomosis. Efforts are ongoing to develop devices that can enhance or replace hand-sewn anastomoses including automated stapling devices, glues, and stents. It is envisioned that the widespread application of total endoscopic bypass grafting will occur only if a safe, effective, and easy-to-use mechanical device capable of producing a coronary anastomosis with short- and long-term patency equivalent to a hand sewn anastomosis is developed.

An intriguing and interesting concept is the adaptation of motion cancellation technology to operations on the beating heart. This technology may allow "virtual immobilization" by creating a frozen video image of a moving target (the beating heart), thereby allowing the surgeon to operate in a virtually immobile environment. Owing to motion cancellation, the surgeon could create the anastomosis on a moving heart that would appear immobile on the video monitor. Such "Star Wars" technology exists *(14)*, but major obstacles need to be overcome before practical application can be considered.

It should be anticipated that as the new generation of cardiac surgeons trained and facile with endoscopic techniques emerges, these approaches will become more widespread and innovative methods of harnessing the benefits of the thoracoscope will evolve.

REFERENCES

1. NIH Consensus Conference 1993 Gallstones and Laparascopic Cholscystectomy. JAMA 1993;269:1018–1024.
2. Calafiore AM, DiGiammarco G, Teodori G, et al. Left anterior descending coronary artery bypass grafting via left anterior small thoracotomy without cardiopulmonary bypass. Ann Thorac Surg 1996;61:1658–1665.
3. Stevens JH, Burdon TA, Peters WS, et al. Port-access coronary artery bypass grafting: a proposed surgical method. J Thorac Cardiovasc Surg 1996;111:567–573.
4. Laborde F, Noirhomme P, Karam J, Batisse A, Bourel P, Maurice OS. A new video-assisted thoracoscopic surgical technique for interruption of patent ductus arteriosus in infants and children. J Thorac Cardiovasc Surg 1993;105:278–280.
5. Nataf P, Lima L, Regan M, et al. Thoracoscopic internal artery mammary artery harvesting: technical considerations. Ann Thorac Surg 1997(Suppl);63:S104–S106.
6. Chitwood WR, Elbeery JR, Chapman WHH, et al. Video assisted minimally invasive mitral valve surgery: the micro-mitral operation. J Thorac Cardiovasc Surg 1997;113:413–414.
7. Ohtsuka T, Wolf RK, Hiratzka LF, Wurnig P, Flege JB. Thoracoscopic internal mammary artery harvest for MICABG using the harmonic scalpel. Ann Thorac Surg 1997(Suppl); 63:S107–S109.
8. Benetti FJ, Rizzardi JL, Pire L, Polanco A. Mitral valve replacement under video assistance through a minithoracotomy. Ann Thorac Surg 1997;63:1150–1152.

9. Burke RP, Wernovsky G, van der Velde M, Hansen D, Castaneda A. Video-assisted thoracoscopic surgery for congenital heart disease. J Thorac Cardiovasc Surg 1995;109:499–507.
10. Burke RP, Rosenfeld HM, Wernovsky G, Jonas RA. Video-assisted thoracoscopic vascular ring division in infants and children. J Am Coll Cardiol 1995;25:943–947.
11. Burke RP, Michielon G, Wernovsky G. Video-assisted cardioscopy in congenital heart operations. Ann Thorac Surg 1994;58:864–868.
12. Duarte IG, Fenton KN, Brown WM III. Video-assisted removal of left ventricular mass. Ann Thorac Surg 1997;63:833–835.
13. Cuschieri A. Whither minimal access surgery: tribulations and expectations. Am J Surg 1995;169:9–19.
14. Hunter IW, Doukoglou TD, Lafontaine SR, et al. A teleoperated microsurgical robot and associated virtual environment for eye surgery. Presence 1993;2:265–280.

6 Techniques of Minimally Invasive Internal Mammary Artery Harvest

Patrick Nataf, MD and M. Anno Diegeler, MD

CONTENTS

INTRODUCTION

Despite the wide application of video-assisted techniques in thoracic surgery, only a few procedures, such as pericardial window and ligation of a patent ductus arteriosus, have been performed by cardiac surgeons *(1–3)*. Owing to the growing clinical interest in minimally invasive coronary surgery, several technical approaches have recently been proposed to perform a left internal mammary artery to left anterior descending (LIMA-LAD) anastomosis on the beating heart through a small anterior thoracotomy. One of the concerns of these less invasive techniques involves the dissection of the IMA. This chapter discusses the various techniques currently used to harvest the IMA with a particular emphasis on the video-assisted (or thoracoscopic) approach.

NONTHORACOSCOPIC PROCEDURE

Method I: IMA Dissection Through Left Anterior Small Thoracotomy

The chest is opened via a left anterior thoracotomy 8–12 cm long in the fourth or the fifth intercostal space as described by Subramanian and Calafiore elsewhere in this book (*see* Chapters 8 and 9). The ribs are retracted and excision of the fourth costal cartilage is performed routinely by most surgeons.

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

The first part of the dissection consists of medial and lateral mobilization of the arterial pedicle and its release from the adjacent intercostal muscles. Transection of the sternocostal joint of the cartilage immediately rostral to the incision and anterior retraction of that cartilage using an external retractor may aid mammary dissection and improve access for the pedicle takedown. The IMA is usually harvested with conventional surgical instruments for a short length (6–10 cm) cephalad to the superior intercostal space and downward to the level of the inferior rib. The IMA may be skeletonized in order to extend its length. After systemic heparinization (1 mg/kg), the IMA is injected with a solution containing papaverine and is distally clipped. Some investigators have proposed the use of a thoracoscope as an adjunct to facilitate IMA takedown *(4)*.

Method II: IMA Dissection Through Anterior Mediastinotomy

Some investigators have alternatively used an anterior mediastinotomy approach via an 8-cm vertical parasternal incision *(5–7)*. Excision of small segments of the third and fourth costal cartilages allows the LIMA to be mobilized between the second and fifth ribs. Advantages to this approach include the performance of the IMA dissection under direct vision with conventional techniques and instruments, and hence, no special training is required. Moreover, the coronary anastomosis is performed through the same approach. Again, the procedure can be facilitated by the use of thoracoscopy *(8)*.

Disadvantages of this approach include the following:

1. Suboptimal visualization of the IMA, resulting in a more difficult disection;
2. The achievement of only a short length of IMA, which may be insufficient to reach the LAD, because only a partial vessel dissection can be performed;
3. Chest wall trauma resulting from the need for rib excision, the use of rib retractors, and the need to perform a larger thoracotomy than that performed with endoscopic procedures;
4. The possibility of coronary steal due to the incomplete harvest of the vessel *(9,10)*.

THORACOSCOPIC IMA TAKEDOWN

An alternative method to harvest the IMA that averts the technical difficulties discussed previously involves the use of video assistance to facilitate complete dissection of the IMA. This technique avoids rib resection and, by providing ample IMA length, results in a tension-free anastomosis with minimal risk of kinking. In addition, this technique allows complete dissection of the LIMA from the subclavian artery proximally to the sixth intercostal space distally, with transection of all collateral branches arising from the LIMA, thus avoiding the risk of coronary steal syndrome *(9–12)*.

Anesthesia and Patient Positioning

General endotracheal anesthesia with a double-lumen endotracheal tube to permit collapse of the left or the right lung is performed (Table 1). It is essential that the patient is able to tolerate single-lung ventilation (SLV); therefore, this technique is contra-

Table 1
Anesthetic Considerations for IMA

Single lung ventilation
High epidural anesthesia for intra- and postoperative analgesia
Clonidine 150 mg premedication to reduce heat rate and need for anesthetics
Warm air sheet over lower body to maintain body temperature
Early extubation

indicated in patients suffering from advanced pulmonary disease who are deemed to lack sufficient pulmonary reserve to permit SLV. Preoperative pulmonary function tests may aid patient selection. Intrathoracic CO_2 insufflation is rarely needed. When it is used, intrapleural pressure should be monitored and maintained below 10 mmHg to avoid mediastinal tension and hemodynamic compromise.

External defibrillation pads are routinely placed on the patient. The patient is placed in a semioblique position supported by an inflatable pillow placed laterally under the left or right thorax, and is draped as for a conventional coronary bypass procedure. In case of LIMA harvesting, the left arm is placed above the head, thus leaving access for a sternotomy, if necessary. The pillow placed laterally under the left thorax is inflated. The surgeons stand on the patient's left side during the IMA harvesting. The video monitor for visualization is placed in front of the surgeons (Fig. 1). Cardiac monitoring includes continuous EKG recording with ST segment analysis and transesophageal echocardiography.

Optimal visualization of the thoracic cavity and especially the course of the IMA is of paramount importance. To achieve this, a surgical assistant who has been trained in the technique and who can guide the camera in a precise fashion anticipating the next move of the surgeon, enlarging the field or homing in on an area as required, is indispensable. The surgical instruments routinely used for thoracoscopic IMA harvest are given in Table 2.

TROCARS POSITIONING

Trocars are introduced via three thoracic incisions of <15 mm at the level of the fourth and sixth intercostal spaces along the medial axillary line and at the level of the fifth intercostal space on the anterior axillary line (Fig. 2). This triangular placement of the trocars keeps the instruments from interfering with each other ("crossing swords") during manipulation. Generally, the thoracoscope is introduced through a rigid trocar at the fifth intercostal space along the anterior axillary line. This position avoids intermittent obstruction of the view, which may be caused by the heartbeats or diaphragmatic movement when the camera is positioned. The instruments are introduced via the other two orifices through flexible trocars. The position of the thoracoscope and the instruments can be modified as required for optimal visualization or to facilitate manipulation of the instruments. In women, the breast and small thoracic cavity may render this technique difficult owing to a different position of the trocars.

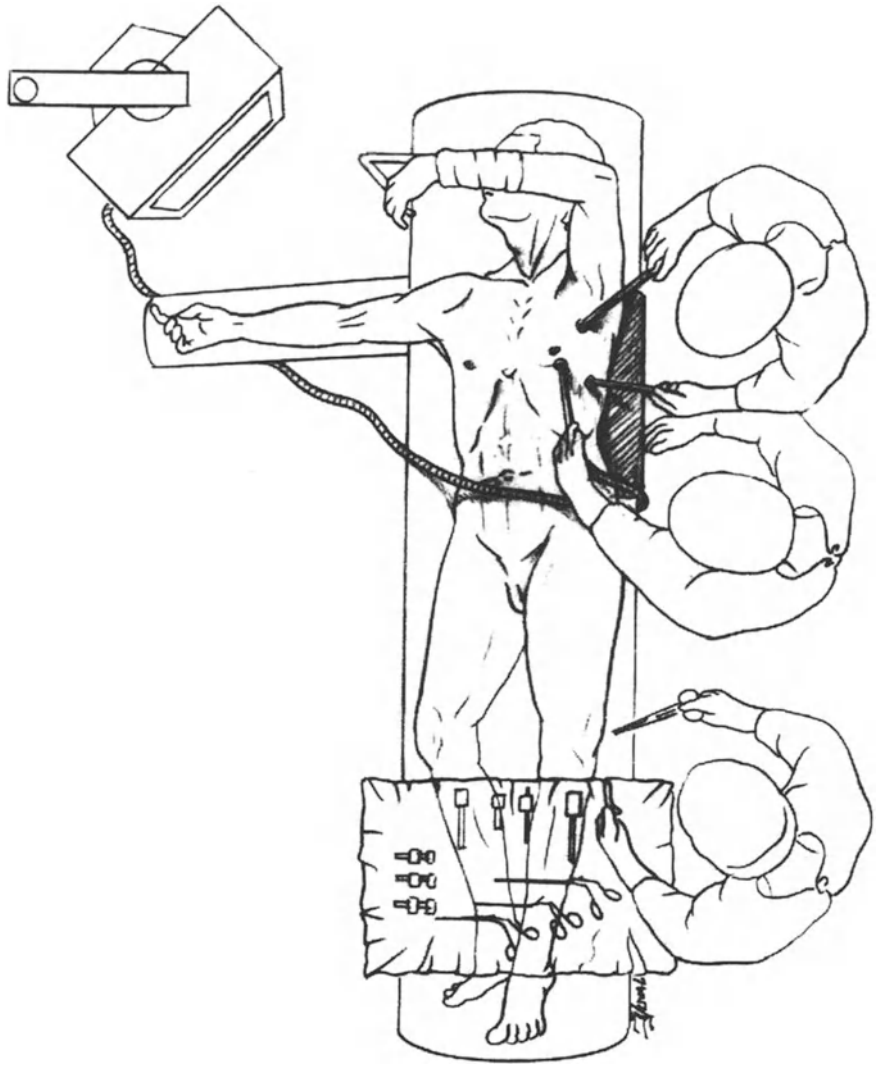

Fig. 1. Patient, nurse, surgeon, and video positioning during thoracoscopic IMA harvest.

Exploration

The first step consists in exposing the IMA. The LIMA is most easily identified just distal to its origin at the subclavian artery, at which point it is only obscured by a thin covering of parietal pleura. The middle third of the artery is sometimes masked by fat and is difficult to identify. The distal third of the IMA is intramuscular up to its bifurcation and therefore, is not visible. In addition, this terminal portion of the artery is sometimes covered by pericardial fat. An endoscopic lung retractor introduced by an additional orifice may be used at times to carefully retract this fat and the pericardium. The use of a 30° scope introduced through the third 10-mm access site at the fifth intercostal space may provide better visualization of this part of the IMA's path.

Table 2
Surgical Instrumentation for Thoracoscopic IMA

Trocars
Size: 5, 10, and 15 mm
Consistency: rigid, for thoracoscope; flexible, for instruments
Instruments
Modified Surgiwand II (United States Surgical Corp., Norwalk, CT)
Spatula diathermy
Irrigation and suction
Endoscopic dissecting forceps
Clip applicator
Endoscopic scissors
Imaging system
Thoracoscope
5 or 10 mm
0° and 30° for distal IMA visualization
Light source
Video camera

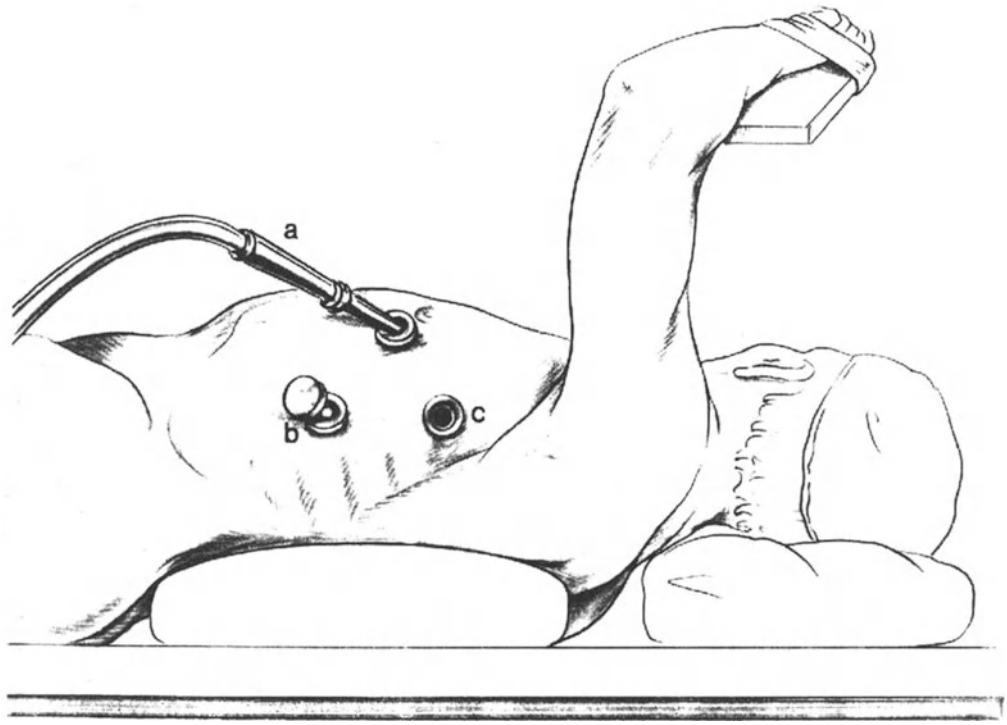

Fig. 2. Trocar placement for thoracoscopic IMA harvest. A 10-mm scope is introduced in the fifth intercostal space over the anterior axillary line (a). Endoscopic forceps are inserted via a trocar placed in the sixth intercostal space overlying the midaxillary line (b). The modified Surgiwand II is introduced via the trocar placed in the fourth intercostal space overlying the midaxillary line (c).

The IMA is not always visualized during initial exploration of the thoracic cavity. In obese patients in particular, the vessel may be covered by a layer of mediastinal fat several centimeters thick extending from the pericardium to the anterior thoracic wall. It is important to first dissect all this fat from the chest wall to visualize the IMA. This part of the procedure can be associated with meddlesome bleeding that may obscure visualization and hamper IMA harvest.

In certain cases, dissection of the IMA is difficult or impossible owing to unfavorable local anatomic conditions. A pleural symphysis may require that the technique be abandoned. Although localized loose adhesions may be dissected without difficulty to free the lung and expose the IMA, diffuse adhesions will preclude safe introduction of the thoracoscope and exploration of the thoracic cavity. In such instances, conversion to a median sternotomy or to a left anterior thoracotomy with direct vision IMA harvesting is undertaken.

IMA Harvesting

The dissection is preferentially begun at the proximal end of the vessel. The parietal pleura is incised at the external border of the artery using diathermy. The dissecting forceps allows retraction of the pleura and mobilization of the arterial pedicle. The collaterals are clipped or coagulated as required. In fact, division of the collateral branches is most efficiently carried out by direct coagulation using diathermy, rather than by the application of a vascular clip. It is more practical and rapid if the introduction of several instruments in turn via the same trocar is avoided. Clipping a collateral branch requires a change of instrument via the trocar, which increases operative time and may interrupt the concentration of the operator, who may lose site of the collateral to be sectioned. Morever, the constant entry and exit of instruments through the trocars is not without risk to the neighboring structures.

A skeletonized IMA is easier to manipulate than an IMA harvested with its surrounding muscle and fascia. Skeletonization of the vessel also allows optimal identification of the collateral branches, which may then be precisely isolated and cauterized or clipped. Control of the IMA branches should always occur at a sufficient distance from the IMA—usually where it penetrates into the intercostal muscle—to avoid the risk of burn or tear. Division of the collateral by diathermy must be definitive and in "one-shot" fashion in order to avoid the risk of bleeding from insufficient coagulation. In cases of collateral branch bleeding, clip application is not always easy. If the stump of the concerned branch is sufficiently long, it may be possible to grasp it with a fine dissecting forceps and apply a small vascular clip. Sometimes the stump is of an insufficient length, or bleeding obscures the visual field. In this situation, the application of a vascular clip is difficult and risks injury to the IMA. Local compression for 2–3 min with endo-peanuts (United States Surgical Corp.) stops the hemorrhage and restores visualization. Hemostasis of the collateral is often perfect in the nonheparinized patient, and there is nothing to be gained in the attempted application of a vascular clip.

The end of the dissection at the distal portion of the IMA may be extremely difficult owing to adverse anatomic characteristics such as extensive pericardial fat and obstruc-

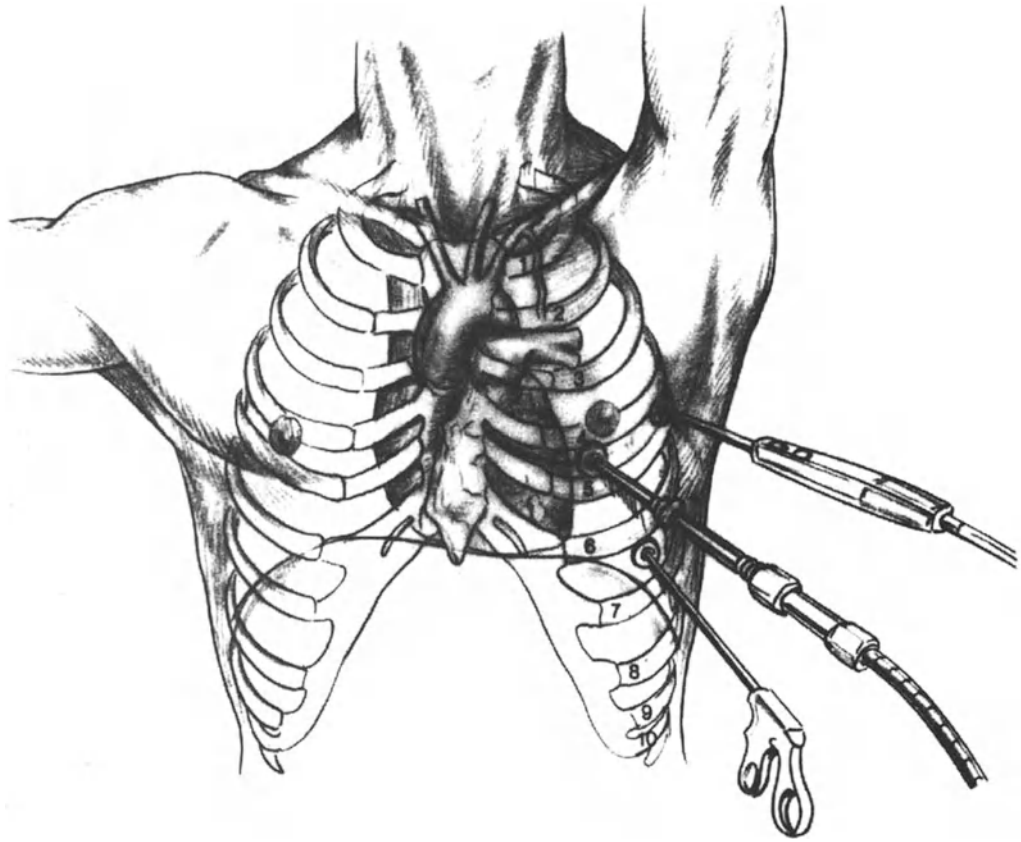

Fig. 3. Once the IMA is harvested, the incision of the most anterior port is extended medially (dotted lines in fourth intercostal space) to gain access for creation of the LIMA-LAD anastomosis.

tion of the inferior portion of the IMA by the cardiac mass. In these cases, the dissection may be facilitated by retraction of the pericardium with a lung retractor introduced via a supplementary port. If the pericardial traction is not well tolerated hemodynamically or if visualization of this part of the IMA is not possible, a 30° thoracoscope may be used to overcome these difficulties. Eventually insufflation with CO_2 may enlarge the operative field by mediastinal deviation and allow continuation of the procedure endoscopically, if well tolerated. If, in spite of these techniques the artery remains difficult to dissect, a direct approach by an extended thoracotomy extending to the sternocostal junction will be necessary.

After systemic heparinization (1 mg/kg), the distal part of the IMA is divided between two vascular clips. An endoscopic forceps is used to place an atraumatic vascular clamp (bull dog) at a distance from the distal aspect of the IMA.

The second step of the procedure may be performed through a 4-cm left anterior thoracotomy along the fifth intercostal space. Usually the port at the level of the fifth intercostal space on the anterior axillary line is extended medially, forming a small anterior thoracotomy (Fig. 3); rib excision is not necessary. The distal segment of the

IMA is withdrawn from the minithoracotomy in order to correctly prepare it, using direct vision, for anastomosis to the LAD.

Chest Closure and Pleural Drainage

On completion of the anastomosis, heparin is neutralized, and a 28-Fr. pleural drain is inserted via the most inferior trocar port and is positioned in the thoracic cavity. The minithoracotomy and the remaining trocar ports are closed in layers.

TECHNIQUE FOR BILATERAL IMA HARVESTING

Thoracoscopic techniques of IMA harvesting may allow the possibility of a second IMA graft while limiting thoracic opening. The patient is placed in the dorsal position with the arms above the head. Inflatable pillows are placed laterally under the right and left thorax. By alternating inflation and deflation of these pillows, the patient can be placed in a right or left anterolateral position with an incline of 30°.

Right IMA harvesting is easier to perform than LIMA harvesting owing to better visualization because of the absence of heartbeats and pericardial fat in this side. The technique used mimics that used for LIMA dissection. Following harvesting of the right internal mammary artery (RIMA); two clips are placed on its distal extremity. The graft is cut between these clips and is then placed on the anterior surface of the right ventricle after fashioning a large pericardial window extending from the right atrium to the pericardial reflection of the superior vena cava. In this way, the right mammary graft may be delivered through the left thoracotomy. The LIMA is then dissected by thoracoscopy. The second stage of the operation consists of performing the left anterior thoracotomy and the two bypasses. The distal segments of the IMAs are withdrawn from the thoracotomy in order to correctly prepare them for anastomoses to the coronary arteries. The RIMA may be anastomosed to the LAD, and the LIMA to the obtuse marginal in cases of left main disease or double-vessel disease.

COMMENTS

The complete dissection of the IMA from its origin at the subclavian artery to the sixth intercostal space afforded by thoracoscopic assistance allows transection of all collateral branches arising from the LIMA, thus avoiding the risk of coronary steal syndrome. Using this technique, a sufficient length of the vessel is harvested, ensuring adequate reach to the LAD target. Postoperative pain is minimized in two ways. First, rib resection is averted. Second, because the IMA is already dissected, a thoracotomy incision of only 4–6 cm is sufficient to approach the LAD and carry out the anastomosis. Moreover, no retraction of the thoracotomy is necessary to expose the IMA.

Most cardiac surgeons currently in practice have little or no experience with videoscopic techniques. A period of training is essential to learn to manipulate the instru-

ments and the thoracoscope. Perfecting the technique of arterial harvesting in animal models before entertaining human application is indispensable. Another option is to practice thoracoscopic IMA in patients undergoing conventional bypass grafting, prior to undertaking the median sternotomy. The extent of dissection and visualization afforded by this technique mimics the conditions attained during conventional open IMA harvest. In conclusion, videoscopic harvest of the IMA represents an additional tool in our quest for a less invasive, safe, and effective myocardial revascularization.

REFERENCES

1. Hazelrigg SR, Mack MJ, Landreneau RJ, Accuff TE, Seifert PE, Auer JE. Thoracoscopic pericardiectomy for effusive pericardial disease. Ann Thorac Surg 1993;56:792–795.
2. Nataf P, Jault F, Pouzet B, et al. Video-surgery of pericardial effusions: technique and results. Arch. Mal. Coeur 1996;89: 223–228.
3. Laborde F, Noirhomme P, Karam J, Batisse A, Bourel P, Saint Maurice O. A new video-assisted thoracoscopic surgical technique for interruption of patent ductus arteriosus in infants and children. J Thorac Cardiovasc Surg 1993;105:278–280.
4. Isik Ö, Daglar B, Kirali K, Balkanay M, Arbatli H, Yakut C. Coronary bypass grafting via minithoracotomy on the beating heart. Ann Thorac Surg 1997;63:S57–S60.
5. de Stanbridge RL, Symons GV, Banwell PE. Minimal-access surgery for coronary artery revascularisation. Lancet 1995;346:837.
6. de Stanbridge RL, Hadjinikolau LK, Cohen AS, Foale RA, Davies WD, Al Kutoubi A. Minimally invasive coronary revascularization through parasternal incisions without cardiopulmonary bypass. Ann Thorac Surg 1997;63:S53–S56.
7. Robinson MC, Gross DR, Zeman W, Stedge-Larsen E. Minimally invasive coronary artery bypass grafting: a new method using an anterior mediastinotomy. J Cardiac Surg 1995;10: 529–536.
8. Benetti FC, Ballester C. Use of thoracoscopy and a minimal thoracotomy, in mammary-coronary bypass to left anterior descending artery, without extracorporeal circulation: experience in 2 cases. J Cardiovasc Surg 1994;36:159–160.
9. Nataf P, Lima L, Regan M, et al. Minimally invasive coronary surgery with thoracoscopic internal mammary artery dissection: Surgical technique. J Card Surg 1996;11:288–292.
10. Nataf P, Lima L, Regan M, et al. Thoracoscopic internal mammary artery harvesting: technical considerations. Ann Thorac Surg 1997;63:S104–S106
11. Tonz M, von Segesser L, Carrel T, Pasic M, Turina M. Steal syndrome internal mammary artery bypass grafting—an entity with increasing significance. Thorac Cardiovasc Surg 1993;41:112–117.
12. Ayres RW, Lu CT, Benzuly KH, Hill GA, Rossen JD. Transcatheter embolization of an internal mammary artery bypass graft sidebranch causing coronary steal syndrome. Cathet Cardiovasc Diag 1994;31:301–303.

7 Myocardial Stabilization During Off-Pump Coronary Artery Bypass Grafting

M. Clive Robinson, MD and Joao Mota, MD

CONTENTS

INTRODUCTION

The key issues for satisfactory results with off-pump coronary artery bypass grafting (CABG) are accuracy with the anastomosis and safe management of the regionally ischemic myocardium. The greatest challenges confronted during creation of the anastomosis under beating heart conditions include performance of a well-aligned coronary arteriotomy without injury to the vessel back wall, accurately placed toe and heel sutures, and prevention of injury to the fragile edge of the arterial conduit and native artery during suture placement. With the concerted focus and development over the last 2–3 years, substantial headway has been made in these areas. There are now formalized and reproducible techniques to ensure optimal presentation of the myocardium and graft artery, for local immobilization of the myocardium, and to control the anastomotic site. As a result of these developments, the previously held hesitations concerning beating heart CABG have been largely averted.

Myocardial contractile physiology varies widely within and between patients, and effective anastomotic site presentation and control requires the ability to both appropriately select and effectively utilize one or a number of the available immobilization

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

methods. Among these methods are mechanical, pharmacological, and electrical techniques; use of each varies according to the location and number of vessels being addressed as well as the incision being used. This chapter reviews the available mechanical, pharmacological, and electric methods of myocardial wall immobilization that have made off-pump CABG a viable alternative to conventional myocardial revascularization.

ANASTOMOTIC SITE PRESENTATION

The application of minimally invasive CABG was at first largely confined to anterior wall vessels, in particular the left anterior descending (LAD) artery. With consolidation of the left internal mammary artery (LIMA) to LAD anastomosis and expansion of techniques, all vessels (albeit with some difficulty) are now accessible and a variety of conduits have been utilized.

Off pump minithoracotomy approaches demand concerted attention to the optimal displacement and positioning of the heart and graft sites. This requires time and often, small and serial adjustments in heart position are necessary to allow for hemodynamic adaptation. The goal must be an optimally positioned heart with the target vessel situated centrally in the wound. In the case of limited anterior thoracotomy, adequate positioning within the pericardial cradle is achieved by placement of lateral traction sutures into the pericardial edge. As the pericardium stretches, the sutures require repositioning more posteriorly in the main body of the pericardial sac until the coronary artery is displaced into the center of the incision. Care is necessary to avoid phrenic nerve traction injury during placement of the posterior sutures in the pericardial sac. These maneuvers are similar whether the LAD, diagonal, or right coronary artery is being grafted. Posterior vessels, on the other hand are not accessible via the anterior minithoracotomy approach.

With off-pump multivessel grafting via median sternotomy, the requirements for lateral and inferior wall presentation are more demanding and elaborate. Using sternotomy access, the parasternal position of the LAD and right coronary artery are immediately apparent and grafting of these vessels requires medial and anterior displacement as previously described. For access to lateral and inferior wall vessels, considerable attention is now being focused on techniques of cardiac displacement and dislocation and on the tolerance and corrective measures for associated hemodynamic changes. The Octopus system *(see below)*, developed by the group at the University of Utrecht *(1)*, is leading the efforts in the field of mechanical displacement. Other methods use variously shaped and compartmentalized balloons with differential inflation to facilitate anterior and medial displacement of the heart. Traction and suspensory systems including slings, mechanical retractors, and surgical packs have also been developed. Other devices exist and many more will be designed to facilitate anastomotic site presentation.

ANASTOMOTIC SITE STABILIZATION

For years, hesitation and skepticism over off-pump CABG related to concerns with grafting on a moving target. Many techniques have been developed to remedy this prob-

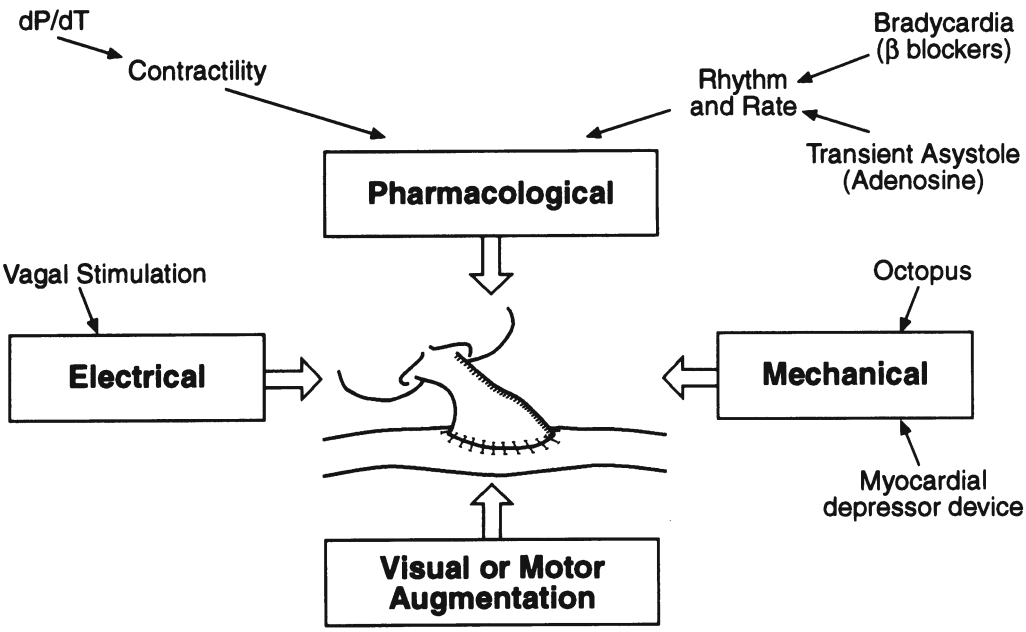

Fig. 1. Available methods to optimize the surgical field for creation of the coronary anastomosis on the beating heart.

lem and each is selected according to the specific myocardial contractile state at the time of grafting. Figure 1 summarizes the available methods.

MECHANICAL IMMOBILIZATION

Mechanical methods of immobilization have become the most successful of all approaches intended to facilitate coronary grafting on the beating heart. The first mechanical principle includes the use of foot-shaped devices that are embedded within the myocardium on either side of the grafted vessel so as to dissipate the propagated systolic wave and immobilize the graft site within a bridge of myocardium. These devices include the Access Platform and Stabilizer (CardioThoracic Systems, Cupertino, CA) and a similar system by the United States Surgical Corporation (Norwalk, CT) (Fig. 2).

The second method involves immobilization with the Octopus device (Medtronic, Minneapolis, MN) that relies on the use of suction cups to provide fixation of the adjacent vessel (Fig. 3) With this device, wide degrees of anterior, medial, and cephalad myocardial displacement are feasible. Angles of up to 90° between the axis of the aorta and the heart are achievable for optimal presentation. The set-up process may require many minutes for optimal tolerance and positioning of the heart for anastomotic site grafting. Further improvement is provided by the effects of gravity from appropriate positioning of the operating room table—Trendelenburg and/or right and leftward movements. The suction cups, carefully attached and with a negative suction pressure of 400 mmHg, allow satisfac-

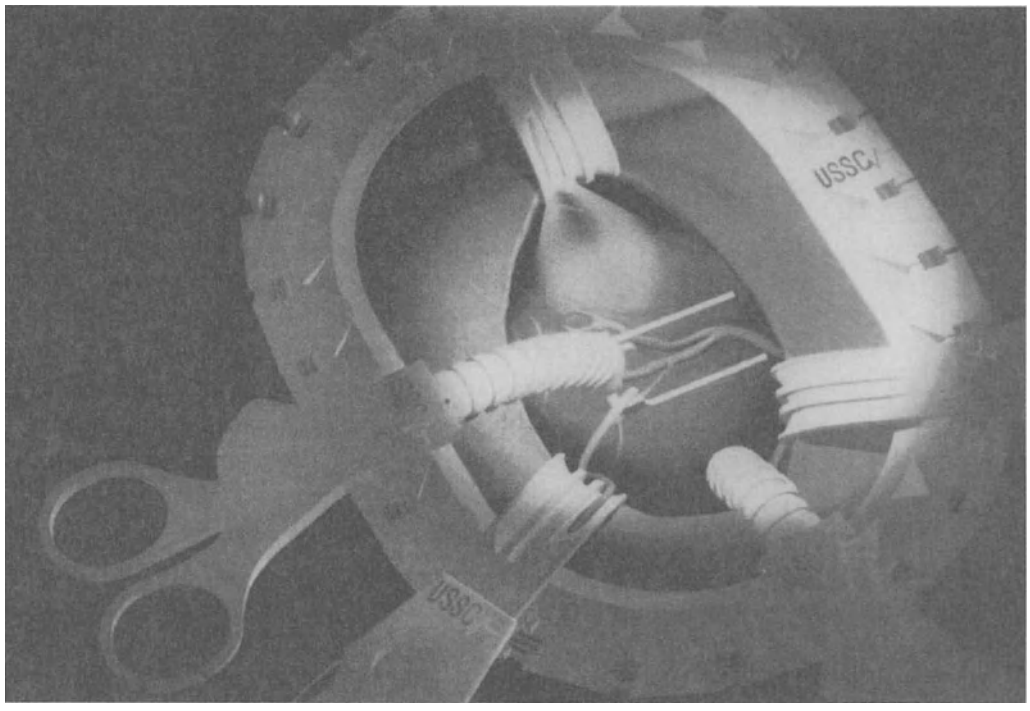

Fig. 2. The United States Surgical Corporation System.

Fig. 3. The Octopus System (Medtronic Inc).

tory traction for access. Besides the anterior wall vessels, the system is particularly useful for the high lateral wall arteries including the ramus and proximal marginal vessels as well as for the inferiorly located posterior descending artery. The left ventricular branch of the right coronary artery and the distal obtuse marginal arteries however, are less accessible.

An integral part of the mechanical displacement technique includes the need for pharmacological and volume therapy to correct and maintain cardiac performance. Judicious use of vasoconstrictors, dilators, volume infusion are often required. Particular care and experience is needed with these interventions to avoid undue hemodynamic swings that may compromise cardiac tolerance during the critical time of anastomosis.

PHARMACOLOGICAL IMMOBILIZATION

Pharmacological interventions incorporate a wide range of methods including myocardial preconditioning prior to vessel isolation, therapy to reduce myocardial oxygen requirements during vessel isolation, reduction in the force of myocardial contractility, and the induction of bradycardia and transient asystole for suture placement.

Induction of Bradycardia

Beta blockers, particularly the short acting agents like Esmolol (Anaquest Inc., Liberty Corner, NJ), have been most widely used. In everyday off-pump clinical practice, use of short-acting β-blockers is associated with wide variation in rate-lowering effect, and undue hemodynamic depression may occur. In our early minimally invasive direct coronary artery bypass (MIDCAB) experience, use of β-blockade for this purpose achieved adequately tolerated rates a the intended level of 35–45 beats/min in approx 40% of cases (unpublished data). In many instances, heart rate may change little yet hemodynamic compromise may occur. The more important role of β-blockers in off-pump grafting may well be in improving ischemic tolerance during the coronary artery isolation *(2)*, in reducing myocardial contractility to facilitate suturing conditions, and in minimizing the potential for tachycardia secondary to other changes and interventions during the procedure. Titrated dose range of Esmolol for these purposes varies from 50–100 μg/kg/min. Several groups use calcium channel blockers, most commonly Diltiazem (Marion Merrell Dow Inc., Kansas City, MO) to achieve the same goals. In general, even when rates of 35–40 beats/min are achieved and tolerated, in the absence of other stabilization measures, the technical demands of suturing remain undue, and hence, the induction of bradycardia alone for suturing should be viewed as a relatively unimportant part of the off-pump grafting method.

Induced Transient Ventricular Asystole

An induction system of controlled pauses of ventricular contraction can be used to provide a transiently still cardiac field that facilitates accurate anastomotic grafting. Epicardial pacing back-up—ventricular or atrioventricular—is used when required to minimize the pause interval. We have developed a method and new application using

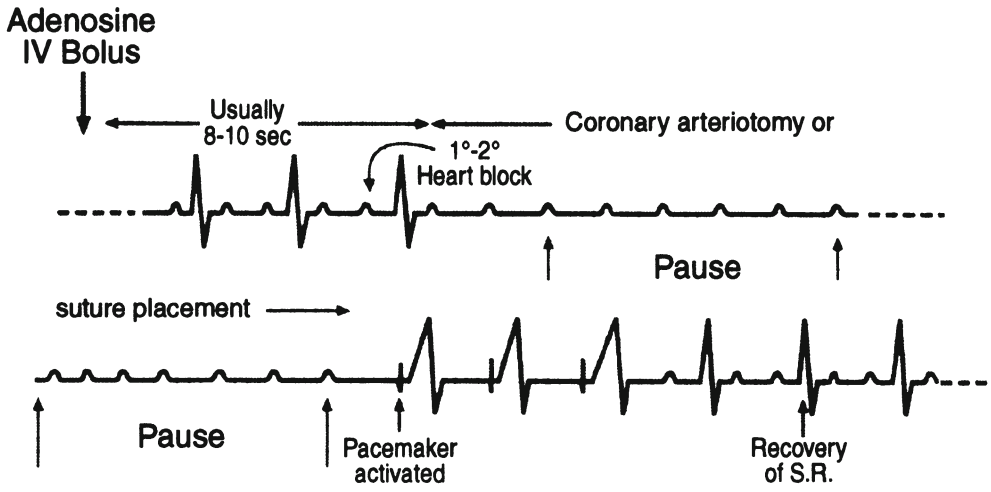

Fig. 4. Typical electrocardiographic recording following rapid intravenous bolus administration of adenosine.

adenosine (Fujisawa USA, Deerfield, IL) for this purpose *(3)*. The properties of adenosine make it ideally suited for this purpose. Adenosine is an endogenous nucleoside with an ultra-short half-life of <10 s that is clinically used for conversion of paroxysmal supraventricular tachycardia to normal sinus rhythm. After intravenous injection, the agent is rapidly eliminated from the blood by erythrocytes and vascular endothelial cells and converted by adenosine deaminase to inosine and adenosine monophosphate (AMP). Sinus node activity is depressed and slowing or blocking of atrioventricular nodal conduction and ventricular arrest can occur. The substance and its metabolites are not toxic to the liver or kidneys. Vasodilation of the coronary bed occurs with often a fourfold increase in coronary blood flow, a response that is utilized in thallium stress testing. The substance is infused in doses ranging from 0.15–0.3 mg/kg with administration by a central venous catheter as a rapid bolus. Test boluses using 0.15 mg/kg are given to assess the initial response and further doses are given based on the response to the preceding bolus and the required duration of the pause. A larger dose for a longer pause is administered for the particularly important coronary arteriotomy. Figure 4 shows the typical EKG changes following a rapid intravenous bolus of adenosine.

Results of our experience with the use of adenosine are shown in Table 1. Hypotension secondary to systemic vasodilation and the asystolic pause is usually self-limiting or easily reversed or controlled with administration of Neosynephrine (Sanofi Winthrop Pharm., New York, NY). Doses of 100–200 mcg are given routinely as a chaser bolus at the time of the original adenosine administration. Adenosine side effects were unimpressive in our experience of 31 cases and the recognized problems of flushing, shortness of breath, asthma, and gastrointestinal discomfort are of little consequence under general anesthesia. In our experience, no patients required prolonged pacing and only one patient (3.2%) developed atrial fibrillation. Occasionally, reflex tachycardia follows the adenosine bolus but this is minimized by the use of background β-blockade. Because the patients

Table 1
Infusion and Hemodynamic Data for 31 Patients Undergoing Off-Pump Revascularization with Adenosine-Induced Transient Asystole[a]

Patient data	*Mean*	*Range*
Infusion		
Boluses per coronary anastomoses	9	6–14
Dose per bolus (mg/kg)	0.24	0.15–0.35
Duration of pause (s)	6	3–19
Time to complete anastomosis (min)	18	14–27
Hemodynamic		
Time for arterial blood pressure recovery to baseline (±5 mmHg, s)	35	13–48
% SVO_2[b] fall per bolus	7	5–11
Time for SVO_2 recovery to baseline (s)	36	12–46

[a]Adapted from ref. *3*.
[b]Mixed venous oxygenation.

are normothermic, care is required to limit the pause interval and to allow full recovery of hemodynamics between pauses. However, as described earlier, the mechanical devices have in most situations become more efficacious alternatives. Adenosine nonetheless, remains of substantial use in particular to provide the ideal conditions of a transient and completely still field for the critical coronary arteriotomy or difficult toe and heel sutures. The method is also beneficial in off-pump situations to facilitate suture placement for anastomotic hemostasis.

Other substances have been used for this purpose. Indeed, acetylcholine was originally used for intentional pausing to provide a still field during coronary angiography *(4)*. However, wide variations in predictability, untoward systemic side effects, and dangerous repolarization arrhythmias make this alternative much less attractive. These problems have arisen in most substances investigated to date.

A similar principle has been used experimentally by induction of more extended intervals of complete heart block and ventricular asystole with secondary support provided by atrioventricular pacing. The method has been proposed and described by Khanna and Cullen *(5)* in a sheep model. Lidocaine (2 mL, 2% solution) is directly infiltrated into the His bundle and proximal bundle branches. Cardiac function is maintained with ventricular or sequential pacing and transient cessation of pacing enables a controlled pause and still surgical field for creation of the coronary arteriotomy and placement of sutures. Using this technique, extended periods of up to 30 min of underlying ventricular asystole were produced. Although in basic principle this method appears valid and promising, several areas of concern exist regarding clinical application. These relate to the ability to provide reliable and atraumatic bundle infiltration, the potential for escape and repolarization arrhythmias, and the possibility of unrecognized intracardiac injury or late conduction system dysfunction. Although limited by these uncertainties, use of advance electrophysiological techniques including bundle localization and transient ablation may in the future render this approach more suitable for clinical application.

MANIPULATION OF MYOCARDIAL CONTRACTILITY

Baseline myocardial contractility and dP/dT varies widely in response to intrinsic physiology, in particular adrenergic activity, as well as in response to a variety of medications. Therapy that causes a reduction in dP/dT provides conditions where excursion of the beating heart becomes significantly diminished and hence, a favorable anastomotic milieu is established. Furthermore, a quieter heart can improve the effectiveness of available mechanical myocardial stabilization devices. Manipulation of this entity can therefore be important in maximizing the ease and accuracy of coronary suturing in off-pump grafting. β-blockade is particularly effective in reducing dP/dT and for this among other reasons, baseline β-blocker administration is an important preliminary to off-pump grafting. In addition, short acting agents are titrated intraoperatively during the anastomosis to achieve optimal effect. Esmolol infused to maximum tolerance and response is most suited for this purpose, and often, multiple gradually infused doses are required. Other agents including α-agonists such as Clonidine (Boehringer Ingelheim Pharm. Inc., Ridgefield, CT) *(6)* and ganglion blocking agents have been used as well. Additional myocardial control can be obtained by deepening the level of anesthesia at the time of the anastomosis. Although little attention has been directed in the past to these aspects of off-pump coronary surgery, it is becoming clear that use of these approaches in combination with mechanical stabilizers can result in optimal conditions for beating heart myocardial revascularization.

It is critical to point out that the concentrated and demanding pharmacological management of the myocardium during off-pump minimally invasive CABG is largely under control and initiative of the cardiac anesthesiologist. The degree of intraoperative participation and intervention by the anesthesiologist is at a much greater level than during conventional CABG and hence, open communication and dedicated anesthesia teams are essential to the success to these approaches.

ELECTRICAL TECHNIQUES OF WALL MOTION IMMOBILIZATION

Electrical stimulation of the parasympathetic nervous system for cardiovascular manipulation has been used extensively in both experimental and clinical conditions *(7,8)*. Using this principle, the vagus nerve can be stimulated by electric current with the potential for induction of profound bradycardia and temporary arrest. The resultant pause is utilized to enhance suturing on the beating heart. Matheny recently reported his limited clinical experience using intermittent vagal nerve stimulation along with cholinesterase inhibition with Neostigmine (ICN Pharm., Inc., Costa Mesa, CA) during full cardiopulmonary bypass support *(9)*. The vagus nerve is accessible by both sternotomy and thoracotomy and can be located as it crosses the aorta just lateral to the phrenic nerve. In their study, temporary pacing wires were attached to the nerve and electric stimulation delivered using a continuous 5-s pulse train of 25 Hz and 20 V with a pulse width of 0.1 msec. The resultant pause duration was in the vicinity of 5 s. Resting periods between stimulations were provided to allow blood pressure recovery. Observations showed that with

incremental stimulation there was increasing vagus nerve fatigue and a wide degree of variation in the induction of bradycardia and the arrest response. In our own experience with electric vagus nerve stimulation in the porcine model, using unilateral and bilateral vagi and with similar stimulus signals, the effect was unpredictable. As suggested by Matheny and Shaar *(9)* the length of time required to isolate the nerve, the variability in response to stimulation, and the possibility of nerve injury, at present, limit the applicability of this technique. For vagal stimulation to gain broad applicability, further improvements in regulation and response must evolve.

SUMMARY

Myocardial presentation and anastomotic site immobilization remain the most critical factors influencing accuracy in off-pump anastomosis. Recent progress has led to a variety of mechanical, pharmacological, and electric methods of control. The final strategy in practice should be tailored to the individual case but, in most instances, will include the combination of a mechanical immobilizing device with one or several pharmacological manipulations.

REFERENCES

1. Grundeman PF, Borst C, van Herwaerden JA, Beck HJ, Jansen EWL. Hemodynamic changes during displacement of the beating heart by the Utrecht Octopus method. Ann Thorac Surg 1997;63:S88–S92.
2. Labovitz AJ, Barth C, Costello R, Ogile M, Kern MJ. Attenuation of myocardial ischemia during coronary occlusion by ultra-short acting beta adrenergic blockade. Am Heart J 1991;121(5):1247–1251.
3. Robinson MC, Thielmeier KA, Hill BB. Transient ventricular asystole using adenosine during minimally invasive and open sternotomy coronary artery bypass grafting. Ann Thorac Surg 1997;63:S30–S34.
4. Bjork L, Hallen A. Coronary angiography during acetylcholine induced cardiac arrest in patients with angina pectoris. J Cardiothorac Surg 1961;6:9–19.
5. Khanna R, Cullen HC. Coronary artery surgery with induced temporary asystole and intermittent ventricular pacing: an experimental study. Cardiovasc Surg 1996;4(2):231–236.
6. Flacke JW, Bloor BC, Flacke WE, et al. Reduced narcotic requirement by clonidine with improved hemodynamic and adrenergic stability in patients undergoing coronary bypass surgery. Anesthesiol 1987; 67(1):11–19.
7. Murphy DA, Armour JA. Human cardiac nerve stimulation. Ann Thor Surg 1992;54: 502–506.
8. Armour JA, Randall WC, Sinha S. Localized myocardial response in stimulation of small cardiac branches of the vagus. Am J Physiol 1975;118:141–148.
9. Matheny RG, Shaar CJ. Vagus nerve stimulation as a method to temporarily slow or arrest the heart. Ann Thorac Surg 1997;63:S28,S29.

8 Minimally Invasive Coronary Artery Bypass Grafting on the Beating Heart

The American Experience

Valavanur A. Subramanian, MD

CONTENTS

INTRODUCTION

Interest in minimally invasive coronary artery bypass grafting (MICABG) on the beating heart is growing. The premise for adopting these less invasive approaches is that patient morbidity can be reduced without compromising the safety and efficacy of conventional CABG. Despite the encouraging early clinical results reported by Benetti *(1)*, Buffolo *(2)*, Pfister *(3)*, Subramanian *(4)*, Calafiore *(5)*, and their associates, CABG without cardiopulmonary bypass (CPB) via midline sternotomy or minithoracotomy has met with concerns of technical limitations and efficacy of anastomosis *(6–8)*. Recently, the introduction of surgical instrumentation to facilitate internal mammary artery (IMA) harvest, mechanical local immobilization and stabilization of coronary artery target sites has enabled standardization of the surgical technique for left internal mammary artery to left anterior descending (LIMA-LAD) anastomosis by a minimally invasive direct coronary artery bypass (MIDCAB) approach, with predictable good results.

INDICATIONS FOR MIDCAB

The indications for MIDCAB have evolved since its inception, and general agreement on this topic has not been reached. At present, candidates for this procedure are patients with:

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

Table 1
Ideal Anatomic Conditions for LIMA-LAD MIDCAB

LAD >2 mm in diameter
Presence of a tublar heart on chest roentgenogram
Thin chest wall with wide intercostal spaces
Reoperative coronary artery bypass with deteriorated saphenous vein grafts
Totally occluded LAD with good collaterals to distal LAD
Noncalcified LAD
Left ventricular dysfunction

1. Prior CABG with failed saphenous vein grafts to the LAD, right coronary artery (RCA), or obtuse marginal (OM);
2. Multiple-vessel disease and significant coexisting morbidities for whom CPB is considered high risk (cancer, renal failure, diffuse cerebrovascular and peripheral vasculopathy, aortic atherosclerosis, advanced age, respiratory insufficiency);
3. Restenosis after percutaneous transluminal angioplasty (PTCA) and stenting; and
4. Unsuitable LAD, RCA, and OM for PTCA because of severe complex stenosis, or chronic total occlusion.

In addition, current evolving indications include MIDCAB for

1. "Hybrid therapy," i.e., single-vessel grafting as part of a combined strategy with PTCA for patients with triple-vessel CAD;
2. LIMA-LAD grafting as an adjunct to major noncardiac surgical procedures, e.g., abdominal aortic aneurysm repair;
3. "Culprit" lesions (is complete revascularization necessary?); and
4. Ischemic cardiomyopathy with anterior wall ischemia.

Table 1 depicts the current ideal anatomic conditions for LAD-MIDCAB today. Relative contraindications for MIDCAB include the presence of an intramyocardial, diffusely calcified or small (<1.5 mm) LAD, or presence of severe pulmonary hypertension with a large left ventricle. Our experience and that of others indicates that if LIMA-LAD MIDCAB is performed under these conditions, graft occlusions are more likely to occur.

SURGICAL TECHNIQUE

Anesthesia and Intraoperative Monitoring

Standard cardiac anesthetic techniques are used for induction and maintenance of anesthesia. Premedication with oral clonidine (Boehringer Ingelheim, Ridgefield, CT) prior to surgery calms the heart during coronary anastomosis. Clonidine inhibits central release of adrenergic amines and decreases anesthetic requirements *(9)*, maintaining a low heart rate and blood pressure during coronary anastomosis.

Recently, routine use of temporary single-lung ventilation (SLV) has facilitated direct vision of the IMA and has resulted in a reduction in harvest time to 15–20 min. However,

caution is to be exercised in using SLV in patients with severe chronic respiratory insufficiency because of an apparent increase in pulmonary complications when the lung is collapsed for longer periods of time. At present, SLV is used only during the last 5 min of the dissection for exposure of the LIMA near the top part of the thorax, beyond the second intercostal space. In patients with advanced obstructive pulmonary disease who do not tolerate SLV intraoperatively, conversion to midline or partial sternotomy is undertaken to complete the procedure.

Anesthetic techniques are fine-tuned to allow rapid awakening and extubation of the patient routinely while in the operating room. The use of epidural anesthesia and narcotics to facilitate extubation and to optimize pain control has recently been initiated. This is particularly helpful for patients undergoing midline sternotomy CABG operations without CPB.

During the period of local coronary occlusion, the depth of anesthesia is increased to reduce left ventricular contractility, blood pressure, and heart rate. This is accomplished with the use of intravenous β-blockers or calcium-channel blockers. The use of adenosine (Fujisawa, Deerfield, IL) for intermittent cardiac standstill during coronary anastomosis has been abandoned. In addition, during the period of LAD occlusion and stabilization, deliberate volume loading is performed to diminish the movement of the heart surrounding the area of local immobilization.

Routine hemodynamic monitoring, continuous transesophageal echocardiographic monitoring of regional left ventricular wall motion, and ST-segment mapping are conducted during the entire procedure. Mixed venous oxygen saturation is continuously monitored in all these patients.

Patient Positioning

All patients undergoing grafting of the LAD, diagonal, proximal, first marginal or ramus intermedius arteries are operated on in the semianterolateral decubitus position with a 20–30° tilt with a roll underneath the left scapula. For grafting of the second and third marginal arteries or posterolateral branch of the circumflex artery, the straight left lateral position is used. Finally, for the grafting of the mid- and distal RCA, and the posterior descending coronary artery, patients are positioned in the supine position.

Incisions

The different incisions used to accomplish optimal exposure are depicted in Fig. 1.

Anterior MIDCAB

Grafting of the mid-LAD and second diagonal branch are performed through an 8-cm submammary incision placed underneath the nipple over the fourth left intercostal space with two-thirds of the incision medial and one-third lateral to the nipple (Fig. 2). The pleura is routinely entered and the lung is pushed away gently with gauze. With the aid of the new retractor systems, this incision creates a wide visual tunnel for the exposure of the entire LIMA, allowing its mobilization up to its origin under the direct vision. The

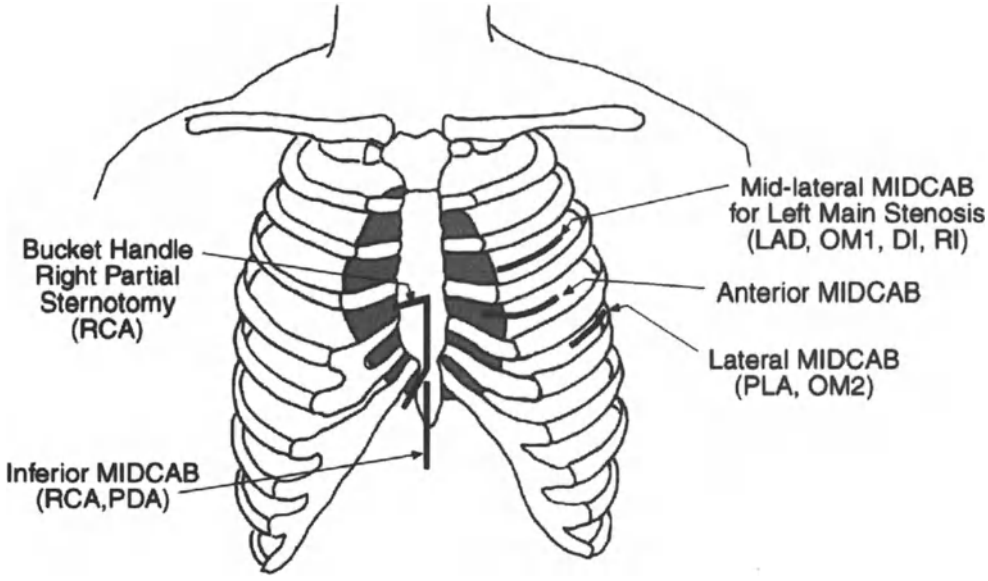

Fig. 1. Skin incisions used for different approaches to MIDCAB procedures.

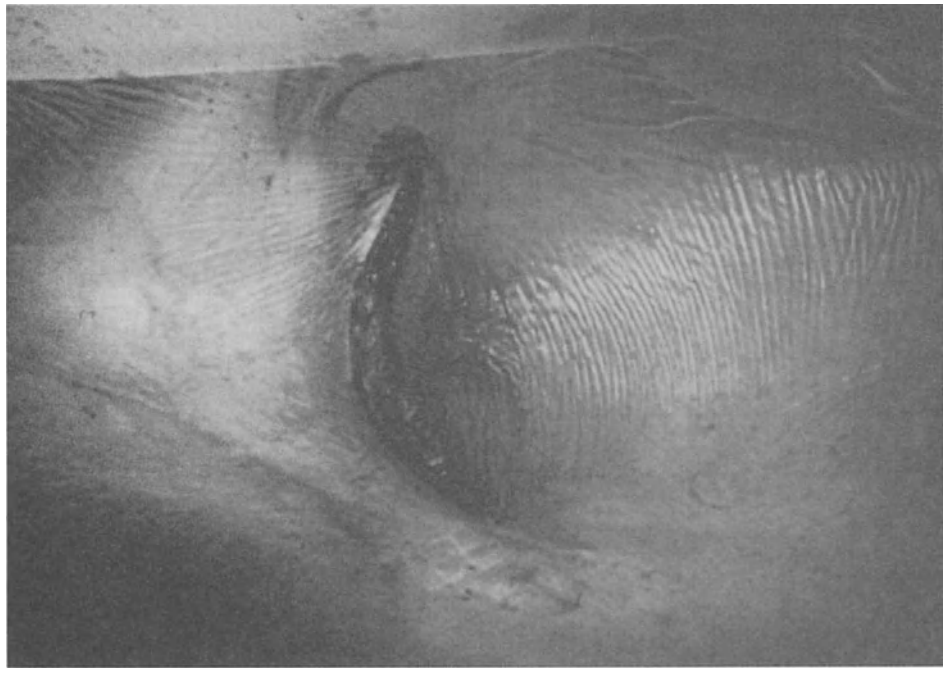

Fig. 2. Anterior MIDCAB submammary incision.

exposure attained is very similar to that achieved during median sternotomy and hence quite familiar to most surgeons. Note that skeletonization of the LIMA pedicle is not crucial with this approach.

Lateral MIDCAB

Grafting of the second and third marginal branches as well as the posterolateral branch of the circumflex artery is accomplished via a 3-in. thoracotomy incision on either side of the tip of the scapula in the lateral decubitus position. A short segment of the fifth or sixth rib is excised, and the thoracic wall muscles are marsupialized by tacking them to the skin edges with heavy sutures. A medium-sized Finnechietto retractor (Codeman Co., Johnson & Johnson, Randolph, MA) is used to spread the interspace, and SLV is routinely used. The inferior pulmonary ligament is incised and the lung is packed away in the upper chest for exposure. The pericardial incision is made posterior to the phrenic nerve, thereby permitting easy location of target vessels are located easily with this approach. The radial artery or saphenous vein graft from the descending thoracic aorta is used to graft the coronary vessels with this approach.

Inferior MIDCAB

The distal RCA and proximal posterior descending artery are exposed with a 2.5-in. subxiphoid incision. The xiphisternum is excised and bilateral release of the costal diaphragmatic attachments is performed. Downward displacement of the diaphragm toward the abdominal retractor with traction sutures achieves excellent exposure of the target vessels. The right gastroepiploic artery is frequently used as a graft. Mobilization of this vessel is performed in the standard fashion *(10)*.

Mid-lateral MIDCAB

An incision is made in the third or fourth intercostal space between the midclavicular and axillary lines, rostral to the scapula in the semi anterolateral position as described above. This allows exposure of the LAD, first diagonal, ramus intermedius, and first OM branches. Composite grafts using the radial artery or saphenous vein from the LIMA have been used as double or triple grafts. Recently, bilateral IMA grafting with RIMA-LAD and LIMA-OM has been accomplished.

Right Coronary Artery MIDCAB

Recent introduction of the bucket handle right partial sternotomy (Fig. 1) in the inferior sternum with extension onto the third and fifth intercostal space has facilitated mobilization of the entire right IMA for anastomosis to the mid- or distal RCA.

LIMA Harvest and Preparation

The introduction of a specialized IMA Access Retractor (CardioThoracic Systems, Cupertino, CA) (Fig. 3) has standardized harvest of the LIMA. Entry into the left thorax is carried out through a submammary incision in the fourth intercostal space. The costal cartilage is not routinely excised. The dissection and mobilization of the entire length is

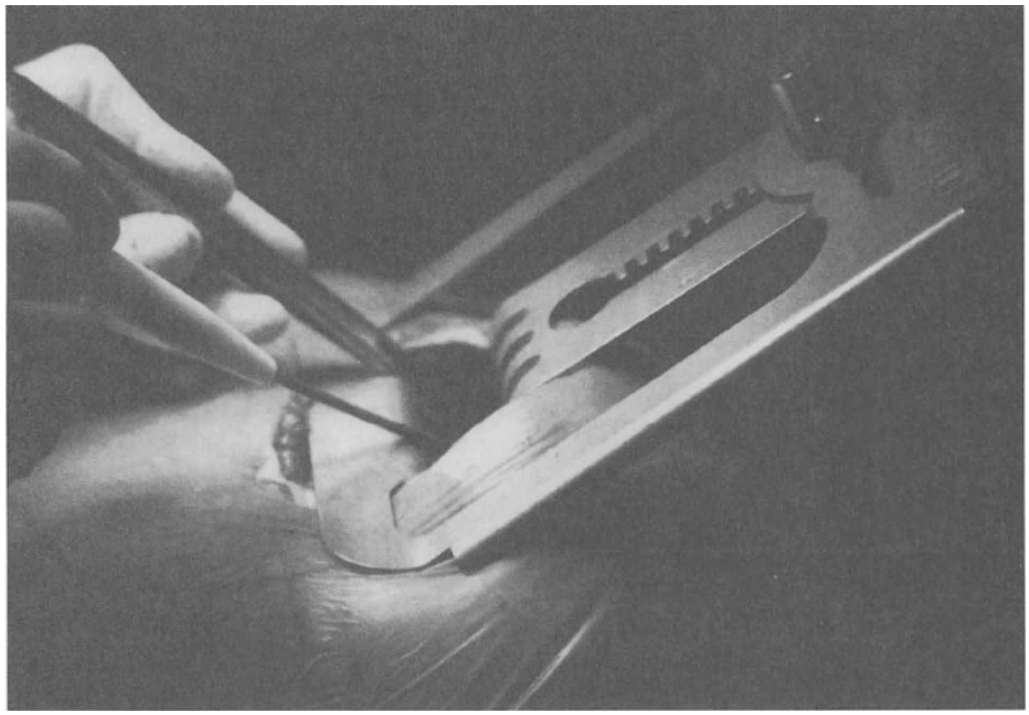

Fig. 3. IMA Access Retractor (CardioThoracic Systems, Cupertino, CA).

performed under direct vision from a lateral approach. The length and integrity of the LIMA is well preserved with this technique. In some centers, thoracoscopic visualization has been used to aid IMA harvesting *(11,12)*. The isolation of a long length of the LIMA is an essential component of the MIDCAB operation because it:

1. Avoids the kinking that occurs at the chest wall takedown when a short IMA is harvested;
2. Allows a tension-free LIMA-LAD anastomosis;
3. Reaches the LAD in a large transverse heart or in patients with chronic obstructive pulmonary disease (COPD) with large residual lung volumes;
4. Avoids the need to extend the LIMA with other conduits;
5. Facilitates sequential grafting of the LAD and diagonal artery; and
6. Alleviates the concern of coronary steal from an incompletely ligated branch of the IMA.

After harvest, the IMA is clipped underneath the fifth costal cartilage and divided. The LIMA distal to this point is frequently smaller and more muscular and, hence, more prone to spasm. Prior to division of the IMA, a systemic bolus of intravenous heparin (2 mg/kg) is administered and the activated clotting time is maintained at twice the baseline value. Next, the IMA is prepared with intraluminal injections of verapamil (Knoll Pharmaceutical, Whippany, NJ), and papaverine hydrochloride (Eli Lilly, Indianapolis, IN) in heparinized saline. Injections are administered without clamping the IMA pedicle, and no hydrostatic dilation of the IMA is performed. Subsequently, the distal end of the IMA

is clipped and allowed to dilate while the coronary artery anastomosis is prepared. Routine use of intraluminal verapamil in more than 750 patients undergoing multiple arterial conduit revascularization over the past 4 yr has completely eliminated IMA spasm. Indeed, the arterial conduits are usually quite large by the time the coronary anastomosis is performed. In situations in which a composite T or Y graft from the LIMA is necessary for grafting to the diagonal, marginal, or ramus intermedius branches, the construction of the composite graft (i.e., radial artery, saphenous vein, inferior epigastric artery) is done prior to the LIMA-LAD anastomosis. Just prior to creation of the anastomosis, the IMA is clamped with a soft, vascular, Fogarty-type bulldog clamp. The IMA is divided at the distal end, spatulated, and suspended from the upper medial edge of the thoracotomy incision with fine sutures of 6-0 Prolene onto the skin.

Access to the LAD and its Branches

After the IMA is prepared, the IMA retractor spreader is replaced by an access platform (CardioThoracic Systems [CTS]) that carries a coronary stabilizer. The pericardium is incised about one fingerbreadth lateral to the IMA pedicle and parallel to the midline. The left ventricle is then inspected, the LAD is located, and the pericardium is suspended by traction sutures. The laterally placed pericardial traction sutures are pulled cephalad toward the patient's suprasternal notch or left shoulder. This maneuver cradles the heart and rotates it anteriorly, bringing it to the wound surface. Usually, a small gauze pad can be placed underneath the left ventricle to further rotate the heart and bring the LAD to the surface. The combination of the pericardial traction sutures and gauze pad under the left lung prevents it from being in the way during the creation of the anastomosis.

After the LAD is deemed suitable, a site for the anastomosis is chosen. Early in our experience, the finding of an intramyocardial or extensively calcified LAD resulted in conversion to conventional CABG. More recently, however, for the calcified LAD, if >1.5 mm, interrupted sutures were used to complete the anastomosis. With an intramyocardial LAD, the intramyocardial tunnel is incised to expose the vessel after adequate stabilization of the heart, and the LAD is then "unearthed" by using two lateral epicardial mattress sutures with Teflon bolsters placed on the sides of the intramyocardial tunnel. In patients with a history of prior CABG to the LAD, very little pericardial dissection is needed. The target site of the LAD below the old saphenous vein graft is usually immediately under the pericardial incision. In this instance, the pleural cavity is not entered, making the operation simpler.

Coronary Occlusion and Preparation for Anastomosis

Two types of suture techniques have been used to achieve local coronary occlusion: A double-looped, 5-0 Prolene suture placed proximally and distally to the selected anastomosis site, encircling the entire coronary artery, epicardial fat, and accompanying veins, with the coronary artery underneath the looped sutures protected by silastic bolsters; and a silastic retractor tape without double loop (Fig. 4).

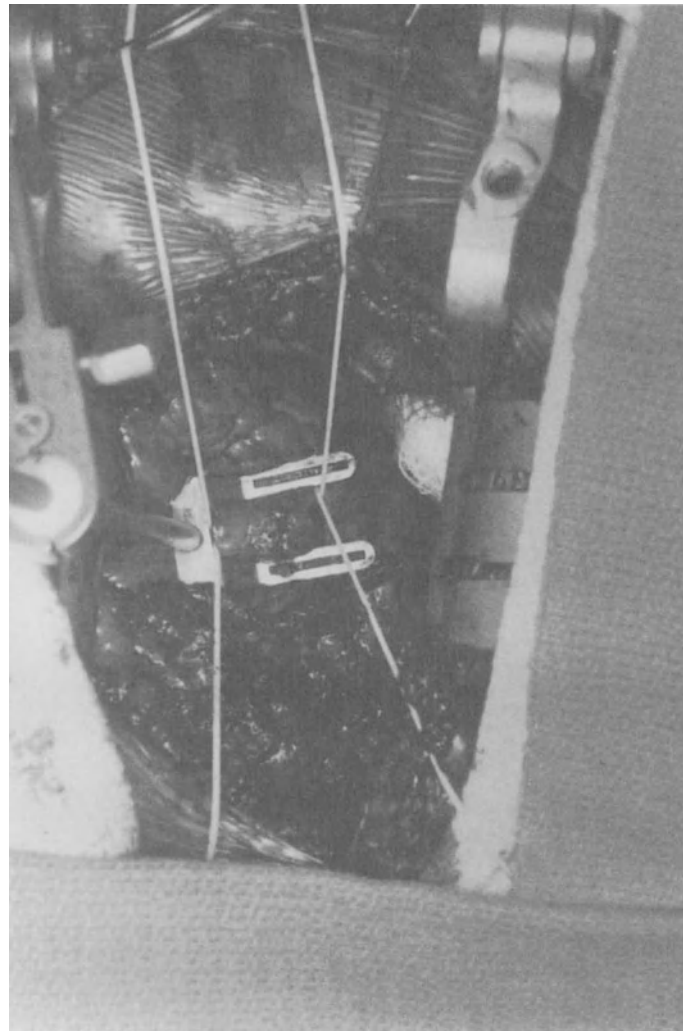

Fig. 4. Silastic retractor tape used to facilitate coronary target immobilization.

Ischemic preconditioning is used almost routinely; it entails 5 min of local coronary occlusion followed by 5 min of reperfusion, and then is completed by occlusion for the coronary anastomosis. Although the exact role of ischemic preconditioning in MIDCAB is not established, our clinical experience with this technique has been favorable. Ventricular tachyarrhythmias have not been observed in any of the patients undergoing LIMA-LAD anastomosis, and unifocal premature ventricular beats were rarely observed.

Immobilization and Stabilization of the Recipient Coronary Artery

The technique for anastomosis on a beating heart is technically demanding. Partial immobilization of the coronary target site by use of pharmacological agents, including intermittent adenosine-induced asystole, has not been successful in predicting or enhanc-

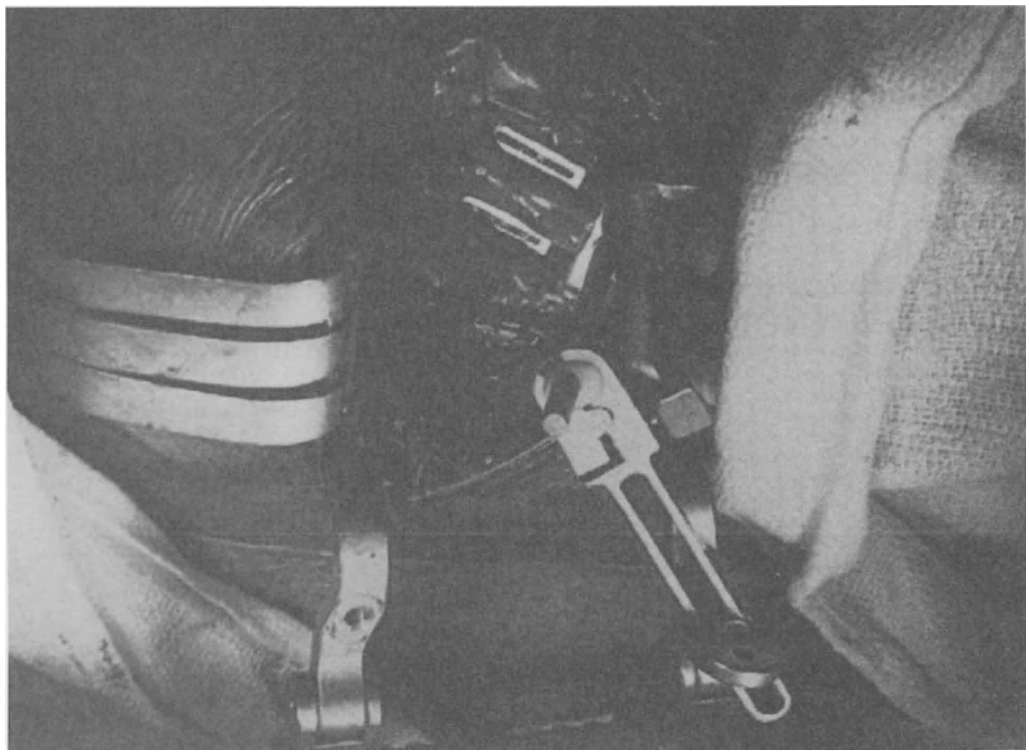

Fig. 5. CardioThoracic Systems immobilizer with immobilizing foot.

ing the early graft patency beyond 90% in our hands. We believe this is a result of the complex movements of the LAD in a beating heart, occurring in three axis in space (longitudinal, transverse, and vertical). The recent introduction of the concept of regional cardiac wall immobilization with mechanical platforms, on the other hand, has eliminated most of the movement of the LAD in all directions, simulating the anastomotic milieu present in the cardioplegic-arrested heart.

Currently, two types of mechanical stabilization devices are available to achieve regional immobilization. The first type relies on local myocardial compression from direct pressure exerted on either side of the recipient coronary artery. A variety of such devices exist including the CTS stabilizer and rigid circles or rectangles that may be handheld or attached to the incisional retractor. To be effective, these devices must indent the myocardium firmly to dissipate the propagated systolic wave across the vessel and immobilize the artery within a bridge of myocardium. Localized compression is usually well tolerated hemodynamically, and it can often be seen on the transesophageal echocardiogram, sometimes mistaken for an ischemic akinetic area. Use of one such stabilizer (Fig. 5) in the last 172 consecutive LIMA-LAD grafts performed via the MIDCAB technique, in our experience, has yielded an early (36 h) graft patency of 96.2%.

The second type of mechanical device its the Utrecht Octopus (Medtronic, Minneapolis, MN) (Fig. 6). This device consists of a system of suction cups on two fixed handles

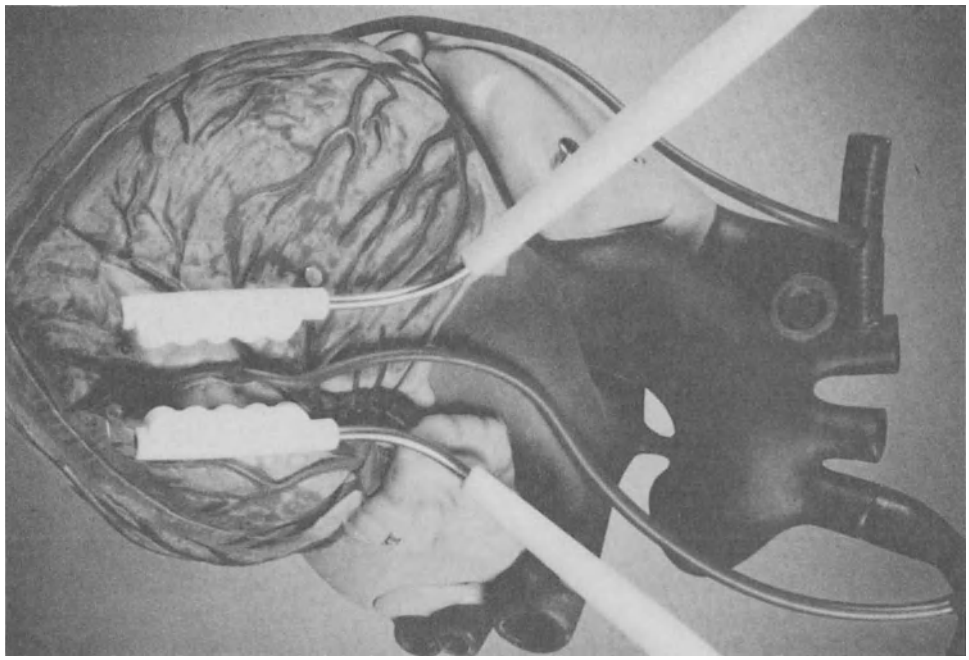

Fig. 6. Utrecht Octopus retractor. "Tentacles" or suction cups are positioned on either side of the target vessel.

that are positioned on either side of the target vessel. This system not only offers immobilization but also enables variable degrees of myocardial traction for access to lateral and inferior wall vessels.

Frequent changes in heart size occur during the anastomosis secondary to variations in intracardiac volume, afterload, ischemia, and tidal volume. These variations often lead to a shift in alignment of the device, and methods to improve these immobilization techniques are necessary and certain to optimize the technically demanding situation of coronary grafting on the beating heart.

Visualization and Control of the Anastomotic Site

Despite the many technical improvements, isolation and control of the anastomotic site remains a contentious area. Effective control requires an atraumatic system that provides isolation of an adequate segment of vessel, free of bleeding, and with provision for dispersing residual blood, which may obscure the anastomosis. We are routinely using a blower device to blow the blood away during the anastomosis. As an added advantage, the blowing action keeps the incised edges of the coronary artery separated like "a spinnaker on a sailboat," greatly simplifying the anastomosis.

The correct length of the isolated artery is a balance between being too long, with the increased potential for excessive and bothersome back-bleeding, and being too short. When feasible, the isolated segment should be chosen in order to exclude inflow from any

significantly sized visible branches. With an unduly short segment, on the other hand, crowding or distortion of the tissues at the anastomotic toe and heel may occur and seriously compromise a secure anastomosis. An allowance also needs to be made for variable degrees of edema and hematoma formation secondary to tissue injury, during or after placement of the vessel-controlling system. With the ongoing beating action of the heart, swelling may occur and extend to encroach on the anastomosis. Selection of the anastomosis site may be relevant to ensure a successful operation. A more proximal site may result in a greater area of distal ischemia and increase the potential for hemodynamic instability and arrhythmias during the critical anastomotic period.

Anastomotic Technique

After the target site has been immobilized and the ischemic preconditioning completed, the LAD is incised for a distance of 4 to 5 mm. The anastomosis is performed with running 7–0 or 8–0 Prolene sutures in standard fashion. Over the last year, our technique has been modified to use two 8–0 Prolene sutures, one at the toe and one at the heel, with three throws at each end; the IMA graft is then parachuted down to the coronary artery, and the anastomosis is finished on either side. When doing composite or multiple grafts to the diagonal and the circumflex arteries, the end-to-side anastomosis to the circumflex is completed first, followed by the side-to-side anastomosis of the diagonal, and then the final LIMA-LAD anastomosis. While the latter is completed, the bulldog clamp is placed distal to the origin of the composite graft. In a sequential LAD-diagonal graft, the side-to-side anastomosis of the diagonal is performed first. Again, the bulldog clamp is placed distal to the diagonal anastomosis to allow perfusion while the LAD anastomosis is completed.

Following completion of the coronary anastomosis, the looping sutures are removed, thus allowing the native coronary artery to fill the anastomosis into the IMA and ensuring good flow through the anastomosis. The stabilizer is then removed, and the bulldog clamp on the IMA pedicle is released. Protamine is not given routinely. The pericardium is widely incised and the IMA pedicle carefully tacked onto the epicardium to achieve a 30–40° angle of LIMA on to the LAD. The wide pericardial incision has greatly decreased the incidence of pericarditis and atrial fibrillation after this operation. The careful alignment of the LIMA-LAD angle has virtually eliminated the "funny shadows" previously seen on early angiography. Routine intercostal block with bupivicaine (Sanofi Winthrop, New York, NY) is used to minimize postoperative pain. A small drainage catheter is placed in either the pericardial or pleural cavity, the wound is closed, and the patient is returned to the intensive care unit (usually extubated).

Routine postoperative care is carried out with emphasis on early extubation within the first postoperative hour and discontinuation of all invasive lines within 6 h. Graft patency is tested by immediate, postoperative echocardiographic Doppler color flow analysis of the LIMA-LAD anastomosis and by routine angiography between 24 and 36 h after surgery. Patients are ambulated within the first 12–24 h after surgery. Follow-up stress testing with the use of thallium and a treadmill, as well as repeat evaluation of the IMA anastomosis with echo Doppler are performed within a 3 to 6 mo interval.

MULTIVESSEL GRAFTING BY MIDLINE STERNOTOMY INCISION ON/OFF PUMP

The exposure used in multivessel grafting by midline sternotomy incision is similar to conventional CABG. Preferably, only arterial grafts are used, no aortic manipulation is done, and the mechanical stabilizers previously discussed are utilized. A recently introduced multivessel platform (CardioThoracic Systems) is the most suitable for approaching the posterior vessels. The foot of the device, which is used as a local immobilization platform, rotates on a swivel that can be placed in different directions to achieve immobilization. The Octopus platform has also been extensively used in approaching posterior vessels, however, experience is too limited to comment on its safety and efficacy. Currently, the LAD, RCA, posterior descending, and a high-diagonal or ramus branches are the most easily approached for multivessel grafting by midline sternotomy incision with the use of these platforms.

Dislocation of the apex of the heart upward 90° while in a Trendelenburg (head down) position is well tolerated hemodynamically in patients with good left ventricular function. In patients with compromised left ventricular function, however, this maneuver is commonly complicated by regional ischemia and moderate mitral regurgitation. To achieve cardiac dislocation, we use a two-sponge technique: one sponge is placed in the transverse sinus and the other around the inferior vena cava, with the right sides of the sponges fixed to the chest wall and the left ends free to move around the heart to expose and present the target to the surgeon. In our experience, maneuvering of the heart in this manner is associated with minimal, if any, hemodynamic compromise. Bilateral detachment of the diaphragm from its costal attachments enhances exposure of the posterior surface of the heart. Closure of the wound and drainage with pleural and mediastinal tubes is performed in standard fashion.

CLINICAL EXPERIENCE

Between April 1994 and September 1997, 290 patients with a mean age of 66 ± 12 yr (range 36–93) underwent MIDCAB in our institution. Anterior minithoracotomy, subxyphoid, lateral minithoracotomy, and right-sided bucket-handle ministernotomy incisions were performed. Using the aforementioned techniques—pharmacological bradycardia, local coronary occlusion on the beating heart, local immobilization of target arteries with traction sutures, and regional cardiac immobilization with mechanical platforms—IMA, gastroepiploic, and radial artery grafting were performed.

Table 2 depicts the preoperative risk factors among the patients undergoing these procedures. Three patients underwent concomitant carotid endarterectomy. Clinical priorities for MIDCAB were elective in 168 patients (154 for chronic stable angina, 14 for ischemic cardiomyopathy), urgent in 119 patients (postmyocardial infarction or unstable angina), and emergent (acute myocardial infarction) in 3 patients. Clinical indications for MIDCAB consisted of high-risk comorbid factors prohibitive for CPB in 78 (27%) patients, reoperative coronary bypass grafting with high-risk factors for CPB in 81 (28%)

Table 2
Preoperative Risk Factors
Among 290 Patients Undergoing MIDCAB Procedures

	N	%
Unstable angina	43	14.8
Postmyocardial infarction angina	70	24.1
Ischemic cardiomyopathy	14	4.8
Emergency acute myocardial infarction	3	1
Reoperative coronary artery bypass	81	27.9
CHF[a] with angina	59	20.3
Ejection fraction <30%	71	24.4
Chronic mitral insufficiency	36	12.4
End-stage renal disease	5	1.7
Prior CVA[b]	39	13.4
Severe COPD[c]	61	21
Prior pneumenectomy	2	0.7
Diffuse vasculopathy	69	23.7
Calcified aorta	11	3.7

[a]Congestive heart failure.
[b]Cerebrovascular accident.
[c]Chronic obstructive pulmonary disease.

patients, restenosis after PTCA and stenting in 95 (33%) patients, religious preference (Jehovah's Witness) in 7 (2.4%) patients, and unsuitable proximal LAD for PTCA in 15 (5%) patients. Conversion rate to midline sternotomy and CPB in the entire series was 4.8% (14/290), and in the recent 190 consecutive cases, this figure was reduced to 1.6%. There has been no mortality in the patients who required conversion to conventional CABG. Among the 14 patients who underwent converted conventional CABG, only one patient required conversion for bradycardic arrest during LIMA-LAD grafting. This patient had successful completion of the operation via sternotomy and CPB. Reasons for additional conversion to conventional CABG include technical difficulties during RIMA-RCA right-sided minithoracotomy (5), intramyocardial LAD (3), LIMA injury (3), fatty heart (1), and bleeding at the LAD proximal occluding snare site (1). The minimal incidence of conversion for hemodynamic deterioration in the 250 patients who underwent LIMA-LAD MIDCAB confirms our impression that the local coronary occlusion of the LAD is well tolerated. We believe this is a result of our routine use of ischemic preconditioning from the onset of our experience with MIDCAB.

The high rate of conversion to sternotomy among patients undergoing RIMA-RCA MIDCAB grafting (26%), is probably related to the difficulty encountered in immobilizing the RCA and the presence of diffuse disease in this vessel. These factors along with the very high early occlusion rate of 20% with the RIMA-RCA graft performed via this incision strongly suggest that this operation should be performed only in cases in which the RCA is of good caliber and quality, and in patients with short anteroposterior chest diameters. Furthermore, the high patency rates obtained with right gastroepiploic graft-

ing to the distal RCA or posterior descending artery (PDA) (92%) combined with the lack of conversions to conventional CABG suggest that an inferior MIDCAB approach may be better to achieve RCA grafting. The introduction of the right-sided bucket-handle incision has recently allowed successful reoperative RIMA to mid- or distal RCA in five patients with 100% early patency. For patients requiring RCA grafting, presence of a totally occluded proximal RCA with collaterals from the left side to the distal PDA and RCA is preferable.

Cardiac-related operative mortality was 1.1%. The number of coronary anastomoses per patient was one in 86%, two in 14%, and three in one patient. Postoperative complications were infrequent. Of interest is the extremely low incidence of neurological and renal adverse sequelae (0.36%), and low incidence of atrial fibrillation (7.2%). Angiographic and transthoracic Doppler flow analyses of the anastomoses at 36 h postoperatively were performed in 96.7% of the patients with an overall patency rate of 92%.

Prior to March 1996, when only conventional immobilization techniques had been used, the angiographic patency of LIMA-LAD grafts was 86%. Since that time, regional cardiac wall mechanic immobilization was used in the last 124 LIMA-LAD MIDCAB patients, resulting in an early angiographic patency of 97%. The only four occlusions that occurred in this latter cohort were owing to an intramyocardial LAD, an extremely calcified artery with a 1.5 mm diameter, and a heparin-induced thrombocytopenia with white thrombus in the anastomotic site and the native LAD after the operation. Therefore, it appears that the graft quality and the proper selection of target site are the sole determinants for graft occlusion when mechanical stabilization platforms are used. A cohort of 15 patients who underwent LIMA-LAD and who had early patent grafts have been sequentially studied at 6–9 mo intervals, and all grafts were found to be patent. During a mean follow-up of 12.4 ± 7.4 mo, four patients had expired (1 mo [1], 3 mo [2], and 7 mo [1] postoperatively). For the remaining 247 patients, cardiac event–free survival (PTCA, reoperative CABG, readmission with recurrent angina, and congestive heart failure) was 95%. Preliminary analysis of the economic impact of MIDCAB compared to elective uncomplicated conventional CABG in our institution has shown a consistent 50% reduction in hospital costs and dramatic reduction in length of stay *(13)*.

The LIMA-LAD grafting is the most important operation advanced by the MIDCAB technique. At our institution, this operation is performed in a fashion that closely mimics the routine conventional CABG except for the incision and the elimination of CPB. The patency of the lateral MIDCAB using radial artery from the descending aorta to the marginal branches has been excellent. This approach has been carried out in 12 patients with a 100% overall patency rate in the 11 patients who underwent the procedure with the aid of mechanical immobilization. The superior exposure obtained in eight patients operated by midlateral MIDCAB incision has uncovered an alternative method of approaching both the circumflex and LAD in patients with left main disease in which composite grafting of LIMA-radial graft to the LAD and circumflex branches have been successfully performed. We are currently entertaining the possibility of RIMA-LAD and LAD-circumflex grafting via the midlateral MIDCAB incision. MIDCAB grafting in primary elective or urgent reoperative coronary bypass patients is a safe and

effective procedure with good early clinical results especially with LIMA-LAD grafting. Regional cardiac wall mechanical immobilization must be incorporated as a standard part of the procedure in all MIDCAB grafting procedures to ensure good graft patency. Also, critical evaluation of early and late angiographic results with this operation is essential. It is envisioned that in the next 5 yr, at least 30–40% of coronary artery bypass surgery will be routinely performed on a beating heart either with midline sternotomy for multiple vessels or with strategically placed minimal access incisions for single- or double-vessel grafting.

REFERENCES

1. Benetti FJ, Naselli G, Wood M, Gefner L. Direct myocardial revascularization without extracorporeal circulation. Chest 1991;100:312–316.
2. Buffolo E, de Andrade JCS, Branco JNR, Teles CA, Aguiar LF, Gomes WJ. Coronary artery bypass grafting without cardiopulmonary bypass. Ann Thorac Surg 1996;61:63–66.
3. Pfister AJ, Zaki MS, Garcia JM, et al. Coronary artery bypass without cardiopulmonary bypass. Ann Thorac Surg 1992;54:1085–1091.
4. Subramanian VA, Sani G, Benetti FJ, Calafiore AM. Minimally invasive coronary bypass surgery: a multicenter report of preliminary clinical experience. Circulation 1995;(Suppl 8) 92:S1645.
5. Calafiore AM, DiGiammarco G, Teodori G, et al. Left anterior descending coronary artery grafting via left anterior small thoracotomy without cardiopulmonary bypass. Ann Thorac Surg 1996;61:1658–1665.
6. Lytle BW. Minimally invasive cardiac surgery. J Thorac Cardiovasc Surg 1996;111:554,555.
7. Ullyot DJ. Look ma, no hands! Ann Thorac Surg 1996;61:10–11.
8. Gundry SR. Discussion of Pfister AJ, Zaki MS, Garcia JM, et al. Coronary artery bypass without cardiopulmonary bypass. Ann Thorac Surg 1992;54:1091–1092.
9. Howie MB, Hiestand DC, Jopling MW, Romanelli VA, Kelly WB, McSweeney TD. Effect of oral clonidine premedication on anesthetic requirement, hormonal response, hemodynamics, and recovery in coronary artery bypass graft surgery patients. J Clin Anesth 1996;8(4):263–272.
10. Suma H. Optimal use of the gastroepiploic artery. Semin Thorac Cardiovasc Surg 1996;8(1):24–28.
11. Nataf P, Lima L, Regan M, et al. Thoracoscopic internal mammary harvesting: technical considerations. Ann Thorac Surg 1997;(Suppl)63:S104–S106.
12. Ohtsuka T, Wolf RK, Hiratzka LF, Wurnig P, Flege JB. Thoracoscopic internal mammary artery harvest for MICABG using the harmonic scalpel. Ann Thorac Surg 1997;63: S107–S109.
13. Subramanian VA. Less invasive arterial CABG on a beating heart. Ann Thorac Surg 1997;63:S68–S71.

9

Minimally Invasive Coronary Artery Bypass Grafting on the Beating Heart

The European Experience

Antonio M. Calafiore, MD, Marco Contini, MD, Giuseppe Vitolla, MD, Teresa Iovino, MD, and Angela Iaco', MD

CONTENTS

INTRODUCTION

The prospect of grafting the internal mammary artery (IMA) to the left anterior descending (LAD) artery via a thoracotomy without the aid of cardiopulmonary bypass (CPB) was first explored by Kolessov in 1967 *(1)*, and further applied by Favaloro *(2)*, Garrett *(3)*, Trapp *(4)*, and others. The early wave of enthusiasm for this technique soon wavered with the widespread availability of CPB and cardioplegia, which allowed for a motionless and bloodless operative field. The unequivocal and widespread success of conventional coronary artery bypass grafting (CABG) limited the use of unsupported bypass grafting. Two developments in the early 1990s revived the technique of myocardial revascularization without CPB: (1) the emergence of minimally invasive technology applicable to the chest, and (2) the promising results of "pumpless" bypass grafting reported by a number of authors *(5–7)*.

The promising clinical reports of minimally invasive coronary artery bypass grafting (MICABG) demonstrating excellent early patency, low morbidity and mortality, and shortened hospital stays stimulated a worldwide interest in these techniques. Our group

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

popularized MICABG through a left anterior small thoracotomy, coining the term the "LAST" operation *(8)*. The purpose of this chapter is to describe our updated experience and to examine the directions of minimally invasive techniques as they are presently evolving in Europe.

SURGICAL INDICATIONS

Presently no consensus exists delineating absolute indications for MICABG. The decision to perform MICABG at our institution is individualized and is by no means generalizable to all patients and to all institutions. Furthermore, we recognize that the field is rapidly evolving and that current indications may change. Nonetheless, certain indications are shared by several of our European colleagues. Candidates for the LAST operation include patients with isolated LAD disease in whom a percutaneous transluminal coronary angioplasty (PTCA) was unsuccessful, impossible (occluded LAD), or contraindicated (proximal and/or complex stenoses). Patients with two-vessel disease (right coronary or circumflex plus LAD) in which the non-LAD vessel is occluded and recanalized or with a mild stenosis or stenosis that could be dilated are also considered. In addition, patients with multivessel disease in which the lesion in the other vessels can be dilated are suitable candidates. Finally, patients for whom CPB is deemed a high-risk undertaking, including patients with malignancies, renal failure, generalized vasculopathy, coagulation disorders, and advanced age, are also considered.

Contraindications to MICABG are limited to anatomic considerations and are strictly related to the impossibility of performing the LIMA-LAD anastomoses because of an unsuitable or unreachable LAD. In some patients, unfavorable conditions can be detected preoperatively. Presence of left subclavian stenosis or occlusion precludes MICABG because it can result in a coronary steal syndrome *(9,10)*. An intramyocardial vessel, often discernible at angiography (Fig. 1), is an absolute contraindication to MICABG. This particular situation is best diagnosed on oblique right anterior projections in which the vessel is seen to progress downward and then, after a few centimeters, turn upward (toward the epicardium). An LAD of <1.5 mm or a calcified LAD preclude MICABG. Exquisite attention must be given to the area 2–4 cm distal to the second diagonal branch because this is the usual anastomotic site. We rely on the evaluation of different angiographic projections to show the internal size of the distal LAD, the quality of its walls, and its position relative to the epicardial surface. In the majority of cases, however, the final decision to proceed or not with MICABG is made at operation.

SURGICAL TECHNIQUE

After establishing hemodynamic monitoring, general endotracheal anesthesia with a single-lumen endotracheal tube is instituted. Early in our experience, we relied on the use of double-lumen endotracheal tubes to optimize left-sided exposure. With increased experience, we have abandoned its routine use. Anesthesia is generally induced with

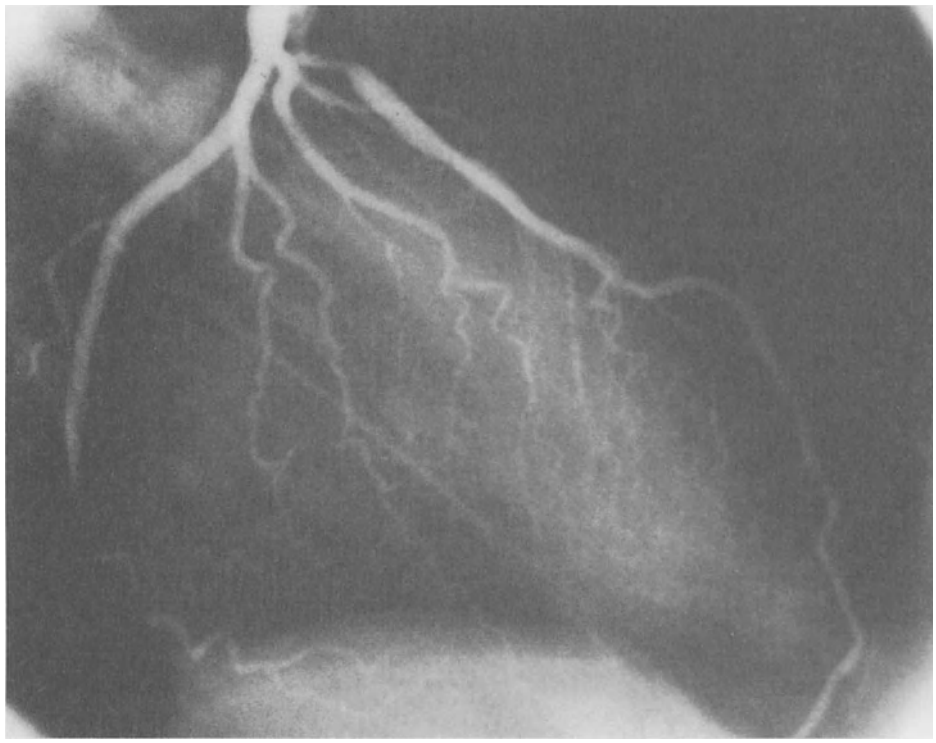

Fig. 1. Angiographic demonstration of an intramyocardial LAD. This constitutes a contraindication to off-pump grafting.

fentanyl and sodium thiopental and maintained with fentanyl and droperidol. Muscular relaxation is obtained with pancuronium bromide. To allow rapid awakening of the patient, a mixture of nitrous oxide and oxygen is used in the final part of the operation.

Access to the heart is obtained via LAST in the fourth or fifth intercostal space, depending on angiographic criteria. The pleural cavity is entered, the ribs are retracted, and the pericardium is incised parallel to the sternum. The LAD is inspected and the feasibility of the operation is considered. In the presence of any contraindication (as described above), the chest is closed and median sternotomy is performed. The LIMA is harvested for a short length (4 to 5 cm), usually extending from the superior intercostal space to the level of the inferior rib. In our early experience, if the LAD lay excessively lateral, the inferior epigastric artery was used to prolong the LAD in an end-to-end fashion (Fig. 2). Occasionally a saphenous vein graft would be used to achieve the necessary length (Fig. 3). This technique has been previously reported *(11)*. More recently, however, increased experience combined with the availability of better instruments, has allowed us to procure a longer segment of the LAD. Indeed, the IMA Access Retractor (CardioThoracic Systems, Cupertino, CA) has allowed extended IMA dissection to the level of the bifurcation inferiorly and first rib superiorly, if necessary. Following systemic heparinization (1 mg/kg), 3 mL of papaverine (1 mg/mL) are injected into the LIMA, and the vessel is clipped distally *(11)*.

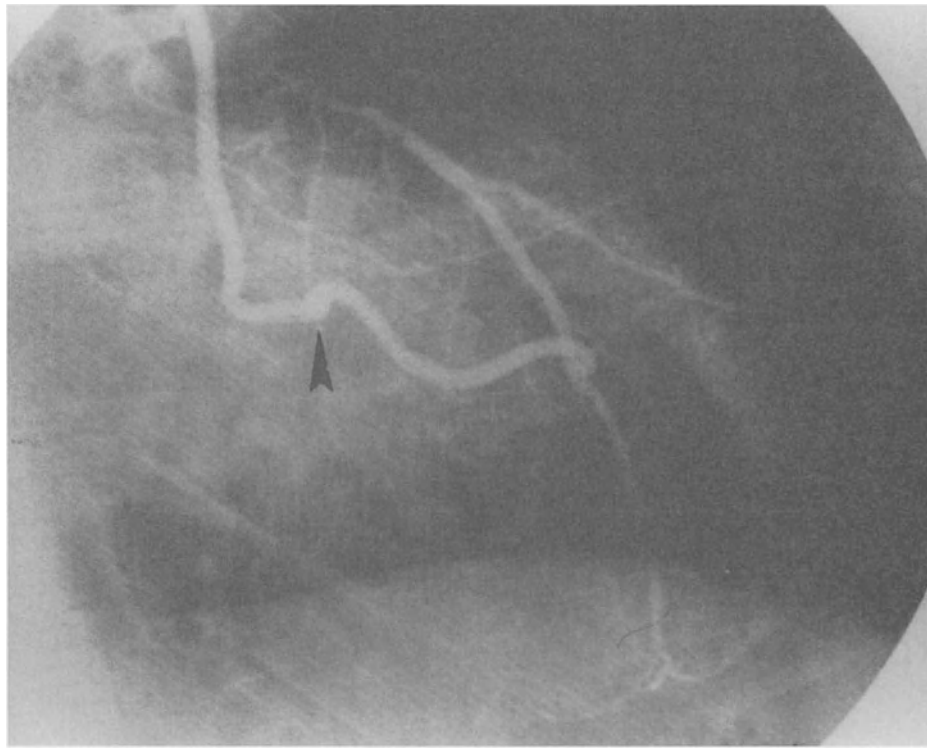

Fig. 2. The inferior epigastric artery is anastomosed end-to-end to the LIMA to allow grafting of an abnormally lateral LAD.

The LAD is then occluded proximally and distally using a 4-0 Prolene suture with a 25-mm needle, which is passed twice to surround the vessel. To avoid direct compression of the suture on the coronary vessel wall, the needle is passed through a small piece of silicon tubing. The Prolene stitch is then gently snared to ensure a bloodless operative field.

A stabilizer with two feet (CardioThoracic Systems) connected to the retractor is positioned parallel to the LAD and pushed down gently. This maneuver minimizes the effect of the beating heart on the operative field, lending the LAD virtually motionless. No preconditioning of the distal LAD territory is performed.

The distal LIMA is prepared in the usual fashion. The anastomotic site of the LAD is dissected and incised with a scalpel for a distance of 4–5 mm. The anastomosis is created using two running sutures of 8–0 Prolene. The anastomosis is created by "parachuting" the stitches at the heel and apex and the anastomosis is completed by running the Prolene sutures in standard vascular fashion. The LIMA and LAD are unclamped and meticulous hemostasis is obtained. During the first part of our experience, we would routinely reverse the heparin with a 1:1 dose of protamine, but we have abandoned heparin reversal more recently. A thoracotomy tube is positioned in the chest along with a small catheter, which is used to infuse analgesics. The wound is closed in the usual manner.

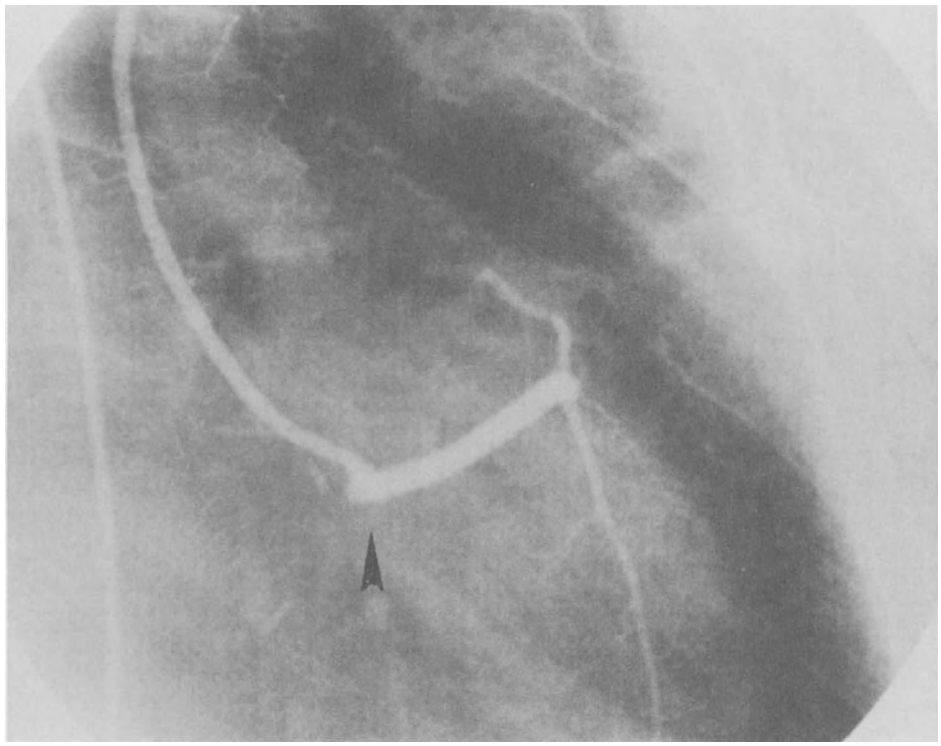

Fig. 3. Use of an interposition saphenous vein graft to achieve LIMA-LAD grafting in a laterally placed LAD.

POSTOPERATIVE COURSE

The patient is extubated in the operating room, or shortly after arrival to the intensive care unit. Routine blood samples, electrocardiogram, and chest roentgenograms are obtained. The flow pattern in the LIMA is assessed by continuous-wave Doppler echocardiography. Because the LIMA partly remains in its normal anatomic position for approximately two to three intercostal spaces, the flow pattern is easily detectable. The demonstration of diastolic flow is considered as evidence for a patent anastomosis. The flow can be compared with that of the unused right IMA, the flow of which is mainly systolic.

After a few hours of observation, the patients are transferred to the ward. The chest tube and pleural catheter are removed on the morning of the first postoperative day. Evaluation of LIMA flow is repeated at rest and after acutely induced hypervolemia, by lifting the patient's legs and instructing him or her to perform an isometric exercise *(12)*. This maneuver induces tachycardia and increases cardiac output. In the absence of a restrictive anastomosis, diastolic blood flow velocity increases owing to the larger amount of blood needed by the coronary territory. Early in our experience, most patients underwent angiography. At present, every patient suspected of having a restrictive anastomosis

undergoes angiography. If no problems are found, the majority of patients are discharged on the second postoperative day.

All patients are followed up at our outpatient clinic and at the end of the first and sixth postoperative months. All patients are subjected to a stress test and, if possible, myocardial scintigraphy is obtained on their second visit. In addition, Doppler evaluation of the LIMA-LAD anastomosis is repeated at rest and during hypervolemia, as previously described.

RESULTS

Between November 21, 1994, and October 20, 1997, 540 patients were scheduled to undergo LIMA-LAD grafting using the LAST approach. In 28 patients (5.2%), the LAST operation could not be accomplished because the LAD was not visible (18), calcified (4), substernal (3), too small (2), or the LIMA was injured during harvesting (1). All these patients underwent uneventful median sternotomy and conventional bypass grafting.

Table 1 details the variables of the LAST operation. Mean LAD occlusion time was under 30 min. The majority of patients were extubated in the operating room or during the first two postoperative hours. Postoperative atrial fibrillation developed in 9% of patients but was easily managed with amiodarone. Pericarditis requiring extended hospitalization occurred in only 1.2% of patients. Two patients developed a pulmonary hernia requiring wound revision. Mean (±SD) length of stay (LOS) was 67.9 ± 30.3 h, in many instances owing to a delay in obtaining a postoperative angiogram. Nevertheless, nearly 70% of patients were discharged within 2 postoperative days.

Six patients underwent concomitant vascular operations at the time of the LAST operation, including carotid endarterectomy alone in 5 patients and carotid endarterectomy and femoro-femoral bypass for limb salvage in 1 patient.

Perioperative mortality was 1%, and included 5 patients who died after a mean (±SD) of 6.8 ± 7.5 d (Table 2). Causes of death were cardiac, but not operation related, in 4 patients. One patient had died suddenly owing to an inferolateral myocardial infarction with a widely patent graft at autopsy; 1 patient succumbed owing to low output syndrome, which was present preoperatively and was not reversed by the LIMA-LAD graft; one patient died of cardiac tamponade after he underwent successful stent PTCA of the right coronary artery 3 d after the LAST procedure; and 1 patient died of cardiac failure early after stent PTCA of the circumflex artery. In addition, massive intestinal infarction was the cause of death in 1 patient.

In late mortality was 1.2%, including 6 patients who died after a mean (±SD) of 130 ± 120 d. Causes of late death were cardiac in 3 patients. One of these was in a patient with renal failure who developed bleeding from the LIMA causing hypotension and eventual multisystem organ failure. Two patients on chronic hemodialysis died of myocardial infarction in previously nondiseased circumflex arteries. One of these patients underwent postmortem examination, which documented a patent anastomosis. In 3 patients, the cause of death was not cardiac but included malignancy (1), cerebral hemorrhage (1), and cirrhosis (1).

Table 1
Intraoperative and Postoperative Variables Among Patients Undergoing the LAST Operation

Variables	*LAST operation*[a]
LAD occlusion time (min)	28.8 ± 7.9
Duration of operation (h)	2.1 ± 0.5
Extubation by 2 h postoperatively	360 (70.3%)
12-h chest tube output (mL)	171 ± 212
Mean creatinine phosphokinase (CPK)-MB (IU)	18 ± 14.7
Mean ICU stay (h)	4.1 ± 4.2
Mean hospital LOS (h)	67.9 ± 30.3
Discharge within 2 postoperative d	352 (68.7%)

[a] $n = 512$. Figures are expressed as mean ± SD.

Table 2
Operative Morbidity, Mortality, and Incidence of Repeat Intervention on the LIMA-LAD Anastomosis Among Patients Undergoing the LAST Operation

	LAST operation[a]
Morbidity	
Need for blood transfusion	17 (3.3%)
Reoperation for bleeding	10 (1.9%)
New onset atrial fibrillation	46 (9%)
Pericarditis	6 (1.2%)
Delayed chest wound healing	15 (2.9%)
Mortality	
Perioperative (30 d) mortality	5 (1%)
Late mortality	6 (1.2%)
Reoperation of anastomosis	
Early (<30 d) repeat intervention	
Reoperation	18 (3.5%)
PTCA	1 (0.2%)
Late (>30 d) repeat intervention	
Reoperation	8 (1.6%)
PTCA	2 (0.4%)

[a] $n = 512$.

In 10 of 11 deaths, a patent anastomosis was documented by angiography (3), Doppler flow velocity assessment during acute hypervolemia (3), or at rest only (1), or at autopsy (3). The remaining patient died of later complications from cirrhosis after a successful conventional CABG reoperation for conduit occlusion.

A total of 26 patients (5.1%) required reoperation for anastomotic stenosis (10) or conduit occlusion (16). Eighteen of these operations occurred within 30 d of the LAST operation and 8 were performed at an average of 138 ± 111 d after the LAST procedure.

Twenty-five of these patients (96%) underwent reoperation via median sternotomy and 1 patient via repeat LAST incision. CPB was used in most patients (92%).

Three patients underwent PTCA for anastomotic stenosis. One patient had a successful infrastent PTCA of the LAD for treatment of an early anastomotic stenosis. An angiogram 4 mo later demonstrated a widely patent anastomosis. A second patient with an asymptomatic stenosis detected after an early routine angiogram underwent successful PTCA 126 d after surgery. The third patient underwent successful dilation 153 d after the LAST procedure. A routine early postoperative angiogram had demonstrated an intact anastomosis.

With increasing experience and better instrumentation, the incidence of reoperation is decreasing in our series. In fact, in the last 100 operations, reoperation was necessary in only one patient owing to conduit occlusion.

Four patients underwent reoperation for disease outside the LAD territory at a mean (±SD) of 55 ± 53.6 d after the index operation. Two of these occurred very early postoperatively (1 and 3 d): in the first case owing to evolving inferior myocardial infarction associated with occlusion of a previously moderately diseased right coronary artery (RCA); in the second case owing to unstable angina associated with subocclusion of a mildly stenosed marginal branch. The two late reoperations (97 and 119 d) were performed for the treatment of recurrent severe pericarditis in one patient, and development of a new LAD lesion, proximal to a distal patent anastomosis and not related to the LAD occlusion during the first procedure in the other patient. In this case, the LIMA was used to create an intermediate anastomosis leaving the previous distal anastomosis intact.

Eleven patients (2.1%) underwent scheduled postoperative stent PTCA on the circumflex or RCAs. All procedures were successful, but two patients died as described previously.

Postoperative angiography was performed in 318 patients (62.1%) during the first year after operation. The anastomosis was patent in 301 cases (patency rate 94.6%) and patent without malfunction in 287 cases (perfect patency rate 90.2%). Combining the results obtained with angiography and Doppler echocardiography, a patent anastomosis was obtained in 495 patients (96.7%) and a nonrestricted anastomosis in 481 patients (93.9%).

In six patients who underwent serial angiography, anastomotic or conduit malfunction resolved without intervention, with a mean interval between angiographic studies of 94 ± 56 d. This observation is likely owing to small clots or adventitial hematomas, both of which are known to resolve. Experience has taught us that in the absence of symptoms, no drastic decisions need to be taken in the early postoperative period. If an angiographic abnormality is documented, repeat angiography is performed 2–3 mo later.

Thirty-eight patients (7.4%) underwent repeat angiography more than 1 yr after surgery (mean ±SD, 17.6 ± 5.3 mo), to evaluate the stability of the anastomosis over time and to examine the development of LAD irregularities or stenosis in the proximal and distal sites used for transient occlusion. No such irregularities or stenoses were found.

At a mean follow-up of 16 ± 9.4 mo, 501 patients (97.8%) are alive and remain asymptomatic with or without medical treatment with documented negative stress tests

in every case. The overall freedom from death, symptoms, and reintervention is 92%, and event-free survival is 90.9%.

No patient has suffered a perioperative or late myocardial infarction in the area targeted by the LAST operation. This observation coupled with the late angiographic data available in a small proportion of patients strongly suggests that temporary LAD occlusion as practiced in this series is a safe and effective technique to allow construction of the anastomosis.

DISCUSSION

Within a short period, great strides have been made in the development and clinical implementation of MICABG on the beating heart. In the past two years, the LAST procedure has gained rapid popularity in Italian centers other than ours and in other European countries. In fact, many of these centers are now concentrating on the development of improved techniques for IMA harvesting and LAD stabilization and are experimenting on the use of facilitated end-to-side anastomotic techniques. Several of these centers participated in the recent MICABG Workshop held in Utrecht in 1996. In these institutes, coronary bypass grafting without CPB constituted 1–43% of current bypass procedures performed *(13)*. Of 2587 operations reviewed at the workshop without CPB, 1071 (41%) were performed through minithoracotomies. The benefits of this approach are most notable in the early postoperative period, with shorter hospital stays, shorter convalescent times and earlier return to full social activities.

The LAST operation, as described herein, is a procedure that can be performed with low risk and acceptable midterm results. Surgical technique is becoming safer and reproducible, and instrumentation is rapidly evolving. Long-term results of MICABG however, remain to be defined. A randomized clinical trial with angiographic follow-up comparing conventional LAD bypass to coronary operation on the beating heart is warranted. Although we believe that long-term patency of the LIMA-LAD anastomosis using either technique should be the same, our intuition remains to be proven.

Concerns regarding development of a steal phenomenon owing to preserved IMA branches have been raised. Two opposing views have emerged regarding the importance of these branches: one is that thoracoscopic operation to harvest the full length of the LIMA and ligate all the branches is necessary; the other is that only a short segment of IMA needs to be harvested and that branches are not physiologically important. Our experience supports the latter view, and in fact, most surgeons performing MICABG have not reported this steal phenomenon; nevertheless, longer follow-up is necessary to resolve this issue.

It is important to recognize that a steep learning curve is inherent in the performance of this operation, particularly for surgeons accustomed to the optimal exposure and stabilization provided by median sternotomy, CPB, and cardioplegic arrest. It may be advisable, as suggested by Benetti *(14)*, to first gain experience with CABG with median sternotomy on the beating heart. Because of the risk of undesirable arrhythmias during

LAD occlusion, it is advisable to have CPB on standby. Some surgeons routinely place percutaneous guide wires into the femoral vessels in case emergent CPB is necessary. Routine use of transesophageal echocardiography is suggested, particularly during the period of LAD occlusion. Should a change in contractility be noted, the artery can be readily unsnared and resnared as necessary.

The role of the LAST procedure vis-à-vis PTCA and stent placement for single LAD disease is a topic of great interest. Recent data derived from a randomized trial *(15)* have revealed a 20% restenosis rate after stent placement. The LAST procedure, in our opinion, can provide more stable results. Even if interventional cardiologists improve their results, the long-term future of a LIMA graft to the LAD is well known in conventional bypass grafting *(16)* and only reproducible by surgical means.

We predict that MICABG will continue to grow and become popular among surgeons, patients, and institutions. It is critical, however, that we continue to evaluate the safety and efficacy of MICABG as it relates to conventional techniques of myocardial revascularization.

REFERENCES

1. Kolessov VI. Mammary artery-coronary artery anastomosis as method of treatment for angina pectoris. J Thorac Cardiovasc Surg 1967;54:535–544.
2. Favaloro RG. Saphenous vein autograft replacement of severe segmental coronary artery occlusion. Ann Thorac Surg 1968;5:334–339.
3. Garrett HE, Dennid EW, DeBakey ME. Aortocoronary bypass with saphenous vein graft. Seven year follow-up. JAMA 1973;223:792–794.
4. Trapp WG, Bisarya R. Placement of coronary artery bypass graft without pump oxygenator. Ann Thorac Surg 1975;19:1–9.
5. Benetti FJ, Naselli G, Wood M, Geffner L. Direct myocardial revascularization without extracorporeal circulation: experience in 700 patients. Chest 1991;100:312–316.
6. Buffolo E, de Andrade CS, Branco JN, Teles CA, Aguilar LF, Gomes WJ. Coronary artery bypass grafting without cardiopulmonary bypass. Ann Thorac Surg 1996;61:63–66.
7. Moshkovitz Y, Lusky A, Mohr R. Coronary artery bypass without cardiopulmonary bypass: analysis of short-term and mid-term outcomes in 220 patients. J Thorac Cardiovasc Surg 1995;110:979–987.
8. Calafiore AM, Di Giammarco G, Teodori G, et al. Left anterior descending coronary artery grafting via left anterior small thoracotomy without cardiopulmonary bypass. Ann Thorac Surg 1996;671:1658–1665.
9. Bryan FC, Allen RC, Lumsden AB. Coronary-subclavian steal syndrome: report of five cases. Ann Vasc Surg 1995;9(1):115–122.
10. Breall JA, Grossman W, Stillman IE, Gianturco LE, Kim D. Atherectomy of the subclavian artery for patients with symptomatic coronary-subclavian steal syndrome. J Am Coll Cardiol 1993;21(7):1564–1567.
11. Calafiore AM, Di Giammarco G, Luciani N, et al. Composite arterial conduits for a wider myocardial revascularization. Ann Thorac Surg 1994;58:185–190.
12. Calafiore AM, Teodori G, Di Giammarco G, et al. Minimally invasive coronary artery bypass grafting on a beating heart. Ann Thorac Surg 1997;63:S72–S75.
13. Borst C, Santamore WP, Smedira NG, Bredee JJ. Minimally invasive coronary artery bypass grafting: on the beating heart and via limited access. Ann Thorac Surg 1997;63:S1–S5.

14. Benetti F. Discussion. In: Calafiore AM, Di Giammarco G, Teodori G, et al. Left anterior descending coronary artery grafting via left anterior small thoracotomy without cardiopulmonary bypass. Ann Thorac Surg 1996;671:1658–1665.
15. Serruys PW, de Jaegere P, Kiemeneij F. A comparison of balloon expandable stent implantation with balloon angioplasty in patients with coronary artery disease. N Engl J Med 1994;331:489–495.
16. Cameron A, Davis KB, Green G, et al. Coronary bypass surgery with internal thoracic artery graft-effect on survival over a 15 year period. N Engl J Med 1996;334:216–219.

10 Port-Access Coronary Artery Bypass

Greg H. Ribakove, MD, Aubrey C. Galloway, MD, Eugene A. Grossi, MD, and Stephen B. Colvin, MD

CONTENTS

INTRODUCTION

Fueled by the success of laparoscopic and thoracoscopic techniques, recent developments in minimally invasive surgery are now being applied to cardiac surgery. The obvious advantages to the patient include a smaller incision, less pain, an improved cosmetic result, and a potentially shorter recovery time. However, owing to the high degree of accuracy and precision required for cardiac surgery and the need for cardiopulmonary bypass (CPB) and myocardial protection for most cardiac surgical procedures, methods of minimally invasive cardiac surgery were slow to develop. Newly proposed techniques for minimally invasive cardiac surgery had to meet the dual challenges of being less invasive while achieving outcomes equivalent to those of established techniques without compromising safety or efficacy. These goals could not be accomplished on a widespread basis with beating heart techniques, nor could these goals be achieved until less invasive methods of extracorporeal perfusion and cardioplegic arrest were developed.

The initial approach to minimally invasive bypass surgery involved working on the beating heart through a limited anterior small thoracotomy (LAST) approach, also known as "keyhole" surgery or minimally invasive direct coronary artery bypass (MIDCAB). Introduced by Calafiore *(1)* in Europe, this innovative technique quickly spread to the United States, and was clinically implemented by Subramanian and Mack et al. *(2–4)*. Early results have been encouraging in select patients, but the technique appears to be

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein © Humana Press Inc., Totowa, NJ

applicable primarily to patients with single-vessel coronary disease, a group that accounts for <5% of the overall cardiac surgical population. Obviously, beating heart procedures are not applicable to valvular operations and other complex open-heart repairs. Furthermore, a disadvantage of the beating heart technique has been the need to perform the coronary anastomosis on a moving heart, which introduces the potential for decreased anastomotic precision. It has been speculated, therefore, that this disadvantage will result in graft patency rates that are lower than those achievable with standard procedures using cardioplegic arrest, especially if the beating heart technique is applied to a wider range of patients. The advantages of less invasive cardiac surgery, however, were readily apparent in the patients treated with the beating heart techniques and included reductions in postoperative pain, hospital stay, and recovery time. Thus, minimally invasive cardiac surgery was not only shown to be feasible but was found to offer significant advantages to the patients and to have immense popular appeal.

The next important milestone in minimally invasive cardiac surgery was the development of an endovascular approach first proposed and described by Stevens and coworkers *(5)* and developed in conjunction with industry. This approach involved the development of a new endovascular system for CPB and cardioplegia delivery (Port-Access, Heartport, Redwood City, CA), which served as a platform allowing wider applicability of minimally invasive cardiac surgery *(5)*. This system relies on the use of peripheral CPB and an endoaortic balloon occlusion catheter, and is designed to achieve standard myocardial protection without the need for a median sternotomy. This approach gives the surgeon the potential to apply fully all the standard techniques of cardiac surgery while minimizing access trauma by the use of small thoracotomy "ports." The Port-Access technique involves the placement of a group of catheters via the femoral artery, femoral vein, and jugular vein. A small thoracotomy "port" incision is then made over the operative target to accomplish the bypass or valvular operation. With this newly developed system, the heart can be stopped, decompressed, and protected, allowing the surgeon to utilize standard anastomotic techniques on multiple coronary targets with reproducible anastomotic precision. Furthermore, the Port-Access approach can be applied to valvular surgery.

The endovascular bypass and balloon endoclamp system was tested extensively at the Stanford University and New York University (NYU) research laboratories *(6–8)*. The initial reports demonstrated the safety and efficacy of myocardial protection using endovascular CPB and cardioplegic arrest. Other studies from the same groups established the feasibility of minimally invasive multivessel bypass grafting and mitral valve surgery with the Port-Access system, providing a sound scientific basis for expanded clinical use of the system.

Port-Access coronary artery bypass grafting (CABG) using the endovascular perfusion and cardioplegic arrest system described previously, was introduced in 1996. An FDA phase I trial was performed at Stanford University, with subsequent controlled clinical trials introduced at NYU and elsewhere. The technique was rapidly adopted in more than 100 centers throughout the country, probably because it immediately expanded the potential application of minimally invasive cardiac surgery, while allowing the surgeon to use standard, reliable techniques of bypass grafting.

The Port-Access technique is applicable to a much wider range of patients than are beating heart methods, including patients requiring multivessel bypass procedures, as well as patients with mitral, tricuspid, and aortic valve disease and atrial septal defects. The early results have been extremely encouraging, achieving a high level of safety and anastomotic reproducibility. In this chapter, we describe the operative technique of Port-Access coronary bypass surgery and report the initial clinical results from our institution.

OPERATIVE TECHNIQUE

Anesthesia and Monitoring

The anesthesiologist is a critical member of the team during Port-Access operations. General anesthesia is induced and a double-lumen endotracheal tube or a bronchial blocker is placed so that the left lung can be collapsed during harvesting of the left internal thoracic artery (LITA). With increasing experience in the mobilization of this vessel, routine single-lung ventilation has become less necessary. For patients undergoing valvular procedures, standard endotracheal intubation is performed. Following induction of anesthesia, special catheters are placed percutaneously via the right internal jugular vein. The first is the endovascular coronary sinus catheter, which is advanced into the mid portion of the coronary sinus under fluoroscopic guidance. This catheter is used to deliver retrograde cardioplegia, which is critical for more complex multivessel procedures and valve operations. The second catheter is the endovascular pulmonary vent, which is similarly placed in select patients. This catheter is used to decompress the heart and to help keep the operative field dry. It is placed fluoroscopically, using a balloon flotation technique similar to that used to place a Swan-Ganz catheter.

The anesthesiologist maintains primary responsibility for patient monitoring, which is critical during Port-Access surgery since the entire heart and many of the devices are not immediately visible to the surgeon. Bilateral radial arterial lines are usually placed. Because an endoaortic balloon is used to occlude the ascending aorta, and because proximal or distal migration could produce either aortic insufficiency or innominate artery occlusion with decreased cerebral blood flow, bilateral radial monitoring provides an easy method of detecting balloon migration. The pressures in the radial arterial lines should remain equal throughout the clamp time. If the pressure in the right radial artery drops compared with the pressure in the left radial artery, this may indicate movement of the balloon endoclamp with occlusion of the innominate artery, and repositioning of the endoaortic clamp may be necessary. In most cases, the balloon clamp can also be visualized or palpated to confirm its position.

Transesophageal echocardiography (TEE) is routinely performed in every patient and is a critical part of the monitoring. The aorta is first carefully evaluated for mobile intraluminal atheromatous disease, because this would preclude passage of the endoaortic clamp. The TEE is then used to assess proper placement of the intracardiac venous drainage catheter and the intra-aortic balloon endoclamp. The combination of visual and manual examination, continuous bilateral upper extremity blood pressure recording, and

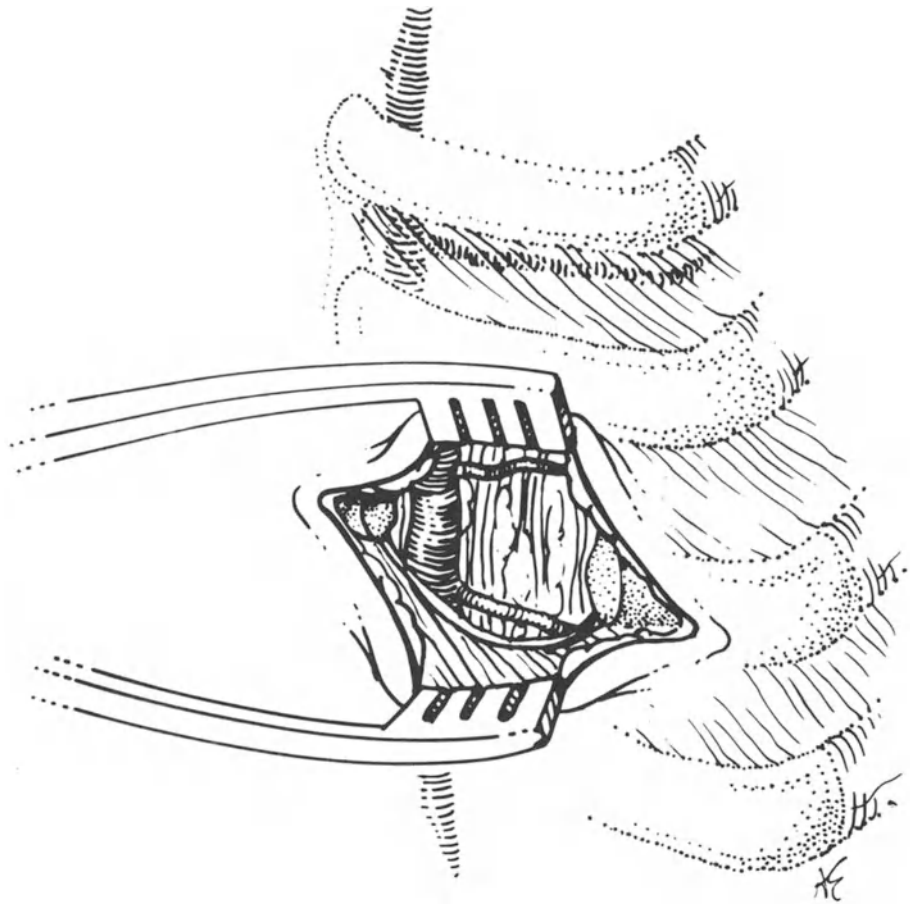

Fig. 1. Diagram of a small left anterior thoracotomy. The fourth costal cartilage is removed, exposing the LITA immediately below.

constant echocardiography ensure that optimal endoaortic balloon clamp position is maintained. In addition to these measurements, the anesthesiologist must carefully follow intraballoon occlusion pressure, proximal aortic root pressure, coronary sinus pressure and EKG activity.

Incisions and Conduits for CABG

A small left (or right) anterior thoracotomy (5–8 cm) is made in the inframammary skin fold and the fourth costal cartilage is usually removed, exposing the LITA (Fig. 1). This approach is virtually identical to that used in MIDCAB beating heart procedures. The left lung is deflated to maximize exposure and the LITA is mobilized as a pedicle with the accompanying veins. Using a specially designed chest retractor, direct visualization is usually adequate for complete mobilization of the LITA proximally to the first interspace. In our experience, the thoracoscope has not been helpful in taking down the LITA and

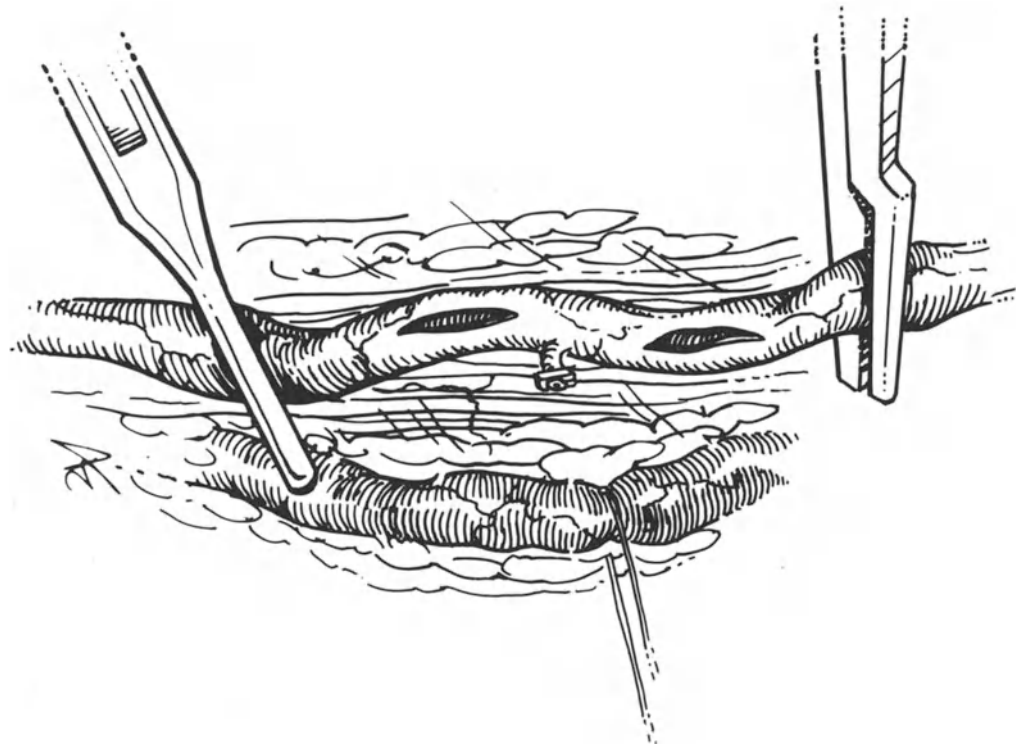

Fig. 2. Diagram of the mid portion of the LITA, which is utilized as the source of inflow for additional conduits. Initially the LITA is not divided but is occluded proximally and distally. For each proximal anastomosis, a 3- to 4-mm longitudinal incision is made in the lateral surface of the LITA.

is unnecessary for achieving good mammary length. Specifically designed angled instruments, forceps, clip appliers, and scissors aid in the dissection. Distal mobilization is possible to below the fifth rib.

Radial artery conduits or segments of saphenous vein are harvested in standard fashion. Papaverine-soaked gauze pads should be kept on most of the radial artery while it is being dissected and mobilized, and the vessel is gently distended with dilute papaverine after removal. This precaution in combination with the liberal use of intravenous calcium-channel blockers may decrease the tendency for spasm *(9)*.

Proximal Anastomoses for Multivessel Bypass

After conduit harvesting is complete, the proximal anastomoses are performed. At present, the mid portion of the LITA is usually utilized as the source of inflow (Fig. 2). Alternatively, proximal grafts can be brought in a standard fashion off the ascending aorta. Full systemic heparinization with 3 to 4 mg/kg of heparin is instituted. The LITA is not divided initially, but is occluded proximally and distally, since it is well positioned on the anterior chest wall directly in front of the surgeon. For each proximal anastomosis,

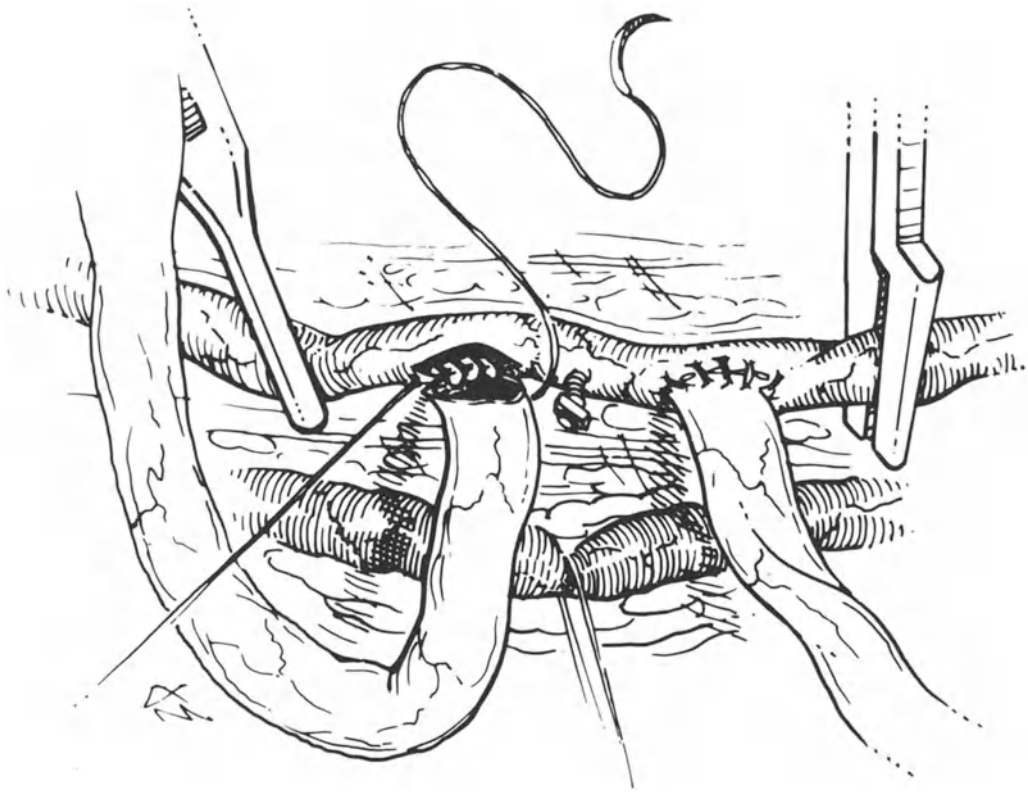

Fig. 3. Diagram of the anastomoses between the LITA and additional conduits, which are performed with continuous 8–0 Prolene suture. Depending on the size and flow characteristics of the LITA, one or two "Y" grafts with either vein or radial artery can originate from the LITA in this fashion.

a 3- to 4-mm longitudinal incision is made in the lateral surface of the LITA with a #11 blade and small fine scissors. The slightly beveled end-to-side anastomosis is performed with continuous 8–0 Prolene suture (Fig. 3). Depending on the size and flow characteristics of the LITA, one or two "Y" grafts, with either vein or radial artery, can originate from the LITA in this manner.

More recently most proximal anastomoses have originated from the ascending aorta. These are performed on CPB with the heart decompressed. The aorta is mobilized into the field with pericardial sutures. A partial occlusion clamp is placed, and anastomoses are performed in the standard fashion.

Endovascular CPB and Endoaortic Clamp System

A 2–3-cm transverse groin incision is made just below the inguinal skin crease overlying the femoral vessels. Proximal and distal control of the common femoral vessels is

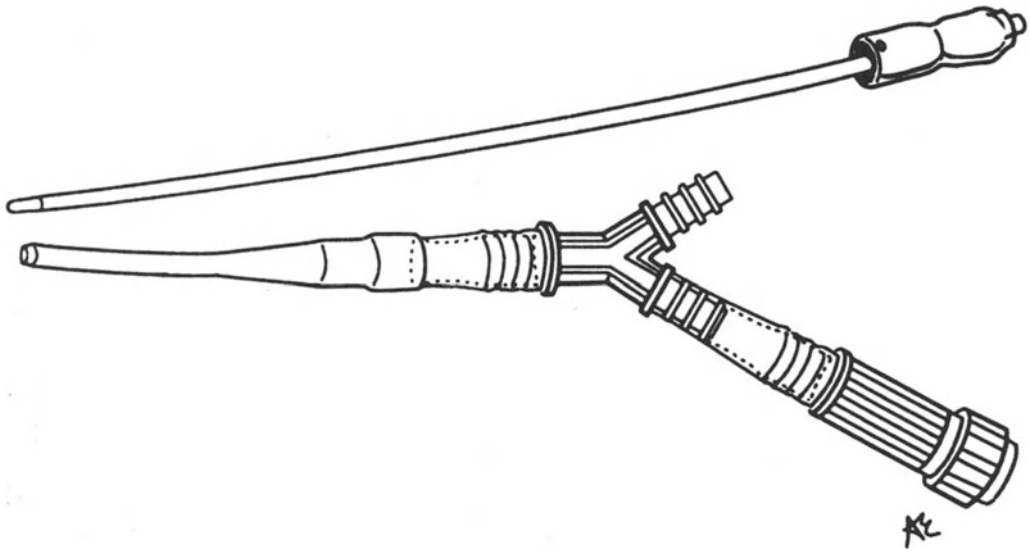

Fig. 4. Illustration of the dual-port endoarterial return cannula with its obturator. The cannula is inserted into the femoral artery over a guide wire. One port is used for peripheral CPB and the other to introduce the endoaortic clamp.

obtained. Under fluoroscopic or echocardiographic guidance, a long venous cannula (DLP, Medtronic, Minneapolis, MN; size 28 or 23 French) is passed from the femoral vein into the right atrium, with the distal tip positioned in the superior vena cava. The venous cannula is then connected to a centrifugal pump (Biomedicus, Medtronic) to enhance venous drainage. This is a very efficient system that results in a well-decompressed heart and a dry surgical field. The common femoral artery is then cannulated with a dual-port arterial return cannula (Heartport). These cannulae are available in 21 and 23 French sizes (Fig. 4) and are inserted using the Seldinger technique to be certain that the cannula passes easily and atraumatically without obstruction or resistance. This safeguard is thought to minimize the risk of aortic dissection that is associated with retrograde femoral perfusion. For this reason, significant peripheral vascular occlusive disease is a relative contraindication to the use of this system. Once placed, the arterial return cannula is secured to the patient to ensure stability during CPB.

The second limb of the arterial return cannula has a hemostatic valve. The endoaortic clamp (Fig. 5) is passed through this limb. Again, a Seldinger technique is used, passing a flexible guide wire into the descending aorta initially and eventually positioning the guide wire and endoclamp in the ascending aorta approx 3 cm above the aortic valve under fluoroscopic or echocardiographic guidance. As our experience has evolved, we have increasingly relied on the TEE solely. If the guide wire or endoclamp cannot be passed owing to occlusive disease, the Port-Access approach should be abandoned because persistant attempts at retrograde perfusion in this situation may result in a fatal aortic dissection. When these circumstances arise, it is safer to extend the incision across the sternum for central cannulation.

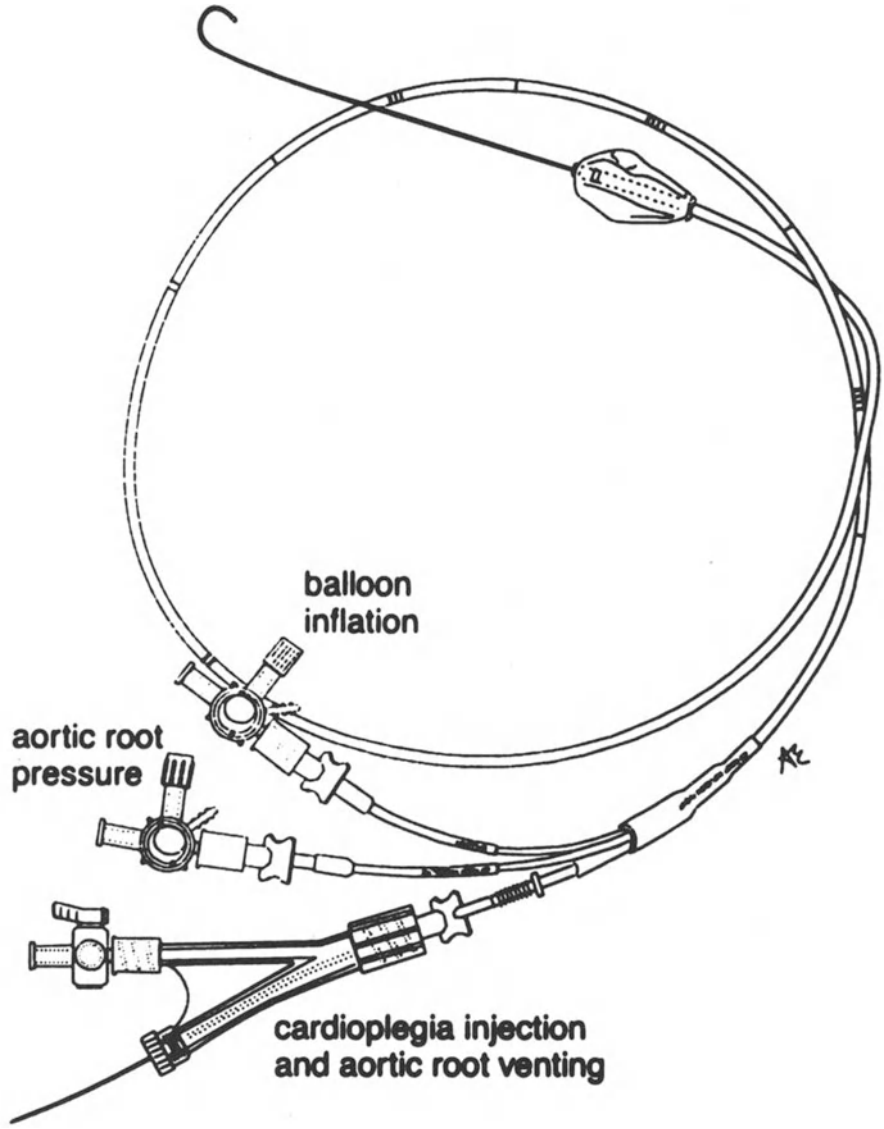

Fig. 5. Endoclamp. One lumen is used to inflate the balloon and occlude the aorta. A second lumen is used to measure the aortic root pressure. A third lumen is used to deliver antegrade cardioplegia when indicated. The latter lumen can also be connected to suction in order to vent the aortic root. In addition, the guide wire used for insertion of the endoaortic clamp is passed through this lumen.

Myocardial Protection

After cannulae placement is completed, CPB is instituted and the temperature is lowered to between 25 and 30°C. Subsequently, the endoaortic clamp is inflated, confirming its position just above the sinotubular junction by TEE. All gradient must be removed from the heart so that ejection of blood from the left ventricle does not cause the endoclamp to migrate distally. Usually 20–30 mL of saline inflation of the endoclamp balloon is

required to occlude the aorta, aiming for a balloon pressure of approx 250–350 mmHg. After occluding the aorta, the heart is arrested with either antegrade (through the endoclamp proximal sideport) or retrograde (through the percutaneous coronary sinus catheter) cold blood cardioplegia. For single-vessel bypass procedures with an intact aortic valve, antegrade cardioplegia is adequate, whereas for more complex operations or for patients with aortic insufficiency, retrograde cardioplegia may be preferable. Repeat injections are given after each distal anastomosis. With this regimen, myocardial protection has been optimal, and results have paralleled the excellent results obtained in our laboratory experience *(6)*.

Coronary Artery Bypass Technique

With the heart empty on CPB, the coronary arteries are marked for grafting. There is usually little difficulty in reaching coronary vessels on both the lateral and inferior walls through this incision while the heart is decompressed on CPB. If proximals are to be taken off the ascending aorta, there are performed first. The LITA is divided and the length needed to reach its proposed position on the LAD artery is determined. The LITA is also ideal for a sequential graft to a diagonal branch, if necessary. The length needed for the other conduits to reach distal anastomotic sites is now determined. Overall graft length is much shorter than usual if the conduits originate from the LITA. Determining the appropriate length of the radial artery is less critical than determining the length of the vein, since the radial artery has a muscular wall and does not tend to kink as does the vein. If anything, a little extra length should be left on the radial artery. Once the heart is arrested and protected, the distal coronary anastomoses can be accomplished in the usual manner. The most distal bypasses are performed first (i.e., inferior wall before lateral wall before anterior wall). We generally use a standard anastomotic technique of continuous 7–0 or 8–0 Prolene. One advantage of the cardioplegic arrest with this system is that anastomotic techniques do not need to be modified. Cardioplegia is given after each anastomosis, and warming is begun prior to starting the last distal graft. The anastomoses are carefully examined for hemostasis while the heart remains arrested and immediately after unclamping while still on bypass.

When all distal grafts have been completed, the balloon endoclamp is deflated and the heart is reperfused. Rewarming is completed and the patient is weaned from CPB. The endoclamp and the femoral venous and arterial cannulas are removed, and the femoral vessels are repaired. Protamine is infused to reverse the heparin. A temporary ventricular pacing electrode remains on the right ventricle, a single pleural chest tube is placed, and the thoracotomy and groin incisions are closed.

PATIENT SELECTION

Most patients with single- or multivessel disease are considered candidates for Port-Access CABG. Aortic insufficiency is not a contraindication to Port-Access CABG, since retrograde cardioplegia can be used, and the aortic root can be vented throughout

the procedure. Similarly, age *per se* is not a contraindication, although severe peripheral vascular disease (PVD) and intraluminal atherosclerosis involving the aortic arch or upper descending thoracic aorta are contraindications. Initial screening for PVD is based on history and physical examination. If PVD is suspected, a distal aortogram with runoffs is performed during cardiac catheterization to assess the iliofemoral circulation. Intraoperative TEE is used to screen for significant intraluminal atheromatous disease in the thoracic aorta. The surgeon should be aware of significant PVD or arch atheromatous disease prior to opening the chest and, if such disease is present, must consider whether to convert to a beating heart or a standard sternotomy approach.

RESULTS

During the first 12 mo of the NYU experience with Port-Access surgery, 49 patients underwent minimally invasive Port-Access CABG. Mean age was 60 yr (range 34–82). Sixteen patients underwent single bypass, and 37 patients underwent multivessel bypass. Early in the experience, the majority of operations were single bypasses, but more recently, most operations were multivessel revascularizations. All but one patient received a graft to the LAD artery. The radial artery (n = l0) and saphenous vein (n = 20) were used when additional conduits were needed for multivessel disease; the LITA served as the site for the proximal anastomosis during the first 6 mo and now more often proximals are brought off the ascending aorta. Sequential grafts were used in five cases. Coronary arteries that were bypassed included the LAD (n = 48), diagonal (n = 14), obtuse marginal (n = 14), posterolateral (n = 3), posterior descending artery (PDA) (n = 5), and right coronary (n = 8). One additional patient had a planned two-vessel Port-Access procedure, but was converted to a beating heart single-vessel bypass to the LAD when significant PVD was encountered intraoperatively. Conversion to sternotomy was not required in any case.

There were no deaths, strokes, or myocardial infarctions. Complications included one early reoperation for pulmonary embolus and graft revision to include an additional graft to a nonbypassed vessel. Two patients required angioplasty. Four patients required reoperations for bleeding or tamponade.

Post operative angiograms were performed in 42 of 49 patients (86%), revealing 100% anastomotic patency of the LITA to LAD (LITA-LAD) anastomosis and an overall graft patency rate of 96%. Three patients were found to have significant spasm in the radial artery graft, which responded to an infusion of intracoronary nitroglycerin and intravenous Cardizem. The median hospital stay was 5 d, and the average length of time required to return to full activity was approx 3 wk.

DISCUSSION

Minimally invasive cardiac surgery represents a significant change in the way cardiac surgeons approach heart disease. The basic premise is that by working through a smaller incision, the patient will experience less pain, have a shorter hospitalization, and have a

quicker overall recovery. Certainly if minimally invasive cardiac surgery is to be widely applicable, the operation must be as safe and efficacious as standard procedures performed through a median sternotomy. The Port-Access approach with full CPB, endovascular aortic occlusion, and cardioplegia delivery allows the surgeon to use standard anastomotic techniques on a still, protected heart. Because the distal anastomotic technique is not changed, this approach should presumably achieve patency results that are similar to open-chest methods, if patients are selected appropriately. The early data from our institution and elsewhere are very encouraging with anastomotic patency rates of >96%, which is significantly higher than the reported patency rates with beating heart procedures. In our hands, the patency rate of LITA-LAD anastomoses has been 100% thus far. In addition, minimally invasive bypass grafting can be used in a significant number of patients with multivessel disease using the system and the techniques described previously.

Ultimately, the goals of minimally invasive heart surgery are less trauma and pain for the patient, shorter hospital stay, and quicker recovery time, while providing an operation that is as safe and effective as conventional surgery. The early results with the Port-Access technique suggest that these goals can be achieved with this system. As minimally invasive cardiac surgery becomes widely available, it can be expected that this and other techniques will be greatly refined, and that minimally invasive surgery will become increasingly applicable to a wide range of cardiac surgical patients.

REFERENCES

1. Calafiore AM, DiGiammarco G, Teodori G, et al. Left anterior descending coronary artery grafting via left anterior small thoracotomy without cardiopulmonary bypass. Ann Thorac Surg 1996;61:1658–1665.
2. Subramanian VA, Sani G, Benetti FJ, et al. Minimally invasive coronary bypass surgery: a multi-center report of preliminary clinical experience. Circulation 1995;(Suppl)92:I-645.
3. Subramanian VA. Clinical experience with minimally invasive reoperative coronary bypass surgery. Eur J Cardiothorac Surg, in press.
4. Landreneau RJ, Mack MJ, Magovern JA, et al. "Keyhole" coronary artery bypass surgery. Ann Surg 1996;224:453–462.
5. Stevens JH, Burdon TA, Peters WS, et al. Port-access coronary artery bypass grafting: a proposed surgical method. J Thorac Cardiovasc Surg 1996;111:567–573.
6. Schwartz DS, Ribakove GH, Grossi EA, et al. Minimally invasive cardiopulmonary bypass with cardioplegic arrest: a closed chest technique with equivalent myocardial protection. J Thorac Cardiovasc Surg 1996;111:556–566.
7. Stevens JH, Burdon TA, Siegel LC, et al. Port-access coronary artery bypass with cardioplegic arrest: acute and chronic canine studies. Ann Thorac Surg 1996;62:435–441.
8. Schwartz DS, Ribakove GH, Grossi EA, et al. Multi-vessel port-access coronary artery bypass grafting with cardioplegic arrest: technique and reproducibility. J Thorac Cardiovasc Surg 1997;114:46.
9. Reyes AT, Frame R, Brodman RF. Technique for harvesting the radial artery as a coronary artery bypass graft. Ann Thorac Surg 1995;59:118–126.

11 Minimally Invasive Saphenous Vein Harvest

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and Michael Gardocki, PA

CONTENTS

INTRODUCTION

The enthusiasm for minimally invasive procedures has extended to include the development of new techniques and instrumentation for saphenous vein harvest. The methods for subcutaneous endoscopic surgery have been widely applied in plastic surgery and the feasibility of performing such procedures through small incisions in remote subcutaneous planes has been clearly demonstrated *(1)*. The concept of smaller, more cosmetic incisions, less subcutaneous dissection, and reduced postoperative pain has broad appeal among both patients and health care providers. Although experience with minimally invasive saphenous vein harvest is still limited and short-term reports are just beginning to appear in the literature, many centers are now utilizing these methods. The techniques and instruments share a set of basic concepts for atraumatic vein harvest and are based either on video endoscopy or direct visualization through multiple small incisions. In this chapter, we present a synopsis of the techniques and principles of minimally invasive saphenous vein harvest.

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

THE NEED FOR AN ALTERNATIVE APPROACH

The most frequent approach to the saphenous vein is through a long, continuous medial skin incision with either scissors or a scalpel. Alternatively, the vein can be harvested through multiple smaller incisions, leaving intact bridges of skin in between. Delayed wound healing associated with cellulitis, lymphangitis, edema, and inflammation is common in patients undergoing saphenous vein excision *(2–4)*. In the prevention of harvest site complications, proper selection of the donor extremity, meticulous closure of all layers, and avoidance of large skin flaps are important factors *(5–6)*. Adherence to these recommendations has decreased the incidence of major wound complications to <1% *(7)*. However, minor complications are much more common, especially if strict criteria are used. Utley et al. *(8)* reported impaired wound healing in 24% of 1047 patients. In this group, impaired healing included cases of mild inflammation, drainage, erythema, or tenderness along the wound edge. Persistent lymphorrhea *(9)* and chronic limb swelling secondary to unavoidable division of intradermal lymphatic channels are also associated with extensive skin incisions *(10)*. In addition, leg pain, dermatitis, and recurrent cellulitis can occur with saphenous nerve injury *(2,11–12)*. Although the incidence of major complications is low, these problems can be devastating in patients with existing peripheral vascular disease (PVD). Skin separation, nonhealing ulcers, progressive wound gangrene, and severe soft tissue infections have significant associated morbidity. These complications require aggressive wound care, additional peripheral revascularization, or, in rare cases, amputation *(13–14)*. Furthermore, wound complications, however defined, most certainly affect the ability to ambulate and return to employment, parameters that are frequently unrecognized and are poorly reported in the literature.

MINIMALLY INVASIVE SAPHENECTOMY: BASIC CONCEPTS

Isolation of the Vein

Current approaches to the saphenous vein involve creation of a 2–3 cm incision directly over the vein in either the transverse or longitudinal direction. Dissection is carried down to the vein using standard instruments, and the vein is encircled. The vein is then harvested under direct vision as far as it is possible through this small opening. Once the limit of dissection has been reached, the remainder of the procedure is carried out by instruments designed to allow visualization of the vein and its branches through a limited number of skin incisions or without any other additional incisions, depending on the approach used.

Creation of Working Space

Unlike the minimally invasive approaches in the abdomen and thorax where cavities naturally exist permitting the introduction and manipulation of instruments, minimally invasive subcutaneous saphenous vein harvest requires the expansion of a potential space. Indeed, creation of a working space for visualization and careful dissection

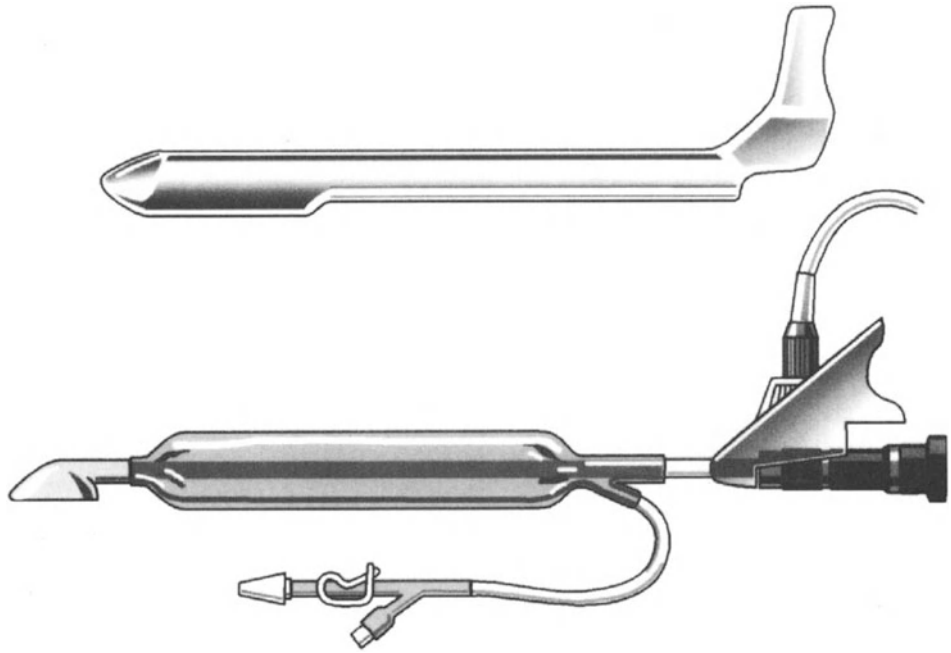

Fig. 1. SAPHtrak (GSI).

mandates the development and maintenance of a cavity separating the vein from the overlying subcutaneous tissues.

This space is generally created bluntly anterior to the vein either by digital dissection, by use of a specially designed long inflatable balloon (SAPHtrak™ , or SAPHfinder™, GSI, Cupertino, CA) (Fig. 1), or by use of a balloon that is sequentially inflated and deflated under direct endoscopic vision as the scope is advanced over the vein (VasoView™, Origin Medsystems, Menlo Park, CA) (Fig. 2). Alternatively, a blunt-tip, transparent dissector mounted on an endoscope that allows this space to be created as the endoscope is advanced with gentle forward motion is commercially available (ENDOPATH Subcu-Dissector™, Ethicon Endo-Surgery, Cincinnati, OH) (Fig. 3). Since there are very few branches rising anterior to the saphenous vein, this dissection is relatively easy and progresses rapidly. Other sequential cutaneous incisions at various intervals can be of aid by allowing this dissection to be performed in the reverse direction. For dissections in the distal thigh that cross the knee, the common presence of a few anterior genicular branches often requires a separate counter incision so that this segment can be mobilized under direct vision using standard open techniques.

Maintenance of Working Space

Once the tunnel has been created, a variety of available mechanical devices can be used to retract the skin and overlying subcutaneous tissues to allow the vein to fall posteriorly. In all cases, it is critical to maintain an adequate working space for manipulation of

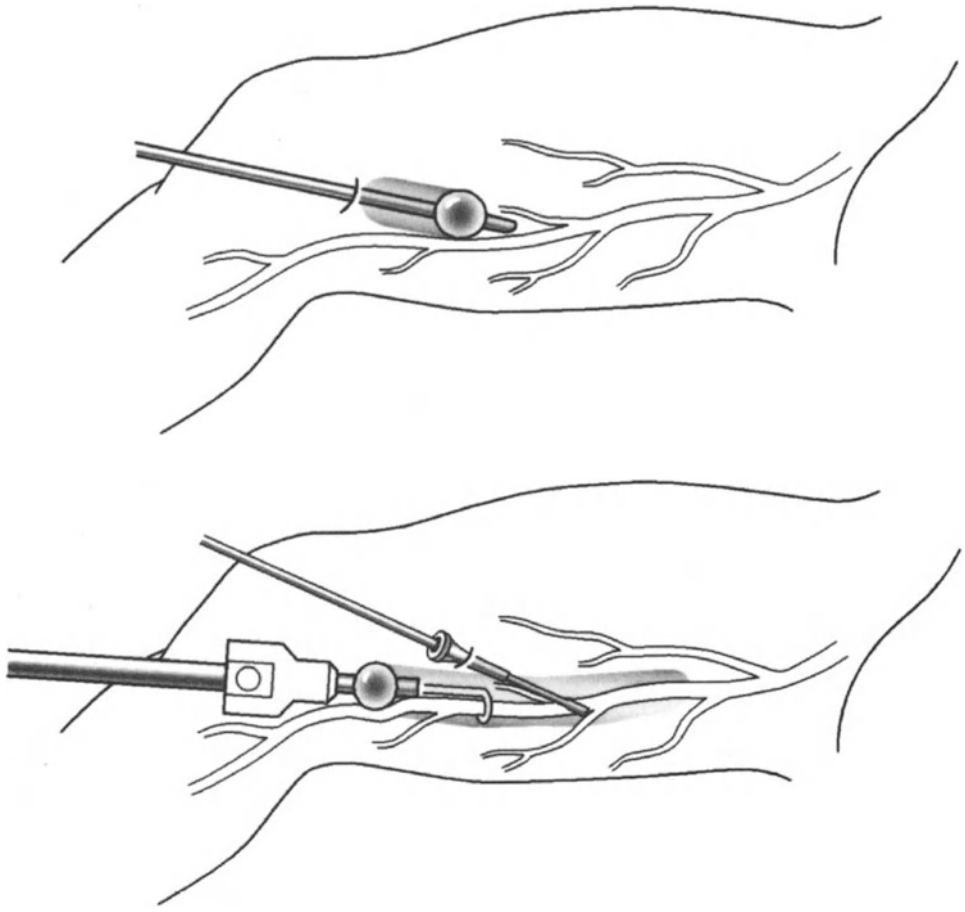

Fig. 2. Vasoview (Origin Medsystems).

instruments so that the dissection can proceed atraumatically with visualization and ligation of side branches within the tunnel.

Maintenance of the working space can be accomplished with a standard mediastinoscope or a rigid, specially designed instrument that allows anterior traction on the overlying soft tissues. In these cases, visualization is only limited by the length of the instrument and the elasticity of the tissues. The VasoView System™ (Origin Medsystems) is the only system that requires the creation of an airtight tunnel that is subsequently insufflated with CO_2 gas. This most closely resembles the techniques currently used in laparoscopic procedures. With this system, additional instruments for dissection and ligation require introducing instruments through trocars placed via separate stab incisions.

Light Source

In all cases, a good fiberoptic light source is needed to adequately illuminate the tunnel and permit visualization of the side branches and the greater saphenous nerve, which lie in close proximity. The light source is either mounted directly on the retractor or is

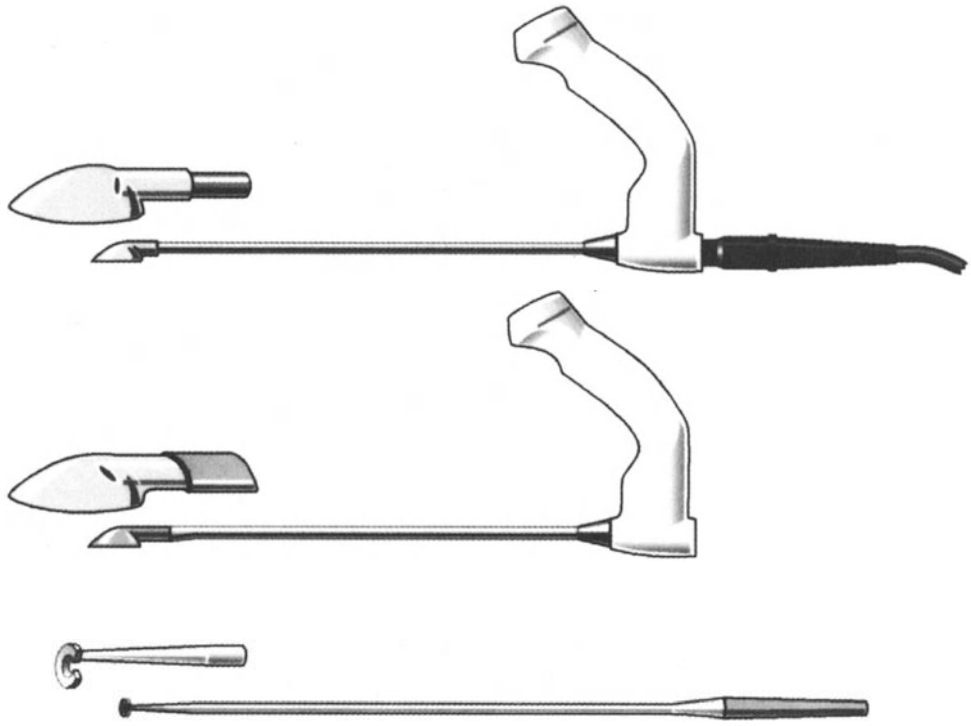

Fig. 3. Special instruments designed for saphenous vein dissection (ENDOPATH Subcu-Dissector, Ethicon Endo-Surgery).

otherwise an integral component of an advancing endoscope so that maximal illumination is present at the leading edge of dissection.

Dissection of Vein and Ligation of Side Branches

Dissection of the vein is generally carried out with a variety of long, blunt V-shaped or U-shaped instruments (Fig. 3). With these instruments, gentle dissection of subcutaneous tissues proceeds until either a branch is identified or resistance is met, suggesting a potential branch point. Bipolar electrocautery or endoscopic clips are then applied 1–2 mm away from the main trunk to prevent damage. The branch is then divided with endoscopic scissors. In addition to aiding the dissection, these instruments can be used to apply traction on the vein to one side or the other, thereby facilitating visualization of the side branches.

CLINICAL EXPERIENCE WITH MINIMALLY INVASIVE VEIN HARVEST

Reports in the literature are just emerging as more centers gain experience with minimally invasive techniques *(15–18)*. One limitation to all reported series has been the small number of patients in whom these approaches have been used. In addition, follow-up is limited, which is important in establishing that the veins are indeed har-

vested atraumatically. For these techniques to be developed universally, the patency of the venous bypass must be shown to be at least equivalent to those removed by standard open surgery. Nonetheless, these reports uniformly emphasize that minimally invasive saphenectomy is feasible with no added immediate morbidity.

Lumsden and colleagues *(16)* described the technique of saphenous vein harvest in 30 patients undergoing lower extremity peripheral bypass. In all cases, the procedure was performed using a 10-mm laparoscope with a handheld retractor. The saphenous vein was harvested from the thighs, legs, or both. The number of incisions used depended on the reach of the retractor blades and the length of vein needed. The average length of vein harvested was 42 cm, with a mean time of 1.25 h. Minimal postoperative discomfort was reported by the patients, although this was not assessed quantitatively. In two patients, wound complications occurred. One patient had a 2×3 cm area of skin necrosis, and the other developed a small blister over the harvest tunnel. Lumsden and colleagues believed that both complications were secondary to conduction by electrocautery used during the harvest, and did not experience any further complications with bipolar electrocautery.

More recently, Tevaerai et al. *(17)* reported the results of a prospective randomized study comparing minimally invasive saphenectomy to the standard open technique in 30 patients undergoing coronary revascularization. Their technique involved multiple skin incisions along the leg, placement of a retractor (Mini Harvest System, United States Surgical Corporation, Norwalk, CT) (Fig. 4), and dissection under direct vision. Using this system, 6–8 cm of vein could be harvested through each incision. They report that the incidence of hematoma and edema were reduced in the less invasive group, that none of the patients had a wound complication, and that none of the patients expressed pain 7 d after the procedure. By contrast, in the open group, one patient developed local skin necrosis and another had a large skin dehiscence. In both groups, the quality of vein was judged to be good (87% in the minimally invasive group vs 93% in the open group, p = NS). The time required for vein harvest was not reported, although in all cases, the vein had been excised and prepared before starting cardiopulmonary bypass.

Finally, Allen and Shaar *(18)* recently reported on their experience in 30 consecutive patients who underwent saphenectomy using a video-endoscopic technique. Although pain, edema, and wound complications were not evaluated prospectively, in all cases the technique proved to be feasible. Most impressive was the reduction in time from 1.5–2 h to 35–45 min after the first eight patients. Also, the number of necessary incisions decreased from the initial three to four, to one or two in the last 15 patients.

EXPERIENCE AT COLUMBIA-PRESBYTERIAN MEDICAL CENTER

Method

To date, 38 patients have undergone minimally invasive saphenous vein harvest at our institution. In 28 of these patients, the saphenous vein was harvested by minimally invasive techniques in one leg and open standard technique in the other leg, to serve as an internal control. In all patients, the greater saphenous vein was identified and cleared of

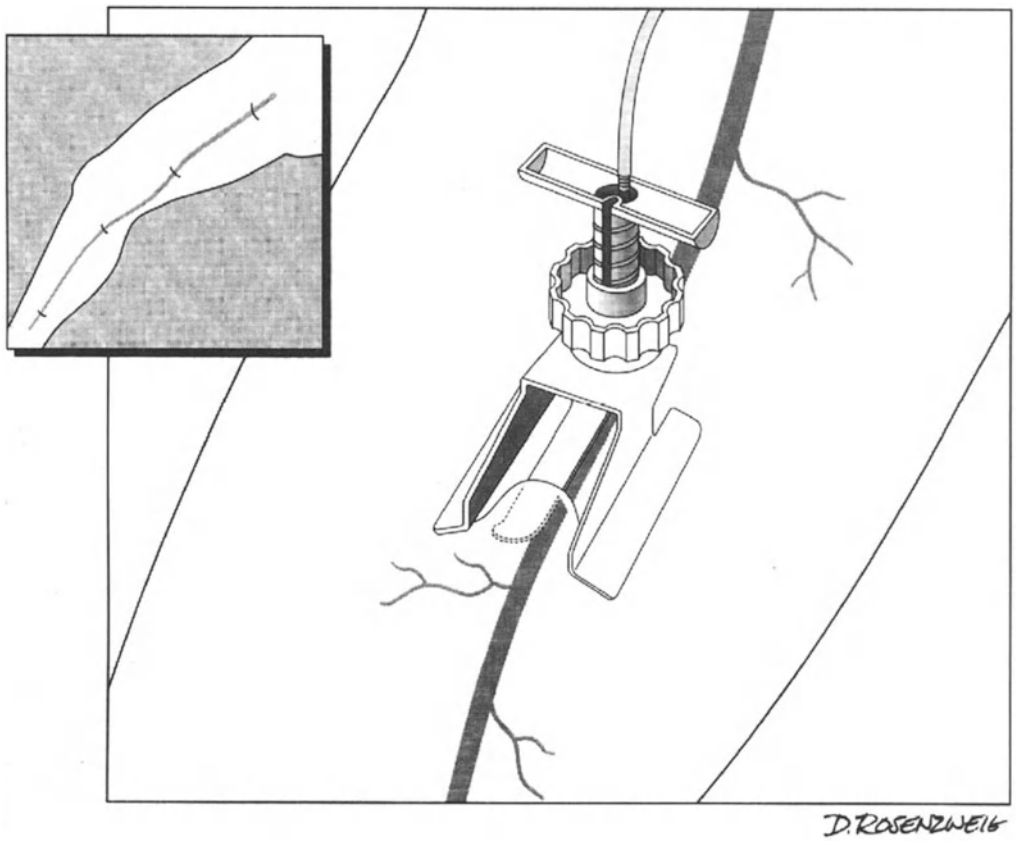

Fig. 4. Mini Harvest System (United States Surgical Corporation).

all adventitia and connective tissue under direct vision. A vessel loop was placed around the vein and the posterior space was enlarged with blunt Metzenbaum scissors. We primarily used the Mini Harvest System because it combines a number of features that facilitate dissection. This instrument can be stabilized on the leg and is equipped with a fixed, fiberoptic, light source. Once an anterior tunnel is created by blunt digital dissection, the prongs are inserted through the incision, allowing anterior traction and adequate visualization of the tunnel at all times. The adventitia along the sides of the vein is dissected using Metzenbaum scissors or a closed-neck blunt dissector. This dissector can be gently pushed alongside the vein separating the subcutaneous tissues. At branch points, the tissue plane does not separate with ease, allowing for ready identification of branches, which are clipped. Caution is used during the entire procedure to avoid damage to the saphenous nerve. A second 2-cm incision is made once the limit of exposure by the retractor is reached. After obtaining the desired length of vein, the same procedure is repeated in the reverse direction. In general, we have found the dissection to be easier if it is performed in the thigh rather than the lower leg. If the desired length of vein is >18 cm, we have found that making additional incisions at approx 10-cm intervals reduces the

amount of time required to harvest the vein. Once the entire length is dissected, the ends are ligated, the vein is removed and inspected, and open, side branches are ligated. At this time, any excessive adventitia that may still be attached to the vein can also be excised. The wound is then irrigated and checked for hemostasis. A medium-sized hemovac may be inserted throughout the length of the incision, if there is evidence of excessive bleeding. The incisions are closed with two layers of absorbable suture, and the legs are wrapped with elastic bandage.

RESULTS

Of the 38 patients, 28 were males. Ages ranged from 37–81 yr, with a mean of 64 ± 7 yr. Hypertension was present in 70%, diabetes in 32%, and PVD in 13% of the patients. None of the patients had undergone previous lower extremity revascularizations. Length of harvested vein ranged from 16–40 cm, with a mean of 30 ± 6 cm. In all cases, the vein was successfully harvested using the described technique, and no conversion to "open" was necessary. Harvest time ranged from 18–44 min, with a mean of 29 ± 5 min. No wound complications occurred, and at 6 wk follow-up, all incisions had healed well with good cosmetic result (Fig. 5). No electrocardiographic or enzymatic evidence of perioperative myocardial infarction was observed. Pain and edema evaluated by visual analog scale on postoperative d 5 was significantly reduced in all extremities in which minimal access techniques had been used ($p < 0.05$). In the subgroup with bilateral leg incisions comparing open to minimal techniques ($n = 28$), pain intensity and satisfaction were similarly improved for the latter group ($p < 0.05$).

ADVANTAGES AND LIMITATIONS

Proponents of minimally invasive saphenectomy advocate that the reduced number of skin incisions and less subcutaneous dissection translate into less pain, fewer wound complications, and earlier hospital discharge and patient ambulation. As mentioned previously, the reported results from different centers have only been in a limited number of patients with short-term follow-up. Preliminary results suggest that pain control is better, that quality of vein (by gross inspection) is adequate, and that a better cosmetic result can be obtained. However, given the relatively low incidence of major wound complications, a large number of patients must undergo this procedure before firm conclusions can be established regarding wound morbidity, earlier discharge, and ambulation. Nevertheless, present reports suggest that minimally invasive saphenectomy is feasible and can be accomplished in a reasonable time without any additional immediate morbidity.

Factors against the possibility of the many benefits of this approach are the limitations that accompany it and the questions that still surround these procedures. As yet unsettled is whether the actual number of skin incisions is important. Should the procedure be done under direct vision with long skin bridges, or should the entire dissection be performed

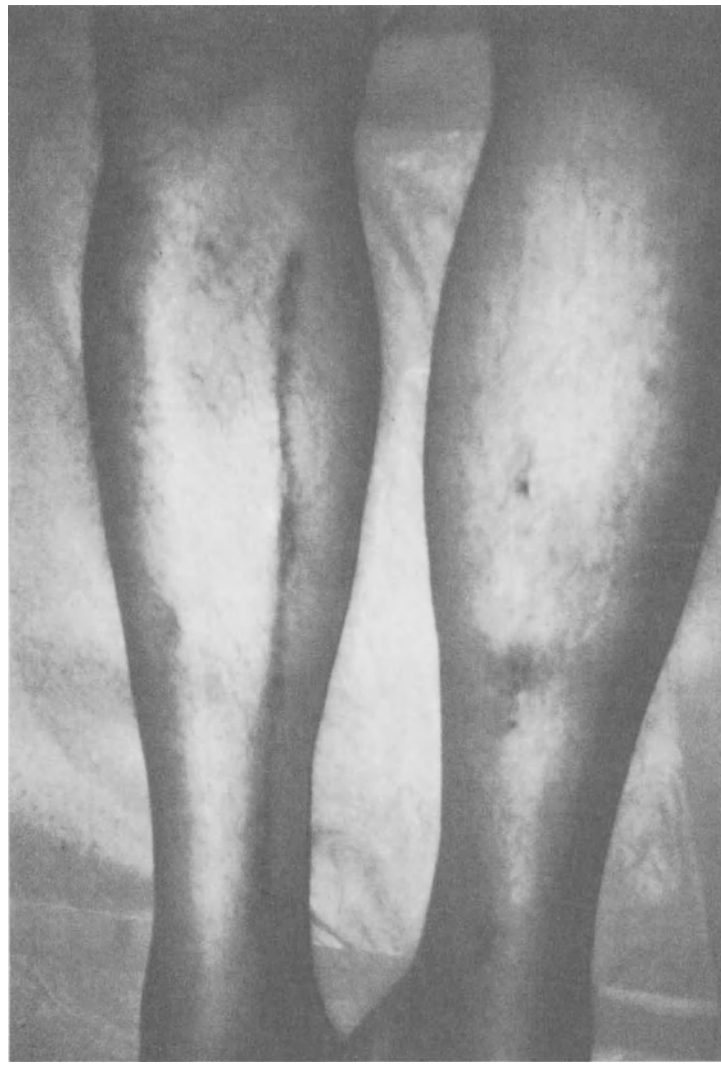

Fig. 5. Lower extremities, 6 wk postoperatively. The right leg saphenous vein was harvested using conventional techniques. The left lower extremity vein was harvested with minimally invasive techniques.

endoscopically with one or two incisions? If performed endoscopically, as with any new technique, it will require personnel training, and because the procedure is technically difficult, a learning curve will be necessary. Also, the harvest times are usually longer and depend on the expertise of the individual performing the procedure. In addition, endoscopic approaches require the presence of a video endoscope and/or gas for insufflation. This additional equipment may not be cost-effective because the operation can be performed with standard instruments available in all operating rooms. Furthermore, extra equipment requires more operating room space.

CONCLUSION

At present, it is unclear whether the techniques of minimally invasive saphenous vein harvest are associated with a lower rate of wound complications. We emphasize that this is a technique in evolution and as with other new procedures, it is associated with a learning curve. Improvements in surgical instrumentation and greater experience has made this approach to saphenectomy a feasible option. The superior cosmetic results, less perioperative pain, and patient satisfaction make it a desirable addition to the cardiac surgery armamentarium, but before widespread application of these techniques is adapted, long-term angiographic evaluation of these veins must be performed. The potential wide application of these approaches ultimately will be determined by the balance between reduced morbidity and patient satisfaction and the additional associated cost.

REFERENCES

1. Bostwick J, Eaves FF, Nahai F. Endoscopic Plastic Surgery. Quality Medical, St. Louis, MO, 1995, pp. 535–547.
2. Baddour LM, Bisno AL. Recurrent cellulitis after coronary bypass surgery. JAMA 1:1049–1052.
3. Baddour LM. Delayed soft tissue infections in saphenous venectomy limbs of coronary bypass patients. Infect Surg 1985;l:243–250.
4. Greenberg J, Descantis RW, Mills RM. Vein donor leg cellulitis after coronary artery surgery. Ann Intern Med 1982;97:565–566.
5. Scher LA, Samson RH, Ketosugbo A, Gupta SK, Ascer E, Veith FJ. Prevention and management of ischemic complications of vein harvest incisions in cardiac surgery—case reports. Angiology 1986;37:119–123.
6. Flemma RJ, Torpy SD. Complications of aortocoronary bypass grafting. In: Cordell AR, Ellison RG, eds. Complications of Intrathoracic Surgery. Little Brown, Boston, 1979, pp.167–168.
7. DeLaria GA, Hunter JA, Goldin MD, Serry C, Javid H, Najafi H. Leg wound complications associated with coronary revascularization. J Thorac Cardiovasc Surg 1981;1: 403–407.
8. Utley JR, Thomason ME, Wallace DJ, et al. Preoperative correlates of impaired wound healing after saphenous vein excision. J Thorac Cardiovasc Surg 1989;98:147–149.
9. Terada Y, Mitsui T, Gomi S, Kanemoto S. Lymphorrhea in the thigh after a saphenous vein harvest. Ann Thorac Surg 1996;62(6):1183 (letter).
10. Miller TA, Turk AE. The lymphatic system. In: Veith FJ, Hobson RW II, Williams RA, Wilson SE, eds. Vascular Surgery: Principles and Practice, 2nd ed. McGraw-Hill, New York, 1994, pp.933–934.
11. Carr RD, Rau RC. Dermatitis at vein graft site in coronary artery bypass patients. Arch Dermatol 1981;117:814–815.
12. Adar R, Meyer E, Zweig A. Saphenous neuralgia: a complication of vascular reconstructions below the knee. Ann Surg 1979;190:609–613.
13. Lavee J, Schneiderman J, Yorav S, Shewach-Millet M, Adar R. Complications of saphenous vein harvesting following coronary artery bypass surgery. J Cardiovasc Surg 1989;30: 989–991.
14. Lee KS, Reinstein L. Lower limb amputation of the donor site extremity after coronary artery bypass graft surgery. Arch Phys Med Rehabil 1986;67:564–565.

15. Cusimano RJ, Dale L, Butany JW. Minimally invasive cardiac surgery for removal of the greater saphenous vein. Can J Surg 1996;39(5):386–388.
16. Lumsden AB, Eaves EF III, Ofenloch JC, Jordan WD. Subcutaneous, video-assisted saphenous vein harvest: report of the first 30 cases. Cardiovasc Surg 1996;4(6):771–776.
17. Tevaerai HT, Mueller XM, Segesser LK. Minimally invasive harvest of saphenous vein for coronary artery bypass grafting. Ann Thorac Surg 1997;63:S119–S121.
18. Allen KB, Shaar CJ. Endoscopic saphenous vein harvesting. Ann Thorac Surg 1997; 64(1):265–266.

12 Alternative Approaches to Vascular Anastomosis Surgery

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Contents

INTRODUCTION

Irrespective of vessel size or specific technique, manual suturing remains the golden standard for the creation of vascular anastomosis. Successful creation of anastomosis, particularly in small vessels, requires a high level of skill, a long learning curve and a substantial amount of time. In addition, the insertion of transmural stitches, even by experienced hands using atraumatic techniques and fine sutures, causes significant damage to the vessel wall *(1,2)*. Suture placement results in exposure of the subendothelial matrix to the blood stream, setting up a nidus for thrombus formation. The same process occurs at the site of the anastomosis in the case of an end-to-end apposition. These thrombotic processes can potentially result in anastomotic obstruction, especially in small vessels. Because of these limitations, a continuous search for alternative methods to anastomose vessels has been at the forefront of vascular surgery and industry alike. The introduction of loupe and microscopic magnification and the development of microsurgical instruments and techniques *(3)*, however, have improved patency rates of small vessel anastomoses. These progresses in surgery have enabled revascularization procedures of the brain and distal limbs, free tissue transfer, replantation of digits, and coronary bypass surgery.

Early efforts to minimize vessel wall damage included the "sleeve" or telescope technique advanced by Murphy *(4)*. In this technique, the upstream vessel is placed inside the downstream vessel end and secured with two to four sutures that do not penetrate all

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

layers of the innermost vessel end *(5)*. Several studies have demonstrated equivalent patency rates when this technique was compared to conventional end-to-end techniques *(6)*. Moreover, this technique was associated with a reduction in operative time.

Although many efforts aimed at circumventing the problems inherent to manual suturing have been tried—including intra—or extraluminal ferrules- the clinical application of these techniques has been limited and disappointing. Renewed emphasis in the development of automatic, semiautomatic, or facilitated methods to create a vascular anastomosis has gained momentum with the recent advances in minimally invasive myocardial revascularization *(7,8)*. In this context, this chapter reviews the relevant anastomotic techniques that deviate from manual suturing. The idea of facilitating the anastomoses of tubelike structures is not unique to vascular surgery; thus, whenever relevant, a description of these devices is included.

In general, anastomotic techniques can be categorized as mechanical appliances, which can be further subdivided into stapling and coupling devices, and bonding techniques that aim to seal the anastomotic site and use glues or laser welding.

MECHANICAL APPLIANCES

Staplers

Staplers were introduced to clinical medicine in 1900s by Hütl *(9)*, a Hungarian surgeon who developed a stapling device to perform a distal gastrectomy. The device was able to insert two double rows of staples at a time, sealing both sides of the stomach, which thereafter could be divided in between the middle of the staple lines. The apparatus was heavy and difficult to use; however, it introduced a standard fashion of stapling that currently remains in practice: the points of the U-shaped staples were driven through the tissues, and as they met the anvil, they were forced to bend, thereby, transforming the staple into a B-shape *(10)*. Countless modifications have resulted in the disposable, easy-to-use systems currently available in gastrointestinal surgery.

In 1935, von Brucke *(11)* introduced an instrument for the serial placement of individual staples, similar to that in a paper stapler. A slight modification of this device was used in the 1960s in cardiac surgery to fixate prosthetic cardiac valves and close atriotomies, and in vascular surgery to close transverse arteriotomies *(12,13)*. Nevertheless, this instrument did not gain wide acceptance, most likely because suture technology had already made major progress and because the use of stitches was much cheaper, simpler and equally effective.

Androsov *(14)* reported on a method of making an end-to-end vascular anastomosis by mechanical means with the use of a circular stapler. The original device, fashioned in the 1940s, could be used for vessels measuring 1.3–15 mm. Briefly, both vessel ends had to be everted 180° and passed over two bushings that were each held by a clamp. One of the bushings contained U-shaped tantalum staples, and the other served as the anvil (Fig. 1A). To complete the end-to-end anastomoses, the two clamps were mounted together, and the staples were driven through the opposed and everted vessel ends and closed. After releasing the clamps, the bushings could be removed. The successful clinical application of this stapler in 71 patients was reported by the developer *(14)*. Although

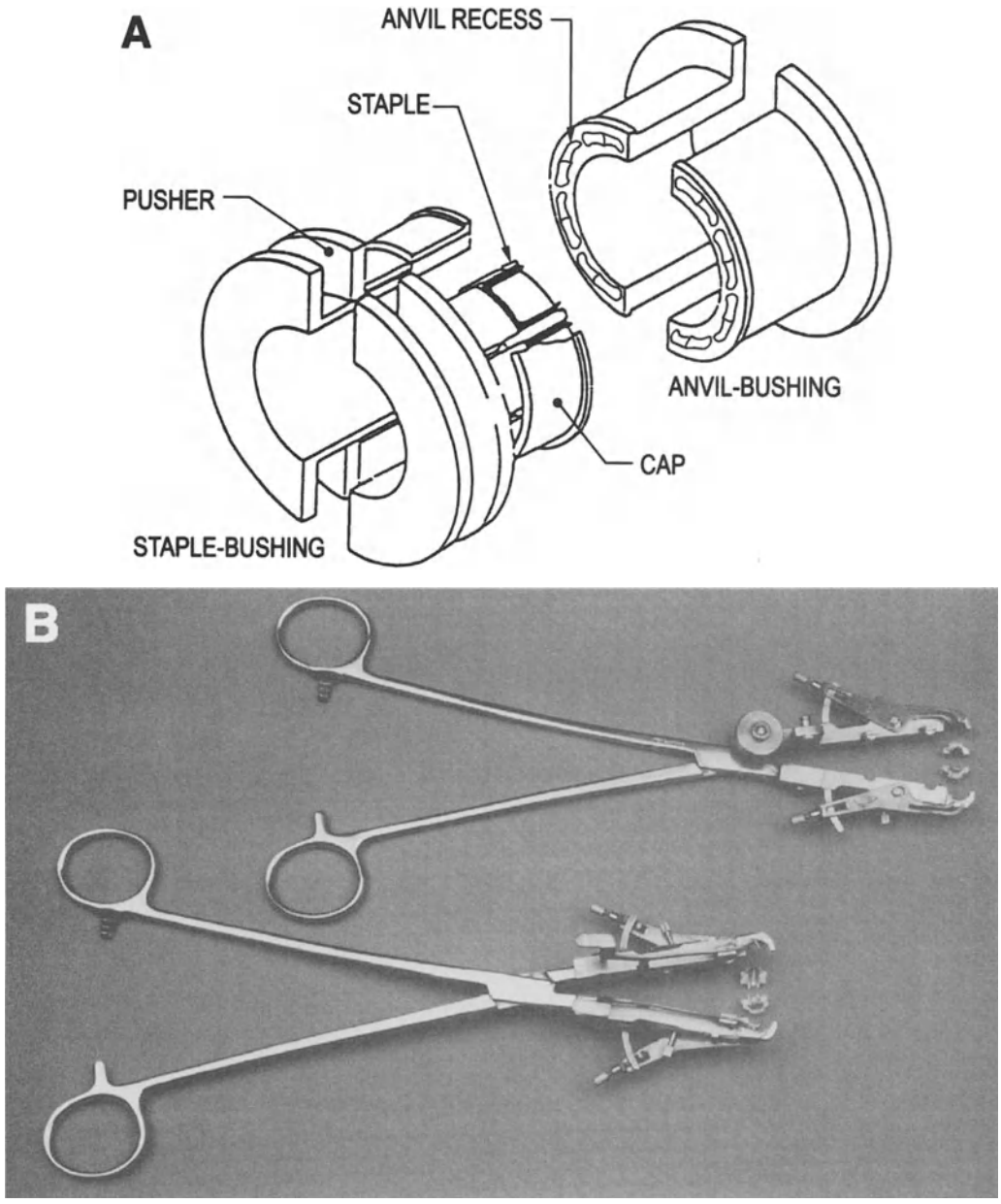

Fig. 1. **(A)** Schematic drawing of the bushings of the ring staple. **(B)** The Codman stapler.

modified versions of this stapler enjoyed some clinical use, none have been adopted for routine clinical use, for several reasons. First, effective use of these devices required the presence of soft distensible vessels to allow for mobilization and eversion. This is difficult, if not impossible, in the presence of diseased atherosclerotic vessels. Second, the prototypes had to be reloaded manually, which was time consuming. In some types (Fig. 1B), this problem was overcome by the use of disposable staple bushings. Finally,

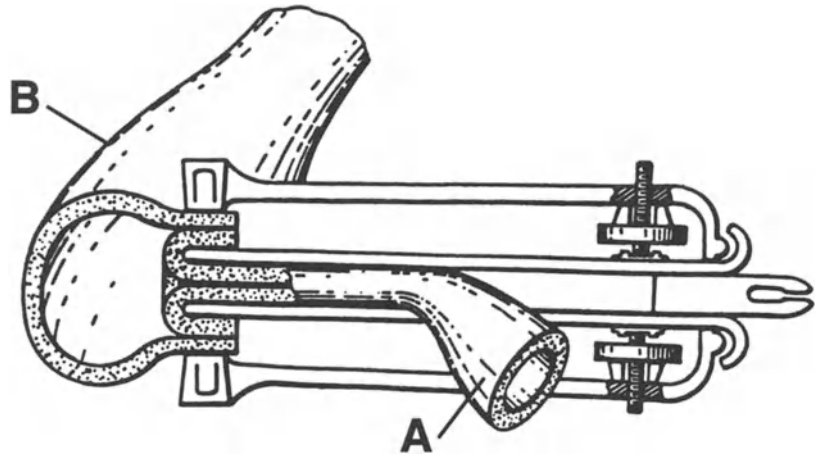

Fig. 2. Schematic drawing of the end-to-side stapler. The donor vessel **(A)** has been everted over the anvil bushing and is placed in the recipient vessel **(B)**. Staples are driven from the outside in.

most independent experts that tested the staplers found their initial use cumbersome *(10)*. The last report of the use of this stapler appeared in the literature in 1982 *(15)*. No circular stapler for creation of an end-to-end vascular anastomosis is currently marketed.

Inokuchi *(16)* developed an end-to-side stapler, and more recently, other staplers have been designed and patented for end-to-side anastomosis *(17)*. The general principle involves the 180° eversion of the donor vessel, which is subsequently placed inside the arteriotomy in the recipient vessel and the vessel walls are then stapled (Fig. 2). Because of the frequent development of anastomotic leakage, the future of such devices remains unclear.

In 1992, Kirsch et al. *(18)* introduced a new method for microvascular reconstruction based on the principle of flanged, nonpenetrating, intimal approximation by an arcuate-legged clip. It has been demonstrated that the use of these clips led to a biologically and technically superior anastomoses when compared to the penetrating microsuture, thereby eliminating most of the problems related to manual suturing previously discussed. These findings have been substantiated by others *(19,20)*, and these clips are currently available in various sizes, packed in self-loading disposable applicators (Fig. 3).

A recently introduced device, the "one-shot device" (United States Surgical Corp., Norwalk, CT) (Fig. 4A–D) permits creation of end-to-side and end-to-end vascular anastomoses and has been successfully used in peripheral vascular and hemodialysis access surgeries.

Coupling

The connection of tubelike structures with the aid of stents, ferrules, or rings without staples predates the introduction of stapling. In 1826 a system to bring together two segments of small bowel in an inverted fashion was experimentally and clinically used *(10)*. In the same year, a ring-pin system for everted bowel anastomoses was presented by Henroz *(10)*. This device was received with much skepticism because it relied on a mucosa-to-mucosa approximation (Fig. 5), a technique believed at the time, to result in failure of healing. Consequently, interest in this device waned.

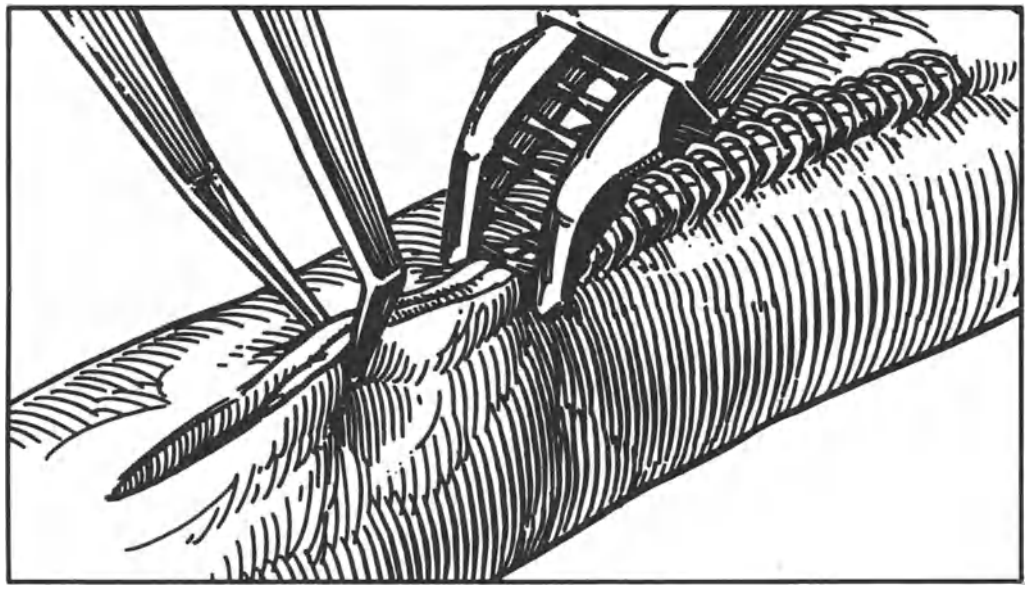

Fig. 3. VCS clip applier. (Reprinted with permission from Autosuture Europe.)

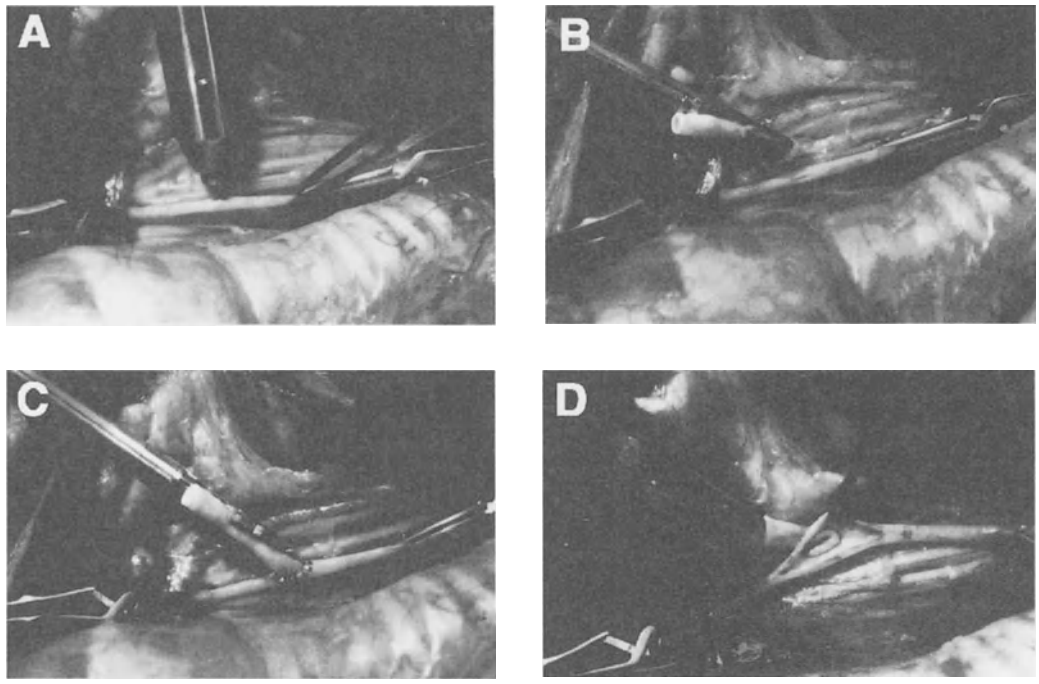

Fig. 4. One-Shot device (United States Surgical Corp.) for creation of vascular anastomoses.

The latter part of the 19th century witnessed the introduction of several intra- and extraluminal prostheses to facilitate vascular anastomosis. These included ivory cuffs, paraffined silver tubes, caramel cylinders, and shin bone of oxen *(21–25)*. The poor

Fig. 5. Henroz's ring-pin system for end-to-end bowel anastomosis. (Reprinted with permission from ref. *10*.).

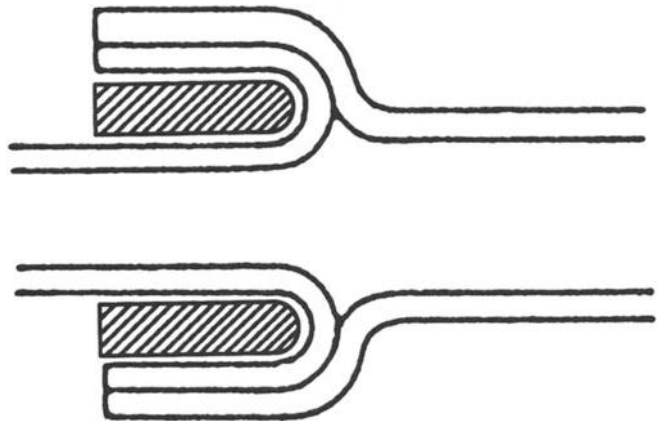

Fig. 6. Schematic drawing of anastomosis made according to the principle of Payr's magnesium ring system: one vessel end is everted over the ring, and the complex is subsequently placed inside the other vessel end.

results attained with these and many such devices were not necessarily owing to poor design, but related to the lack of sterility, immunohistoincompatibility, and ischemia-reperfusion injury. Many of the developments in the early part of the 20th century were spearheaded by Payr *(26)*, who published the use of an absorbable magnesium ring for end-to-end anastomoses. The proximal vessel end had to be passed through the ring and was everted over it. Subsequently, the distal vessel end was dilated, and the proximal end, everted over the magnesium ring, was placed inside the distal vessel end and secured with a suture (Fig. 6). This technique was revived in the 1960s *(27–29)*. One of the problems encountered with all variants of this technique was vessel wall necrosis; this problem was alleviated by the use of tantalum perforated rings by Haller *(30)* in 1965, who reported a 92% patency rate in 4-mm diameter vessel anastomosis.

The 20th century witnessed the development and introduction of several systems designed to facilitate vascular anastomoses (*see* Table 1) *(31–41)*. The basic principle of the commonly used ring-pin systems entailed the passage of rings over vessel ends that were everted and hooked onto pins. When the two rings were brought together, the pins were bent and the anastomoses was secured (Fig. 7). Unlike most previous models, a

Table 1
Important Contributions to the Development of Facilitated Suture and Sutureless Anastomoses in the 20th Century

Year	*Author/Developer*	*Device*
1904	Payr *(31)*	Magnesium-flanged ring-pin system
1913	Landon *(32)*	Metal ring with everted teeth to secure vessel ends in lieu of ligature
1940	Smith *(33)*	Paraffin-coated dextrose rods to facilitate hand-sewn anastomoses
1956	Donetskii *(34)*	Modification of the Landon ring for end-to-side and side-to-side anastomoses
1958	Tibbs *(35)*	Diamond-shaped ice cone with ring clamps to facilitate suturing
1960	Holt *(36)*	Teflon ring-pin system
1962	Nakayama *(37)*	Modified ring pin for small diameter vessels
1976	Östrup *(38)*	Simplified Nakayama ring
1979	Yamagata *(39)*	Intraluminal polyvinyl alcohol stents and extraluminal cyanoacylates for sutureless anastomoses
1984	Daniel *(40)*	Absorbable anastomotic device for microvascular surgery
1994	Siebert *(41)*	Renewed application of intraluminal stents

device introduced by Östrup et al. *(38,42–44)* in 1976 gained wide acceptance in reconstructive surgery after extensive testing by the group. It is the only available system for semiautomated vascular anastomoses. In addition, it is very suitable for the creation of venous end-to-end anastomosis; the designers also support its use in arterial end-to-end and end-to-side surgeries (Fig. 8).

SEALANTS AND SEALERS

Glues

Application of adhesives in surgery has been widespread *(46)*. Their use has, in part, emerged out of the frustration with suture-related problems including fistulization, granuloma formation, insufficient holding capacity, wound dehiscence owing to early disintegration of suture material, and strangulation of wound margins. In vascular surgery in particular, adhesives have been used as an adjunctive to sutures. Two groups of tissue adhesives can be distinguished: biological glues (e.g., fibrin glue) and synthetic glues (e.g., cyano-acrylate).

Fibrin Glue

The first use of fibrinogen as a hemostatic agent dates back to the first decades of the 20th century *(47–49)*. The clinical use of fibrin as an adhesive was first described by Cronkite et al. *(50)* to fixate skin grafts. The inability to obtain high concentrations of fibrinogen led to poor graft fixation and waning enthusiasm for this technique. Rediscov-

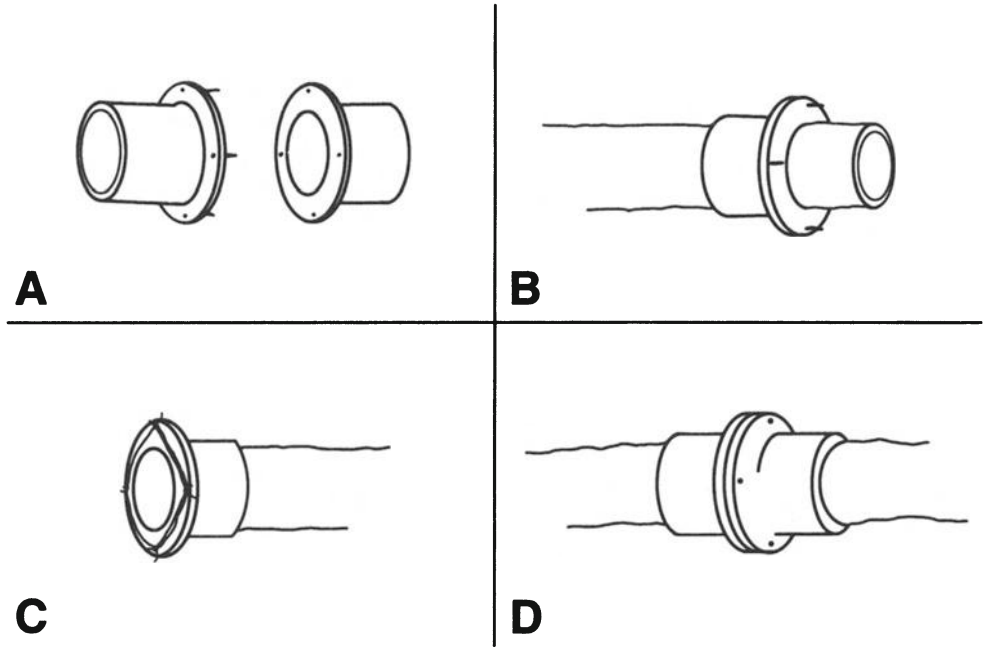

Fig. 7. Payr's ring-pin system of 1904: vessel ends are passed through the ring and everted over pins after the rings are joined together.

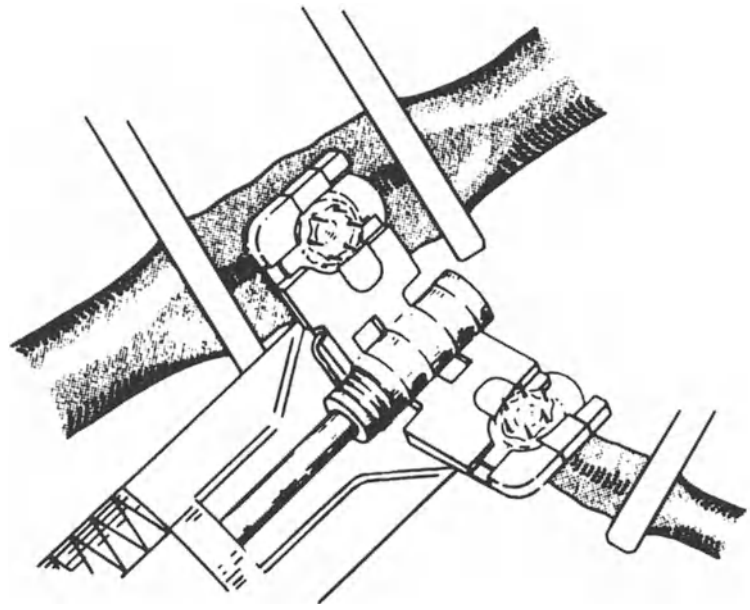

Fig. 8. Schematic drawing of the 3M Microvascular Anastomotic (ring-pin) System in use for an end-to-side anastomosis.

ery and application of fibrin glue was delayed until the 1970s, when advances in laboratory technology enabled the isolation of highly concentrated clotting factors from plasma. Shortly thereafter, Matras et al. *(51)* described the successful application of fibrin glue for microneurorrhaphy in rabbits and reported the first clinical uses of fibrin glue in trauma patients and in microvascular surgery *(52,53)*. Arterial anastomoses of the common carotid artery were created using a hybrid technique that combined sutures with fibrin glue. Histologic examination of these anastomoses showed no necrosis of the tunica media in contrast to what is frequently observed in conventionally sutured anastomoses *(54)*. The first report of this hybrid technique in a clinical setting presented patency rates of 94% *(55)*. Aksik et al. *(56)* confirmed the validity of this hybrid technique, substantiated the histologic findings of Matras's group, and pointed out the time-saving effect of this technique.

More recent experience with fibrin glue has raised concerns regarding potential long-term adverse effects. Moskovitz et al. *(57)* noted a decreased late patency as compared to a sutured anastomosis owing to pseudoaneurysm formation. They concluded that fibrin glue could generate adequate strength to prevent bursting but that the seal was not durable enough to hold the media of the vessel ends in close enough apposition to allow proper healing over time. Therefore, they suggested the addition of factor VIII or the use of an anastomotic cuff to prevent this problem. Dowbak et al. *(58)* reached the same conclusion regarding the tensile strength of fibrin-glued femoral arteries.

In addition to the troubling incidence of pseudoaneurysm formation, investigators have described an increased risk of thrombogenicity with the use of fibrin glue. This prothrombotic property appears to be related to the presence of positively charged amino groups. Indeed, Dowbak and his group found that the use of positively charged fibrin glue resulted in a 50% reduction in patency rate at 7 d, whereas anastomoses created with negatively charged fibrin glue had a patency rate of 100% over the same time period *(58)*.

Cyanoacrylate Glue

Cyanoacrylate glue has been in use since 1960 *(59)*. Its major limitation lies in its potential toxicity. Results of experimental application of methyl cyanoacrylate as well as butyl cyanoacrylate have been disappointing. Use of these plastic adhesives caused thinning of vascular walls, leading to aneurysm formation *(60–63)*. Recently a new glue, polyethyleneglycol 400 diacrylate, has been tested in a microvascular setup *(64)*. It has been reported to remain stable when properly stored and is polymerized by exposure to ultraviolet light. Furthermore, it does not augment local vascular thrombogenicity and is nontoxic to living tissues *(65)*. The glue was found to be able to seal small holes in vessels, but not strong enough in early testing to support a sutureless anastomosis.

Laser Welding

Jain et al. first reported the use of a neodymium yttrium-aluminum-garnet (Nd-YAG) laser for vascular anastomosis *(66)*. Soon thereafter, a favorable report using the argon laser appeared *(67)*. Since then, numerous publications have reported the use of lasers for vascular anastomosis surgery. Results of these studies paralleled those that emerged from the

fibrin glue experience: their use as part of a hybrid technique that combines a few stay sutures with laser requires less time than conventional techniques and results in equivalent patency rates. Despite initial favorable clinical results *(68,69)*, a high incidence of pseudoaneurysm formation and rupture at the anastomotic site *(70)* has precluded widespread clinical use.

At least seven different laser techniques have been proposed for creation of vascular anastomoses. Many questions remain unanswered, including how laser welding is achieved and what the most appropriate settings are for their use. Bass et al. *(71)* suggested that noncovalent interactions between denatured collagen may be responsible for tissue bonding. When a CO_2 laser is used at high power, the tissue temperature is reported to rise to 80–120°C and adhesion, therefore, is thought to occur through melting (denaturation) of collagen and coagulation of cells in the media and adventitia *(72–76)*. In the process of wound healing, this coagulum is gradually replaced by fibrous and muscular tissues. It is conceivable that this laser technique may result in a high incidence of complications, and, hence, use of low-power CO_2 lasers has been advocated *(77)*. Argon lasers used for vascular anastomoses generate a surface temperature of 43–48°C, which is well below the temperature at which collagen denatures *(73)*. While the mechanism by which an argon laser fuses tissue remains uncertain, most researchers believe that protein bonds are degraded thermally, allowing proteins to rebind to adjacent proteins. This results in smooth tissue–tissue connection *(78)*. Chikamatsu et al. *(79)* used low-energy conditions in applying the argon laser and obtained tissue growth without disturbance of the laminar architecture of the vessels and without aneurysm formation.

The diode laser has been used as a contact laser in microvascular surgery since 1989 *(80)*. Equal patency rates and incidence of aneurysmal dilation were found when compared to a conventionally sutured anastomosis. However, diode laser use was associated with faster endothelial healing, a smoother inner vessel surface, less inflammation, and normal orientation of collagen and elastic fibers when compared to manual sutures. Recently, Godlewski et al. *(81)* reported on the use of the diode laser in a noncontact fashion in a comparative study using the rat carotid artery model. A purported benefit of noncontact diode laser application is the lack of the need for an intraluminal stent. The avoidance of stent use results in lesser incidence of stenosis and thrombus formation. Moreover, the penetration depth of the 830-nm diode laser is said to be more optimal than that of the CO_2, the argon, and the Nd-YAG lasers, giving rise to a better and more complete sealing of the anastomotic site. Diode lasers cause a shallow injury that occupies the entire thickness of the vessel wall and facilitates slight protein denaturation and collagen fusion of media and adventitia, while being less thrombogenic than the Nd-YAG laser and less incisive than the CO_2 and argon counterparts *(79,82,83)*.

CREATION OF AN ANASTOMOSIS IN A BLOODLESS FIELD WITHOUT FLOW INTERRUPTION

All techniques that have been covered in the above necessitate a relatively lengthy interruption of the bloodflow. In the mid-70s various types of shunts have been advocated to circumvent this *(84)*. However these techniques have never become widely used. Recently two new interesting techniques have been described in this respect. In one of

them the donor vessel is stitched to the exterior of the recipient vessel, whereafter an Excimer laser catheter (Medolas GmbH, Amberg, Germany), introduced through a sidebranch of the donor vessel, is used to create the arteriotomy *(85)*. In the other technique the bloodflow in the recipient vessel is very shortly interrupted and the arteriotomy is made. Subsequently a polyurethane shield is introduced into the vessel after which the bloodflow is restored and the anastomosis is created *(86)*.

CONCLUSIONS

Despite significant advances in the use of mechanical devices, sealants, and laser welding, manual suturing remains the golden standard for the creation of vascular anastomoses. Almost all stapling, clipping, and coupling techniques, when applied to small-diameter vessels, require a temporary interruption of blood flow. This factor, until now, has limited the acceptance of these devices. With increasing understanding of ischemic preconditioning and better methods to achieve myocardial immobilization and new shunting techniques, it is expected that a method for facilitated coronary anastomosis that is reliable, easy to operate, versatile, and cost-effective will become available in the foreseeable future.

ACKNOWLEDGMENT

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REFERENCES

1. Ramos JR, Berger K, Mansfield PB, et al. Histologic fate and endothelial changes of distended and non-distended vein grafts. Ann Surg 1976;183:205–228.
2. Zhong-Wei C, Dong-Yue Y, Di-Sheng C, eds. Microsurgery. New York:Springer Verlag, New York, 1982, p. 72.
3. Jacobson JH, Suarez EL. Microsurgery in the anastomosis of small vessels. Surg Forum 1960;11:243,244.
4. Murphy JB. Resection of arteries and vein injured in continuity: end-to-end suture: experimental and clinical research. Med Rec 1897;51:73.
5. Lauritzen C. A new easier way to anastomose microvessels. Scan J Plast Reconstr Surg 1978;12:291–294.
6. Zhang L, Moskovitz M, Baron DA, Siebert JW. Different types of sleeve anastomosis. J Reconstr Microsurg 1995;11:461–465.
7. Borst C, Janssen EWL, Tulleken CA, et al. Coronary artery bypass grafting without cardiopulmonary bypass and without interruption of native coronary flow using a novel anastomosis site restraining device. Surgery 1996;27:1356–1364.
8. Borst C, Santamore WP, Smedira NG, Bredee JJ. Minimally invasive coronary artery bypass grafting: on the beating heart and via limited access. Ann Thorac Surg 1997;(Suppl 6)63:S1–S5.
9. Hütl H. Surgical stitching instrument for the suture of the stomach and intestines according to Victor Fischer. Budapest, 1911.
10. Steichen FM, Ravitch MM. History of mechanical devices and instruments for suturing. In: Ravitch MM, Steichen FM, Austen WG, Scott HW Jr, Fonkalsrud EW, Polk HC, eds. Current Problems in Surgery Vol. 3. Yearbook Medical, Chicago and London; 1982, pp. 3:3–51.
11. von Brucke H. Uber ein neuartiges chirurgisches Nahininstrument. Zentralbl Chir 1935;62:1684.

12. Rygg IH, Westengaard E, Fredricksen T. A new method for fixation of prosthetic cardiac valves and closure of the atriotomy with staples. J Cardiovasc Surg 1963;4:467.
13. Bertelsen S, Rygg IH. A simple stapling device for vascular surgery. Surg Gyn Obstet 1967; 125:1087–1090.
14. Androsov PI. New method of surgical treatment of blood vessel lesions. AMA Arch Surg 1956;73:902.
15. Oka N, Yamada T, Ikeda T, Furuyama M, Shiramizu T, Kusaba A. Construction of internal arteriovenous fistulas for hemodialysis using Inokuchi's vascular stapler. Jpn J Surg 1982;12:262–265.
16. Inokuchi K. Stapling device for end-to-side anastomosis of blood vessels. Arch Surg 1961;82:337–341.
17. Barak JH. Patent filed February 15, 1990, date of publication August 29, 1990. European patent #Ep 0 384 647 A1.
18. Kirsch WM, Zhu YH, Hardesty RA, Chapolini R. A new method for microvascular anastomosis. Am Surg 1992;58:722–727.
19. Boeckx W, Darius O, van der Hof B, van Holder C. Scanning electron microscopic analysis of the stapled microvascular anastomosis in the rabbit. Ann Thorac Surg 1997;(Suppl 6)63:S128–S134.
20. Nataf P, Kirsch W, Hill AC, et al. Non-penetrating clips for coronary anastomosis. Ann Thorac Surg 1997;(Suppl 6)63:S135–S137.
21. Carrel A. La technique operatoire des anastomoses vasculaires et la transplantation des visceres. Lyon Med 1902;98:859.
22. Nitze M. Kongress in Moskau. Centralbl Chir 1897;24:1042.
23. Tuffier M. De l'untubation dans les plaies des gross artères. Bull Acad Natl Med (Paris) 1915;74:455.
24. Carrel A. Results of the transplantation of blood vessels, organs and limbs. JAMA 1908;51:1662.
25. Muir ES. A new device for anastomosing blood vessels. Lancet 1914;34:211.
26. Payr E. Beitrage zur Technique der Blutgefass und Nrevennaht nebst Mittheilungen uber die Verwendung eines resorbirbaren Metalles in de Chirurgie. Arch Klin Chir 1900;62:67–93.
27. Carter EL, Roth EJ. Direct non-suture coronary anastomoses in the dog. Ann Surg 1958;148:212–218.
28. Rohman M, Goetz RH, Dee R. Double coronary artery internal mammary artery anastomoses: tantalum ring technique. Surg Forum 1969;11:236,237.
29. Ratan RS, Leon M, Lovette JB, Levowitz BS, Magovern GJ, Kent EM. Modified non-suture anastomosis of coronary artery and internal mammary artery in dogs. Surg Forum 1960;11:239–241.
30. Haller JD, Kripke DC, Rosenak SS, Roberts DR, Rohman M. Long-term results of small vessel anastomoses with a ring technique. Ann Surg 1965;161:67–72.
31. Payr E. Zur Frage der circularen Vereinigung von Blutgefasse mit resorbirbaren Prothesen. Arch Klin Chir 1904;72:32–54.
32. Landon LH. A simplified method of direct blood transfusion with self retaining tubes. JAMA 1913;61:490.
33. Smith S. The soluble rod as an aid to vascular anastomosis. Arch Surg 1940;41:1004–1007.
34. Donetski DA. A new method of a circular vascular suture. Eksperimetn Al'naia Khirurgiia (Moscow) 1956;1:53–59.
35. Tibbs GJ, Leslie WG. Arterial replacement with minimal interruption of the blood flow. Lancet 1958;1:292–294.
36. Holt GP, Lewis FJ. A new technique for end-to-end anastomosis of small arteries. Surg Forum 1960;11:242–243.
37. Nakayama K, Tamiya T, Yamamoto K, Akimoto S. A simple new aparatus for small vessel anastomosis. Surgery 1962;52:918–923.

38. Östrup LT. Anastomosis of small veins with suture or Nakayama's apparatus. Scand J Plast Reconstr Surg 1976;10:9–17.
39. Yamagata S, Handa H, Taki W, Yonekawa Y, Ikada Y, Iwata H. Experimental nonsuture microvascular anastomosis using a soluble PVA tube and plastic adhesive. J Microsurg 1979;1:208–215.
40. Daniel RK, Olding M. An absorbable anastomotic device for microvascular surgery: clinical applications. Plast Reconstr Surg 1984;74:337–342.
41. Moskovitz MJ, Bass L, Zhang L, Siebert JW. Microvascular anastomoses utilizing new intravascular stents. Ann Plast Surg 1994;32:612–618.
42. Östrup LT, Berggren A. The Unilink instrument system for fast and safe microvascular anastomosis. Ann Plast Surg 1986;17:521–525.
43. Berggren A, Ostrup LT, Ragnarsson R. Clinical experience with the Unilink/3M precise anastomotic device. Scan J Plast Reconstr Hand Surg 1993;27:35–39.
44. Ragnarsson R, Berggren A, Ostrup LT. Microvenous end-to-side anastomosis: an experimental study comparing the Unilink system and sutures. J Reconstr Microsurg 1989;5:217–224.
45. Ragnarsson R, Berggren A, Ostrup LT, Gilbert RW. Arterial end-to-side anastomosis with the Unilink system. Ann Plast Surg 1989;22:405–415.
46. Lerner R, Binur NS. Current status of surgical adhesives. J Surg Res 1990;48:165–181.
47. Bergel S. Uber Wirkungen des Fibrins. Dtsch Med Wochenschr 1909;35:633.
48. Grey EG. Fibrin as a hemostatic in cerebral surgery. Surg Gynecol Obstr 1915;21:452.
49. Harvey SC. The use of fibrin papers and forms in surgery. Boston Med Surg J 1916;174:658.
50. Cronkite EP, Lozner EL, Deaver JM. Use of thrombin and fibrinogen in skin grafting. JAMA 1944;124:976.
51. Matras H, Dinges HP, Lassman H, Mamoli B. Zur nahtlosen interfaszikularen Nerventransplantation im Tierexperiment. Wien Med Wochenschr 1972;122:517–523.
52. Kuderna H, Matras H. Die klinische Anwendung der Klebung von Nreveanastomosen bei der Rekonstruktion verletzer peripherer Nerven. Wien Med Wochenschr 1975;87:495.
53. Matras H, Chiari F, Fletter G, et al. Zur Klebung von Microgefäßanastomosen. Proceedings, 13th Annual Meeting Dtsch Ges f Plast Wiederherstellungschirurgie. Stuttgart, Thieme, 1977, p. 357S.
54. Baxter TJ, O'Brien B, Henderson PN, Bennet RC. The histopathology of small vessels following microvascular repair. Br J Surg 1972;59:617–622.
55. Kletter G, Matras H, Dinges HP. Zur partiellen Klebung von Microgefabanastomosen im intrakraniellen Bereich. Wien Klin Wochenschr 1978;90:415–419.
56. Aksik IA, Kikut RP, Apshkalne DL. Extraintracranial anastomosis performed by means of biological gluing materials: experimental and clinical study. Microsurg 1986;7:2–8.
57. Moskovitz MJ, Bass L, Zhani L, Siebert JW. Microvascular anastomosis utilizing new intravascular stents. Ann Plast Surg 1994;32:612–618.
58. Dowbak GM, Rohrich RJ, Robinson JB, Peden E. Effectiveness of a new non-thrombogenic bioadhesive in microvascular anastomoses. J Reconstr Microsurg 1994;10:383–386.
59. Nathan HS. Nonsuture closure of arterial incisions using a rapidly polymerizing adhesive. Ann Surg 1960;152:648.
60. Vinters HV, Galil KA, Lundie MJ, Kaufman JCE. The histotoxicity of cyanoacrylates. Neuroradiology 1985;27:279–291.
61. Green AR, Milling MAP, Green RT. Butylcyanoacrylate adhesives in microvascular surgery: an experimental pilot study. J Reconstr Microsurg 1986;2:103–105.
62. Weissberg D, Goetz RH. Necrosis of arterial wall following application of methyl-2-cyanoacrylate. Surg Gynecol Obstr 1964;119:1248.
63. Woodward SC, Hermann JB, Cameron JL, et al. Histotoxicity of cyanoacrylate tissue adhesive in the rat. Ann Surg 1965;162:113.
64. Dumanian GA, Dacombe W, Hong C, et al. A new photopolymerizable blood vessel glue that seals vessel anastomoses without augmenting thrombogenicity. Plast Reconstr Surg 1995;95:901–907.

65. Pathak CP, Sawhney AS, Hubbell JA. Rapid photopolymerization of immunoprotective gels in contact with cells and tissue. J Am Chem Soc 1992;114:8311.
66. Jain KK, Gorisch W. Repair of small blood vessels with the Neodymium-YAG laser: a preliminary report. Surgery 1979;85:684–688.
67. Gomes OM, Macruz R, Armelin, et al. Vascular anastomosis by argon laser beam. Texas Heart Inst J 1981;10:145.
68. White RA, White GH, Fujitani RM, et al. Initial human evaluation of argon laser-assisted vascular anastomoses. J Vasc Surg 1987;9:542–547.
69. Okada M, Simizu K, Ikuta H, Horii H, Nakamura K. An alternative method of vascular anastomosis by laser: experimental and clinical study. Lasers Surg Med 1987;7:240–248.
70. McCarthy WJ, Hartz RS, Yao JS, et al. Vacular anastomoses with laser energy, J Vasc Surg 1986;2:32–41.
71. Bass LS, Moazami N, Pocsidio J, et al. Changes in type I collagen following laser welding. Lasers Surg Med 1992;12:500–505.
72. Serure A, Whithers EH, Thomsen S, Morris J. Comparison of carbon dioxide laser-assisted microvascular anastomosis and conventional microvascular sutured anastomosis. Surg Forum 1983;34:634.
73. Kopchok GE, White RA, White GH, et al. CO_2 and argon laser welding: acute histologic and thermodynamic comparison. Lasers Surg Med 1988;8:584–588.
74. Danielsen CC. Precision method to determine denaturation temperature of collagen using ultraviolet difference spectroscopy. Coll Rlat Res 1982;2:143.
75. Epstein M, Colly BC. Electron microscopic study of dosimetry for microvascular tissue welding. Laser Surg Med 1986;6:202.
76. Frazier OH, Painvin GA, Morris JR, Thomsen S, Neblett CR. Laser-assisted microvascular anstomoses: angiographic and anastomopathologic studies on growing microvascular anastomoses: preliminary report. Surgery 1985;97:585–590.
77. Sartorius CJ, Shapiro SA, Campbell RL, Klatte EC, Clark SA. Experimental laser-assisted end-to-side microvascular anastomosis. Microsurgery 1986;7:79–83.
78. White RA, Kopchok GE, Donayre C. Mechanism of tissue fusion in argon laser-welded vein-artery anastomoses. Lasers Surg Med 1988;8:83–85.
79. Chikamatsu E, Sakurai T, Nishikimi N, Yano T, Nimura Y. Comparison of laser welding, interrupted sutures, and continuous sutures in growing vascular anastomoses. Lasers Surg Med 1995;16:34–40.
80. Unno N, Sakaguchi S, Koyano K. Microvascular anastomosis using a new diode laser system with a contact probe. Lasers Surg Med 1989;9:160–168.
81. Godlewski G, Rouy S, Tang J, Dauzat M, Chambettaz F, Salathe RP. Scanning electron-microscopy of microarterial anastomoses with a diode laser: comparison with conventional manual suture. J Reconstr Microsurg 1995;11:37–42.
82. Oz MC, Bass LS, Chuck RS, et al. Strength of laser vascular fusion: preliminary observations on the role of thrombus. Lasers Surg Med 1990;10:393–395.
83. Godlewski G, Frapier JM, DeBalman B, et al. Diode laser and microvascular carotid anastomosis: a preliminary study. Laser Med Sci 1991;8:33.
84. Ludington LG, Kafrouni G, Peterson MH, Verska JJ, Mulder A, Brewer LA III. Technique for using soft, flexible stents in aortocoronary vein bypass operations. Ann Thorac Surg 1976;21:328–332.
85. Tulleken CAF, Verdaasdonk RM, Mansvelt Beck HJ. Nonocclussive excimer laser assisted end-to-side anastomosis. Ann Thorac Surg 1997;63:S138–S142.
86. Heijmen RH, Borst C, van Dalen R, Gruendeman PF, Verlaan CWJ. Temporary luminal arteriotomy seal for bypass grafting. Ann Thorac Surg 1998;65:1093–1099.

13 Device-Supported Myocardial Revascularization

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and Robert K. Jarvik, MD

Contents

INTRODUCTION

Cardiopulmonary bypass (CPB) elicits a well-described systemic inflammatory response that results in significant end organ dysfunction in a subset of high-risk patients *(1–3)*. Contact of blood with the nonphysiologic surfaces of the bypass machine causes coagulopathy and bleeding *(4)*, complement activation *(5)*, neutrophil-mediated pulmonary injury *(6)*, hemodilution, and capillary leak *(7,8)*. In patients with left ventricular dysfunction, myocardial arrest can result in ischemia with temporary or permanent cardiac impairment.

To avoid these potential deleterious effects, myocardial revascularization has been performed on the beating heart without the use of CPB *(9–11)*. Despite the development of new minimally invasive techniques, at present, complete revascularization is limited by the difficulty in visualizing and stabilizing vessels on the lateral and posterior surfaces of the heart. The absence of a safety net should the heart fail, further limits cardiac manipulation in off-bypass coronary revascularization.

Great strides have been made in optimizing the surgical field for beating heart revascularization. Indeed, the use of pharmacological agents to slow the heart and the development of mechanical stabilization devices to reduce cardiac wall motion have

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

Table1
Available Pumps Used for Device-Supported Myocardial Revascularization

Pumps	*Examples*
Nonpulsatile	
Centrifugal (rotary) flow	Biomedicus™ (Medtronic, Minneapolis, MN)
	Sarns (3M Healthcare, Ann Arbor, MI)
Axial flow	Hemopump™ (Medtronic)
	Jarvik Cannula Pump[a] (United States Surgical Corp., Norwalk, CT)
Pulsatile	
Pneumatic	Abiomed™ BVS 5000 (ABIOMED, Danvers, MA)

[a]Not yet clinically tested.

resulted in a more controlled environment for coronary grafting. However, the creation of an anastomosis under beating heart conditions remains a technical challenge. In an effort to further facilitate grafting onto a moving target, pumps capable of unloading the left ventricle while maintaining coronary and systemic perfusion present an attractive strategy. Some such pumps have been successfully used clinically whereas others are at various stages of preclinical development (Table 1). This chapter examines the rationale for the use of these devices and reviews the available data regarding their safety and efficacy.

PHYSIOLOGY

Circulatory assistance can be used in uni- or biventricular configurations. In either situation, the patient's lungs act as the oxygenator, eliminating the costs and potential sequelae of an in-line oxygenator. Mechanical ventilation maintains normal pulmonary metabolism and avoids the transient pulmonary hypertension often associated with long periods of pulmonary collapse during CPB. Additional advantages of this method of cardiac assistance include the following:

1. Avoidance of hemodilution;
2. Reduction of heparin use, blood loss and blood use;
3. Elimination of protamine reversal;
4. Faster recovery and convalescence; and
5. Reduced costs.

The absence of a cardiotomy sucker on the other hand, necessitates the use of an intraoperative cell-saver and rapid blood infusers.

Decisions regarding univentricular vs biventricular support are usually made on the basis of the preoperative pulmonary artery pressures and right ventricular function. Moreover, β-blockade during revascularization may precipitate pulmonary hypertension in patients with profoundly depressed preoperative cardiac function. Such situations may require biventricular support or avoidance of pharmacological cardiac depression.

MYOCARDIAL PROTECTION

Minimally invasive surgical techniques for myocardial revascularization of the normothermic beating heart are associated with temporary coronary occlusions and regional ischemia. The working heart has limited tolerance to ischemia under these conditions, and the risk of myocardial damage may be considerable.

Ischemic preconditioning has been shown to limit myocardial adenosine triphosphate (ATP) wasting and to improve postischemic cardiac function *(12,13)*. The mechanisms involved in ischemic preconditioning include the stimulation of adenosine (A_1) receptors, the modulation of ATP-regulated potassium channels, the release of oxygen-derived free radicals, and the expression of stress-induced proteins *(14)*. A number of pharmacological manipulations exist to effect these mechanisms, but the most common include adenosine stimulation and adrenergic β-blockade. The use of these agents in beating heart revascularization not only helps to stabilize the coronary target but also has profound effects on myocardial oxygen demand and myocardial reperfusion injury. Although their use may be limited in the unsupported heart, device-assisted revascularization could potentially allow for marked pharmacological myocardial depression and improved myocardial protection.

Device-supported revascularization likewise offers the protective effect of mechanical unloading on the ischemic myocardium. The beneficial effects of left heart unloading have been well described *(15–18)*. Several investigators have experimentally demonstrated reductions in acute infarct size when a mechanical decompression is created *(16,19)*. Mechanical decompression results in both pressure and volume unloading and a subsequent decrease in myocardial oxygen demand *(17,20)*. The relative contribution of pressure unloading is significantly increased in the experimentally β-blocked state resulting in a logarithmic reduction in myocardial oxygen requirements. By reducing myocardial wall tension, resistance to flow through obstructed coronary arterial beds may also be decreased. If coronary flow is maintained, an increase in perfusion to the ischemic regions of the ventricle can occur *(21)*.

CLINICAL RESULTS

Left Ventricular Dysfunction

In view of the theoretical benefits afforded by device-supported revascularization, initial clinical applications of this evolving technology were used in patients with compromised left ventricular function. Sweeney and Frazier *(22)* first reported the use of device-supported revascularization among a population of patients with profoundly depressed preoperative left ventricular function (average ejection fraction = 22%). It was hypothesized that avoidance of CPB, aortic cross-clamping, and cardioplegic arrest in this high-risk population of patients might reduce postoperative morbidity and mortality. The presence of mechanical ventricular assistance also allowed for continued circulatory support in the postoperative period should postcardiotomy cardiogenic shock ensue.

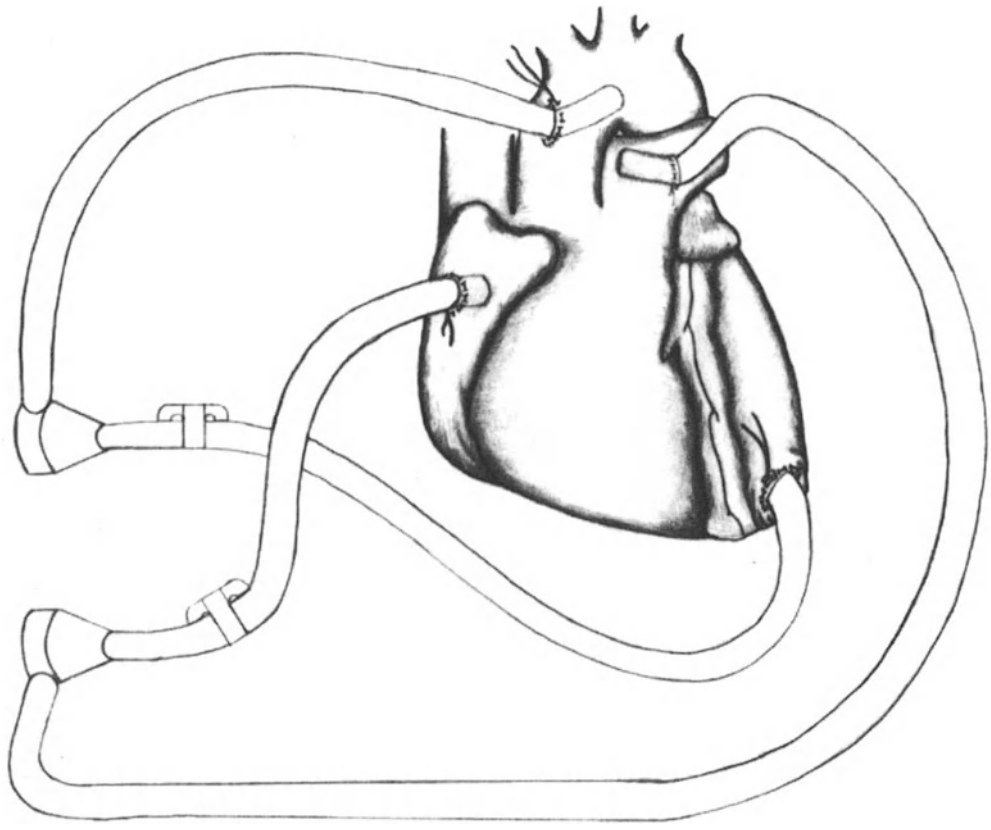

Fig. 1. Cannulation scheme used for biventricular support with the Biomedicus centrifugal pump during beating heart revascularization.

The majority of the 43 patients initially reported by Sweeney and Frazier *(22)* underwent biventricular support using the Biomedicus centrifugal pump (Fig. 1). Inflow from the left heart was established via direct left ventricular apical cannulation. Patients with documented left ventricular thrombus had inflow cannulations via the left atrial appendage, the right superior pulmonary vein, or the aorta by advancing the cannula retrograde across the aortic valve. Blood was returned to the patient via standard aortic cannulation. Inflow to the right-sided ventricular assist device was created via standard right atrial cannulation, and outflow was established by cannulating the main pulmonary artery. By decompressing the right heart, right ventricular support facilitated optimal exposure of the posterior ventricular and obtuse marginal vessels.

An average of 3.7 bypass grafts was constructed in this series, and 20 patients required at least one coronary endarterectomy, demonstrating the degree of stabilization that could be achieved with this system. All the patients were weaned from right-sided support in the operating room; however, five patients required prolonged left ventricular assistance postoperatively. All but one was weaned from left-sided support in the intensive care unit. There were two deaths (4.6%): one from low cardiac output in a patient with preoperative

cardiogenic shock, and one from a cerebrovascular accident in a patient with a preoperative fluctuating neurological exam. Average hospital stay was 10.5 d and no patient experienced a worsening of cardiac function when compared with preoperative status.

Given these initial clinical results, device-assisted beating heart coronary artery bypass grafting (CABG) has become an attractive alternative for patients at extremely high risk for postcardiotomy cardiogenic shock. Although centrifugal pumps have been used in the majority of patients, a newer generation of pumps including temporary pneumatic devices (e.g., Abiomed BVS 5000) and axial flow pumps (e.g., Hemopump) may also be used for uni- or biventricular support. If weaning from such devices is not possible in the postoperative period, excellent results may be obtained with early conversion to implantable devices *(23,24)*.

Normal Ventricular Function

With the feasibility of device-assisted CABG demonstrated in high-risk patients, short-term left ventricular assist devices (LVADs) are now being explored as an alternative to CPB for routine myocardial revascularization. The most widely studied device for this purpose has been the Hemopump.

The Hemopump is a catheter-mounted axial flow pump with an inflow catheter that can be advanced retrograde across the aortic valve into the left ventricular cavity (Fig. 2). The cannula measures 8.5 cm in length and 8.1 mm (24 Fr.) in diameter. The outflow is via a second port in the catheter, which ejects blood into the ascending aorta. The Hemopump must be placed through either a graft or a purse-string in the ascending aorta and advanced through the aortic valve, into the left ventricle *(25–27)*. The position of the cannula in the left ventricle is confirmed by manual palpation. At a maximum speed of 26,000 rpm and a pressure difference of 70 mmHg, the device can provide non pulsatile flow approximating 5 L/min. A smaller 14 Fr. version provides only 1 to 2 L/min of flow but can be inserted percutaneously via the femoral artery.

In experimental studies, the Hemopump demonstrates excellent unloading of the normal and β-blocked ventricle with corresponding decreases in myocardial oxygen consumption *(17,18,28)*. It has been used as a support system for high-risk angioplasty, as a ventricular assist device in the setting of postcardiotomy cardiac failure, and as a percutaneously introduced device for ischemic cardiogenic shock *(25–27,29,30)*. Sweeney and Frazier *(22)* used the Hemopump in five of their patients undergoing device-assisted CABG as a left ventricular assist device in combination with right-sided Biomedicus support *(22)*.

Presently, Lonn et al. *(31)* have the most experience with the Hemopump as an alternative to CPB for routine myocardial revascularization. Patients with normal ventricular function have undergone isolated left heart support and myocardial depression via β-blockade. In their initial report of 25 patients undergoing multivessel revascularization with Hemopump support, they demonstrated promising results with no patients requiring blood transfusions and no patients experiencing postoperative renal or pulmonary failure. In contrast to the early experience of device-assisted

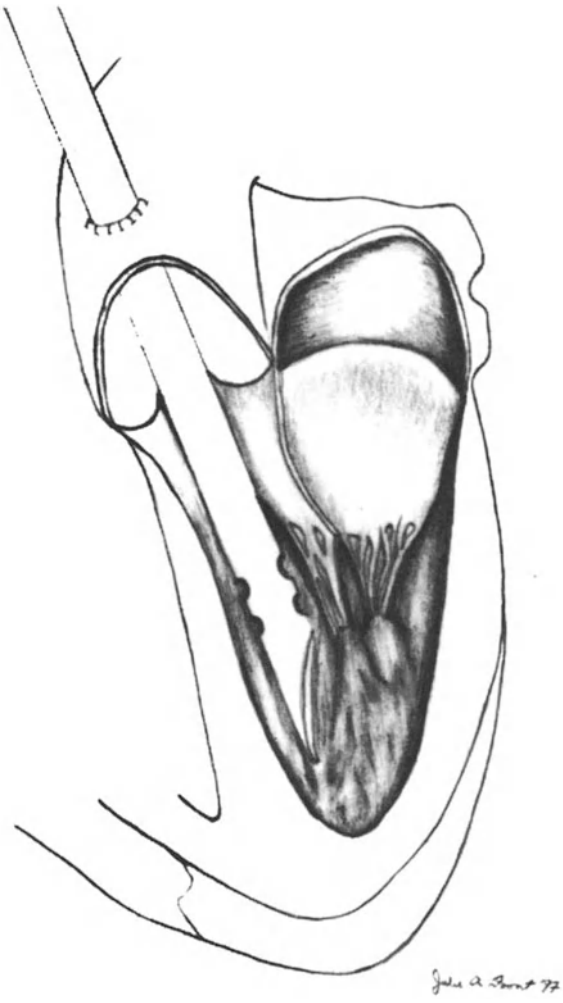

Fig. 2. Catheter-mounted 24 French Hemopump. The device must be advanced across the aortic valve either through a graft sewn to the ascending aorta or through an aortic purse-string.

revascularization for high-risk patients, no patients with normal cardiac function and left ventricular Hemopump support required right ventricular assistance despite aggressive β-blockade.

With the emergence of minimally invasive direct coronary artery bypass (MIDCAB) via smaller incisions, some researchers have advocated the use of the percutaneous Hemopump as an adjunct to present techniques. The application of this approach awaits further investigation, but it may improve the stabilization, visualization, and myocardial protection now encountered with MIDCAB. Randomized studies will be necessary before device-assisted CABG can claim major outcome advantages over the standard CPB-supported myocardial revascularization techniques successfully used in most patients.

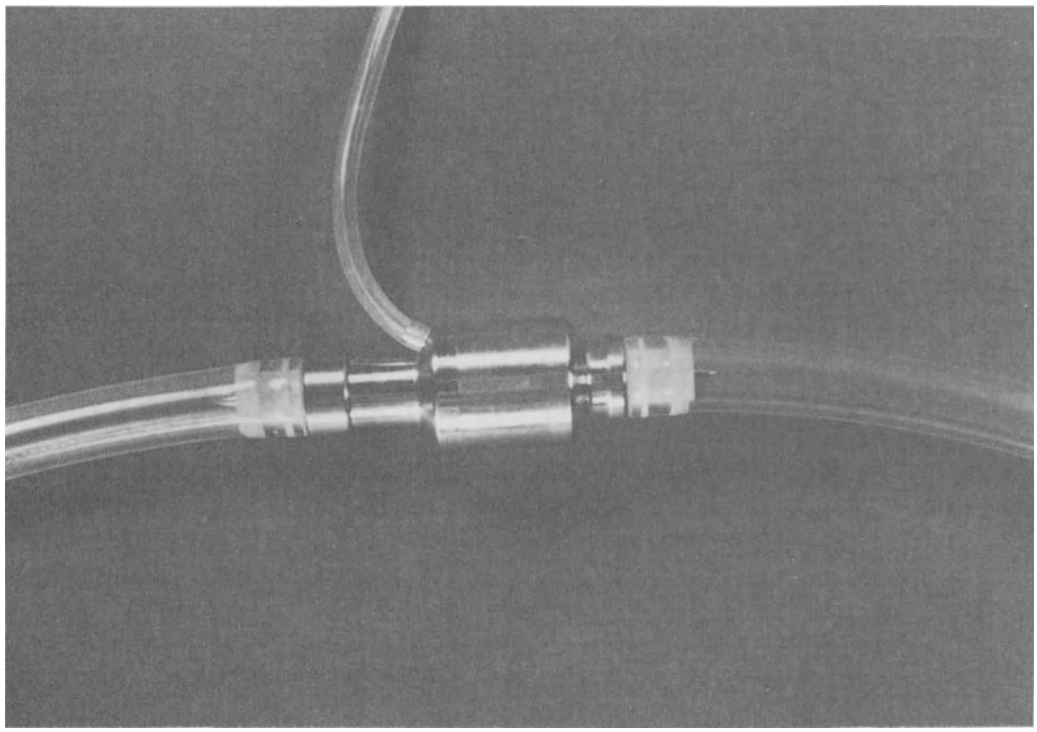

Fig. 3. Compact axial flow pump (Jarvik Cannula Pump) being developed by the United States Surgical Corporation. Standard cannulas are attached to either end of the device and provide isolated left heart bypass. Inflow cannulation can occur via the left ventricular apex (pictured) or the left atrium, and outflow is via standard aortic cannulation.

FUTURE DEVELOPMENTS

Developments are currently under way to design compact, easily inserted, left heart bypass systems for device-assisted beating heart myocardial revascularization. One such system, the Jarvik Cannula Pump, uses a small axial flow pump in line with standard bypass cannulas and tubing (Fig. 3) *(20,32,33)*. The device, a modification of the Jarvik 2000, is a 10-mm diameter axial flow pump that incorporates a tiny electric motor within its housing. The motor drives the pump impeller via a short shaft that is supported on blood-immersed bearings. In its current design, the pump is inserted into the left ventricular apex. A flexible wire-reinforced outflow cannula dotted with inlet holes permits blood to enter the pump directly from the ventricular chamber. At a low wattage, and operating at 10–15% overall efficiency, nonpulsatile flows of 5 L/min and 80 mmHg of pressure can be obtained *(34)*. At a speed of 15,000 rpm, the Jarvik pump can completely unload the left ventricle and achieve non-pulsatile systolic aortic wave tracings while maintaining optimal left atrial pressures (0–5 mmHg) *(20)*. Reductions in left ventricular end-diastolic and end-systolic pressure result in a 66% reduction in left ventricular external work under baseline conditions, and an 83% reduction in the depressed ventricle. More

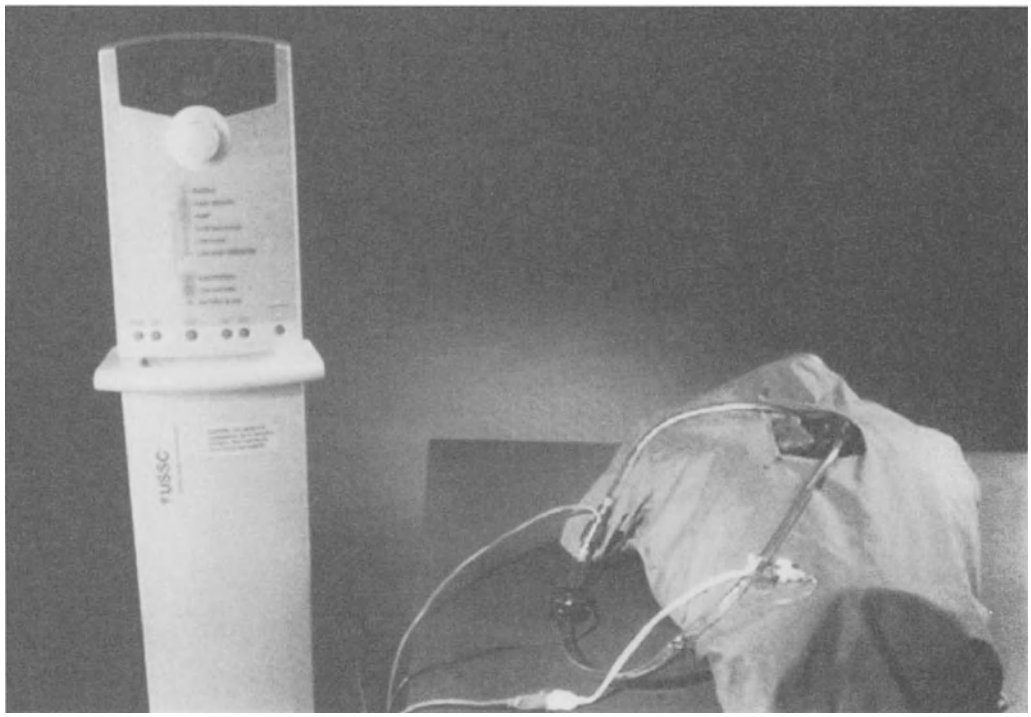

Fig. 4. Jarvik Cannula Pump controller. Entire bypass loop fits comfortably on operating room table.

important, right ventricular pressures, pulmonary artery flow, left ventricular filling, and systemic oxygenation remain unchanged during axial flow unloading, even under conditions of profoundly depressed ventricular contractility.

The entire bypass loop fits comfortably on the operating table (Fig. 4). A single electrical cable and a pressure monitoring line are connected to an easy-to-use controller. An electromagnetic flow probe can be attached around the outflow tubing, to display continuous pump flow. The pump is equipped with a bubble sensor that triggers immediate cessation of function should air be detected at the inflow cannula. A ventricular pressure transducer regulates ventricular unloading.

Experimental results indicate that complete myocardial unloading can be achieved without hemolysis or end organ damage *(32)*. In animal models, internal mammary artery to left anterior descending anastomoses can be performed easily, and access to all coronary territories is possible without hemodynamic collapse. Clinical trials are currently being designed to test the safety and efficacy of this system as an alternative to CPB for routine myocardial revascularization.

CONCLUSIONS

Device-assisted myocardial revascularization is an evolving technique to be added to the coronary surgeon's growing armamentarium of surgical options. Although presently

used only at skilled LVAD centers, emerging device developments may serve to broaden the use of this technique, particularly in patients undergoing beating heart revascularization. Randomized clinical studies will be necessary to determine if device-assisted CABG offers outcome advantages to standard CPB.

REFERENCES

1. Kirklin JK. Prospects for understanding and eliminating the deleterious effects of cardiopulmonary bypass [editorial]. Ann Thorac Surg 1991;51:529–531 (editorial).
2. Westaby S. Organ dysfunction after cardiopulmonary bypass: a systemic inflammatory reaction initiated by the extracorporeal circuit. Intensive Care Med 1987;13:89–95.
3. Kirklin JK. The postperfusion syndrome: inflammation and the damaging effects of cardiopulmonary bypass. In: John Tinker, ed. Cardiopulmonary Bypass: Current Concepts and Controversies. Monograph. Saunders, Philadelphia, 1989:pp. 131–146.
4. Friedenberg WR, Myers WO, Plotka ED, et al. Platelet dysfunction associated with cardiopulmonary bypass. Ann Thorac Surg 1978;25:298–305.
5. Chenoweth DE, Cooper SW, Hugley TE, et al. Complement activation during cardiopulmonary bypass: evidence for generation of C3a and C5a anaphylatoxins. N Engl J Med 1981;304:497–503.
6. Kirklin JK, Westaby S, Blackson EH, et al. Complement and the damaging effects of cardiopulmonary bypass. J Thorac Cardiovasc Surg 1983;86:845–857.
7. Komai H, Yomamoto F, Tanaka K, et al. Increased lung injury in pulmonary hypertensive patients during open heart operations. Ann Thorac Surg 1993;55:1147–1152.
8. Smith EJ, Naftel DC, Blackstone EH, Kirklin JW. Microvascular permeability after cardiopulmonary bypass. J Thorac Cardiovasc Surg 1987;94:225–233.
9. Buffolo EA, Andrade JCS, Branco JNR, Aquiar LF, Ribiero EE, Jatene AD. Myocardial revascularization without extracorporeal circulation: seven year experience in 593 cases. Eur J Cardiothorac Surg 1990;4:504–508.
10. Benetti FJ, Naselli G. Wood M, Geffner L. Direct myocardial revascularization without extracorporeal circulation: experience in 700 patients. Chest 1991;100;312–316.
11. Pfister AJ, Zaki MS, Garcia JM, et al. Coronary bypass without cardiopulmonary bypass. Ann Thorac Surg 1992;54:1085–1192.
12. Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium. Circulation 1986;74:1124–1136.
13. Alkhulaffi AM, Jenkins DP, Pugsley WB, Treasure T. Ischemic preconditioning and cardiac surgery. Eur J Cardiothorac Surg 1996;10:792–798.
14. Flemeng WJ. Role of myocardial protection for coronary artery bypass grafting on the beating heart. Ann Thorac Surg 1997;63:S18–S22.
15. Pierce WS, Aaronson AE, Prophet GA, Williams DR, Waldenhausen JA. Hemodynamic and metabolic studies during two types of left ventricular bypass. Surg Forum 1972;23:176–178.
16. Pennock JL, Pierce WS, Waldenhausen JA. Quantitative evaluation of left ventricular bypass in reducing myocardial ischemia. Surgery 1976;79:523–533.
17. Shiiya N, Zelinsky R, Deleuze PH, Loisance DY. Changes in hemodynamics and coronary blood flow during left ventricular assistance with the Hemopump. Ann Thorac Surg 1992;53:1074–1079.
18. Waldenberger FR, Meyns B, Wouters P, de Ruyter E, Pongo E, Flameng W. Mechanical unloading properties of axial flow pumps and their effect on myocardial stunning. Int J Artif Organs 1995;18:766–771.

19. Lachterman BS, Felli P, Smalling RW. Improved infarct salvage by left ventricular unloading with the Hemopump immediately prior to and during reperfusion after 2-hour coronary occlusion. J Am Coll Cardiol 1991;(Suppl 2A)17:134A.
20. DeRose JJ Jr, Umana JP, Madigan JD, et al. Mechanical unloading with a miniature in-line axial flow pump as an alternative to cardiopulmonary bypass. ASAIO J 1997;43:M421–M426.
21. Brazier J, Cooper N, Buckberg GD. The adequacy of subendocardial oxygen delivery: the interaction of determinants of flow, arterial oxygen content and myocardial oxygen need. Circulation 1974;49:968–977.
22. Sweeney MS, Frazier OH. Device-supported myocardial revascularization: safe help for sick hearts. Ann Thorac Surg 1992;54:1065–1070.
23. DeRose JJ Jr, Argenziano M, Sun BC, Reemtsma K, Oz MC, Rose EA. Implantable left ventricular assist devices: an evolving long-term cardiac replacement strategy. Ann Surg 1997;226:461–470.
24. DeRose JJ Jr, Umana JP, Argenziano M, Gardocki MT, Catanese KA, Flannery MA, Levin HR, Sun BC, Rose EA, and Oz M. Improved results for postcardiotomy cardiogenic shock using implantable left ventricular assist devices. Ann Thorac Surg 1997;64:1757–1763.
25. Casmir-Ahn H, Lonn U, Peterzen B. Clinical use of the hemopump cardiac assist system for circulatory support. Ann Thorac Surg 1995;59:S39–S45.
26. Wampler RK, Frazier OH, Lansing AM, et al. Treatment of cardiogenic shock with the Hemopump left ventricular assist device. Ann Thorac Surg 1991;52:506–513.
27. Wampler RK, Aboul-Hosn W, Cleary M, Saunders M. The sternotomy Hemopump: a second generation intraarterial ventricular assist device. ASAIO J 1993;39-M218–M223.
28. Waldenberger FR, Wouters P, deRuyter E, Flameng W. Mechanical unloading with a miniaturized axial flow pump (Hemopump): an experimental study. Artif Organs 1995;19:742–746.
29. Meyns BP, Sergeant PT, Daenen WJ, Flameng W. Left ventricular assistance with the transthoracic 24F hemopump for recovery of the failing heart. Ann Thorac Surg 1995;60:392–397.
30. Wiebalck AC, Wouters PF, Waldenberger FR, et al. Left ventricular assist with an axial flow pump (Hemopump): clinical application. Ann Thorac Surg 1993;55:1141–1146.
31. Lonn U, Peterzen B, Granfeldt H, Casimir-Ahn H. Coronary artery operation with support of the Hemopump cardiac assist system. Ann Thorac Surg 1994;58:519–523.
32. Kaplon RJ, Oz MC, Kwiatowski PA, et al. Miniature axial flow pump for ventricular assistance in children and small adults. J Thorac Cardiovasc Surg 1996;111:13–18.
33. Macris MP, Parnis SM, Frazier OH, Fuqua JM, Jarvik RK. Development of an implantable ventricular assist system. Ann Thorac Surg 1997;63:367–370.
34. Westaby S, Benetti FJ. Less invasive coronary surgery: consensus from the Oxford meeting. Ann Thorac Surg 1996;62:924–931.

14 Economic Impact of Less Invasive Cardiac Operations

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CONTENTS

INTRODUCTION

Cost-containment policies have required a fundamental reexamination of surgical practice. Increasingly government, third-party payers, and the public have expected that surgical treatment will be delivered on an ambulatory or short-term basis. This environment, coupled with the success of laparoscopic interventions in reducing postoperative trauma and shortening the length of stay (LOS) without increased morbidity or mortality, has recently extended to affect the practice of cardiac surgery.

The result has been the emergence of less invasive surgical approaches for the treatment of patients with congenital and acquired heart disease. Nowhere has the effect been more pronounced than in the care of patients with coronary artery disease. Indeed, increasing numbers of patients are undergoing less invasive surgical approaches to myocardial revascularization. Although the early results of these approaches are encouraging, long-term patency and survival rates are unknown. Coupled with these uncertainties is the question of whether these less invasive operations provide an economic benefit. At first glance, reduced intensive care unit (ICU) and hospital stay, lower morbidity, and accelerated return to work translate into lower costs. However, these advantages may be mitigated by longer operating room times and unsuspected hidden costs such as reductions

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

in the threshold for surgical intervention and increases in the demand for these procedures *(1)*. This chapter examines the data available regarding the cost analysis of less invasive coronary bypass grafting.

CLINICAL EXPERIENCE AT CHRISTIANA HOSPITAL

Between April 1996 and April 1997, 67 patients underwent minimally invasive direct coronary artery bypass (MIDCAB) procedures at Christiana Hospital. All procedures were performed on an elective basis except for two patients who underwent urgent revascularization after institution of intra-aortic balloon pump support. The study population consisted of two subgroups of patients. The first was comprised primarily of young patients facing high-risk angioplasty (± stent placement) or failed repeated procedures. This group were not considered to be candidates for conventional coronary artery bypass grafting (CABG) because of patient preference or because of the limited nature of their coronary artery disease. The second cohort consisted of patients not considered to be candidates for either conventional CABG or angioplasty ± stent. Most of these patients had undergone prior coronary grafting.

COST ASSESSMENT

Charts of all patients undergoing MIDCABG procedures were examined to identify the charges associated with the procedures. Ratio of cost to charges was calculated as needed using standard conversion factors for the facilities included. Preoperative risk factors and postoperative complications were tallied to identify outliers skewing the hospitalization expenses. Charge information for DRG 107 from the Medical Center of Delaware was compared with cost data gathered from the "Cardiology Preeminence Roundtable," an advisory board that evaluated the clinical and financial impact of minimally invasive cardiac surgery by evaluating changes occurring within the 1200 member institutions.

Additional cost information was extrapolated from the New York State Database, which is a nonvoluntary mechanism for studying all CABG procedures performed in the state. Only data from 1995 were used for analysis. In addition to identifying major patient comorbidities and demographics, specific complication and LOS information is available for 52 MIDCABG patients, 548 conventional single CABG patients, and a total of 19,224 coronary bypass patients receiving no other cardiac procedure. No direct financial information is available within the Database.

OPERATIVE TECHNIQUES

At the Medical Center of Delaware, all patients underwent standard induction of general endotracheal anesthesia, as per cardiac anesthesia protocols, with a double-lumen endotracheal tube and were placed in the supine position. One of three thoracic

incisions was used to gain cardiac exposure—full sternotomy, hemisternotomy, or left anterior thoracotomy.

Myocardial stabilization was performed in several fashions as the technique evolved, but most recently has been performed with the suction octopus device (Medtronic, Minneapolis, MN). This stabilizer has the advantage of minimal myocardial depression and excellent visualization because the area of interest is retracted into the field rather than compressed into the pericardium. Two-dimensional epicardial beacon motion measurements on beating pig hearts has demonstrated that the baseline cardiac motion in all three dimensions of 12–18 mm can be reduced reliably to 1 mm *(2)*. Postoperatively, suction hematomas are visible; however, in animal studies at 6 wk postoperative follow-up, no evidence of trauma was evident, even by light microscopy. In our series, 10 patients had multiple bypasses, 2 had partial femoro-femoral bypass, and 1 had intraoperative conversion to a conventional CABG.

SHORT-TERM RESULTS

All patients were extubated in the operating room. There were no intraoperative deaths nor returns to the operating room during the same hospital stay. Two postoperative deaths occurred owing to arrhythmia and myocardial infarction in a nongrafted territory. Mean hospital stay was 2 d. These factors were important variables in allowing hospital charges to average approximately half ($14,676) that of conventional CABG ($22,817) and to approximate that of stenting ($15,000). When only the higher risk CABG patients are studied, the MIDCABG cohort charges are higher than the lower risk cases, but progressively less expensive than conventional procedures performed in higher risk patients. Part of the divergence in cost is owing to renal insufficiency and the neurologic sequelae of placing older, sicker patients on cardiopulmonary bypass (CPB). If hospital reimbursement for CABG without catheterization is equivalent to the 1997 Medicare rates for large urban areas ($17,687), the break-even point looms close.

Similar estimates for hospital costs (rather than charges) were made by the Advisory Board Company for two U.S. institutions. For DRG 107, the conventional approach cost was $6000 compared with $5309 for MIDCAB and $4477 for average risk transcatheter approaches. For a second hospital, the conventional CABG cost was $12,197 compared with $8018 for single-stent intervention and $7174 for the MIDCAB and $5455 for a percutaneous transluminal coronary angioplasty (PTCA). Much of this advantage resulted from a reduction in LOS from an average of 5.6 d for conventional CABG to 1.8 d for MIDCAB. The additional savings were owing to an elimination of perfusion expenses including disposables, which averaged $1200 per case. Reduction in ICU, ventilation, and rehabilitation time were additional contributing factors. Overall, MIDCAB procedures resulted in average profits per case to the hospital of just over $10,000 in comparison to approx $5000 per conventional CABG, $3500 for PTCA alone, and less than $1000 for stents. Indeed, when multiple stents were used, facilities generally lost revenue on the procedure. Needless to say, managed care companies are already attempting to capture

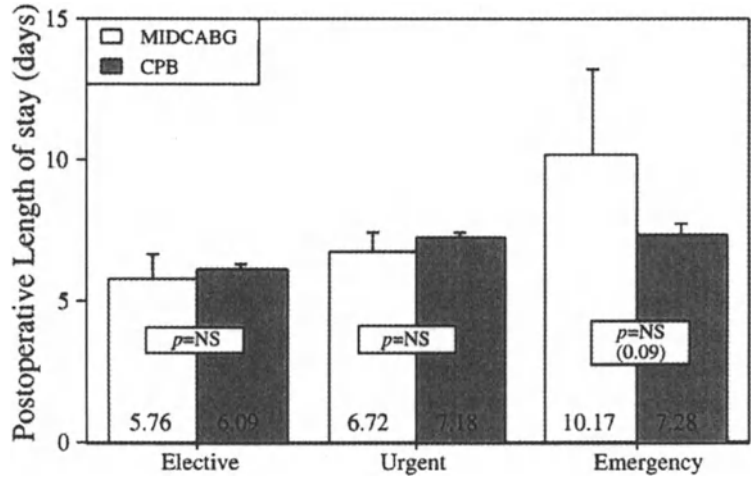


Fig. 1. LOS by surgical priority. Postoperative LOS did not differ significantly between MIDCABG and conventional CPB cases for elective, urgent, and emergency cases. However, urgent and emergency cases overall had significantly longer recovery times than elective cases ($p < 0.0001$).

this potential revenue stream by identifying and specifically reimbursing for MIDCAB procedures.

From the New York State Database for 1995, the importance of acuity (elective, urgent, or emergency), age (70-yr-old divide), and ejection fraction (40% divide) as predictors of LOS becomes evident (Figs. 1–3). Interestingly, younger patients did not benefit from MIDCAB as much as older patients in terms of LOS over conventional procedures. The number of grafts created did not affect LOS. LOS for patients undergoing conventional CABG was 6.8 ± 3.3 d, not significantly different from the LOS for MIDCABG patients (6.8 ± 4.2 d) (Fig. 4). This overall similarity was owing to the inclusion of extremely high risk cases within the MIDCABG group who had an inordinately long LOS even in comparison to the conventional high-risk CABG population (10.2 vs 7.3 d). Therefore, cost savings from these procedures were mainly related to avoidance of perfusion expenses and shorter operative times. In the Columbia-Presbyterian database, a conventional single-vessel CABG operation had an intraoperative time of 179 ± 51 min compared with 112 ± 24 for a traditional MIDCABG approach.

Although not directly germane to the immediate perioperative expenses, longer-term complications will raise the societal costs of this approach, as has been demonstrated in high-risk or three-vessel angioplasty. In our series, follow-up was at 1-, 6-, and 12-mo intervals. Catheter intervention was required within 3 mo in 8.9% of patients; no further interventions were required in these or any other patients during the study period.

DISCUSSION

Since its introduction in 1967, CABG has become a reliable surgical treatment for severe coronary atherosclerosis. Three major randomized trials performed in the 1970s—

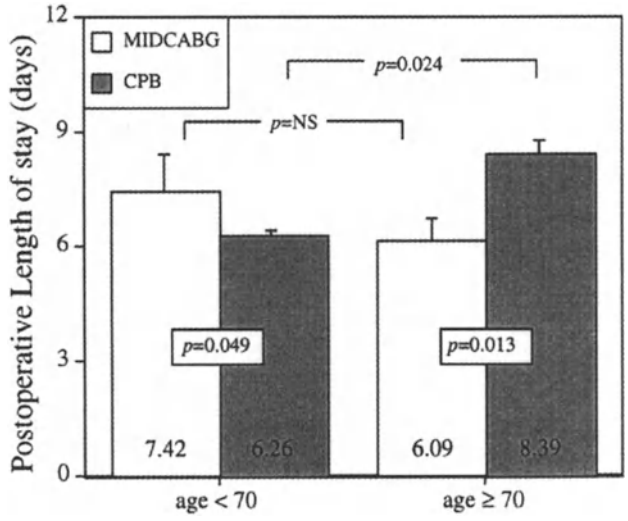


Fig. 2. Age stratification. Patients older than 70 yr recover more quickly from MIDCABG than from conventional CPB. Older and younger MIDCABG patients had similar recovery times; however, older patients receiving CABG on CPB had a longer recovery time than younger CPB patients.

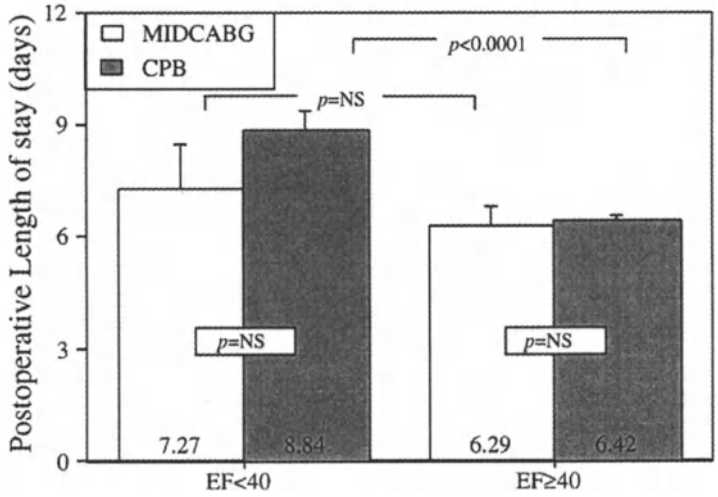


Fig. 3. Ejection fraction stratification. Patients with normal ejection fractions (≥40%) had similar recovery times from MIDCABG and conventional CPB, as was the case for those with depressed ejection fractions. CPB patients with depressed ejection fractions, however, had significantly longer recovery times than CPB patients with normal ejection fractions, a difference not seen in MIDCABG patients.

the VA Study *(2)*, the European Cooperative Surgical Study (ECSS) *(3)*, and the Coronary Artery Surgery Study (CASS) *(4)*—compared surgical with medical management of coronary artery disease, and identified patient populations in which surgery achieved

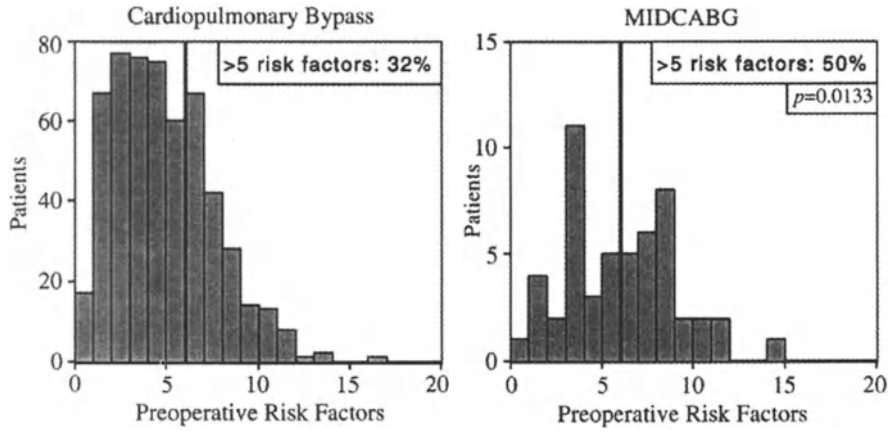


Fig. 4. Risk histogram. The percentage of MIDCABG patients with more than five preoperative risk factors (50%) was significantly greater than the CPB population (32%), suggesting that a higher risk group of patients are being selected for MIDCABG.

superior results. These conclusions provided the framework for the establishment of today's indications and reimbursement for coronary artery bypass surgery.

More recently, these data have been extrapolated to justify referring patients for less invasive angiographic procedures ranging from percutaneous transluminal angioplasty to intraluminal stenting. The success of these modalities has varied and has impacted the perceived financial benefits to society of the procedures, especially since longer-term complications are often not evident early and are not captured in cost accounting.

CPB with pump oxygenation is used for nearly all conventional coronary bypass operations *(5)*, and is associated with a wide variety of adverse effects, which will increase postoperative costs. In particular, pulmonary *(6,7)* and central nervous system complications (stroke, seizures, and impaired consciousness) are leading sources of morbidity and cost increases and have been attributed, in large part, to the effects of CPB *(8–10)*. Myocardial dysfunction occurs commonly following CPB and may require prolonged inotropic support, particularly in patients with poor preoperative ventricular function, older age, or prolonged duration of aortic cross-clamping *(11)*. In a recent study in which 220 cardiac operations were performed without CPB, and compared with similar operations done on bypass, the off-bypass group demonstrated no differences in mortality but significant decreases in transfusion requirements and incidence of postoperative myocardial dysfunction, which translates into reduced costs *(12)*.

Candidate patients for MIDCABG have more of a bimodal distribution of comorbid factors than the more classic bell-shaped pattern in which conventional CABG patients fall (Fig. 4). The high-risk cohort skews the cost data of this group of patients, as can be seen in the New York State Database in which the LOS for the two groups were almost identical. Preoperative morbidity factors were much more predictive of LOS than the number of grafts performed. However, the cost of managing sicker patients appears to be reduced if managed by MIDCAB rather than by conventional approaches, based on our

limited early experience. Despite the high-risk nature of many of these cases, the inability to demonstrate a reduced LOS in a statewide survey reflects the inability of physicians in 1995 to adapt to the possibility of discharging patients early, even if the less-invasive procedure would allow this prospect. Changing practice patterns are equally important to the technical learning curve of the procedure if potential cost-saving benefits of the procedure are to be recognized.

For the healthier patients able to undergo any potential revascularization procedure, the early cost data support the superiority of the MIDCAB approach. However, long-term efficacy data are lacking, so the overall financial benefits may be limited. As was seen in the EAST trial *(13)*, early financial benefits will evaporate if medium-term complications require repeat interventions with some crossover to conventional CABG.

Other studies have supported these findings. Fonger et al. *(14)* demonstrated in a cohort of 100 patients that MIDCABG patient charges were $13,415 in comparison to $21,414 for conventional CABG and $13,415 for stents and $7803 for PTCA. However, this study was performed prior to the rapid anticoagulation and hospital discharge protocols now used for stent cases, and overstates the cost of these procedures.

Additional and more recent support of these findings by King et al. *(15)* confirmed that in the early perioperative period, MIDCABG costs ($10,129 ± 1104) approximate PTCA ($9113 ± 3039) and are less than conventional CABG ($17,816 ± 1043), $p = 0.0028$. Much of this benefit resulted from the reduced LOS of the MIDCABG cohort (2.7 ± 0.3 d) compared to conventional CABG (4.8 ± 0.5 d), $p = 0.009$. The authors in this study argue that since 20% of invasive cardiology procedures will require repeat interventions within 6 mo, these costs should be included in the decision to pursue this approach *(15)*. In a similar fashion, if MIDCABG procedures are found to have a predictable early failure rate, the estimated costs of the procedure must be increased accordingly.

Ultimately, the cost-effectiveness of this approach to revascularization, like the many that have preceded it, will be dependent on the longevity of the benefit. We should be interested in the annual cost of quality life gained rather than simply the early periprocedural cost information. Quality, not cost, must be established first.

REFERENCES

1. Lawrence K. Minimal access surgery: harnessing the revolution. Lancet 1994;343:308–309.
2. Takaro T, Hultgren HN, Lipton MJ, Detre KM. The VA cooperative randomized study of surgery for coronary arterial occlusive disease II. Subgroup with significant left main lesions. Circulation 1976;54(6 Suppl):III107–III117.
3. European Coronary Surgery Study Group (ECSS). Coronary artery bypass surgery in stable angina pectoris: survival at two years. Lancet 1979;1(8122):889–893.
4. Coronary Artery Surgery Study (CASS): a randomized trial of coronary artery bypass surgery: Survival data. Circulation 1983;68(5):939–950.
5. Subcommittee on Coronary Artery Bypass Graft Surgery. Guidelines and indications for coronary artery bypass graft surgery. A report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures. J Am Coll Cardiol 1991;17(3):543–589.

6. el-Fiky MM, Taggart DP, Carter R, Stockwell MC, Maule BH, Wheatley DJ. Respiratory dysfunction following cardiopulmonary bypass: verification of a non-invasive technique to measure shunt fraction. Respir Med 1993;87(3):193–198.
7. Louagie Y, Gonzalez E, Jamart J, Bulliard G, Schoevaerdts JC. Post-cardiopulmonary bypass lung edema. A preventable complication? Chest 1993;103(1):86–95.
8. Mills SA. Cerebral injury and cardiac operations. Ann Thorac Surg 1993;56(Suppl 5):S86–S91.
9. Kuroda Y, Uchimoto R, Kaieda R, et al. Central nervous system complications after cardiac surgery: a comparison between coronary artery bypass grafting and valve surgery. Anesth Analg 1993;76(2):222–227.
10. Rankin JM, Silbert PL, Yadava OP, Hankey GJ, Stewart-Wynne EG. Mechanism of stroke complicating cardiopulmonary bypass surgery. Aust N Z J Med 1994;24(2):154–160.
11. Royster RL. Myocardial dysfunction following cardiopulmonary bypass: recovery patterns, predictors of inotropic need, theoretical concepts of inotropic administration. J Cardiothorac Vasc Anesth 1993;7(4 Suppl 2):19–25.
12. Pfister AJ, Zaki MS, Garcia JM, et al. Coronary artery bypass without cardiopulmonary bypass. Ann Thorac Surg 1992;54(6):1085–1091.
13. King SB, Lembo NJ, Weintraub WS, Kosinski AS, Barnhart HX, Kutner MH, EAST Investigators. Emory Angioplasty Versus Surgery Trial (EAST): design, recruitment, and baseline description of patients. Am J Cardiol 1995;75:42–59C.
14. Fonger JD, Nicholson CF, Sussman MS, Salomon NW. Cost analysis of current therapies for limited coronary artery revascularization. Circulation 1996:94;51 (abstract).
15. King RC, Reece TB, Hurst JL, et al. Minimally invasive coronary artery bypass grafting decreases hospital stay and cost. Ann Surg 1997;225(6):805–811.

15 Minimally Invasive Coronary Artery Bypass Grafting

Quality of Life Issues

Lorraine Choi, BA, Windsor Ting, MD, and Prashant Sinha, SB, MENG

CONTENTS

INTRODUCTION

In addition to the achievements in technique and technology that off-pump myocardial revascularization presents, minimally invasive coronary artery bypass grafting (MICABG) has subtly made quality of life (QOL) a major concern of cardiac surgeons around the world. Advances in treatment and the subsequent decline in CABG surgery mortality rates over the last 20 yr introduced a need to incorporate these subjective measures in studies evaluating treatment efficacy *(1)*. The most recent elevation of QOL to the forefront of the medical decision-making process stems directly from the unfailing invocation of patient preference as a primary benefit balancing the known risks of MICABG. This may present a renewed opportunity to commit the focus of medicine more closely and consistently toward patient preferences for outcomes.

The objective and subjective outcome goals for MICABG have already been defined by the known risks and benefits of the two alternative methods of revascularization: conventional CABG with cardiopulmonary bypass (CPB), and percutaneous transluminal coronary angioplasty (PTCA). Any conversation on outcomes will necessarily require understanding of the substantial body of research already accomplished by investigators of these two procedures. A second challenge to fruitful discussion is the inconsistency in methods and reports from studies on MICABG. Off-pump myocardial revascularization

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

is offering a surgical alternative not only to patients with single-vessel disease not amenable to PTCA, but also to subpopulations of patients with coronary artery disease for whom CPB represents a considerable risk. This diversity disallows blanket statements on treatment efficacy for a single MICABG population. The delineation of preoperative risk factors, surgical technique, and outcomes is essential for the MICABG learning curve and any long-term comparative evaluation. Furthermore, standardization of outcome measures across treatments will be vital to our understanding of MICABG and its role as an alternative or adjunct procedure to PTCA and CABG.

Our discussion will proceed as follows:

1. MICABG's role as an intervention vis-à-vis the shortcomings of current treatment alternatives.
2. The techniques currently used to measure QOL and the standards set by PTCA and CABG.
3. Our recommendations for a battery of QOL measures to standardize these outcomes for this field in its infancy.

BASELINES SET BY PTCA AND CABG

For the convalescing individual, QOL is not separable from medical outcome. Postoperative pain, time to extubation, intensive care unit (ICU) length of stay (LOS), incidence of complications, need for reoperation, and length of hospitalization are parameters by which the surgeon measures a successful operation. They also clearly affect the QOL of a patient. It is reasonable to suggest that a protracted hospitalization and convalescent course will significantly alter patient QOL in the early postoperative period. Similarly, longer term variables by which both physician and patient mark operative success, such as the relief of angina, exercise tolerance, need for repeat interventions, incidence of myocardial infarction, and longevity, have a close correlation with QOL issues.

The cohort of coronary artery disease patients with only proximal left anterior descending (LAD) artery stenosis resembles most closely the patients who currently undergo MICABG *(2)*. In a randomized trial comparing the results of PTCA to grafting of the left internal mammary artery to the LAD on the arrested heart for isolated proximal LAD stenosis in 134 patients, Goy et al. *(3)* reported that the rates of cardiac-related death and myocardial infarction were not significantly different between the groups at a median follow-up of 2.5 yr *(3)*. However, there were substantial differences between the groups. PTCA patients were taking more antianginal medications than the CABG cohort. Freedom from adverse events was 86% in CABG-treated patients and 43% in PTCA-treated patients. The rate of restenosis in the PTCA group was 32%, with repeat angiography in 44%, repeat PTCA in 15%, and the need for CABG in 16%. Furthermore, a 58% restenosis rate was reported among the patients who underwent repeat PTCA. By contrast, only 3% of CABG patients required any repeat intervention. Even though the authors described restenosis in the PTCA group as benign, it is reasonable to infer from the relatively high frequency of adverse events in the PTCA group that the QOL among these patients may have been adversely affected. This study suggests one of the primary potential benefits

of MICABG: providing the angina-suffering patient with a long interval free of symptoms and repeat interventions.

Ovrum et al. *(2)* recently reported perioperative data for 99 patients undergoing elective CABG for single vessel disease. The risk profile indicates a younger population (57.7 ± 7.3 yr) with normal ejection fraction and low incidence of diabetes mellitus. The average ischemic time for this patient population was 15.3 ± 9.6 min and total bypass time was 29 ± 13 min. No homologous blood products were given, minimal morbidity was noted, and no deaths were observed *(2)*. These near optimal results demonstrate the challenge that MICABG faces in attempting to provide a superior clinical result to this relatively healthy population.

Zenati and associates *(4)* showed the potential impact of MICABG on early recovery in a small study comparing 17 minimally invasive direct coronary artery bypass (MIDCAB) recipients with 33 routine CABG patients. The authors reported that 41% of the MICABG patients and none of the conventional CABG patients were extubated in the operating room; in addition, 42% of conventional CABG patients received blood products whereas none in the MICABG cohort were transfused. The LOS in the ICU was 12.3 ± 3.3 h for the MICABG group and 32.3 ± 12.6 h for the conventional group. Moreover, 59% of MICABG recipients were discharged home within 48 h compared with none in the conventional cohort.

Data obtained from the New York State Database, a mandatory registry of all coronary bypass procedures performed in the state, demonstrates that the early experience with MICABG procedures is associated with complication rates similar to those seen for conventional single-vessel graft procedures (Table 1).

Within the CABG population, gender and age, as well as factors such as low ejection fraction and diabetes, are associated with higher complication rates. MICABG may therefore prove to be the better surgical decision for certain at-risk subpopulations, but not others. Additionally, we may see a trade-off in postoperative comorbidity factors, such that patient preference may indeed prove to be the single most vital component to the surgical decision-making process. Aiding in that process will be objective data such as that compiled by the New York Database that outlines rates of complications for a given profile and a given surgery, but also reasonable data on how others have seen their QOL affected by these postoperative complications.

Gender Differences

Gender differences acquire greater acceptance with ongoing investigation. Several studies have noted that women present with more preoperative risk factors at the time of surgery (e.g., age, history of smoking, diabetes, small frame size) *(5–7)*. But even when matched for age, angina class, and severity of coronary artery disease, women still have operative mortalities that are twice that of their male counterparts *(8)*. Women are more likely to undergo single- or double-graft procedures and, consequently, experience shorter operative, cross-clamp, and CPB times. Nevertheless, men spend less time on mechanical ventilation, in the ICU, and in the hospital postoperatively *(9)*. Women have lower 2-yr graft patency rates and inferior early, late, overall, and event-free survival *(10)*.

Table 1
New York State Database Complication Rates for Single-Vessel Graft Procedures: Comparison of Conventional and Minimally Invasive Techniques

	MICABG[a]	*Conventional CABG*[b]	p *value*
Age (yr)	65.9 ± 1.4	61.8 ± 0.5	0.013
Complication (%)			
Cerebrovascular accident	0	5	NS[c]
Transmural myocardial infarction	0	2	NS
Nontransmural myocardial infarction	0	5	NS
Deep wound infection	0	2	NS
Reoperation for bleeding	0	3	NS
Return to OR	1	2	NS
Heart block requiring pacemaker	2	2	0.04
Sepsis/endocarditis	0	3	NS
Gastrointestinal bleeding/perforation/infarct	0	4	NS
Renal failure/dialysis	0	2	NS
IABP[d] inserted in OR	1	10	NS
Respiratory failure	3	17	NS
Brachial plexopathy	1	0	0.08
Phrenic nerve palsy	0	0	NS
Malignant ventricular arrhythmia	4	10	0.03

[a] $n = 52$.
[b] $n = 548$.
[c] Not significant.
[d] Intra-aortic balloon pump.

In the short-term, women have reported different recovery profiles than men. Measuring physical recovery, emotional affect, and symptoms 1, 3, and 6 wk post-CABG, Artinian and Duggan *(11)* observed that women reported greater ambulatory difficulty, higher depression scores, and were less able to manage household activities than men. The investigators also found that women complained more of symptoms of illness at each of the time points. Similarly, Carey et al. *(12)* observed that women consistently ranked their health status as lower than their male counterparts annually for up to 15 yr post-operatively. Because a smaller frame is anatomically preferable for most MICABG approaches and because women appear to be more sensitive to the adverse effects of CPB, one may speculate that MICABG may improve both subjective and objective outcomes for women by the avoidance of CPB and by decreased operative and anesthesia time.

Elderly and Others

An increasing number of patients in their 80s and 90s are undergoing myocardial revascularization *(13,14)*. Indeed, Chocron et al. *(15)* reported that in 1993, 15% of patients who underwent open-heart surgery were over 75 yr old and that the percentage was increasing yearly, reflecting a general trend toward an older population *(15)*. For this

cohort of patients who undergoes CABG, perioperative mortality and morbidity rate are high and length of hospitalization and duration of convalescence are increased. Glower et al. *(16)* and colleagues reported a 30-d mortality of 10% and a rate of significant in-hospital complications of 29%. Similarly, Cane et al. *(17)* reported a 9.1% hospital mortality rate and a 49% incidence of perioperative events among their cohort of older patients who underwent CABG.17 At our institution, a statistically significant difference in the incidence of cerebral dysfunction was noted between elderly open-heart patients when compared with both younger open-heart surgery patients or with elderly patients undergoing noncardiac procedures *(18)*.

In another study, a 7% operative mortality and a 3-yr survival rate of 73% was observed among more than 200 octogenarians who underwent isolated CABG. At a mean follow-up of 36 mo, this elderly cohort of patients rated their overall state of health as 77 (0–100 scale) on a QOL instrument measuring mobility, self-care, pain, daily activities, and anxiety *(19)*.

Pain, fatigue, and sleep disturbance are frequent complaints among elderly CABG patients at long-term follow-up. A strong correlation in health satisfaction with the ability to accomplish basic functions (e.g., ambulation and self-care) was reported among CABG patients 80 yr old and older, but despite a 92% improvement in New York Heart Association (NYHA) class, 22% of this patient population reported dissatisfaction with their health *(20)*.

PTCA has been an attractive option among these older patients because of its lower morbidity and mortality in the short term. Life expectancy for the very elderly (80 yr) is approx 6 yr *(20,21)*, therefore, QOL has even more importance as an outcome for this patient population. MICABG represents a potentially attractive third option to provide a single medical intervention without the associated disadvantages of a major operation. Initial results for MICABG in the elderly and high-risk populations have been reported by several institutions *(1,22–25)*.

Because mortality rates remain high for patients with substantial comorbidities such as renal failure, diffuse vasculopathy, or pulmonary insufficiency *(26)*, QOL has not been sufficiently addressed for survivors of high risk CABG and PTCA.

As Nielsen et al. *(27)* pointed out, there is a striking absence of QOL data for survivors of procedures associated with high rates of mortality. But the decision-making process for the high-risk patient would certainly benefit from better understanding of QOL outcomes for each of the medical choices now available to them. Our treatment of coronary artery disease, which may consist of a lifelong series of interventions, can be made more successful with the comprehensive understanding of the risks and benefits of repeat or complementary PTCA, the various surgical approaches and techniques, and patient expectations.

MEASURING QOL

The trinity of QOL end points for cardiac patients in the past has consisted of return to work, freedom from angina, and physical activity. The increasing age and illness of candidates for myocardial revascularization often precludes the relevance of the first of

these, while the latter two, often closely correlated, provide a limited view of outcomes based primarily on functional status, rather than the patient's opinion of the same.

The Randomized Intervention Treatment of Angina (RITA) trial compared the results of initial treatment strategies of PTCA and CABG on patients with angiographically proven CAD and angina. Although interim results at the 2.5-yr follow-up showed no significant difference in prognosis between treatment groups, Pocock et al. *(28)* were able to elucidate QOL differences using the Nottingham Health Profile (NHP). This tool has been utilized successfully as an indicator of the limitations on health imposed by disease and has been validated in several studies on treatment evaluations *(29,30)*. The 38-item questionnaire delineates the realm of QOL into six fields: physical mobility, pain, energy, sleep, emotional reaction, and social isolation. Items are weighed so that a continuous distribution of scores is possible. The NHP was administered to 1011 patients in the RITA trial at baseline, then 6 mo and 2 yr postrandomization to treatment group. Improvements were noted in both groups over time, but statistically significant differences between the two treatments were not observed in the six individual fields. However, because CABG results consistently showed slightly better results over PTCA in each category, the overall NHP score showed a statistically significant improvement in CABG patients compared with PTCA recipients. At 6 mo, the mean difference in favor of CABG was 1.21 items ($p = 0.07$); at 2 yr, the difference was reduced to 0.79 items ($p = 0.1$). The impaired scores in the PTCA group were correlated to an increased chance of persistent or lingering anginal pain *(28)*.

In the Bypass Angioplasty Revascularization Investigation trial, results again showed no significant differences in mortality and myocardial infarction at 5 yr postoperatively between treatment arms *(28)*. Recently investigators reported the results of the annual administration of the Duke Activity Status Index (DASI) to 934 randomized patients of this trial *(31)*. This index, which consists of 12 questions measuring functionality in activities common to daily living, weighs scores based on known metabolic equivalents expended in each activity *(32)* (Table 2).

For the first 3 yr following the initial treatment, CABG-treated patients had better scores than PTCA patients. This suggests that the relief of angina symptoms has a profound effect on physical function, discernible in an index specific to that field of QOL *(31)*.

Physical function and alleviation of disease symptoms, however, are insufficient determinants of QOL. Low self-esteem, lack of interest in social interaction, sexual dysfunction, and depression have been noted in patients, despite good physiological outcomes *(33)*. For example, Eriksson *(34)* reported a 10% incidence of postoperative depression following CABG; 22% of 101 male patients were dissatisfied with the results of their surgery, despite an improvement in NYHA classification. Sjoland et al. *(35,36)* convincingly demonstrated the limitations of a focus on physical functionality. In a 2-yr follow-up to CABG surgery, patients underwent exercise testing as well as the NHP profile. Moderate to mild correlation between overall QOL and exercise tolerance was observed, most closely between exercise tolerance and the two fields of physical mobility and pain. Yet, although the greatest improvement in exercise tolerance was seen in men,

Table 2
DASI to Measure Functional Capacity in Daily Living Activities

Can you

1. Take care of yourself, i.e., eat, dress, bathe, or use the toilet?
2. Walk indoors, such as around your house?
3. Walk a block or two on level ground?
4. Climb a flight of stairs or walk up a hill?
5. Run a short distance?
6. Do light work around the house such as duesting or washing dishes?
7. Do moderate work around the house such as vacuuming, sweeping floors, or carrying in groceries?
8. Do heavy work around the house such as scrubbing floors or lifting heavy furniture?
9. Do yardwork such as raking leaves, wedding, or pushing a power mower?
10. Have sexual relations?
11. Participate in moderate recreational activities such as golf, bowling, dancing, doubles tennis, or throwing a baseball or football?
12. Participate in strenuous sports such as swimming, singles tennis, football, basketball, or skiing?

the better improvements in overall QOL came from women *(35,36)*. This suggests that physiological well-being and physical functionality represent an incomplete image of QOL, one that needs to be complemented by impressions of emotional status, social functionality, cognitive performance, and general perception of health and disease.

A final point of QOL and surgical intervention is made by Chocron et al. *(37)* and associates. These investigators prospectively enrolled 215 elective open-heart patients in a study utilizing the NHP. CABG significantly improved QOL parameters as early as 3 mo postoperatively, most markedly among patients who were younger than 70 yr of age. Of all the parameters evaluated, the only one that failed to match a normal population at 3 mo postoperatively was sleep. This study suggests that any potential improvement in NHP QOL variables in a MICABG population would be limited primarily to the immediate postoperative period. These QOL parameters would likely include items such as length of hospitalization, strength and early mobility, pain and discomfort of the surgery, and duration of early convalescence *(37)*.

Our institution has begun a number of studies that will provide useful baseline data for comparative QOL studies. Our own functional recovery index, in development, began with an intent to look at the effect of different surgical incisions on patient recovery in the immediate postoperative period. Using a series of range of motion exercises and pulmonary function tests, we intend to bring quantitative and qualitative data to the debate on surgical approaches for MICABG. Patients scheduled for elective bypass surgery are tested preoperatively to establish baseline values of vital capacity, minute ventilation, range of upper body motion, and pectoral muscle strength. The pulmonary function tests measure respiratory muscle range and pain associated with breathing. A handheld Wright spirometer measures the expiratory flow volumes. The range of motion tests are horizontal adduction, lateral abduction, and forward flexion of the shoulder. The

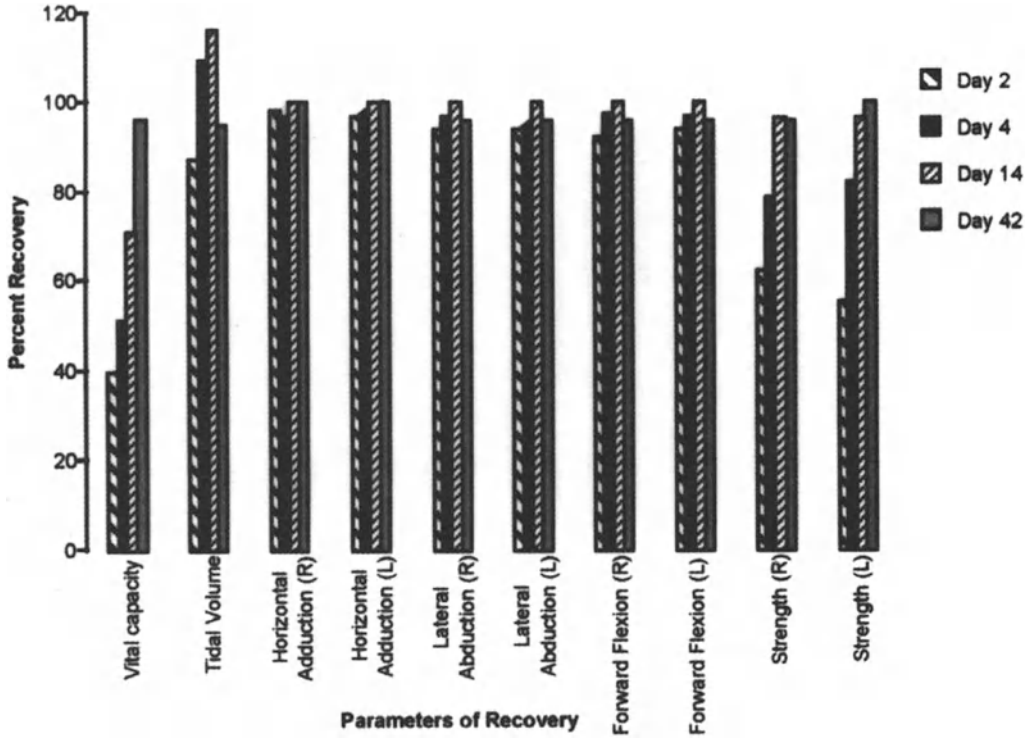


Fig. 1. Short-term functional recovery following elective median sternotomy for open-heart surgery. Pulmonary function tests and pectoral muscle strength are evaluated regarding pain caused by these activities at different time points and graded on a visual analog scale (0–10).

normal ranges for these test are 90°, 180°, and 180°, respectively. Pectoral muscle strength is assessed with the patient supine: horizontal shoulder adduction is repeated with hand weights of 1–5 lb. Each measure is followed by patient assessment of pain, using an 11-point visual analog scale. Physiological parameters are investigated postoperatively every 2 d during in-patient stay, and then at the 2- and 6-wk points again.

Preliminary results on 50 CABG patients demonstrate quick recovery from median sternotomy (Fig. 1). Patients deny overall pain greater than mean = 5 (on visual analog scale) by the second postoperative day. By the time of discharge (6.8 ± 2.4 d), the mean pain report is 2.4, with recovery to baseline of range of motion and pectoral muscle strength. Vital capacity is approx 70% at the 14th postoperative day, with no reported pain from exertional use of the relevant muscle groups. During postoperative interviews on d 14 or 42, the major complaint is related to generalized fatigue, not localized pain related to the surgical wound.

Our protocol has been revised to incorporate greater participation from the patient and the patient's family. Provided with written and verbal instructions, patients perform the range of motion exercises, pulmonary function tests, and strength assessment regularly

during the interim between discharge and the 6-wk surgical follow-up visit. Emotional effect is monitored during this period, as well as during the in-patient stay, with visual analog scales and relevant portions of the NHP. Likewise, overall physical recovery is assessed with repeat administration of the DASI and the physical function and pain sections of the NHP. In collaboration with our institution's Health Outcomes Department, long-term QOL changes are examined by follow-up NHP administration every 6 mo for 2 yr. The Division of Cardiac Anesthesiology has standardized a battery of neuropsychometric exercises, administered perioperatively, to elucidate the risk of cerebral dysfunction not only between groups of patients undergoing on- or off-pump myocardial revascularization, but also among the various risk profiles. Our efforts, we believe, provide the comprehensive examination of QOL and functional recovery in both the short- and long-term frames of reference that are needed for comparison between surgical treatments.

CONCLUSION

We are today under the influence of two often conflicting forces pushing cost-effective medicine and high-tech science. MICABG is an example of this conflict. In terms of resource utilization, this surgery is reflecting highly desirable short-term outcomes such as decreased operating times, decreased ICU time, and shorter overall hospital stays. But as a result, our outcome measures are less scientific. By sending our patients home sooner, we drive them that much more quickly out of our reach and call that a favorable outcome when in fact it is only a questionable one. In our subjective and objective assessments, we all too often leave out precisely what it might mean to a patient to be sent home 48 h after open-heart surgery.

In the same way that we have not examined truly the correlation between economic benefit and patient preference, we have not evaluated the relationship between psychological well-being and patient satisfaction with that state of well-being. What is perhaps most unique about MICABG procedures is the mythology surrounding their ability to produce higher levels of patient satisfaction, so reported without the sustained focus and analysis that surgical problems typically receive. Since this superficial treatment of subjective outcomes will not likely survive beneath the scrutiny of well-controlled clinical trials investigating MICABG efficacy, we are facing a new opportunity to define and standardize a valid and meaningful method of measuring patients' QOL. The interest and participation of surgeons and physicians in this process may prove as instrumental to the improvement of patient outcomes as MICABG, the technique that serves as both subject of and catalyst to this welcome discussion.

REFERENCES

1. Lachat M, Vogt PR, Miederhauser U, et al. Minimally invasive coronary artery bypass techniques as adjunct to extracardiac procedures. Ann Thorac Surg 1997;63:S61–S63.
2. Ovrum E, Tangen G, Am Holen E. Facing the era of minimally invasive coronary grafting: current results of conventional bypass grafting for single vessel disease. Ann Thorac Surg 1997;64:159–162.

3. Goy JJ, Eeckout E, Burnand B, et al. Coronary angioplasty versus left internal mammary artery grafting for isolated proximal left anterior descending artery stenosis. Lancet 1994;343:1449–1453.
4. Zenati M, Domit TM, Saul M, et al. Resource utilization for minimally invasive direct and standard coronary artery bypass grafting. Ann Thorac Surg 1997;63:S84–S87.
5. Kudenchuk PJ, Maynard C, Martin JS, Wirkus M, Weaver WE. Comparison of presentation, treatment and outcome of acute myocardial infarction in men versus women (the myocardial infarction triage and intervention registry). Am J Cardiol 1996;78:9–14.
6. Bergelson BA, Tommaso CL. Gender differences in clinical evaluation and triage in coronary artery disease. Chest 1995;108:1510–1513.
7. Majeed FA, Cook DG. Age and sex differences in the management of ischemic heart disease. Public Health 1996;1010:7–12.
8. Loop FD, Golding LR, Macmillan JP, Cosgrove DM, Lytle BW, Sheldon WC. Coronary artery surgery in women compared with men: analysis of risks and long-term results. J Am Coll Cardiol 1983;1:383–390.
9. Christakis GT, Weisel RD, Buth KJ, et al. Is body size the cause for poor outcomes of coronary artery bypass operations in women? J Thorac Cardiovasc Surg 1995;110:1344–1358.
10. Richardson JV, Cyros RJ. Reduced efficacy of coronary artery bypass grafting in women. Ann Thorac Surg 1986;42:S16–S21.
11. Artinian NT, Duggan CH. Sex differences in patient recovery patterns after coronary artery bypass surgery. Heart Lung 1995;24:483–494.
12. Carey JS, Cukingnan RA, Singer LKM. Health status after myocardial revascularization: inferior results in women. Ann Thorac Surg 1995;59:112–117.
13. Glock Y, Faik M, Laghzaoui A, Moali I, Roux D, Fournial G. Cardiac surgery in the ninth decade of life. Cardiovasc Surg 1996;4:241–245.
14. Cheitlin MD. Coronary bypass surgery in the elderly. Clin Geriatr Med 1996;12:195–205.
15. Chocron S, Rude N, Dubussaucy A, et al. Quality of life after open heart surgery in patients over 75 years old. Age Ageing 1996;25:8–11.
16. Glower DD, Christopher TD, Milano CA, et al. Performance status and outcome after coronary bypass grafting in persons aged 80 to 93 years. Am J Cardiol 1992;70:567–571.
17. Cane ME, Chen C, Bailey BM, et al. CABG in octagenarians: early and late events and actuarial survival in comparison with a matched population. Ann Thorac Surg 1995;60:1033–1037.
18. Heyer EJ, Delphin E, Adams D, et al. Cerebral dysfunction after cardiac operations in elderly patients. Ann Thorac Surg 1995;60:1716–1722.
19. Sollano J, Greene R, Williams D, Cannavale G. A model for determining cost-effectiveness of coronary artery bypass graft surgery in octagenarians. Abstract presented at the International Society for Technology Assessment in Health Care Thirteenth Annual Meeting. May 1997; Barcelona, Spain.
20. Murphy SF, Nickerson NJ, Kouchoukos NT. Functional outcome in the elderly after coronary artery surgery. Medsurg Nurs. 1996;5:107–110.
21. Projections of the Population of the United States by Age, Sex, and Race 1983 to 2080. Washington D.C., U.S. Department of Commerce, Bureau of Census, 984; Current Population Reports, Population Estimates and Projection Series P-25. No. 952.
22. Arom KV, Emery RW, Nicoloff DM, Flavin TF, Emery AW. Minimally invasive direct coronary artery bypass grafting: experimental and clinical experiences. Ann Thorac Surg 1997;63:S48–S52.
23. Mohr R, Moshkovitz Y, Gurevitch J, Bnetto FJ. Reoperative coronary artery bypass without cardiopulmonary bypass. Ann Thorac Surg 1997;63:S40–S43.
24. Moshkovitz Y, Sternik L, Paz Y, et al. Primary coronary artery bypass grafting without cardiopulmonary bypass in impaired left ventricular function. Ann Thorac Surg 997;63:S44–S47.

25. Subramanian VA, McCabe JC, Geller CM. Minimally invasive direct coronary artery bypass grafting: two-year clinical experience. Ann Thorac Surg 1997;64:1638–1655.
26. Calafiore AM, Teodori G, Di Giammarco G, et al. Minimally invasive coronary artery bypass grafting on a beating heart. Ann Thorac Surg 1997;63:S72–S75.
27. Nielsen D, Sellgren J, Ricksten SE. Quality of life after cardiac surgery complicated by multiple organ failure. Crit Care Med 1997;25:52–57.
28. Pocock SJ, Henderson RA, Seed P, Hampton JR, For the RITA Trial Participants. Quality of life, employment status, and anginal symptoms after coronary angioplasty or bypass surgery. Circulation 1996;94:135–142.
29. Hunt SM, McEwen J, McKenna SP. Perceived health: age and sex comparisons in a community. J Epidemiol Comm Health 1984;38:156–160.
30. Hunt SM, McEwen J. The development of a subjective health indicator. Soc Health Illness 1980;2:231–246.
31. Hlatky MA, Rogers WJ, Johnstone I, et al. Medical care costs and quality of life after randomization to coronary angioplasty or coronary bypass surgery. N Engl J Med 1997;336:92–99.
32. Hlatky MA, Boineau RE, Higginbotham MG, et al. A brief self-administered questionnaire to determine functional capacity (The Duke Activity Status Index). Am J Cardiol 1989;64:651–654.
33. Gundle M, Reeves B, Tate S, Raft D, McLaurin L. Psychosocial outcomes after coronary artery surgery. Am J Psychol 1980;137:159–154.
34. Eriksson J. Psychometric aspects of coronary artery bypass surgery: a prospective study of 101 male patients. Acta Psychiatr Scan Suppl 1988;340:1–112.
35. Sjoland H, Wiklund I, Caidahl K, Haglid M, Westbeg S, Herlitz J. Improvement in quality of life and exercise capacity after coronary artery bypass surgery. Arch Intern Med 1996;156:265–271.
36. Sjoland H, Wiklund I, Caidahl K, Albertsson P, Herlitz J. Relationship between quality of life and exercise test findings after coronary artery bypass surgery. Int J Cardiol 1995;51:221–232.
37. Chocron S, Etievent JP, Viel JF, et al. Prospective study of quality of life before and after open heart operations. Ann Thorac Surg 1995;61:153–157.

III Noncoronary Minimally Invasive Cardiac Surgery

16 Minimally Invasive Mitral Valve Surgery

W. Randolph Chitwood, Jr., MD

Contents

INTRODUCTION

This chapter focuses on a new approach to minimally invasive mitral surgery, performed via a minithoracotomy incision using telescopic video assistance. The term "minimally invasive" has different connotations, even among those surgeons considered pioneers in the field. For some, the term implies reduction of access trauma by use of a smaller incision; for others, the term connotes avoidance of cardiopulmonary bypass (CPB). Yet others consider the combination of both necessary to merit this rubric.

At present, "less invasive" valve operations require CPB support, and hence, considerations have related to size and location of the access incision, direct aortic clamping vs intraluminal balloon occlusion, use of modified perfusion technology, and adequacy of myocardial preservation.

EVOLUTION

Whereas clinical experience with minimally invasive approaches to the mitral valve is limited to 2 yr, these operations hold significant promise because, unlike coronary bypass procedures, their success is not contingent on detailed vascular anastomoses.

The use of limited sternal incisions has been shown to provide excellent exposure to the mitral and aortic valves, allowing good operative results with low perioperative mortality *(1–5)*. The Port-Access™ (Heartport Technology, Redwood City, CA) technique,

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein © Humana Press Inc., Totowa, NJ

which relies on the use of limited incisions, intra-aortic balloon occlusion, and cardioplegic arrest, was first adapted to mitral valve procedures by Pompili et al. *(6)*, who performed mitral valve replacements in a canine model and four in-patients. Shortly thereafter, Falk et al. *(7)* from the University of Leipzig and Colvin and associates *(8)* described early successful clinical experiences with port-access minimally invasive mitral valve surgery. At present, the New York University group has performed over 100 mitral valve repairs and replacements with low mortality and minimal morbidity.

By the end of 1997, 412 patients worldwide had undergone port-access minimally invasive mitral valve operations with a 3.2% overall mortality and 2.2% stroke rate (unpublished results). Recent reports have raised concerns regarding the potential of retrograde aortic dissection and occlusive balloon displacement in patients undergoing these procedures *(9)*. These and other concerns have prompted the examination of alternative balloon catheter designs and the evaluation of video-assisted techniques to the mitral valve.

The first description of video-assisted mitral valve surgery was reported by Kaneko et al. *(10)*. Carpentier et al. *(11)* performed the first video-assisted mitral valve repair via a minithoracotomy using ventricular fibrillation. Three months following this report, the first completely video-assisted mitral valve replacement using a minithoracotomy, a percutaneous transthoracic aortic cross clamp, and retrograde cardioplegia was reported *(12,13)*. Most recently, the spectrum of operations using video-assisted techniques has expanded, including the repair of atrial septal defects *(14)* and mitral valve reoperations *(15)*. Vanermin and colleagues in Aalst have performed nearly 50 operations using port-access technology and video assistance.

The early clinical experience with minimally invasive mitral valve surgery performed by Mohr et al. *(9)* relied on the use of three-dimensional (3D) secondary vision. They authors found that video assistance was most helpful for replacement operations; however, the ability to perform mitral reconstructions was limited by this approach. Chitwood et al. *(16)* reported on 31 patients undergoing mitral valve surgery with the aid of telescopic video assistance. In these operations, secondary vision was advantageous for both extirpative and reparative surgeries. Recently, Loulmet et al. *(17)* described the use of a tiny intracardiac camera to repair mitral valves through limited thoracotomy or sternotomy incisions. The intracardiac device was found to be particularly useful for the visualization of subvalvular structures; however, two-dimensional visualization was limiting. At present, 3D digital imaging (Vista™, Boston, MA), using a headset display, is undergoing evaluation, and early results are encouraging. It is foreseeable that the development of improved visualization methods, tactile feedback mechanisms, and tiny ports and incisions may lead cardiac surgeons to an era of "virtual" mitral valve surgery.

THE "MICRO-MITRAL OPERATION"

At the East Carolina University, modifications of conventional operative technology have been used to develop the Micro-Mitral Operation (MMO). The surgical approach includes the use of a minithoracotomy, direct transthoracic aortic clamping, telescopic

video assistance, atrial centrifugal pump-assisted venous return, peripheral arterial perfusions, and modified instrumentation (Fig. 1) *(12,13,16)*.

Preoperative Preparation

Independent left lung ventilation is obtained with a double-lumen endotracheal tube or a right-sided bronchial blocker. A Swan-Ganz catheter is inserted into the pulmonary artery via a left internal jugular vein approach. Subsequently, the patient is positioned as shown in Fig. 2. The right chest is elevated 40° with the shoulders tilted back. The right arm is suspended across the chest on a padded holder or positioned by the side, but residing behind the posterior axillary line. In women, a 6-cm inframammary line is drawn just rostral to the anterior axillary line. The location of the right femoral artery is marked and external defibrillator pads are positioned posterior to the right scapula and at the left anterior axillary line near the fifth interspace, thereby covering the greatest cardiac mass. A transesophageal probe is inserted and a baseline echocardiogram is obtained.

Technical Considerations

A small incision is made overlying the right common femoral artery and the vessel is exposed. A 5-0 polypropylene purse-string suture is placed longitudinally. Following heparinization, a 17–19 Fr. Biomedicus™ Medtronics, Minneapolis, MN) arterial cannula is advanced over progressive dilators into the proximal iliac artery using the Seldinger technique (Fig. 3, p. 192). Avoidance of arterial clamps allows distal perfusion to be maintained throughout cardiopulmonary perfusion. When femoral cannulation is contraindicated or not possible, central cannulation is performed. A purse-string suture is placed just proximal to the innominate artery and an arterial cannula is introduced using the Seldinger technique via an incision or a thoracoport under videoscopic assistance.

The right fourth rib is exposed via a 6–7-cm submammary skin incision with extrapectoral cephalad dissection. A bony fragment of the fourth lateral rib was removed in the early experience (Fig. 4, p. 193). More recently, the fourth rib has been divided and a Tuffler or a "thoracic lift" retractor (United States Surgical Corp., Norwalk, CT) is positioned to deflect soft tissues while minimizing rib spread (this maneuver reduces postoperative pain).

Following entry into the parietal pleura, the right lung is deflated and the pericardium is opened under direct vision, 2 cm ventral to the phrenic nerve. The incision is carried cephalad to the aortic reflection. Silk retraction sutures are placed to approximate the anterior pericardial edge and skin incision tightly. A transthoracic hook (Scanlan International, Minneapolis, MN) is used to withdraw the posterior pericardial edge retraction sutures through the chest wall (Fig. 5, p. 194). This maneuver rotates the heart in a counterclockwise fashion, effectively displacing the left atrium ventrad. Lateral pericardial edge retraction minimizes telescope obstruction and lens contamination. Optimal direct-vision exposure allows access to the base of the aorta, the atrio-caval junction, and the right superior pulmonary vein (Fig. 6, p. 195).

Because the right atrial appendage is not ordinarily reachable through the incision, three alternative approaches to attain venous return have been used. A 2-0 pledget-reinforced Ticron suture is placed in the midright atrium and a thin-walled 24 Fr. Biomedicus

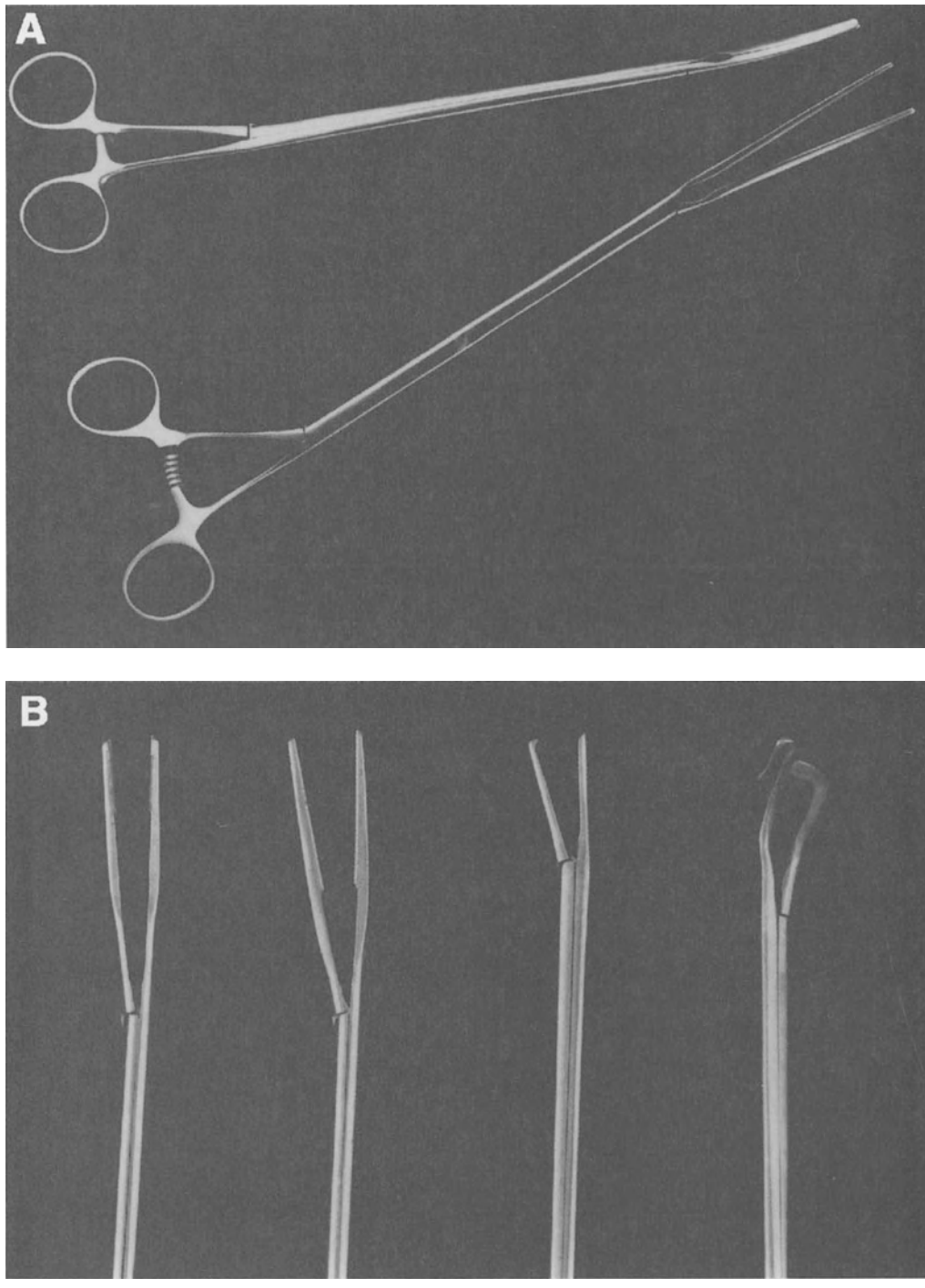


Fig. 1. Instruments: Custom instruments designed for the video-assisted MMO. **(A)** The transthoracic aortic cross clamp is shown in two "pincer tip" lengths. The sliding mechanism precludes wound impingement. **(B)** Specially designed forceps and knot-tier used for the MMO. Note the specialized diamond platform–tipped forceps used for (*left to right*): needle retrieval, delicate tissue manipulation, thickened valve tissue, and knot-tying/valve prosthesis seating (Scanlan International, Minneapolis, MN).

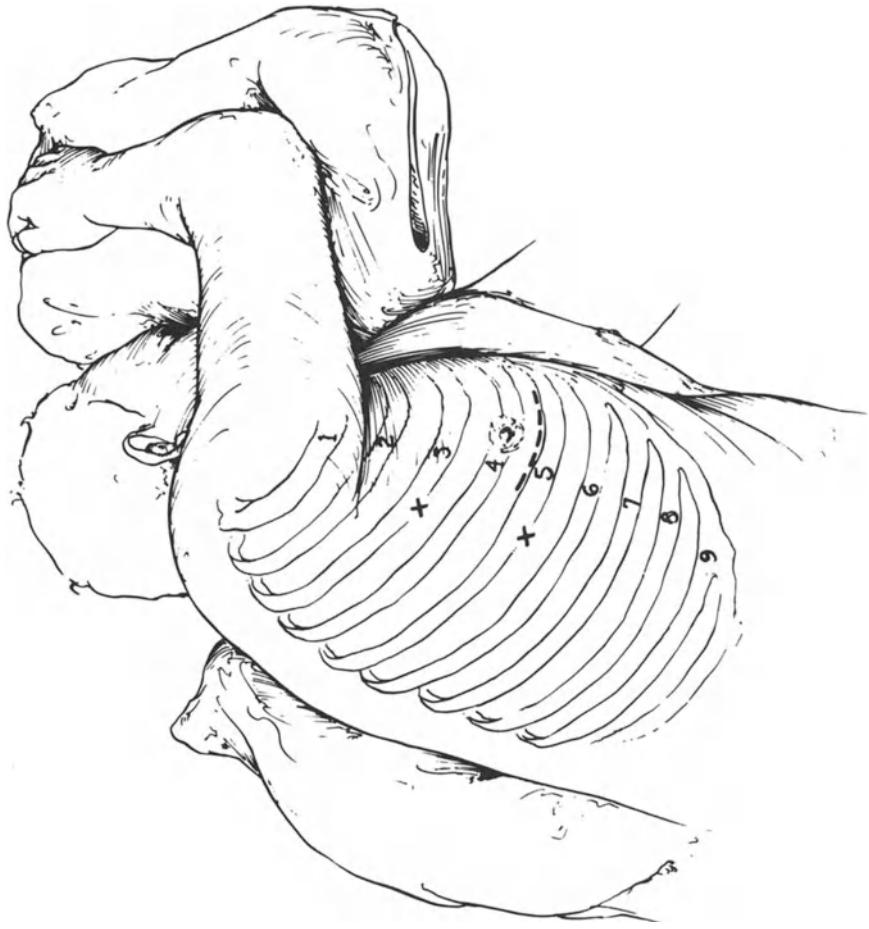


Fig. 2. The patient is positioned with the right chest turned upward 40°. The inframammary incision is made just anterior to the axillary line. Recently we have made a more lateral incision. The cephalad "x" mark represents the prospective insertion site for the transthoracic cross clamp in the third intercostal space, and the caudal "x"mark indicates the location of the thoracoport for the 5-mm telescope.

venous cannula is introduced through the purse-string. Alternatively, a 19 or 21 Fr. venous cannula may be inserted percutaneously into the right atrium through the right internal jugular vein or via the femoral vein. A Biomedicus centrifugal pump is used for assisted venous drainage. Perfusion is begun and the systemic temperature is lowered to 26°C.

A 5-mm thoracoport (Genzyme-DSP, Boston, MA) is inserted through the fifth intercostal space, posterior to the thoracic incision (Fig. 4). Prior to camera insertion, the position of the distal tip of the port should be anterior to the pericardial edge and in direct line with the superior pulmonary vein, and should be verified. A 5-mm 0° telescopic camera is then passed through the port.

With videoscopic assistance, a purse-string suture is placed along the anterior ascending aorta, just distal to the right coronary origin (Fig. 6). A suction-vent cardioplegia catheter is

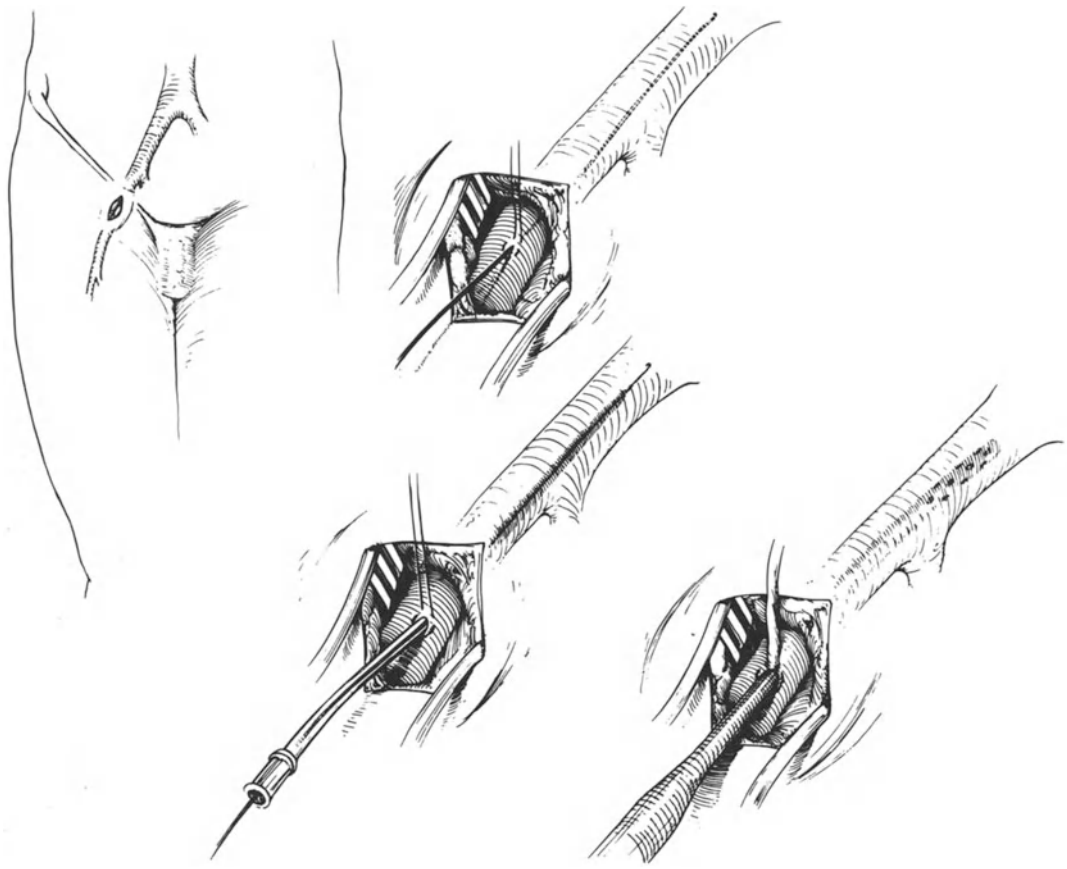


Fig. 3. Femoral arterial cannulation (*left to right*): Either a 2-cm vertical or transverse incision is made over the femoral vessels. A small 5-0 prolene purse-string suture is placed in the common femoral artery. A guide wire is introduced using a blunt-tipped needle and is passed into the proximal aorta. Using the Seldinger technique, progressive coaxial dilators are passed over the guide wire. Finally, a 19–21 Fr. Biomedicus perfusion cannula is passed into the proximal iliac artery over the wire. Venous cannulation can be attained using similar techniques.

inserted either through the wound or via a separate port. A 4-mm incision is then made in the third intercostal space just cephalad to the videoport to allow passage of the transthoracic aortic clamp. Under videoscopic guidance, and with great care not to injure the right pulmonary artery, the clamp is positioned with one prong behind the ascending aorta through the transverse sinus (Fig. 7, p. 196). Proper positioning of the clamp should be confirmed with the video camera. Using this technique, the heart becomes less displaced than when the operation is performed via median sternotomy, which minimizes introduction of air into the aortic root. Although antegrade cardioplegia has provided excellent myocardial protection, occasional retrograde cardioplegia is administered via an echocardiographically guided coronary sinus catheter.

Sondergaard's groove is dissected for only 1–2 cm. A small left atriotomy is made just medial to the right superior pulmonary vein entrance, and a small ribbon retractor is

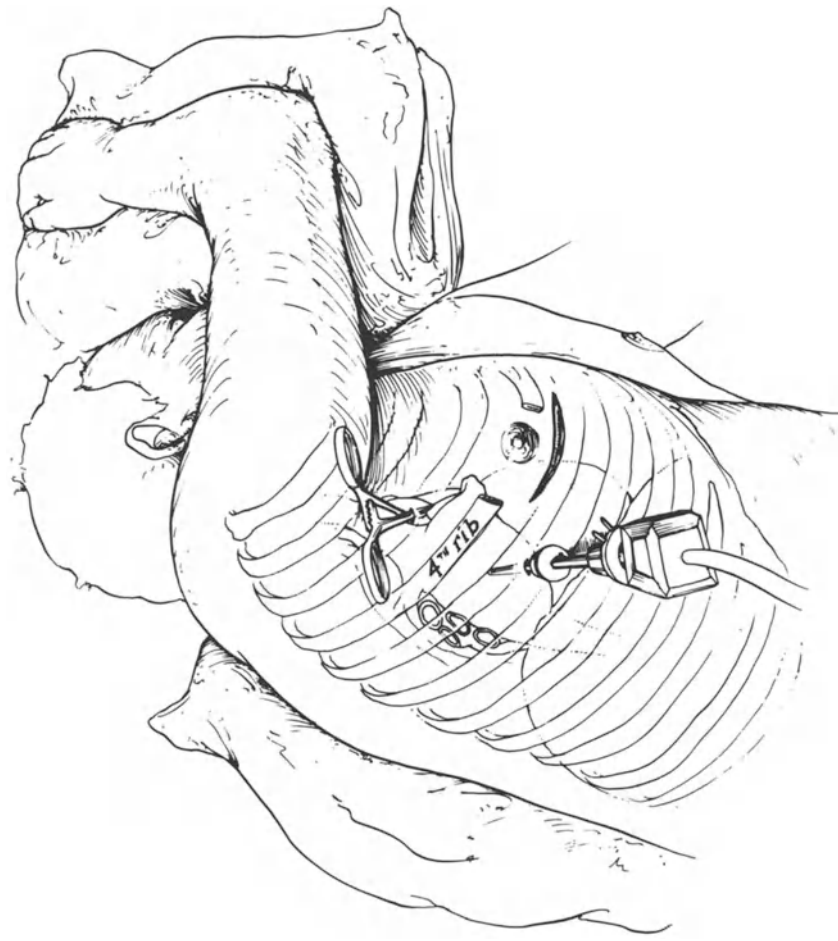


Fig. 4. External operative view. A segment of the fourth rib has been removed. Recently we have only divided this rib anteriorly and distracted it inferiorly. The transthoracic cross clamp is shown inserted through the third intercostal space and in front of the superior vena cava. The aortic clamp is shut. The 5-mm camera transverses the chest wall via the thoracoport. Note that the camera tip is in direct line with the superior pulmonary vein.

introduced to expose the mitral valve. The retractor is configured so that "towing in" will elevate the interatrial septum, allowing the anterior mitral leaflet to hang freely. Transthoracic retractors (Heartport™ and Genzyme-DSP) also may be used to maximize exposure (Fig. 8, p. 197). In the presence of large left atria, the lateral walls tend to fall in, and, hence, early placement of commissure sutures establishes correct anatomic orientation and facilitates exposure.

For mitral valve repair, our technique includes the use of the Carpentier-Edwards Physio™ annuloplasty ring and the Baxter-Cosgrove™ band. Because the latter extends posteriorly between the fibrous trigones, fewer sutures are required. Early placement of annuloplasty sutures clearly facilitates camera visualization. These sutures are placed in a counterclockwise fashion starting at the right fibrous trigone or the commissure

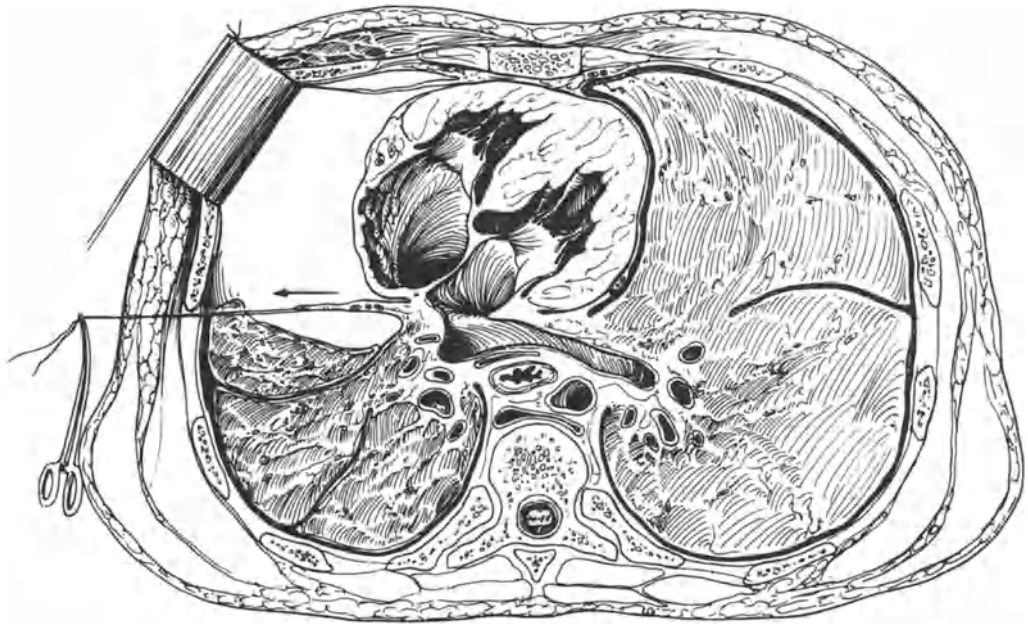


Fig. 5. Operative exposure. Cross-section of the human thorax as seen from the below. The soft tissue retractor is inserted at the fourth rib level through the removed segment. The lung is partially deflated. The pericardial incision lies 2 cm anterior to the phrenic nerve and in juxtaposition to the interatrial groove. A 2-0 silk retraction suture has been placed through the edge of the pericardium and passed through the lateral chest wall to retract the dorsal pericardial edge slightly toward the posterior chest wall, preventing camera obstruction. The anterior suture retracts the heart toward the posterior chest wall to retract the dorsal pericardial edge slightly toward the posterior chest wall, preventing camera obstruction (arrow). The anterior suture retracts the heart toward the incision, bringing the aorta and mitral annulus close to the wound for access.

(Figs. 9 and 10, pp. 198–199). The sutures exiting posteriorly are placed last because they tend to obstruct camera visualization. The sutures are arranged serially and suspended tightly from external suture guides. Reorientation after annular passage becomes very difficult via the small incision. Only after the annular sutures are in place should reconstructive procedures be performed.

For mitral valve replacement, subannular pledgeted 2-0 sutures are placed serially while the anterior leaflet is progressively "snipped" in counterclockwise fashion. This is carried along the anterior annulus; the posterior leaflet and subvalvular apparatus are left intact. In some instances, supra-annular everting mattress sutures are placed. The combination of these two suture techniques has resulted in no early perivalvular leakage. Moreover, this method facilitates videoscopic anterior placement while minimizing the risk of posterior leaflet impingement into the mechanical prosthesis. We favor the use of the standard St. Jude™ (St. Paul, MN) mechanical prosthesis, although rotatable valves preserve maximal flexibility for best orientation. In those instances in which tissue valves are used, only sub- or supra-annular pledgeted sutures are used, and both native leaflets are preserved.

Fig. 6. Thoracoscopic view. This view should be available after introduction of the telescopic camera in the third intercostal space. A purse-string for the cardioplegia cannula is placed on the anterior aorta (*left*). An atrial purse-string suture has been placed for direct atrial cannulation through the incision (*right*). The junction between the superior vena cava, superior pulmonary vein, and right atrium is the major "sighting" point when inserting the camera. Note that the pericardium has been distracted from camera view.

For both mitral valve repair and replacements, anterior sutures require video assistance whereas posterior sutures often can be placed by direct vision. Maneuvers at the left trigone and commissure are best accomplished with the left hand and with the aid of a 30° telescope. Optimal needle stability is essential while placing sutures through the mitral annulus. This is best achieved by the use of short grip, thin-bodied needle holders. Following completion of the annular sutures, the extrathoracic prosthesis is lowered into place through the small atriotomy.

The left trigone suture is tied first, followed by the right trigone and the posterior-middle sutures. A modified valve positioner/knot tier (Fig. 1) is used to seat the valve and secure the knots. It is critical that the first two knots slip in order to affect ideal prosthesis tissue apposition while precluding suture breakage. Using a guillotine-type suture cutter (Scanlan International), the remaining sutures are tied and cut.

The left atriotomy is closed under direct vision using monofilament suture. A transvalvular vent is not used routinely. Prior to aortic clamp release, venous return is decreased while both lungs are ventilated and the intracardiac air is evacuated through

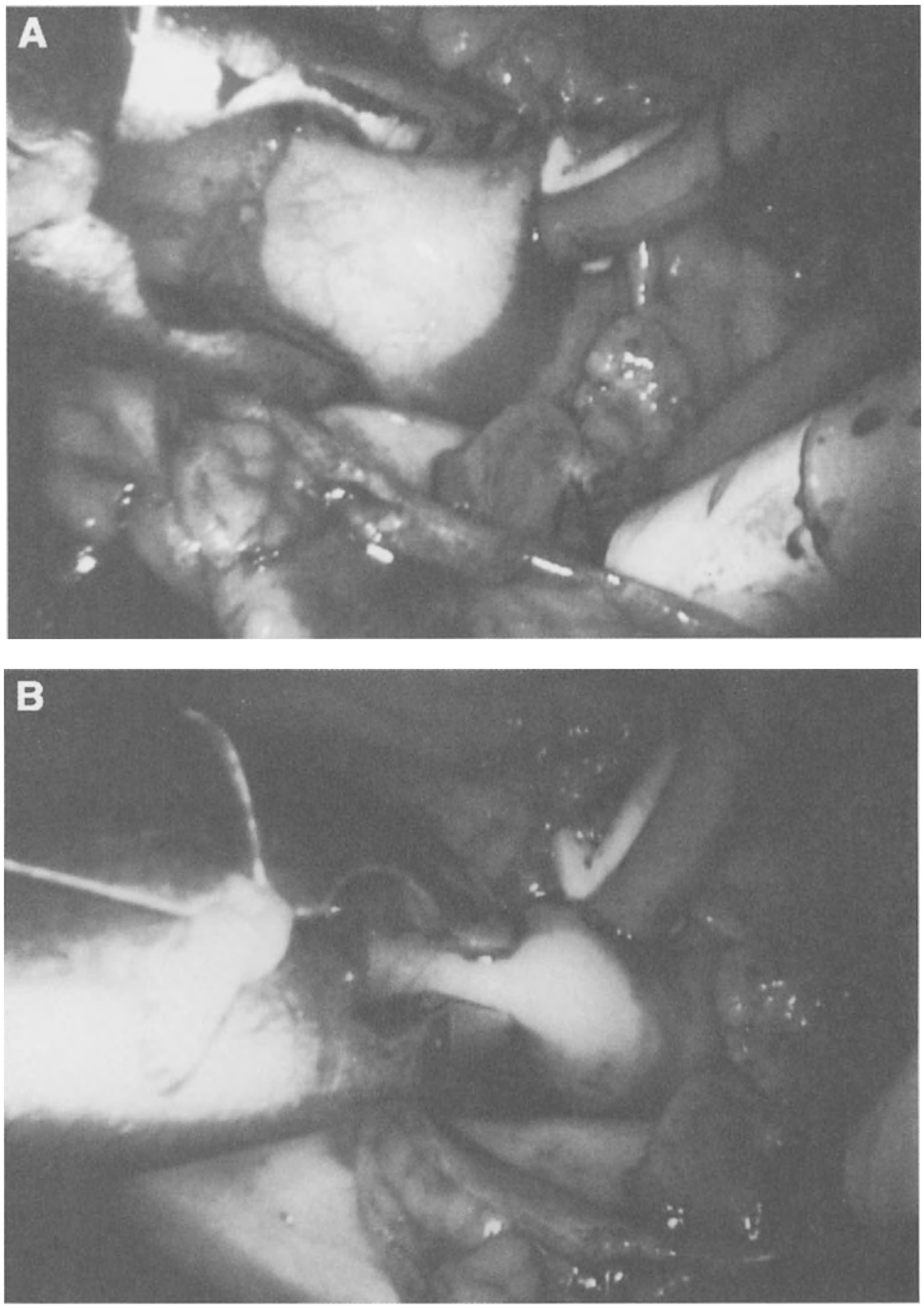


Fig. 7. Transthoracic aortic occlusion. **(A)** Intraoperative photograph depicts the transthoracic clamp jaws being positioned around the aorta. The posterior jaw is positioned, using video assistance, through the transverse sinus. Care must be taken to avoid injury to the right pulmonary artery and to assure total aortic occlusion. **(B)** The clamp has been closed and antegrade cardioplegia is being administered via the aorta. The venous cannula can be seen in the lower right foreground.

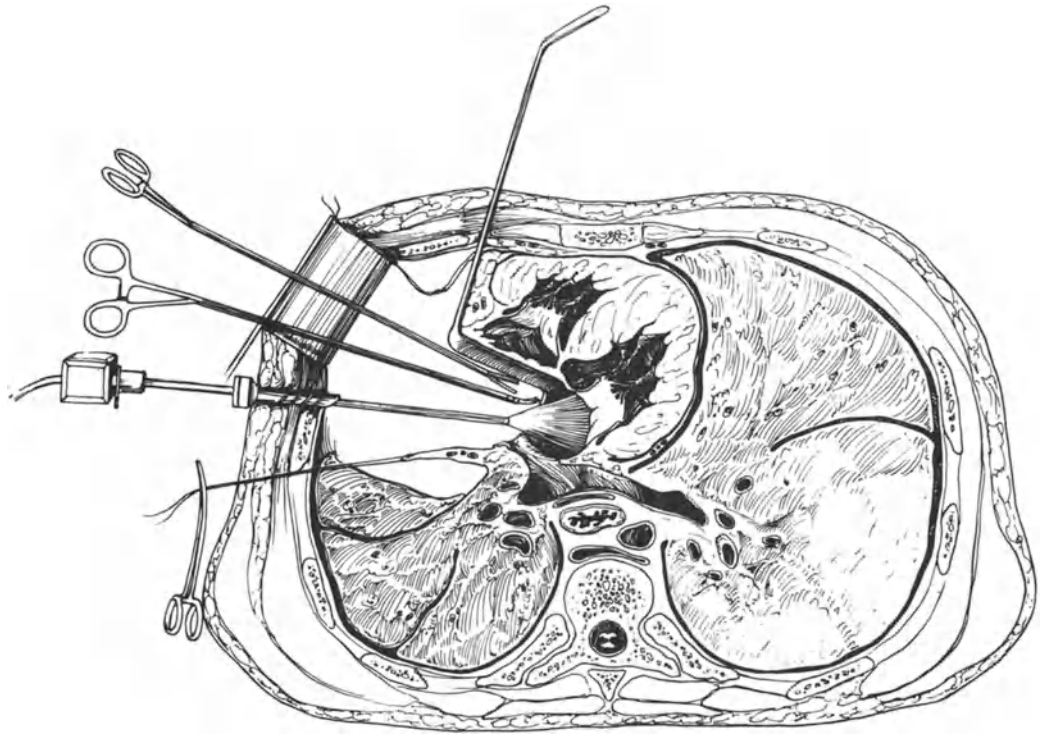


Fig. 8. Intrathoracic operative view. The interatrial septum is being retracted ventrally using a transthoracic retractor. The thoracoscopic camera provides an excellent view. The tip of the camera should be behind the operating instrument to minimize conflicts.

the atriotomy suture line and the aortic vent. Other de-airing maneuvers are performed with the patient in the Trendelenburg position. Under transesophageal echocardiographic guidance, partial aortic occlusions and other de-airing maneuvers are carried out until complete evacuation of air is documented. Recently, we have insufflated CO_2 into the left atrium to displace air. After the transthoracic aortic cross clamp is removed, the posterior aorta is examined with the aid of the videoscope. Thereafter, the patient is weaned from CPB, and a thoracotomy tube is placed through the camera port-site. In most instances, temporary epicardial pacing wires have not been necessary. However, when needed, they are best placed before weaning from bypass.

CLINICAL EXPERIENCE

The experience at East Carolina University (ECU) with the MMO includes 43 cases with a single perioperative mortality owing to arrhythmia 27 d after discharge. These consecutive patients were operated upon by one surgeon between May 1996 and October 1997, and are compared with a contemporary historical cohort. This latter group is comprised of the previous 100 conventional mitral operations performed by the same surgeon

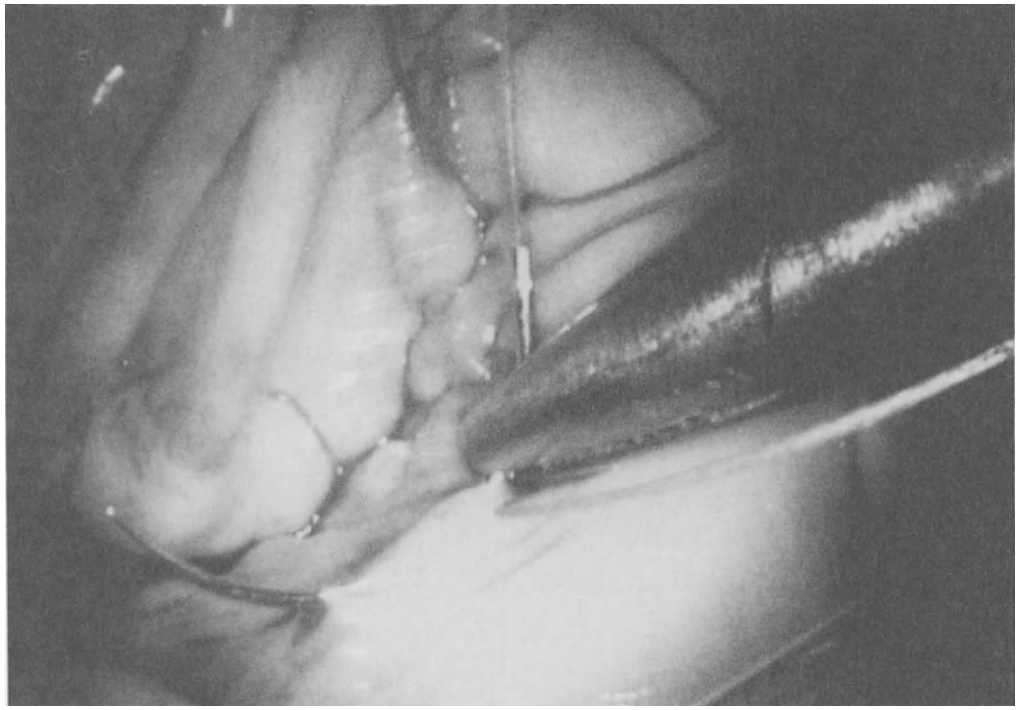


Fig. 9. Intrathoracic suture placement. Annuloplasty sutures are being placed along the posterior portion of the mitral annulus. Note that short-nosed needle holders are used. These prevent needle slippage when placing sutures at the odd angles often necessary with this videoscopic method.

between January 1992 and January 1997. Patients who underwent concomitant coronary artery bypass grafting were excluded from both groups. We have done five MMOs successfully in Europe that are not included in the ECU studies.

Table 1 gives demographic profiles for both groups. The cohorts were similar for age, gender, and New York Heart Association (NYHA) functional class. Fifteen MMO patients (36%) underwent mitral valve replacement, and 28 (64%) had mitral valve repair. Pathological findings in patients undergoing MMO were similar to those of patients undergoing conventional operations and included degenerative changes in 23 patients, annular dilation in 2, rheumatic disease in 15, and healed endocarditis in 3. Table 2 gives the operative techniques for both groups. No MMO patients required conversion to larger incisions or sternotomy, and no mitral valve repairs required secondary replacement. MMO patients had statistically significant longer cardiopulmonary and cross-clamp times but still benefited from a reduced need for packed red blood cell transfusions. No aortic clamp injuries occurred and all patients were easily weaned from bypass. Early postoperative electrocardiograms demonstrated inferior lead changes, which were transient in nature in several patients in our early experience; no Q-wave myocardial infarctions were seen. As assessed by transesophageal echocardiography, postoperative ventricular function did not deteriorate in any patient.

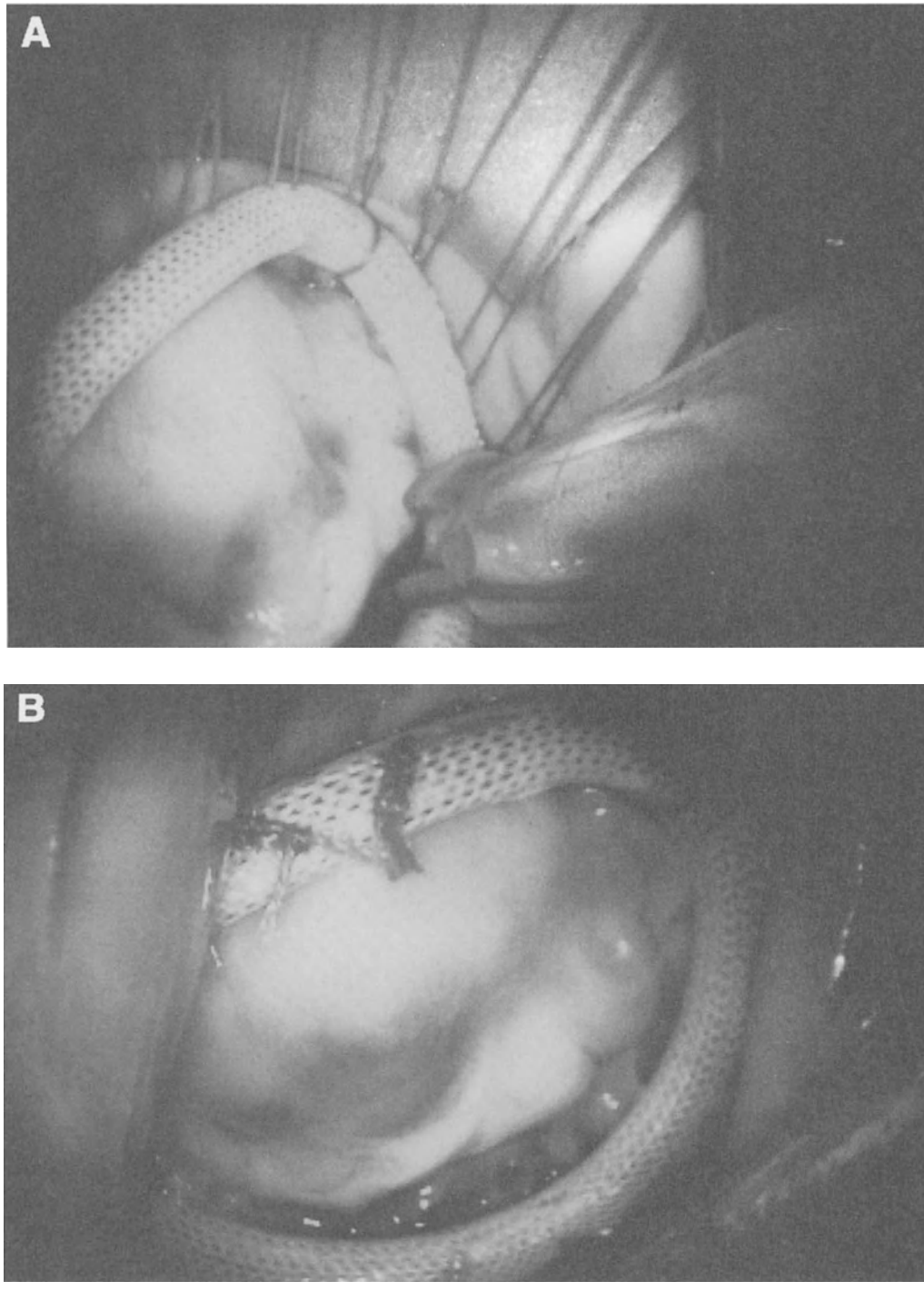


Fig. 10. Intraoperative mitral valve repair. **(A)** Multiple 3-0 tgon annuloplasty sutures have been placed videoscopically with an annuloplasty ring lowered into place. Medial commissure and anterior valve leaflet are seen. A sucker tip is being used to position the ring. **(B)** The completed videoscopic mitral repair is shown, and the saline test demonstrates no leakage.

Table 1
Demographic Profile of 143 Patients Who Underwent Mitral Valve Surgery with Minimally Invasive or Conventional Approaches

	MMO[a]	*Conventional mitral valve surgery*[b]
Age		
Mean ± SEM	59 ± 2.2	59.3 ± 1.4
Range	18–77	29–78
% Female	58	53
Preoperative NYHA class		
I	7%	8%
II	47%	42%
III	40%	40%
IV	7%	10%
Ejection fraction (%)		
<40%	9%	0.37 [c]
>40%	91%	0.63 [c]

[a] $n = 43$.
[b] $n = 100$.
[c] $p = 0.001$.

Table 2
Type of Surgery and Intraoperative Variables in Patients Undergoing Mitral Valve Surgery

	MMO[a]	*Conventional mitral valve surgery*[b]
Operative technique		
Valve replacement	15 (35%)	43 (43%)
Valve repair	28 (65%)	57 (57%)
Annuloplasty alone	16 (57%)	27 (47%)
Annuloplasty + quadrangular resection	10 (36%)	17 (30%)
Annuloplasty + chordal replacement	2 (7%)	5 (9%)
Annuloplasty + chordal transfer	0 (0%)	8 (14%)
Intraoperative variables		
Cross-clamp time (min)	125 ± 4.9	92 ± 3.6[c]
CPB time (min)	125 ± 4.9	92 ± 3.6[c]
Perioperative packed red blood cell transfusion (U)	1.0 ± 0.1	3.0 ± 0.1[d]

[a] $n = 43$.
[b] $n = 100$.
[c] $p = 0.0001$.
[d] $p = 0.01$.

In one patient who underwent MMO, a moderate leak was detected postoperatively, and the patient underwent valve replacement 15 mo later.

Table 3 depicts intensive care unit (ICU) parameters including length of respiratory support, length of stay (LOS), postoperative blood loss, and complications. Patients

Table 3
Comparison of ICU Parameters and Postoperative Complications Among Patients Undergoing Mitral Valve Surgery

	MMO[a]	*Conventional mitral valve surgery*[b]
ICU Parameters		
ICU stay: if ventilated <48 hr (hr)	21.1 ± 2.2	48.7 ± 8.2[c]
ICU stay: total group (hr)	30.2 ± 6.7	48.7 ± 8.2[d]
Respiratory support (hr)	13.6 ± 2.7	23.7 ± 5.3
Total thoracotomy tube output (mL)	578 ± 84	687 ± 84
Complications		
New onset atrial fibrillation	7 (16%)	20 (20%)
Deep venous thrombosis	1 (2.3%)	0 (0%)
Phrenic nerve injury	1 (2.3%)	0 (0%)
Neurologic deficit	0 (0%)	3 (3%)[c]
Reexploration for bleeding	0 (0%)	4 (4%)[c]
30-d mortality (%)	1 (2.3%)	2.20%

[a] $n = 43$.
[b] $n = 100$.
[c] $p = 0.04$.
[d] $p = 0.02$.

undergoing the MMO benefited from reduced ventilatory support times and reduced ICU stay. Forty-one of 43 MMO patients (95%) required less than 48 h of respiratory support; for this cohort, overall ICU stay was significantly shortened compared with the conventionally operated group. Eighty-four percent of MMO patients were discharged from the hospital between the third and fifth postoperative day; in the last half of the series, the length of hospitalization was reduced to 3.5 ± 0.1 d.

An identical proportion of patients in both groups developed postoperative atrial fibrillation. Among MMO patients, major complications included one episode of deep venous thrombosis and one instance of phrenic nerve palsy. Two patients required more than 48 h of ventilatory support. The conventional group had a significantly higher incidence of perioperative neurological deficits and reoperations for bleeding; in fact, no such adverse sequelae were seen in the MMO group. Whereas MMO patients received significantly fewer transfusions than the sternotomy cohort, 40% of MMO patients still required some blood product transfusion. No in-hospital deaths were recorded for MMO patients; one patient died at home 27 d after operation from a presumed arrhythmia; postmortem examination demonstrated an intact prostheses. Perioperative (30 d) mortality was similar for both groups. One late death occurred in the MMO group related to prosthetic valve endocarditis.

Follow-up for MMO patients was 100% and averaged 24 ± 2.5 wk. With the exception of the two patients who developed major complications, all patients reported little or no postoperative pain and a rapid return to normal activities. At follow-up 95% of MMO patients were in NYHA class I or II, compared with 54% preoperatively. Charge and cost reductions in the MMO patients (27% and 34% less than the sternotomy group, respectively, $p = 0.02$) resulted mostly from reduced LOSs.

SUMMARY

The initial experience with the MMO is encouraging and demonstrates that complex mitral valve repairs and replacements can be approached safely and performed using limited incisions and video assistance. Although difficult to quantify, our experience suggests that resection or division of a bony portion of the rib, rather than the costal cartilage, results in improved cosmesis and reduced postoperative pain. This approach reduces the amount of retraction that must be exerted on the chest wall to optimize exposure and perhaps explains the diminished postoperative pain experienced by these patients.

The mitral valve exposure afforded by the MMO precludes the need for an extended atrial incision, which is often necessary with ministernotomy or parasternal approaches. The transthoracic aortic clamp method appears safe and effective and requires few additional resources or customized supplies; in addition, anterograde cardioplegia alone provides excellent cardiac protection. Video assistance during clamp placement reduces the risk of right pulmonary or left atrial appendage injury and serves to confirm adequate aortic occlusion. Although intraluminal balloon occlusion catheters have been developed and clinically implemented, concerns regarding the possibility of aortic dissection and balloon migration—with potential disastrous neurological complications—remain. Furthermore, the we of these devices may be limited in patients with small-diameter aortas or significant aorto-iliac disease. Antegrade perfusion catheters with an aortic occlusion balloon are being developed and may be safer than retrograde perfusion methods.

Our experience with MMO in 13 patients suggests that, using small atriotomies, video assistance is essential for providing optimal instrument access and exposure. Indeed, visualization of the trigonal/commissural regions, anterior mitral annulus, and intracardiac subvalvar structures would have been difficult without videoscopic assistance. Furthermore, excision of tissue, placement of sutures, positioning of the prosthetic valve, and tying of knots are all greatly facilitated by thoracoscopic vision. For reconstructive work, the thoracoscope is of the utmost help in papillary and subvalvar repairs (Figs. 10 and 11). Secondary vision is of particular benefit in patients with large anteroposterior diameters, obese body habitus, and in patients with large left atria. The operation will be greatly enhanced with the advances in 3D visualization and the development of tactile feedback mechanisms. Practice of the above techniques during conventional mitral valve operations enhances the development of video dexterity.

The use of vortex venous drainage allowed for adequate cardiac decompression; however, care must be taken to prevent air leakage around purse-string suture sites. Although retrograde aortic dissection has been reported, we were able to establish excellent arterial perfusion with the use of thin-walled arterial cannulas placed using the Seldinger technique without any instances of dissection in our published report. Since that time, however, one patient developed an aortic dissection requiring conversion to a sternotomy. It is clear that advances in cannula design are necessary to facilitate aortic insertion through a port or small incision.

Increases in the numbers of laparoscopic cholecystectomies performed have been attributed, among other factors, to the ease of performing the operation, particularly in instances when the indication for the operation is not entirely clear. Clearly the decision to repair a

mitral valve should not be driven by the operative approach, but by the pathology of the valve and the patient's symptoms. The optimal mitral valve operation should take primacy over the approach, and quality should never be compromised to minimize hospital cost, improve cosmesis, or to lessen discomfort. In this series, the same selection criteria used for patients undergoing conventional mitral valve surgery were applied to potential candidates for the MMO. Although the operative times were longer for patients undergoing the MMO, the costs were offset by the shorter ICU stay and shorter overall hospital stay. Quality of life issues including satisfaction with the procedure, return to work, discomfort, and performance of daily activities are difficult to evaluate in retrospect. A prospective evaluation of these parameters is important to assess fully the potential benefits of this and other minimally invasive approaches.

Our experience suggests that a minimally invasive approach to mitral valve surgery based on the use of small incisions and videoscopic assistance is safe and feasible and results in reduced ICU and hospital stays, transfusion requirements, postoperative discomfort, and cost. The long-term reliability of this and other minimally invasive approaches to mitral valve surgery, however, remains untested. Thus, despite rapid developments in this field, we must embrace the new technologies with cautious enthusiasm and healthy skepticism. Only when the morbidity, mortality, quality of life, and long-term reliability of these approaches approximates the excellent results obtained with conventional operations, should these procedures find a solid niche in the armamentarium of the cardiac surgeon.

REFERENCES

1. Cosgrove DM, Sabik JF. Minimally invasive approach for aortic valve operations. Ann Thorac Surg 1996;62:596–597.
2. Cosgrove DM, Sabik JF, Navia J. Minimally invasive valve surgery. Ann Thorac Surg 1997;65, 1535–1539.
3. Koenertz W, Waldenberger F, Schutzler M, Ritter J, Liu J. Minimal access valve surgery through superior partial sternotomy: a preliminary study. J Heart Valve Dis 1996;5:638–640.
4. Arom KV, Emery RW. Minimally invasive mitral operations.(letter) Ann Thorac Surg 1996;62:1542–1544 (letter).
5. Navia JL, Cosgrove DM. Minimally invasive mitral valve operations. Ann Thorac Surg 1996;62:1542–1544.
6. Pompili MF, Stevens JH, Burdon TA, et al. Port-access mitral valve replacement in dogs. J Thorac Cardiovasc Surg 1996;112:1268–1274.
7. Falk V, Walther T, Diegeler R, et al. Echocardiographic monitoring of minimally invasive mitral surgery using an endoaortic clamp. J Heart Valve Dis 1996;5:630–637.
8. Spencer FC, Galloway AC, Grossi EA, Ribakove GH, Delianides J, Baumann FG, Colvin SB. Recent developments and evolving techniques of mitral valve reconstruction. Ann Thorac Surg 1998;65:307–313.
9. Mohr FW, Falk V, Diegeler A, Walther T, van Son J, Autschbach R. Minimally invasive port-access mitral valve surgery. J Thorac Cardiovasc Surg 1998;115:567–574.
10. Kaneko Y, Kohno T, Ohtsuka T, Ohbuchi T, Furuse A, Konishi T. Video assisted observation in mitral valve surgery. J Thorac Cardiovasc Surg 1996;111:279,280.
11. Carpentier A, Loulmet D, et al. Chirurgie à coeur ouvert par video-chirurgie et mini-thoracotomie—premier cas (valvuloplastie mitrale) opéré avec succès. Complet Rendus De L'Academie des Sciences: Sciences de la Vie 1996;319:219–223.

12. Chitwood WR, Elbeery JR, Chapman WHH, et al. Video-assisted minimally invasive mitral valve surgery: the "Micro-Mitral" operation. J Thorac Cardiovasc Surg 1997;113:413,414.
13. Chitwood WR, Elbeery JR, Moran JM. Minimally invasive mitral valve repair: using a minithoracotomy and transthoracic aortic occlusion. Ann Thorac Surg 1997;63:1477–1479.
14. Chang CH, Lin PJ, Chu JJ, et al. Video-assisted cardiac surgery in closure of atrial septal defect. Ann Thorac Surg 1996;62:697–701.
15. Tsai FC, Lin PJ, Chang CH, Liu HP, Tan PP, Chang CW. Video-assisted cardiac surgery: preliminary experience in reoperative mitral valve surgery. Chest 1996;110:1603–1607.
16. Chitwood WR, Wixon CL, Elbeery JR, Moran JF, Chapman WHH, Lust RM. Video-assisted minimally invasive mitral valve surgery. J Thorac Cardiovasc Surg 1997;114:773–782.
17. Loulmet DF, Carpentier A, Cho PW, Berrebi A, d'Attellis N, Austin CB, Couetil JP, Lajos P. Less invasive techniques for mitral valve surgery J Thorac Cardiovasc Surg 1998;15: 772–779.

17 Aortic Valve Surgery via Limited Incisions

Steven R. Gundry, MD

CONTENTS

INTRODUCTION

New incisions, foreign to "traditional" cardiac surgeons, are now being touted as a new answer to approach cardiac valvular structures. We and others, convinced that access to the heart could be achieved via a modification of the traditional sternotomy, have elected to perform pediatric heart operations via a partial sternotomy; i.e., only a portion of the sternum is divided in the midline. This approach incorporates traditional cannulation techniques with more limited exposure to the heart.

Owing to the flexibility of children's tissues, the partially divided sternum is stretched open with a retractor. We have also adopted a less invasive approach to aortic (and mitral) valve operations in adults. The rationale for this approach was simple: both the aortic and mitral valves are midline structures and both lie in a plane that can best be viewed obliquely from above the patient's right shoulder. Furthermore, upper sternal division brings the surgeon directly down on the aorta and right atrial appendage for traditional cannulation of structures for venous return and arterial inflow. However, unlike children, the inflexible adult sternum was "T'd" off at the second, third, or fourth intercostal space in addition to dividing it in the midline. Although many terms can be used to describe these sternal divisions and many variations of the inverted "T" now exist such as hemisternotomy, partial sternotomy, limited sternotomy, etc., we have added the term "ministernotomy" to describe this form of limited access to the heart and great vessels. This chapter presents an overview of the first consecutive 100 patients who underwent aortic valve procedures at our institution. The operative technique is detailed and the clinical results are reviewed for this less invasive approach to aortic valvular surgery.

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

OPERATIVE TECHNIQUE

An upper sternal ministernotomy is utilized for all work on the aortic (and mitral) valves, as well as the ascending aorta. As mentioned previously, because of its inflexibility, the partial sternotomy must be extended with a transverse incision into an intercostal space. It is important to emphasize that the sternal incision merely cuts the sternum; the surrounding tissues including the internal mammary arteries (IMAs) are left undisturbed. Once the sternal edge is cut, no further advancement into the intercostal space is necessary.

The level of sternal division necessary to provide access to the base of the heart varies greatly with body habitus, presence of emphysema, and heart position within the chest. Early in our experience, the sternum was divided routinely at the third intercostal space. However, with increasing experience and with the aid of transesophageal echocardiography (TEE) to locate the aortic annulus, the proper intercostal space can be located. The position of the aortic annulus is determined, and by measuring with a tape measure from the edge of the manubrium to the depth of the echo probe, the skin overlying the appropriate intercostal space is marked. In general, a third or fourth interspace T will suffice; however, in the presence of severe emphysema or when aortic root replacement is contemplated, the fourth intercostal space is chosen. As familiarity with this technique increases, higher intercostal spaces can be used. Usually, a 3-in. skin incision is made (Fig. 1).

All sternal divisions are performed using an oscillating saw with a narrow blade as routinely carried out in conventional redo sternotomies. Once divided, a small Finochetti retractor is placed to separate the upper sternal edges (Fig. 2). Thymic tissue is divided with electrocautery and the pericardium is opened. Traction on the lower sternal edge allows further opening of the pericardium. Once opened, the pericardial edges are sewn to the skin, delivering the cardiac structures further into the incision. Smaller pericardial needles are used to aid in this process.

Cannulation sutures are placed on the ascending aorta in the standard location. In the case of aortic valve work, a dual-stage oval venous cannula is utilized through an atrial purse-string (Fig. 3). This and an additional purse-string for retrograde cardioplegia are most easily placed by the first assistant who has the best view of the right atrium. A retrograde cardioplegia cannula (Gundry RCSP, DLP, Grand Rapids, MI) is placed through a second purse-string, just inferior to the atrial appendage. The retrograde cannula is placed blindly, flushing the pressure line to the distal port and watching for a rise in pressure to indicate engagement of the coronary sinus. Once engaged the balloon is inflated. Rising coronary sinus pressure confirms placement *(1)*. If unsuccessful, TEE can be used to guide insertion of the retrograde cannula *(2)*. If access is still not achieved, placement on bypass with the lungs collapsed will allow the surgeon to place a finger near the inferior vena cava to push the cannula into the sinus.

Once on bypass, venting of the left heart can be accomplished in one of several different ways. First, the right superior pulmonary vein can be cannulated easily once the lungs are deflated and the heart is emptied (this maneuver is also the easiest when per-

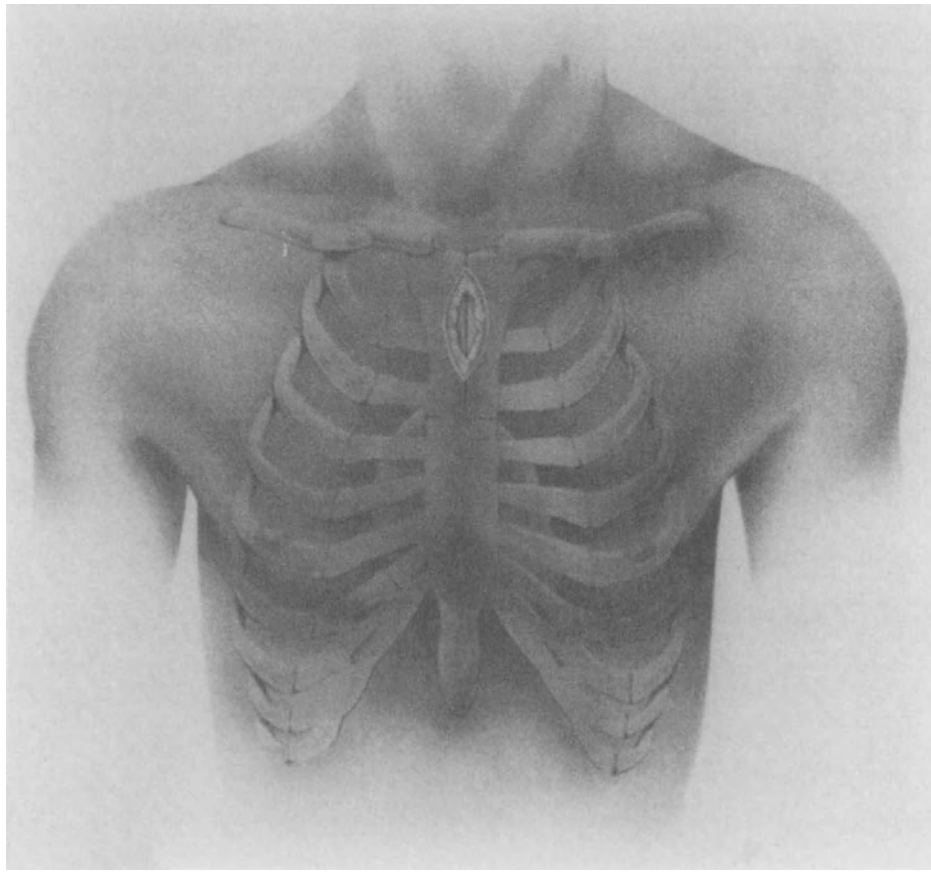


Fig. 1. Skin and sternal incisions for ministernotomy. Note the inverted T at the level of the third intercostal space.

formed by the first assistant). Second, a vent can be placed through the dome of the left atrium or dropped through the aortic valve annulus. Finally, direct venting of the pulmonary artery can be utilized.

The aortic valve is visualized easily via ministernotomy. Visualization is improved by allowing the surgeon access to the patient's right shoulder, permitting him or her to "look down the barrel" of the aortic valve. A right-angle aortic cross clamp is placed on the aorta (Fig. 3). Aortotomy and the remainder of the aortic procedure proceeds following standard techniques. To aid visualization, gentle traction on the venous cannula further pulls the aortic annulus into view.

Standard techniques for aortic valve repair or replacement are utilized. Sutures may be tied directly (Fig. 4). De-airing techniques are aided greatly by TEE, locating pockets of air. Gentle shaking of the heart combined with lung ventilation and momentarily limiting the venous return is usually all that is needed to de-air the left cardiac chambers. If necessary, forceps handles or pediatric defibrillator paddles can reach all areas of the heart, even through this limited incision.

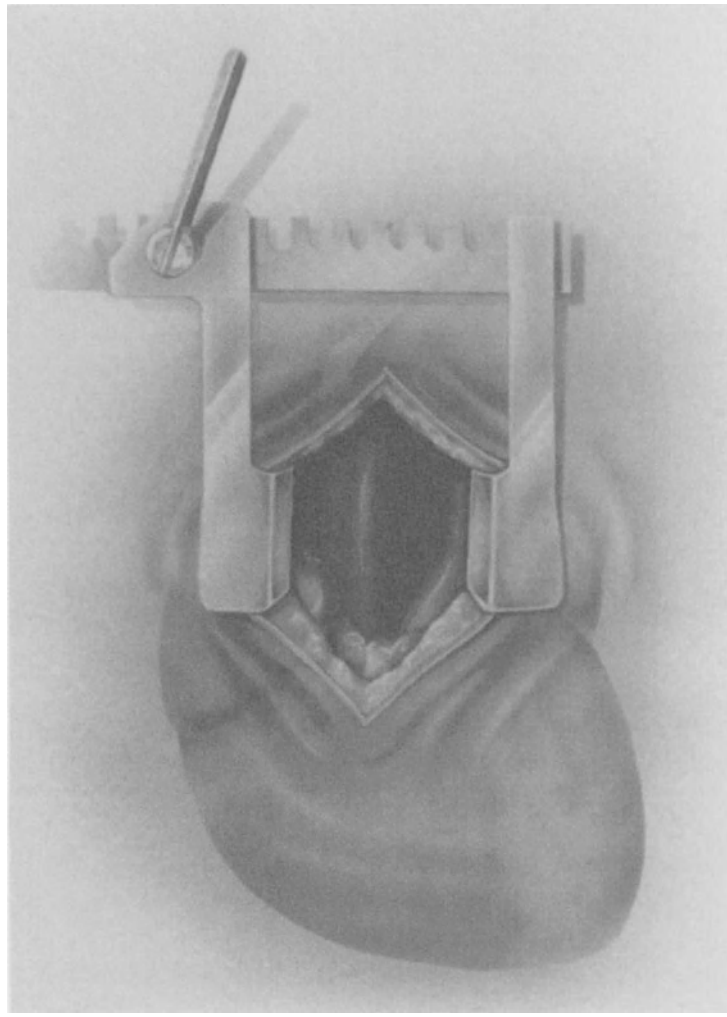


Fig. 2. A small sternal retractor exposes the ascending aorta and right atrial appendage for conventional cannulation.

Myocardial protection has been accomplished primarily via retrograde, continuous warm blood cardioplegia, but we have also used cold, intermittent blood anterograde and/or retrograde cardioplegia without difficulty. Because replacement of a dislodged retrograde catheter may prove difficult in a tiny incision, arrangements to change to antegrade or direct coronary ostial cannulation are recommended, particularly in cases in which only retrograde cardioplegia via ministernotomy is being entertained. In 5% of cases, we were unable to place the retrograde catheter and modified our technique to cold blood antegrade cardioplegia instead. Defibrillation was rarely necessary. Pacing is not routinely instituted, but atrial or ventricular wires can be placed and brought out through an interspace. In this regard, it is important to place the ventricular wires on the right ventricle while the heart is still decompressed.

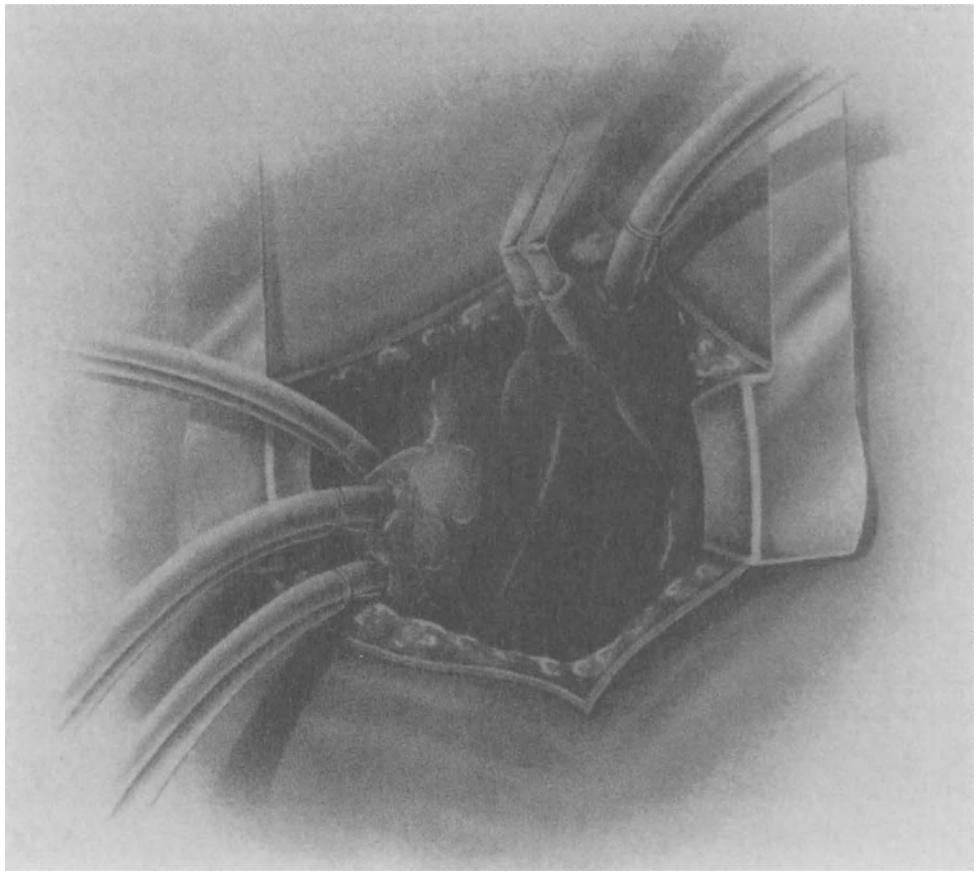


Fig. 3. Right atrial and aortic purse-string sutures have been placed, and cannulation for institution of cardiopulmonary bypass (CPB) including arterial, venous, retrograde, and venting cannulas have been inserted. The aorta is being cross clamped with a right-angle clamp.

Following completion of the procedure and removal of cannulas, a 19 Fr. Blake (J & J, Cincinnati, OH) drain is placed around the heart within the pericardium and brought out lateral to the IMA in an intercostal space and connected to a Heimlich valve grenade suction device (Fig. 5). The upper and lower sternal edges are wired together with separate wires, and then the two upper edges are reclosed with wires. Extubation is anticipated within the operating room or shortly thereafter.

CLINICAL EXPERIENCE

The results of our first consecutive 100 patients is reported herein. Ministernotomy was accomplished in all patients. In four other patients, all adults, planned ministernotomy was aborted when the aortic annulus was found to be at or below the xyphoid ($n = 2$), or when adhesions were felt to be too difficult to dissect in a reoperation for aortic root replacement ($n = 1$), or when anasarca rendered the sternum to be 4 in. below the skin

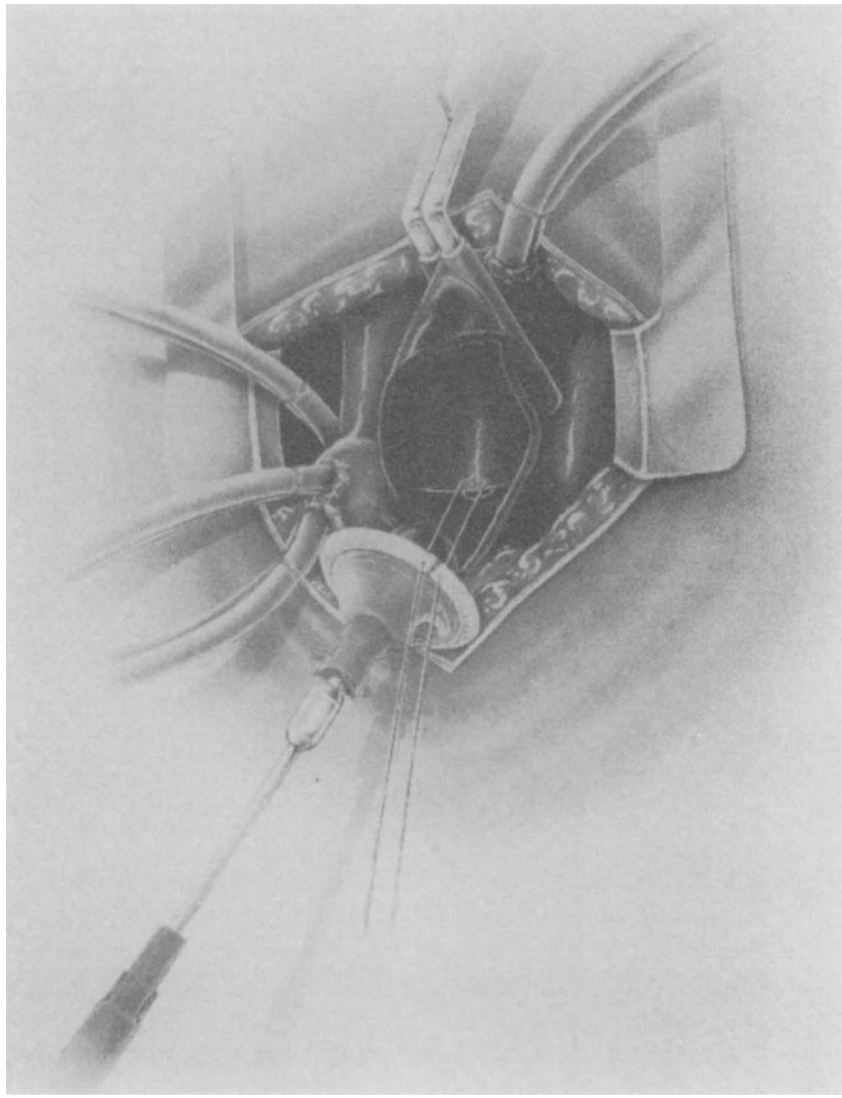


Fig. 4. The ministernotomy approach allows excellent exposure of the aorta for aortotomy and aortic valve repair or replacement.

surface ($n = 1$). In these cases, conventional median sternotomy was carried out and the operation proceeded uneventfully.

Once CPB was under way, no patient required conversion to full sternotomy. Defibrillation was required in 2% of patients. No patient required inotropic support to be weaned off bypass, and most patients (98%) were extubated immediately or within 4 h of operation. Two patients with severe new onset aortic regurgitation required overnight support with mechanical ventilation.

Hospital stay ranged from 1–20 d (median 2.6 d). Patients were generally discharged home on postoperative d 2 or 3, although five patients (including one redo aortic valve

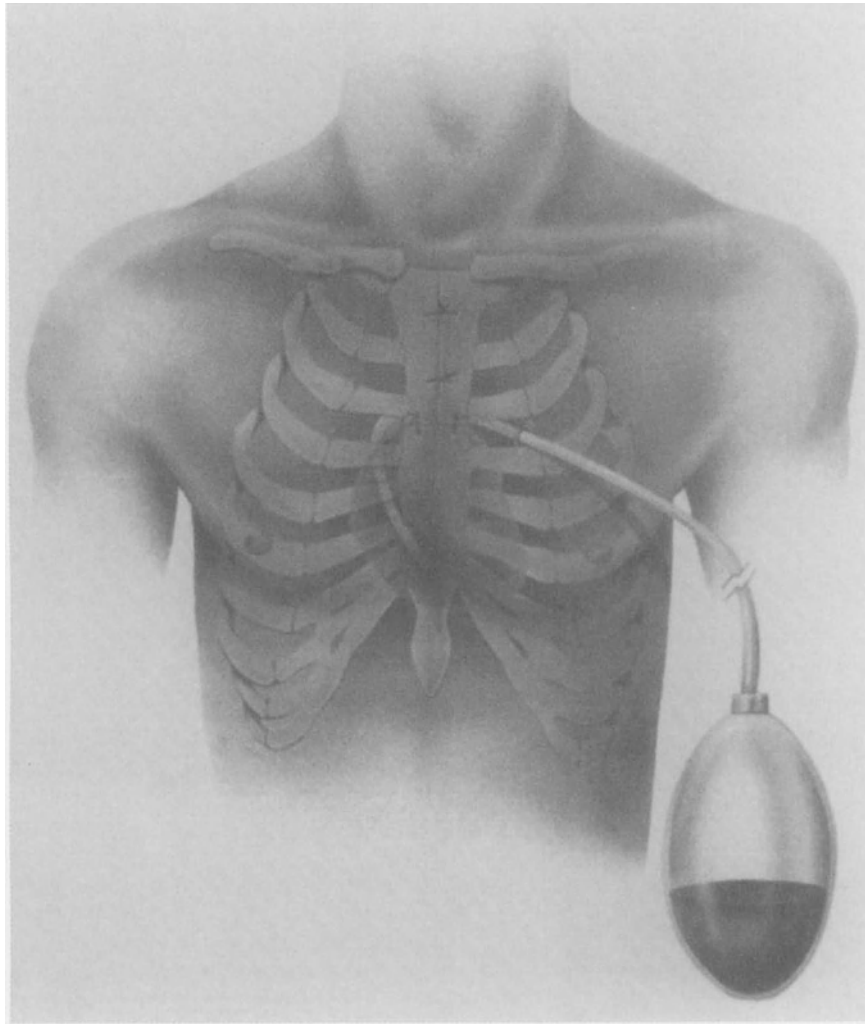


Fig. 5. A drain has been placed around the heart within the pericardium and brought out lateral to the IMA in an intercostal space and connected to a Heimlich valve grenade suction. Sternal incision is closed with four wires as depicted.

replacement) went home on the first postoperative day. There were no readmissions, no wound complications, and no deaths. One patient receiving oral anticoagulation developed a late pericardial effusion that was tapped uneventfully. Two postoperative cerebrovascular accidents were observed, including a patient who was maintained on suboptimal Coumadin therapy.

COMMENTS

Minimally invasive surgical access to most areas of the body is available and increasingly expected by the public. Minimally invasive procedures frequently force upon the

surgeon limited access or control, both anathemas to heart surgeons accustomed to being ready to control directly almost any untoward situation. Moreover, many minimally invasive cardiac operations propose utilizing incisions that are foreign to many practicing surgeons, and involve cannulations of structures such as the femoral vessels, which, although routinely used in the past, are now rarely utilized owing to the known sequelae associated with their use *(3,4)*. Although thoracoscopic techniques will undoubtedly be applied with increased frequency to cardiac surgery *(5)*, we would make a plea that a transitional step utilizing known techniques performed through smaller "holes" seems logical, allowing the cardiac surgeon to operate readily within a comfort zone based on years of practice and training.

With these concepts in mind, we proposed and now utilize ministernotomy to access the heart for all adult valvular and ascending aortic operations. In our early experience with retrograde cardioplegia and redo operations, we determined that CPB could be initiated and cardioplegia delivered with only the ascending aorta and a small portion of the right atrium freed from adhesions *(1)*. With increasing experience, it becomes clear that there is no reason to dissect the entire heart in redo aortic and mitral valve operations, when all the surgeon is operating on is the valve(s). If exposure of the entire heart is not necessary in reoperative cases, why then would it be necessary in supposedly simpler first-time operations?

The ascending aorta and right atrial appendage, the two structures necessary for institution of CPB, are essentially upper midline structures and hence easily reached following upper sternal division. These two structures are also within the reach of paramedian or transverse sternal incisions, but one or both IMAs are sacrificed with these alternative approaches. Additionally, neither of these approaches approximates the intrinsic exposure of the base of the heart with which cardiac surgeons are so familiar. It is true that L, J, or reverse J incisions can also provide similar exposure. However, we believe that symmetric division of the sternum allows each IMA to be stretched slightly, rather than one side being stretched considerably.

The use of a parasternal incision for aortic valve operations has been described recently by Cosgrove and Sabik *(6)*. The technique requires a 10 cm right parasternal incision and common femoral vessel cannulation. The incision extends from the lower edge of the second costal cartilage to the superior edge of the fifth costal cartilage. The third and fourth costal cartilages are excised, and the right internal thoracic artery is ligated. Aortic replacement or repair was undertaken in 25 patients using this limited access with no postoperative deaths, reoperations for bleeding, cerebrovascular accidents, or wound complications.

Benetti et al. *(7)* and colleagues in Argentina described their limited experience with a 6-cm incision in the third intercostal space, an Access Platform device (CardioThoracic Systems, Portola Valley, CA), and femoral vessel cannulation to replace the aortic valve in two patients.

Minimally invasive heart surgery ideally should allow the practicing surgeon to continue to utilize tools and approaches familiar to cardiac operations. In this sense, ministernotomy utilizes standard retractors, cannulas, myocardial protection strategies,

and surgical techniques. Furthermore, the approach, although limited, allows for the introduction of fingers to tie knots and large instruments to remove or cut calcified valves. The only difference between conventional exposure and ministernotomy is that the latter permits the surgeon access to only that portion of the heart with which he or she is interested, rather than "seeing" the entire cardiac structure. However, unlike other "mini" approaches, should the surgeon want or need to have immediate access to the entire heart, simple completion of sternal division provides full cardiac exposure.

The role that small incisions play in patient well-being and comfort should not be underestimated. Because we haven't been able to correlate patient discomfort with extent of sternal division, we have used small skin incisions and a somewhat larger sternal incision to accomplish aortic root replacement. The small skin incisions have been uniformly praised by the patients, and to date, there have been no wound complications. Prospective evaluation of the impact of limited incisions and sternotomies on quality of life and length of stay parameters will require randomized studies comparing conventional approaches with "mini" techniques.

Our clinical experience with 100 adult aortic valve operations suggests that ministernotomy in combination with standard cannulation techniques and the use of smaller pericardial drainage devices results in rapid extubation, decreased LOS, and improved patient comfort and mobility without compromising surgical outcome.

REFERENCES

1. Gundry SR, Razzouk AJ, Vigesaa RE, Wang N, Bailey LL. Optimal delivery of cardioplegia solution for "redo" operations. J Thorac Cardiovasc Surg 1992;103:896–901.
2. Sardari F, Schlunt ML, Applegate RL, Gundry SR. The use of transesophageal echocardiography to guide sternal division for cardiac operations via mini-sternotomy. J Cardiac Surg 1997;12:67–70.
3. Gundry SR, Brinkley J, Wolk M, et al. Percutaneous cardiopulmonary bypass to support angioplasty and valvuloplasty—technical considerations. ASAIO Trans. 1989;35:725–727.
4. Retiz BA, Stevens JA, Burdon TA, St. Goar FG, Siegel LC, Pompili MF. Port access coronary artery bypass grafting: lessons learned in a phase I clinical trial. Circulation 1996;1(Suppl):I–52.
5. Lin PJ, Chang CH, Chang JP, et al. Video assisted cardiac surgery (VACS): the preliminary experience in one center. Circulation 1996;1(Suppl):I–174.
6. Cosgrove DM, Sabik JF. Minimally invasive approach for aortic valve operations. Ann Thorac Surg 1996;62:596–597.
7. Benetti FJ, Mariani MA, Rizzardi JL, Benetti I. Minimally invasive aortic valve replacement. J Thorac Cardiovasc Surg 1997;113:806–807.

18 Minimally Invasive Approaches to Congenital Heart Surgery

Gregory P. Fontana, MD

CONTENTS

INTRODUCTION

Minimally invasive cardiac surgery for the treatment of congenital heart disease (CHD) continues to expand from simple extracardiac procedures to repair of intracardiac defects. The incentive for the development of such techniques is the avoidance of the known long-term morbidity of thoracotomy and sternotomy in children, as well as the reduction of postoperative pain, respiratory dysfunction, and length of hospital stay.

Most extracardiac procedures can be performed through multiple 2- to 4-mm incisions (thoracostomies). They avoid muscle division and do not require rib retraction. Table 1 lists these procedures. Advances in endoscopic suturing techniques and instrumentation should allow for continued expansion to more complex extracardiac procedures including repair of coarctation of the aorta.

Repair of intracardiac congenital heart defects has been performed successfully and requires novel cannulation strategies, specialized instrumentation, and advanced visualization technology. Repair of atrial and ventricular septal defects and tetralogy of Fallot have all been reported using a variety of minimally invasive approaches.

The long-term goal is to perform surgery for CHD totally by thoracoscopic or transvascular techniques maintaining the precision, accuracy, and safety of conventional

From: *Contemporary Cardiology: Minimally Invasive Cardiac Surgery*
Edited by: M. C. Oz and D. J. Goldstein

Table 1
Congenital Heart Operations Currently Performed with Minimally Invasive Approaches

Ligation of PDA
Division of complete vascular rings
Ligation of systemic-to-pulmonary artery collaterals
Creation of pericardial window
Thoracic duct ligaton
Aortopexy for airway compression syndromes
Diaphragmatic plication

open surgery. This chapter presents an overview of the most commonly performed operations for pediatric patients with congenital heart defects.

HISTORICAL PERSPECTIVE

Application of minimally invasive thoracic surgery in children began over 20 yr ago when Rodgers *(1)* and others first used thoracoscopic techniques to the diagnosis of intrathoracic lesions. Thoracoscopy for biopsy of pulmonary parenchymal and mediastinal masses was performed in 800-g infants to adult-sized adolescents. The principles established during this early experience are the foundation for current techniques.

In 1991, Laborde *(2)* was the first to perform a minimally invasive video-assisted thoracoscopic procedure for CHD by successfully ligating a patent ductus arteriosus (PDA) with a titanium surgical clip. This early experience was outstanding and inspired others to pursue the extremes of patient size and complexity. Subsequently, Burke et al. *(3)* reported on the closure of the PDA in premature infants as small as 575 g.

Complete vascular ring division has been accomplished in those patients with either right aortic arch, aberrant left subclavian artery, and a left-sided ligamentum arteriosum or a double aortic arch with an atretic left (anterior) segment *(4,5)*. Division of patent segments of complete vascular rings has, to date, required a limited thoracotomy to introduce conventional vascular clamps because instrumentation to achieve thoracoscopic control of vascular structures has not been sufficiently miniaturized.

Subsequently, additional procedures have been performed utilizing the same instrumentation and endoscopic techniques. In addition to those listed in Table 1, ligation of persistent left superior vena cava, placement of permanent epicardial pacemaker leads, and placement of central nervous catheters directly into the right atrium all have been accomplished *(3,6)*.

The repair of intracardiac congenital defects presents a number of challenging obstacles; however, several centers have reported successful operations. Atrial septal defects (ASDs) have been closed via subxyphoid *(7,8)*, limited right anterior thoracotomy *(6,9–11)*, mini right posterolateral thoracotomy *(12)*, partial sternotomy *(13)*, and totally thoracoscopic *(6,9)* approaches. Early experience with repair of ventricular septal

defects (VSDs), tetralogy of Fallot and transposition of the great arteries has been limited but encouraging *(11–13)*.

Open-chest procedures may be facilitated by endoscopic visualization of remote anatomic structures. Cardioscopy has been performed as a method to visualize intracardiac structures or pathology that are challenging to access without ventriculotomy *(14)*. Repair of atrioventricular valves and muscular VSDs, and removal of misplaced clam-shell devices and intraventricular thrombus have been accomplished *(6,13)*.

RATIONALE

Justification for a video-assisted thoracoscopic approach in the pediatric patient must be compelling because the results for conventional surgery via median sternotomy have been excellent. The primary advantage of this approach is the reduction in tissue trauma and its consequences. Clearly, reduced acute morbidity from painful incisions and shorter length of intensive care and hospital stay are important incentives; however, the long-term effects of thoracotomy are far more significant. With regard to the latter, musculoskeletal defects such as scoliosis, winged scapula, shoulder girdle abnormalities (decreased strength and range of motion), chest wall asymmetry, and chronic pain syndromes have been reported with the more severe manifestations seen in younger patients *(15–18)*. Additionally, significant breast deformities have been reported in up to 20% of female patients.

Sternotomy is well tolerated in children but may be associated with a number of potential cosmetic issues. Wound healing may lead to an unattractive scar in an obvious location, and the sternum may heal with bony prominences or asymmetry.

EXTRACARDIAC PROCEDURES

Patent Ductus Arteriosus

After induction of general anesthesia, a transesophageal echocardiography probe is positioned, and the patient is placed in the right lateral decubitus position. Four thoracostomies (2–4 mm) are performed (Fig. 1), and the pleura is entered via muscle-splitting incisions. Reusable ports are placed through the thoracostomies to aid the manipulation and reintroduction of instruments. A 30° high-resolution videoscope (2.7 mm for patients <4 kg, 4.0 mm for patients >4 kg) is placed first to allow introduction of all instruments under direct vision. Through a second port, a lung retractor is placed. The remaining two ports are used for passage of the operating instruments and electrocautery.

Once the lung is retracted anteriorly and inferiorly, the mediastinal pleura is incised with electrocautery from the mid-descending aorta distally onto the left subclavian artery proximally. The PDA is then exposed with electrocautery and blunt dissection. Careful attention is paid to avoid injury to the recurrent laryngeal nerve. Once the dissection is complete, an appropriately sized titanium clip is applied. Transesophageal monitoring allows confirmation of complete interruption of flow with echo-Doppler technology. If

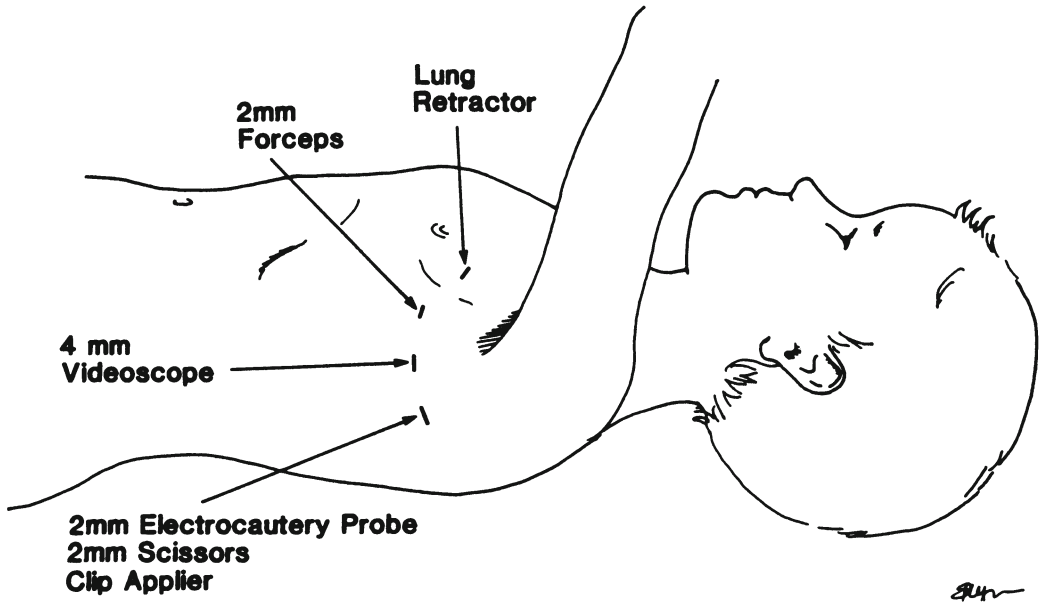


Fig. 1. Port placement for video-assisted thoracoscopic surgery.

persistent flow is documented, a second clip is applied. If adequate dissection of the PDA has been performed and the ductus is not >1 cm in diameter, one or two clips should suffice. For a larger PDA, the duct may first be encircled with suture and ligated with endoscopic knot-tying techniques. Once the PDA diameter has been reduced with the application of sutures, a surgical clip may be easily applied.

Once hemostasis is attained and lymphatic vessels have been controlled with electrocautery, all instruments are removed under direct thoracoscopic vision. A small chest tube is placed via one of the thoracostomies, and the lung is reexpanded. The incisions are closed with absorbable suture. The patient is extubated in the operating room, and the chest tube is removed if there is no significant drainage or pneumothorax. After 2–4 h in the recovery room, the patient is transferred to a monitored bed overnight and then discharged home the next morning.

Over 700 procedures have been performed in the four centers with largest experience in patients ranging in age from 1 d to adulthood (CMC Porte de Choisy, Boston Children's Hospital, Cedars-Sinai Medical Center, Miami Children's Hospital). There have been no operative mortalities or significant intraoperative hemorrhage. Transient recurrent laryngeal nerve palsy has been very rare. In most instances, length of hospital stay for elective patients is 1 d *(2,3,6)*.

Division of Vascular Ring

Following induction of general anesthesia, tracheobronchoscopy is performed to assess the baseline extent of upper airway compression. The technique for the division of complete vascular rings is similar to that of PDA ligation. Four thoracostomies are made.

Exposure is achieved by retracting the inflated lung inferomedially. The left subclavian artery is easily seen and is used to guide the dissection. Using cautery dissection, the ring elements are dissected free from the underlying esophagus and surrounding structures. Patients with a double aortic arch, an atretic anterior segment distal to the left subclavian artery, and a left ligamentum arteriosum require division of the latter two structures between surgical clips (Fig. 2A–C). By contrast, patients with a right-sided aortic arch and an aberrant left subclavian artery require only division of the ligamentum arteriosum (Fig. 2D,E). Fibrous bands over the esophagus are fully divided. A thoracostomy tube is placed through one of the aforementioned incisions, and the remainder of the wounds are closed in standard fashion. Tracheobronchoscopy is repeated to assess acute changes in the degree of airway compression. The degree of reduction in compression varies from subtle to dramatic depending on the severity of tracheomalacia.

If a patent vessel requires division to accomplish vascular ring division, i.e., PDA or anterior aortic arch, the posterior two thoracostomies may be connected to improve vascular access and allow introduction of vascular clamps. To minimize chest wall trauma, the ribs are not spread. Proximal and distal control is achieved and the vascular structures are divided between surgical ligatures. Visualization can be maintained thoracoscopically.

The largest experience with this procedure has been reported by Burke et al. *(4)* who described eight patients with a median age 5 mo (range 40 d–5.5 yr) and a median weight of 6.2 kg (1.8–17.1 kg) who underwent video-assisted thoracoscopic vascular ring division. All had successful ring division with symptomatic relief and no mortality. One patient required prolonged hospitalization for management of a chylothorax.

Other Extracardiac Procedures

Modification of the thoracostomy locations allows for the performance of many tasks. The basic principles of endoscopic surgery are applied to afford adequate visualization and instrument access to operative sites. Ligation of systemic-to-pulmonary artery collaterals, creation of pericardial window, ligation of the thoracic duct, aortopexy, and other simple extracardiac procedures can be readily accomplished.

INTRACARDIAC PROCEDURES

The repair of intracardiac defects with minimally invasive techniques requires modification of cannulation, cardiopulmonary bypass (CPB), and myocardial protection strategies. There are several options for cannulation including femoral, cervical (carotid artery, jugular vein), thoracoscopic, as well as through limited thoracotomies (Fig. 3A–D). Several factors influence the choice of site—most important is the size of the patient. For infants and children under 10 kg, use of the carotid artery, jugular, and femoral veins is an option to direct cannulation. For larger patients, femoral arterial and venous cannulation will allow full cardiopulmonary support. The option of partial or full cannulation via thoracostomies or limited thoracotomy has become increasingly feasible and offers the advantage of limiting the number of incisions and avoiding the disadvantages of groin

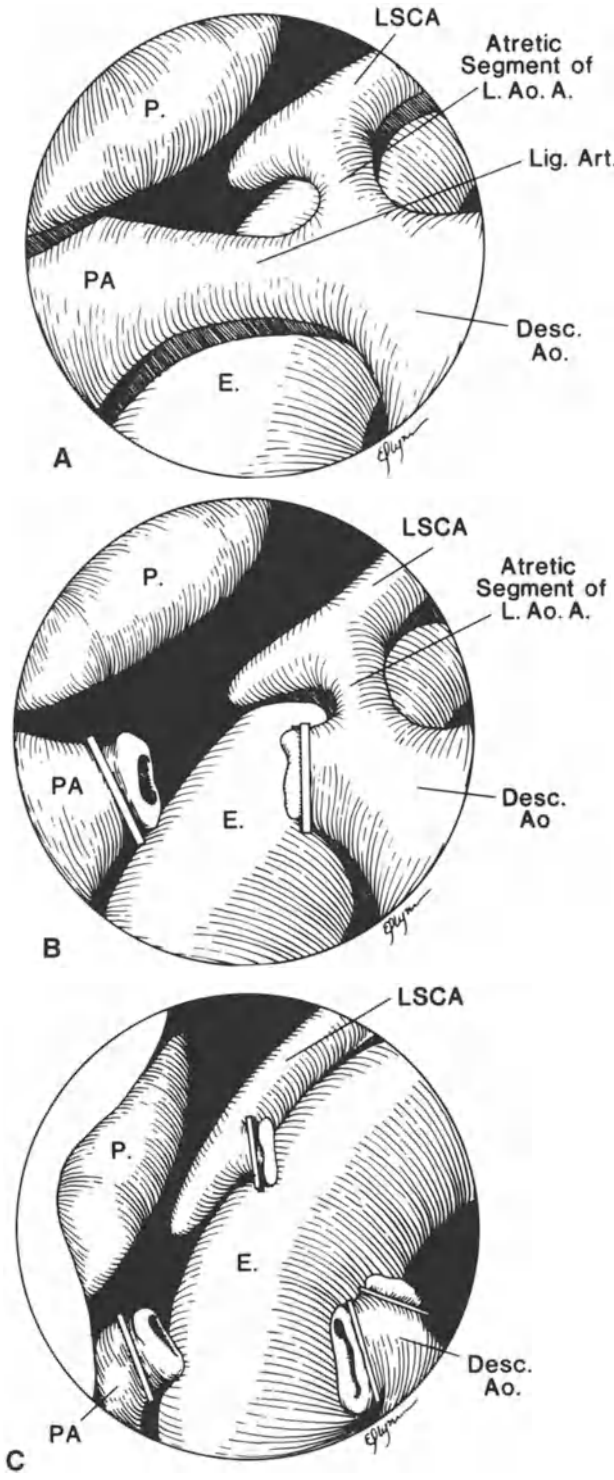


Fig. 2. (A–C) Vascular ring division in patients with a double aortic arch, an atretic anterior segment distal to the left subclavian artery, and a left ligamentum arteriosum. E, esophagus; LSCA, left subclavian artery; PA, pulmonary artery.

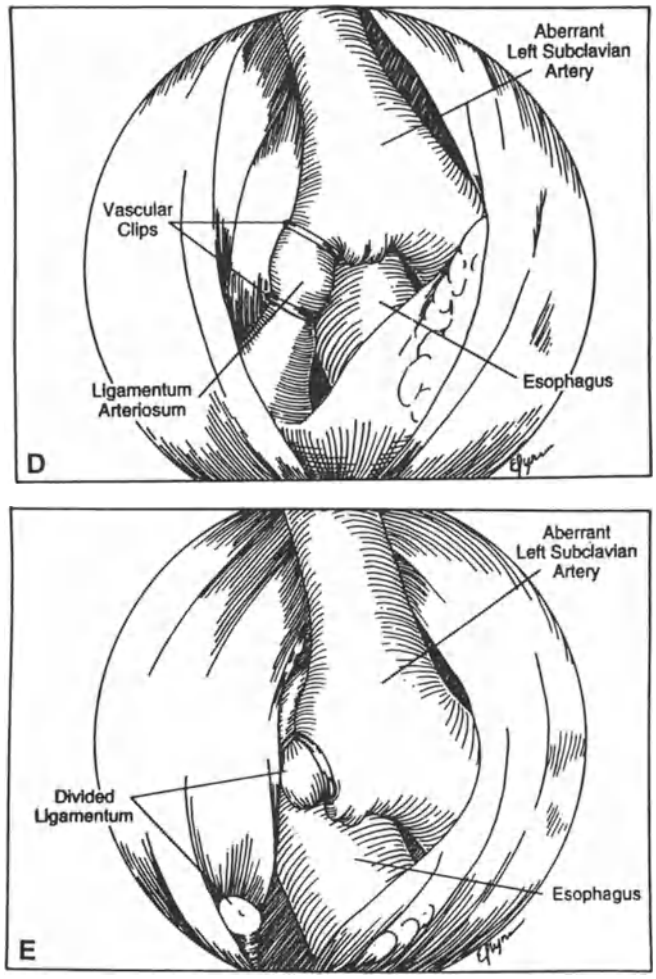
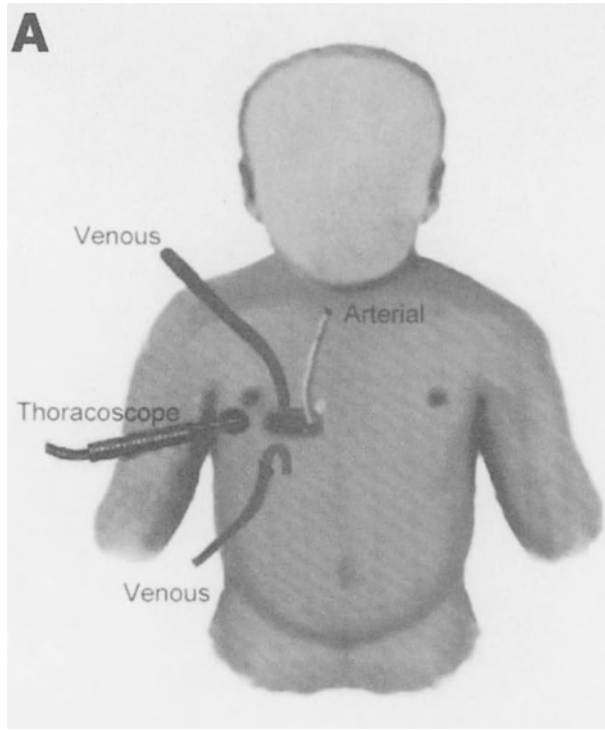


Fig. 2. (D,E) *(continued)* Vascular ring division in patients with a right-sided aortic arch and an aberrant left subclavian artery.

cannulation. Myocardial protection may be provided with fibrillatory or cardioplegic arrest depending on the procedure performed and the size of the patient. Secundum ASD closure can usually be performed with fibrillatory arrest. If more complicated procedures are to be accomplished, cardioplegic arrest may be performed with the aortic cross clamp placed through the wound, through a separate incision/port, or via endoaortic occluder. The latter is currently available only for patients larger than 40 kg.

ASD Closure

As mentioned earlier, several approaches have been applied to close ASDs, including totally thoracoscopic methods (Fig. 4). All provide excellent exposure to the ASD and substantially decrease the morbidity and cosmetic effects of a full sternotomy.



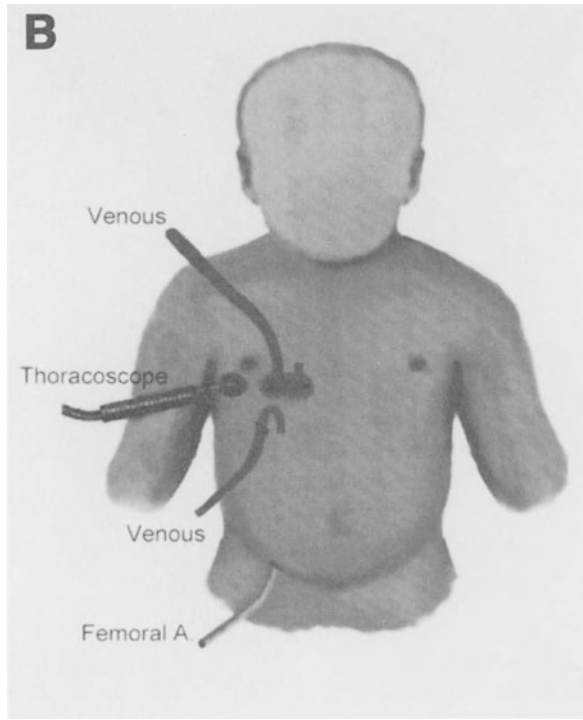
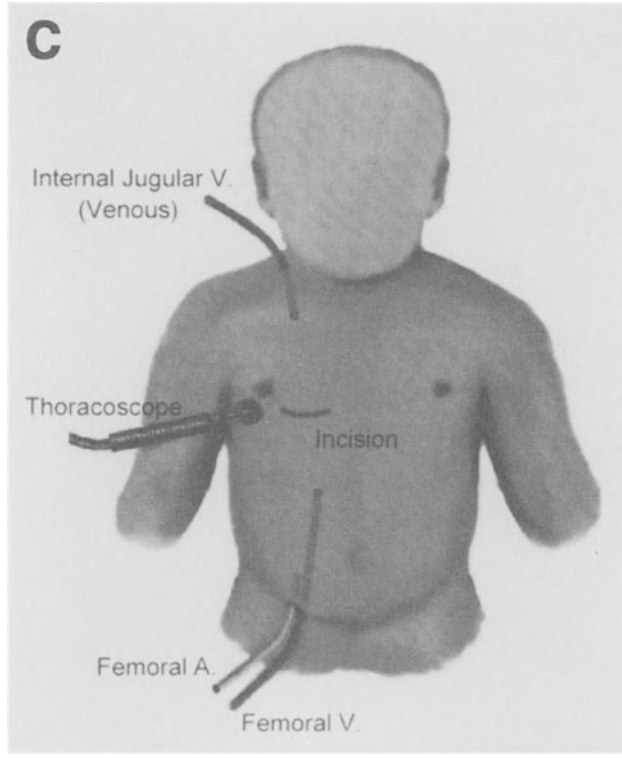


Fig. 3. (A,B) Cannulation options.



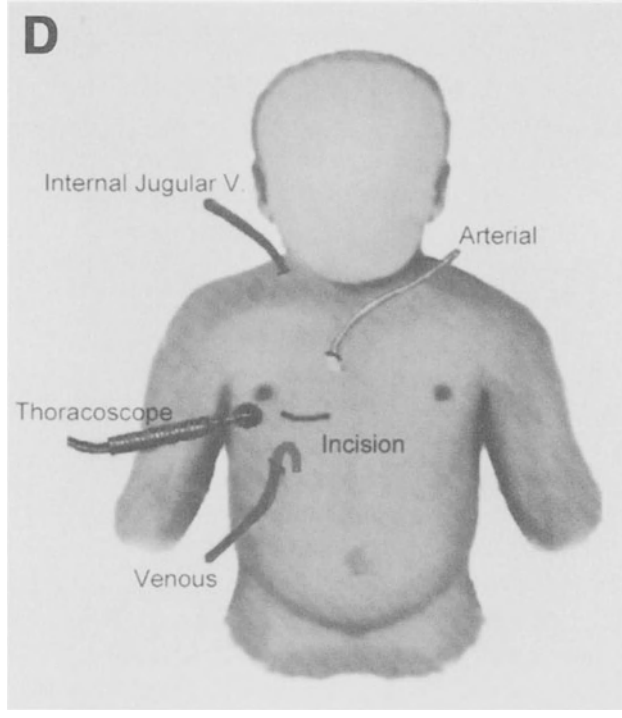


Fig. 3. (C,D) *(continued).*

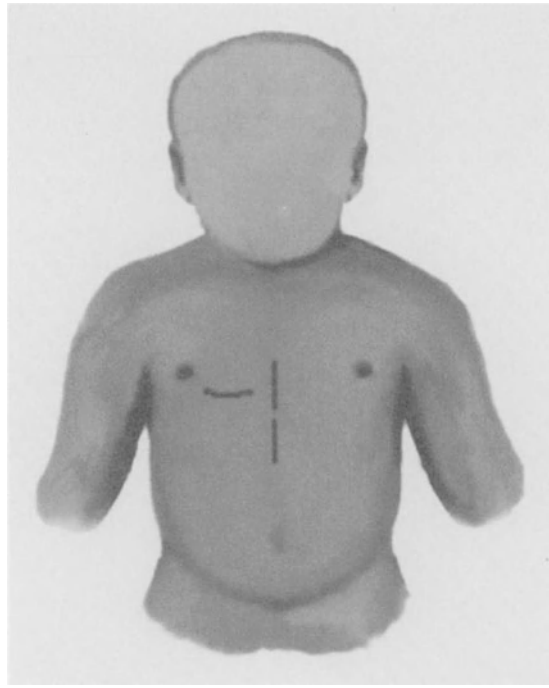


Fig. 4. ASD incisions.

Through a limited right anterior thoracotomy, all cannulae may be placed, however, this requires a larger incision. Therefore, direct cannulation of the femoral artery, internal jugular vein, and either the femoral vein or the inferior vena cava can be used to minimize the length of incision and degree of retraction (Fig. 3B,C). If the inferior vena cava cannula is exteriorized through the future site of the tube thoracostomy, the incision may be reduced to 4–5 cm. Furthermore, if a videoscope is used, minimal rib retraction is necessary. A caval snare is required around the inferior vena cava; however, if active venous drainage is used, a caval snare around the superior vena cava may not be necessary. Drainage is excellent and there is minimal air return as the superior vena cava collapses just proximal to the right atrium. Clearly, this arrangement is appropriate only for fibrillatory arrest. The leads from the fibrillator are easily placed through the incision. Direct suture or patch closure of the ASD is performed. Care should be taken to avoid excessive suction of blood from the left atrium to minimize trapped air in the pulmonary veins. Standard de-airing techniques are performed with the patient rolled to the left so that the plane of the ASD is horizontal. The fibrillator is then discontinued and the right atrium is closed in the usual fashion. Normal sinus rhythm generally returns spontaneously; however, if this is not the case, cardioversion via transcutaneous R2 pads is performed. A right pleural drain is placed and the patient is weaned from CPB. Once hemodynamic stability and hemostasis are ensured, all wounds are closed with absorbable suture. The patient is extubated in the operating room and transferred to the recovery room for 4–6 h, and then discharged home on postoperative d 1 or 2.

The transxyphoid approach may be performed through a midline or transverse incision over the xyphisternum *(7,8)* (Fig. 4). A Rultract (Cleveland, OH) suspension retractor is used to elevate the sternum while a self-retaining retractor is used for lateral exposure. The femoral artery is generally utilized for arterial cannulation; however, the aorta may be reached directly through the subxyphoid incision in some patients. The superior vena cava is cannulated through a purse-string suture in the right atrium using a balloon-tipped catheter. The inferior vena cava may be drained either directly or via the femoral vein. Once CPB is initiated, the heart is fibrillated and a right atriotomy is performed. The ASD is directly exposed *en face* and easily closed with conventional instrumentation.

Partial sternotomy can be used to perform ASD repairs through a low midline incision. The sternotomy is extended to a level that allows adequate exposure, typically to just below the sternal angle of Louis (second interspace). All cannulae are placed through the incision and standard techniques are utilized.

The most recent report on thoracoscopic ASD closure was presented by Chang et al. *(9)* who described eight patients ranging in age from 2–69 yr, and with a mean pulmonary blood flow to systemic blood flow ratio of 3.4 ± 1.3, who underwent the procedure via a right anterior minithoracotomy and femoro-femoral or femoro-atrial CPB. Mean operative time was 2.2 ± 4.5 h. Successful primary closure with no morbidity or mortality was achieved in all patients.

Other Intracardiac Repairs

VSDs may be approached through limited right anterolateral or posterolateral thoracotomies, or via partial sternotomy. By and large, the repair is most effectively accomplished with a cardioplegically arrested heart. The aorta may be occluded by cross clamping through the limited incision, or via separate endovascular access with an endoaortic occluder in larger patients.

Repair of a VSD and tetralogy of Fallot has also been described utilizing a controversial right ventriculotomy via a limited *left* anterior thoracotomy *(11)*. Attempts to minimize or eliminate the ventriculotomy have reduced the long-term morbidity of VSD or tetralogy of Fallot repairs, and, therefore, this approach has clear disadvantages. VSD repair has also been successfully carried out through right posterolateral minithoracotomy with all cannulae and instrumentation placed through a single incision *(12)*.

Finally, repair of complex CHD has been performed via partial sternotomy *(14)*. It requires no specialized instrumentation or endoscopy. Upper partial sternotomies are carried from the suprasternal notch to the third or fourth intercostal space and offer excellent exposure to the great vessels as well as the aortic and mitral valves. A lower partial sternotomy is usually carried from the xyphisternum below to the second or third interspace and offers excellent exposure to the right atrium and right ventricle. Both incisions offer adequate exposure for cannulation and repair.

CARDIOSCOPY

The use of the videoscope during open procedures to allow access to remote or poorly accessible intracardiac locations has been an important advance in surgery for

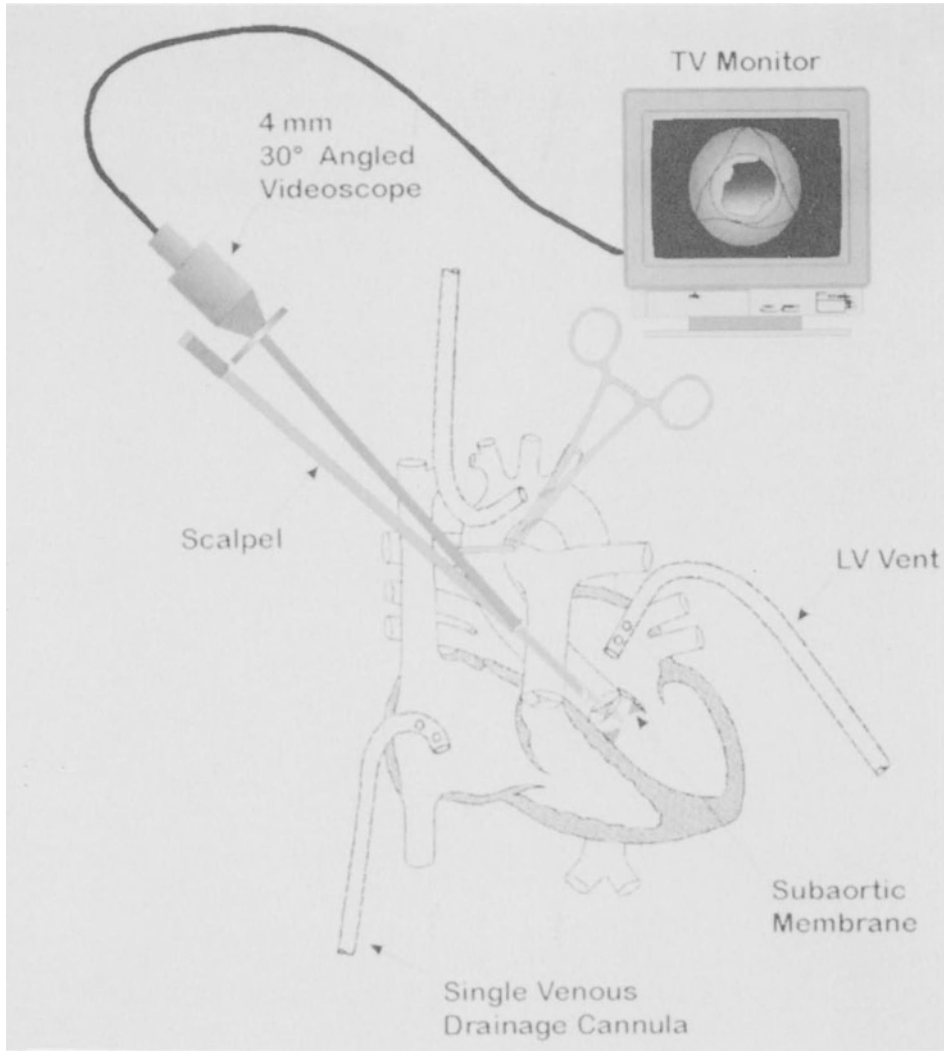


Fig. 5. Cardioscopy.

congenital acquired heart disease *(13)*. This technique allows accurate technical maneuvers to be performed while minimizing retraction, dissection, and/or the need for ventriculotomies. Examples of its application include removal of left ventricular thrombus, repair of difficult to expose mitral valves (especially in malrotated or positioned hearts), removal of displaced septal occlusion (clam shell) devices, repair of subaortic stenosis, and closure of muscular ventricular septal defects. In addition, this technique provides a videoscopic record of repairs that may prove to be helpful in the subsequent care of individual patients, as a method to illustrate techniques not visible to those other that the surgeon and as an investigative tool to further understand the results of current techniques (Fig. 5).

FUTURE DIRECTIONS

For further progress toward accomplishing the goal of complete repair of congenital heart defects by thoracoscopic and/or transvascular techniques, miniaturization and refinement of instrumentation, cannulae, visualization equipment (through flexible scopes) and development of innovative new techniques must be pursued. The concept of performing intracardiac repair of a variety of pathologies on the beating heart is under investigation and will require a new generation of technology including through-blood imaging (blood-displacement videoscopes), as well as task-specific instruments. Robotics may offer additional assistance in the performance of complex and/or fine maneuvers.

It was recently stated that minimally invasive surgery for intracardiac repair of CHD was "avant garde" therapy whose time has "not yet come" *(19)*. If recent progress is any gage of the pace of future development in this field, not only has the time come, but minimally invasive surgery is becoming standard practice.

REFERENCES

1. Rodgers BM. Pediatric thoracoscopic surgery. In: Kaiser LR, Daniel TM, eds. Thoracoscopic Surgery. Little, Brown, Boston, 1993.
2. Laborde F, Noirhomme P, Karam J, Batisse A, Burel P, Saint Maurice O. A new video-assisted thoracoscopic surgical technique for interruption of patent ductus arteriosus in infants and children. J Thorac Cardiovasc Surg 1993;105:278–280.
3. Burke RP, Wernovsky G, van der Velde M, Hansen D, Castaneda A. Video-assisted thoracoscopic surgery for congenital heart disease. J Thorac Cardiovasc Surg 1995;109:499–508.
4. Burke RP, Rosenfeld HM, Wernovsky G, Jonas RA. Video-assisted thoracoscopic vascular ring division in infants and children. J Am Coll Cardiol 1995;25:943–947.
5. Burke RP, Chang A. Video-assisted thoracoscopic division of a vascular ring in an infant: a new operative technique. J Cardiac Surg 1993;8:537–540.
6. Fontana GP. Minimally invasive repair of intracardiac congenital heart defects [abstract]. Presented at the World Congress on Minimally Invasive Cardiac Surgery, 1997, Paris, pp. 2,3.
7. Levinson MM, Fonger JD. Minimally invasive atrial septal defect closure using the subxyphoid approach [abstract]. Presented at the World Congress on Minimally Invasive Cardiac Surgery, 1997, Paris, pp. 2,10.
8. Barbero-Marcial M, Tanamati C, Jatene MB, Atik E, Jatene A. Transxyphoid approach without sternotomy for the correction of atrial septal defects [abstract]. Presented at the World Congress on Minimally Invasive Cardiac Surgery, 1997, Paris, pp. 2,10.
9. Chang CH, Lin PJ, Chu JJ, et al. Video-assisted cardiac surgery in the closure of atrial septal defect. Ann Thorac Surg 1996;62:697–701.
10. Shetty DP, Dixit MD, Gan MD, et al. Video-assisted closure of atrial septal defect. Ann Thorac Surg 1996;62:940.
11. Lin PJ, Chang C-H, Chu JJ, et al. Minimally invasive cardiac surgery for intracardiac lesions [abstract]. Presented at the World Congress on Minimally Invasive Cardiac Surgery, 1997, Paris, p. 2,12.
12. Serraf A, Belli E, Lacour-Gayet F, Petit J, Planche CI. The mini posterolateral thoracotomy for closure of intracardiac defects [abstract]. Presented at the World Congress on Minimally Invasive Cardiac Surgery, 1997, Paris, p. 2, 12.

13. Gundry SR. Minimally invasive aortic valve surgery: technical considerations and results [abstract]. Presented at the World Congress on Minimally Invasive Cardiac Surgery, 1997, Paris, 2,3.
14. Burke RP, Michelon G, Wernovsky G. Video-assisted cardioscopy in congenital heart surgery. Ann Thorac Surg 1994;58:864–868.
15. Dajezman E, Gordon A, Kreiman H, Wolkove N. Long-term post thoracotomy pain. Chest 1991;99:270–274.
16. Wesfelt JN, Nordwall A. Thoracotomy and scoliosis. Spine 1991;16:1124,1125.
17. Shelton JE, Julian J, Walburgh E, Schneider E. Functional scoliosis as a long-term complication of surgical ligation for patent ductus arteriosus in premature infants. J Pediatr Surg 1986;48A:855–857.
18. Jaureguizar E, Vasquez J, Murcia J, Diez Pardo J. Morbid musculoskeletal sequelae of thoracotomy for tracheoesophageal fistula. J Pediatr Surg 1985;20:511–514.
19. Mavroudis G. VATS ASD closure: a time not yet come. Ann Thorac Surg 1996;62:638,639 (editorial).

INDEX

C

D

N

O

P

Q

R

S

T

U

V

W

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