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Short Stay Management of Acute Heart Failure

Third Edition

Humana Press

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Short Stay Management of Acute Heart Failure

Third Edition

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Preface

Heart failure is the most common reason for patients over the age of 65 to be hospitalized. It is the most common reason for their re-hospitalization within the next 30 days, and after an emergency department visit that results in hospitalization for acute heart failure, the 2-year mortality rate approaches 50 %. This is not a disease anyone wants to have, and it is occurring more frequently at an alarming rate. Heart failure is the final common pathway of an aging population and a consequence of the remarkable success that has been attained in managing the other chronic cardiovascular diseases that historically resulted in an early mortality before the presence of heart failure could be realized.

Heart failure is expensive. In fact, it is the number one most expensive diagnosis, as reported by the Centers for Medicare and Medicaid Studies. As a country, the United States spends more on heart failure than any two cancers combined, a fact that just represents the financial costs. From a quality of life perspective, patients with advanced heart failure are miserable. Symptoms include shortness of breath with the slightest effort, sleeping disorders, and the inability to eat or drink normally. This is not a symptom constellation that is easily ignored or appreciated.

Short Stay Management of Acute Heart Failure, Third Edition, presents opportunities for improving the management of patients likely to have, and ultimately be diagnosed with, acute heart failure. Few patients wish to be in the hospital. It is only when the severity of their illness makes it impossible to stay at home do they present and ask for help. By focusing on rapid diagnosis, early intervention, and stabilization, followed by symptom relief and optimization of life-prolonging therapies, a short stay strategy has the potential to maximize the quality of life for the patient. Quality of days alive and outside of the hospital is the measure by which patients will judge our successes in their care. The authors of this text hope that you will find it useful in providing the best outcomes possible for your heart failure patients.

Houston, TX, USA — W. Frank Peacock, MD, FACEP, FACC

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Part I

Administrative and Regulatory Issues

Society of Cardiovascular Patient Care Heart Failure Accreditation

1

Maghee Disch

Introduction

The Society of Cardiovascular Patient Care (SCPC) was founded in 1998 after a meeting held in Dearborn, Michigan, where a partnership between emergency department physicians and cardiologists was born. This collaboration established the goals of breaking down the silos in the care of the acute coronary syndrome (ACS) patient and reducing cardiovascular mortality. SCPC has two primary strategies to accomplish these goals—education and accreditation. In the years that followed, these strategies expanded to include not only the care of the ACS patient but also heart failure (HF) and atrial fibrillation (AF) populations.

SCPC introduced Chest Pain Accreditation in 2003 as a vehicle to provide facilities with a road map to improve their processes and decrease variances in the care of the cardiac patient. The entire accreditation process is designed and built upon the principles of process improvement science. It is important to approach the work of accreditation as a comprehensive process improvement initiative. If approached in this manner, facilities will gain insight into the beginning of the process (baseline gap analysis) and the direction they need to take (process improvement plan/charter) to improve their processes of care for the cardiovascular patient.

SCPC recognized that heart failure is a leading cause of morbidity and mortality within the United States of America and is a growing burden for healthcare facilities and emergency departments. Thus, SCPC first offered Heart Failure Accreditation in 2009 as a natural transition from Chest Pain Accreditation and because many of the underlying strategies and structure of accreditation work to improve the care of the heart failure patient. According to studies by [1] and [2], accredited chest pain centers performed significantly better on both their chest pain and heart failure CMS core measures, respectively. This suggested that Heart Failure Accreditation would

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have the same quality improvement outcomes as that established by accreditation of chest pain centers, in respect to patients presenting with suspected acute coronary syndromes.

In January 2016, SCPC and the American College of Cardiology (ACC) announced the merger of these two organizations. Together a combined venture began, pioneering a new institutional program that combines accreditation services, registry services, quality initiatives, and education with the goal of enhancing quality improvement in cardiovascular patient care and to reduce morbidity and mortality. This merger brings new thinking and new perspectives to ongoing efforts to provide a continuous approach to quality improvement. The now combined mission of both SCPC and ACC will move to transform cardiovascular care delivery and improve patient outcomes.

The shared goals of both SCPC and ACC include the establishment and offering of a comprehensive quality improvement solution to hospitals and other facilities that combines SCPC accreditation and ACC's registry services, quality initiatives, education, collaboration, and data utilization. This includes the continued development and sharing of best practices that optimize the care and outcomes of patients with acute cardiovascular disease worldwide through innovative cross-disciplinary processes and education by Taking Science to the Bedside™.

Heart Failure Accreditation

The growing heart failure burden on our healthcare systems now effects close to 7 million people annually, attributing to over 6.5 million hospital days. Yearly, over 700,000 emergency department visits are for a primary diagnosis of heart failure leading to over 80 % of these patients being admitted to the inpatient level of care. Heart failure patients have an average return to hospital rate of 22 % within 30 days and 61 % of these patients return within 15 days [3]. The heart failure patient population is increasingly difficult to manage due to their chronic state, need for long-term self-management, and encumbrance on healthcare resources. In addition to complexity in management, facilities must also focus resources on decreasing risk for penalty and lower reimbursement due to CMS scrutiny and regulation. Healthcare facilities will benefit from a standardized approach for this patient population to guarantee appropriate patient placement, follow-up care, decreased hospital readmissions, and improved quality of life.

Heart Failure Accreditation encompasses the entire multidisciplinary team, facility, and care continuum. Accreditation is not a specification or an inspection of compliance but rather an effort to engage facilities in a multidisciplinary, all-inclusive improvement process. The quality of care for the heart failure patient should be measured in some manner to demonstrate improvement not only in process but also end outcomes such as 30-day readmission rates, average length of stay, and inpatient mortality. To the degree possible, the entire accreditation process is designed to be collegial and collaborative. The philosophy at SCPC is one of respect and realization of the uniqueness of facilities and the populations they serve.

The Process

The accreditation tool is laid out into seven essential components which are then made up of mandatory, recommended, and innovative items. The essential components span the entire care continuum and process related to the care and management of the heart failure patient. The line items contained within these components are the pieces, processes, team members, and systems that must be in place for best practice, management, and outcomes. All mandatory items are based on Class I recommendations from the *2013 ACCF/AHA Guideline for the Management of Heart Failure Report* and founded in science. Recommended and innovative items are those processes and systems that are recognized as best practice in literature and observation but have not yet received a Class I recommendation.

In addition to the essential components, SCPC has created a unique Accreditation Conformance Database (ACD) to collect patient level data related to process improvement and patient outcomes. Patients who are discharged with a primary diagnosis of heart failure from all levels of care are included in the ACD. From the data collected, facilities are given reports through calculated measures specific to the patient level data that is entered. This data collection and utilization was added to the accreditation process to aid in the process improvement plan and for continued evaluation of progress.

Once the accreditation process has begun, facilities will complete a baseline gap analysis within 30 days; this entails entry of 30 patient encounters into the ACD as well as determining what processes they already have in place versus those that will have to be developed during the application phase to reach accreditation. Following the submission of baseline gap analysis, facilities have 11 months to submit their application for accreditation (12 months total). In order to successfully achieve accreditation, when evaluated, facilities must show evidence that they have met all mandatory criteria and satisfied the data entry component. In addition to the supporting documentation review, the accreditation review specialist (ARS) will complete an onsite visit to validate the facility's documentation and processes. The ARS also will submit a final report to an oversight committee (Accreditation Review Committee), which makes the final determination to grant accreditation. Accreditation is valid for a 3-year period from the date that the Accreditation Review Committee makes its determination. Throughout the application and accreditation phases, facilities have access to all SCPC resources including an assigned ARS, clinical experts, workshops, education, monthly Ask the Experts calls, and all of the references and shared practices held within the essential components.

Essential Components

Governance

Governance serves as the platform for designing, orchestrating, monitoring, and optimizing a hospital's processes. Goals include removing barriers to achieve optimum enterprise performance, improving operational performance by aligning

people and services more effectively, enabling transparency across the system, and enhancing decision-making processes.

Community

Community outreach focuses on public awareness activities through selected community interactions. Community outreach initiatives attempt to directly affect public behavior in order to reduce the incidence and prevalence of cardiovascular diseases. Successful community outreach focuses on improving or maintaining community health and acknowledges any community challenges in addressing the issue. Community outreach can be accomplished with efforts aimed directly to the public and/or by partnering with local businesses, employers, and healthcare providers. It is imperative for outreach to include activities targeting the behavior of youth within the community.

Prehospital

Prehospital care begins with out-of-hospital interventions delivered by community healthcare providers and first responders whenever 9-1-1 services are accessed. Critical care decisions about advanced care in life-threatening conditions are made using remote assessment and evidence-based protocols based upon contemporary guidelines. Patients with HF are heterogeneous and thus require differing treatment strategies. Reversible/treatable causes for decompensation are addressed whenever able.

Early Stabilization

Early stabilization refers to efforts to quickly assuage immediate life-threatening conditions within the emergency department and roughly comprises the first 12–18 h of care. Effective interventions for treating HF are time sensitive and require rapid assessment, diagnosis, and prompt treatment in order to improve outcomes. Subsequent evaluation of the initial response to therapy, followed by adjustment as indicated, are required for efficient risk stratification and appropriate patient disposition. Patients treated and released from the ED and those placed in observation services are included in this component.

Acute Care

Acute care covers inpatient care, from the point of admission to discharge. Using a multidisciplinary approach, acute care encompasses the vast majority of hospital-based care and employs contemporary guideline recommendations.

Transitions

Transitional care occurs whenever the service, provider, intensity, or location of care changes. "Handoffs" in care must be communicated and coordinated for optimal patient perception and financial and quality outcomes. Discharge should not be viewed not as an event but rather as a process. Open communication, coordination, and partnerships that provide patient-centered care across the spectrum are imperative for success.

Clinical Quality

Clinical quality measures monitors the effectiveness of systems across departments in order to positively enhance the patient's experience and improve clinical outcomes, while simultaneously reducing expenditures and maximizing profits. Evidence-based guideline-driven care serves as the foundation for this EC.

Why SCPC Heart Failure Accreditation?

- Requires risk stratification protocols to ensure appropriate placement of patients based on their clinical presentation, comorbidities, and response to treatment
- Encourages facilities to identify gaps, revise processes of care, create standardization, and measure results
- Breaks down silos among departments to bring teams together to improve care
- Ensures that operational efficiencies gained meet clinical and financial goals, such as a decrease in 30-day readmissions, length of stay, and inpatient mortality
- Engages emergency medical services in the process to include airway and medication protocol development as well as documentation to describe the patient's status prior to treatment that can support reimbursement
- Promotes the use of standardized guideline-driven order sets to improve patient safety, ensure appropriate documentation, and provide evidence-based care
- Avoids costly readmissions due to unclear medication discharge instructions, lack of post-hospital follow-up care, and ineffective patient education
- Decreases exposure risk for audits from third-party providers and regulators through appropriate documentation and patient placement
- Decreases liability exposure when using protocol driven, evidence-based medicine
- Educates the community about recognizing symptoms of heart failure and provides a sense of partnership between patients, their families, and the healthcare team

Summary

SCPC has an international reputation as the leader in process improvement through accreditation and education. Currently, there are over 1,100 accredited facilities and this number continues to grow. Once accredited, 93 % of facilities choose to retain

their accredited status, and the growth for accreditation continues at a rapid rate through all service line offerings. Heart Failure Accreditation differs from Chest Pain Accreditation only because heart failure is more difficult to diagnose and treat as well as the patient population tends to be more chronic than acute. SCPC has embraced this challenge to provide facilities with the means to improve both patient care and financial outcomes.

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The Economics and Reimbursement of Congestive Heart Failure

2

Sandra Sieck

Introduction

Cardiovascular disease (CVD) remains entrenched as the leading cause of mortality in the United States [1]. Although the overall death rates due to CVD have been decreasing due to the increased incorporation of evidence-based therapies, the overall incidence of heart failure (HF) has remained relatively unchanged over the last two decades while the prevalence of HF has increased [2]. Innovative and exciting new treatment options offer the promise of improvement in activity-limiting symptoms, enhanced quality of life, and possibly reduced mortality. Yet the economic burden of HF continues to impose a staggering challenge to all segments of the healthcare system. This challenge is particularly prominent for the acute care facility in the era of tightening budgets, diminishing reimbursements, quality of care mandates, government regulation, and an aging population.

While HF is indeed a chronic medical condition that physicians strive to optimally control, it is acute decompensated heart failure (ADHF) that most adversely affects the hospital's balance between providing effective acute care to patients and sustaining the economic viability of the institution. As hospitals are faced with the relentless shift toward caring for only the most acutely ill patients, they will be forced to develop more efficient, efficacious, cost-minimizing, evidence-based treatment paths in order to remain viable and competitive in the rapidly changing healthcare market place.

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Burden of Disease

Heart failure represented approximately 7.4 % of the total burden of all cardiovascular disease deaths (CVD) [3]. In the United States, over 2 % of the total population has HF. The absolute incidence of HF is estimated at 870,000 new cases in a year and is age related [4, 5]. Gains in survival with current therapies have resulted in an increase in the overall prevalence of HF [6]. In 2005, HF prevalence was 5.3 million adults [7]. By 2012, the prevalence of HF in the United States increased to 5.7 million or roughly 2.6 % of the adult population, and by 2030 it is expected to increase to 8 million [8]. While the disease does occur in all ages, it is predominantly a disease of the elderly, with incidence and prevalence increasing with age. Among 40–59 year olds, 1–2 % has HF. In the 60–79 age range, the prevalence increases to 4.8 % for women and 6.6 % for men. In those >80 years of age, the prevalence is 10.6 % in men and 13.5 % in women [9]. With the aging US population, the number of people with HF is likely to continue to increase.

The increasing prevalence of HF also translates to substantial healthcare resource utilization. Physician visits with a primary diagnosis of heart failure were 1,801,000 in 2010, and there were 676,000 ED visits [10]. HF is the most frequent Medicare diagnosis-related group (Medicare Severity or MS-DRG) payment system for hospital billing [11]. HF is responsible for more elderly hospitalizations than any other medical condition [12]. Hospital discharges for HF were 1,023,000 in 2010 and have somewhat stabilized from 2000 to 2010 (Fig. 2.1). Although the average length of stay has decreased over the last decade, the 30-day readmission rate has increased to 23 % and is roughly 50 % at 6 months. It is estimated that up to 25 % of readmissions are avoidable [13, 14].

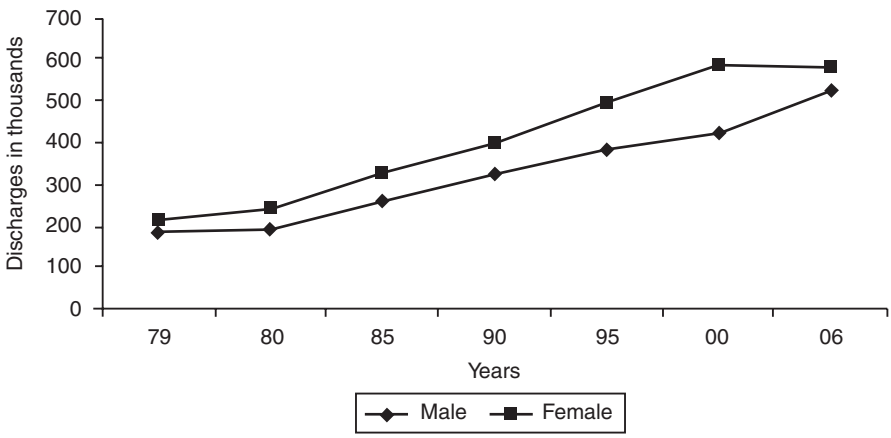

Fig. 2.1 Hospital discharges for heart failure in the United States (1979–2010). Trends in hospital discharges for heart failure in the United States (From the American Heart Association Heart Disease and Stroke Statistics, Update 2010 and American Heart Association Heart Disease and Stroke Statistics, Update 2015. Source: http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.109.192667)

HF represents a resource-intense and costly condition to treat. The total cost of care for HF continues to rise each year. HF accounted for approximately $30.7 billion in total costs in 2012. By 2030 total costs are estimated to reach $69.7 billion. Direct costs account for 68 % of total costs [15]. Heart failure costs represent 7–8 % of the total care costs for all cardiovascular diseases. Of the subsets of healthcare costs, hospital charges account for 62 % of the direct costs, with nursing home charges a distant second place at 8.6 % just ahead of total physician charges at 8.5 % (Fig. 2.2). These figures substantiate the importance of the hospital in the overall economic burden of HF. Hospitals bear both the brunt of the costs of care and the onus to provide more cost-efficient care to these patients.

Hospital Care

Most ADHF patients are treated in the inpatient environment. The emergency department (ED) is the point of entry for three out of every four ADHF patients, and 75–90 % of HF patients presenting to the ED are ultimately admitted to the hospital [16]. Since most HF patients are of Medicare age, facilities are reimbursed on a fixed inpatient payment under the current MS-DRG system effective since October 2008 and, therefore, must provide extremely efficient care in order to maintain financial viability. Today the average MS-DRG (291, 292, and 293) reimbursement $6,842 for the acute care facility, which often does not receive sufficient reimbursement to cover the costs of care for the ADHF patient. Under the former DRG payment system for a typical hospital, the financial breakeven point was roughly 5 days, but the average ADHF patient has a length of stay greater than 5 days, resulting in a fiscal loss for the hospital. A review of cost data in 2001 demonstrated an average loss of $2,104 per ADHF (any new data?) patient [17]. The new MS-DRG system was designed to more appropriately align financial compensation to severity and should offset some but not all of these losses.

In addition to the challenges of providing optimal efficiency in caring for the ADHF patient to avoid financial losses, CMS has placed further burdens on

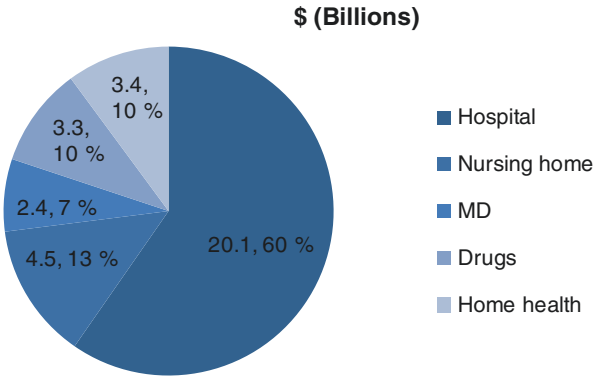

Fig. 2.2 Costs for heart failure in the United States (2012). Projected direct costs of total cardiovascular disease by type of cost (2010 $ in billions) (Mozaffarian D, et al. *Circulation*. 2015;131:e29–e322. American Heart Association)

facilities by targeting inappropriate 1-day length of stay admissions and readmissions within 30 days. Review of such admissions could result in the hospital potentially losing reimbursement for such admissions and thus further compounding an already fiscally austere situation. In light of the high readmission rates noted earlier, the hospital is vulnerable to even further losses as they could become fully financially responsible for the care of such patients. Facing such fiscal pressures in an already challenging overall economic environment, hospitals have been forced to reevaluate current practices and redesign care models for the ADHF patient.

The Observation Unit and Heart Failure

Over the last 10 years, emergency departments (ED) saw patient volume increasing substantially. In 2007, there were 117 million visits to the ED in the United States [18]. As the volume of ED visits continued to increase, admissions to acute care facilities increased, thus decreasing the access to inpatient beds. In an effort to improve access and reduce costs, hospitals have focused on efforts to further reduce length of stays and shift care from the inpatient to the outpatient arena.

In the 1990s, certain patients were often held in the ED for observation in an attempt to make a more clinically educated decision about the need for admission versus the safety of discharge after appropriate intensified treatment [19]. More formal chest pain centers (CPC) emerged and marked the initial attempts to evaluate low-risk chest pain patients for myocardial infarction in a short stay unit, often within the emergency department. This approach represented an operational mechanism to improve quality of care, enhance clinical outcomes, and reduce overall costs. The success of the CPC showed that quality of care was not compromised in this fiscally sound model. The CPC led the way for the development of a more formalized observation unit (OU) that could be expanded to treatment of other medical conditions, providing the same level of care in the outpatient setting as in the acute care setting.

As the OU evolved, the Centers for Medicare and Medicaid Services (CMS) initially targeted asthma, chest pain, and ADHF for efforts to reduce morbidity and mortality through the use of efficient evaluation and intense treatment in non-acute care settings. CMS defines observation care as a "well defined set of specific, clinically appropriate services, which include ongoing short-term treatment, assessment, and reassessment before a decision can be made regarding whether a patient will require further treatment as hospital inpatients or if they are able to be discharged from the hospital" [20]. OU services are less than 48 h and often less than 24 h. Under unusual circumstances, it may exceed 48 h.

In the typical ED evaluation of the ADHF patients, over 75 % of patients ended up being admitted to the acute hospital setting [21]. With intense and focused treatment, the OU affords the opportunity to reduce inpatient admissions. In a study of a hospitalist-run short stay unit, a heart failure diagnosis predicted stays longer than 72 h [22]. In this study, need for consultations and the lack of accessibility to diagnostic tests resulted in longer stays. OUs can accelerate accessibility to these services. Studies show that institution of evidence-based aggressive treatments in the

OU, 75 % of HF patients can be discharged home from the OU. Benefit also exists for those who require inpatient admission after OU treatment, as their overall hospital length of stay is shorter than for those admitted directly to the inpatient setting [23] (Fig. 2.3).

Use of OU days has increased substantially over the decade. Between 2003 and 2007, there was a 403 % increase in OU separately payable observation days. The number of OU days increased from 65,000 in 2003 to over 262,000 in 2007 [24]. In 2013, 18.6 % of 133 million ED visits were admitted to the OU [25]. Use of the OU is likely to continue to increase in the current healthcare environment (Fig. 2.4).

The high cost for patients with heart failure is attributed to high rates of hospital admissions and long lengths of stay for acute decompensation of this condition. The OU emerged as a viable strategy for putting into play efficient and aggressive diagnostic and therapeutic urgent services in an intensely monitored situation [26]. Addition of case management, disease management, and discharge planning activities has been shown to avoid subsequent hospitalizations.

Disease Management in Heart Failure

Disease management (DM) programs have targeted heart failure from their inception. Early DM programs focused on high-risk patients, predominantly those recently discharged from the hospital following decompensation in CHF. Programs

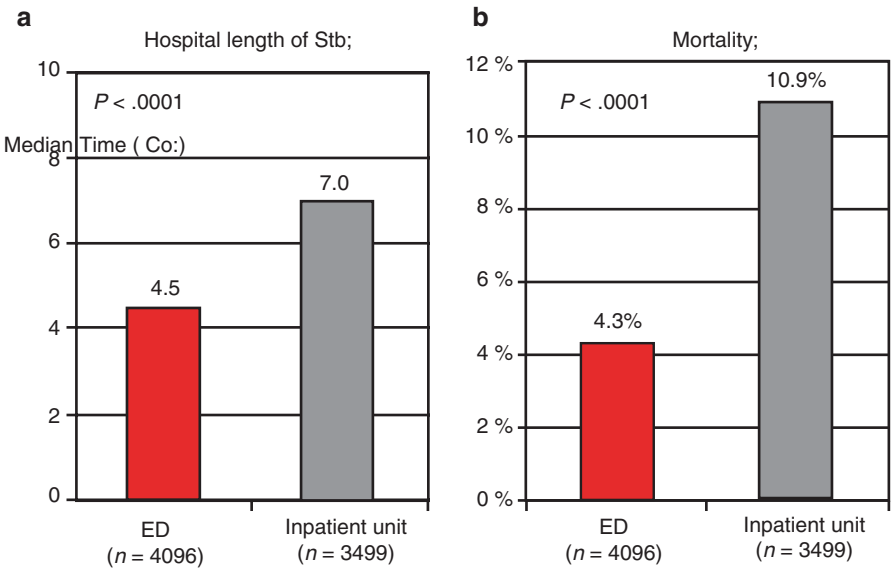

Fig. 2.3 Effect of site of initiation of therapy on LOS and mortality. Effect of site initiation of therapy on length of stay and mortality. ED, emergency department (From Emerman et al. [23])

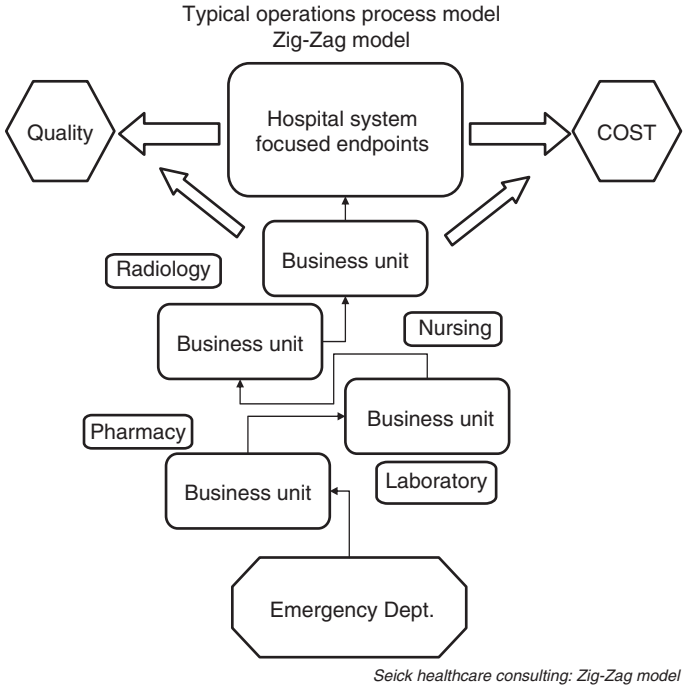

Fig. 2.4 Zigzag model of 2008 update (Sieck [57])

subsequently expanded to those HF patients who were at high risk but who had not yet been hospitalized. The processes and interventions were similar for both target groups.

Patients in the acute care facility, whether as inpatients or in the OU, attentive and thorough discharge planning is a critical piece of the successful DM program [27].

From the societal point of view, DM programs in heart failure benefit the patient with respect to clinical outcomes and quality of life and perhaps in individual costs of care. Early studies on HF DM programs showed mixed clinical outcome results. Some DM programs have shown reductions in hospitalization and mortality in short-term efforts in high-risk patients [28, 29]. Most recent studies have suggested cost-effectiveness may be demonstrated over the long term and in a broader-risk patient [30, 31]. A recent cost estimation model of an integrated care approach utilizing telemedicine monitoring showed a potential for 8 % total healthcare cost savings over a 3-year period [32]. Overall program costs are often higher in the DM group but the QALY (quality-adjusted life year) gained is beneficial. The cost savings in reduced hospitalizations are often offset or exceeded by the costs of the intervention [33]. Insurers benefit from lowered costs of readmission. Hospitals experience less revenue from readmissions, but they benefit on national quality measures by showing reduced readmissions. Those stakeholders responsible for the payment of the costs of the programs may or may not

financially benefit; only if they too are financially responsible for future hospitalizations are they likely to benefit.

DM provides focused and evidence-based treatment approaches to patients with HF. Medically, it is the most appropriate comprehensive management approach for this group and it shows improved outcomes. The healthcare system will have to evolve in its methods for paying for such program to put the burden for intervention costs on the stakeholders most likely to benefit from the outcomes.

Clinical Outcomes

The importance of the OU to the healthcare system is in the benefit on clinical and financial outcomes. The use of nationally recognized clinical guidelines and pathways for the treatment of ADHF is the first step toward optimizing HF care. The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) has created a set of quality performance indicators for HF. These Advanced Certification in Heart Failure (ACHF) inpatient indicators for 2016 include beta blocker therapy at discharge, post-discharge evaluation and follow-up appointment, transmission of transition report, and discussion and execution of advance directive. There are seven optional outpatient performance measures: beta blocker therapy, ACEI or ARB therapy for LV systolic dysfunction, aldosterone antagonist for LV dysfunction, NYHA classification, outpatient activity recommendations, and discussion/execution of advance directives [34].

Despite treatment advances in HF that include medications and device-based therapies, many HF patients do not receive treatment according to these guidelines [35]. The lack of adherence to guidelines may be related in part to a lack of knowledge, but more likely is the result of operational inefficiencies. Intense DM efforts to incorporate evidence-based treatments that focus on the accepted quality indicators can impact the ADHF patient. A study from the Veterans Affairs San Diego Healthcare System demonstrated significant improvement in nationally established performance measures for HF using a multidisciplinary, computerized care pathway [36]. The well-designed OU can provide the operational efficiencies necessary to put treatment guidelines into effect and thereby achieve optimal clinical outcomes.

Although OU management has been demonstrated to reduce morbidity and a trend toward reduced mortality, further studies are needed to assess the full impact of focused OU care – diagnosis, treatment, intensity of service, and staffing—on quality measures.

Cost-Effectiveness of the OU

The OU provides a location for the provision of intense medical therapy and services under close observation and frequent monitoring of response to such treatment. In the ADHERE data registry (a multicenter, observational database of

patients discharged from the hospital with a DRG diagnosis for HF), the time to initiation of administration of certain intravenous medicines specifically directed at acute HF was 1.1 h if the patient's treatment was initiated in the ED compared with 22 h if therapy was begun in an inpatient unit [37]. The OU protocols for both treatment and timely adjustments in treatment plans lead to more intense and timely initiation of therapy, which can have remarkable differences in clinical outcomes, as well as a dramatic impact on financial implications.

Treatment of ADHF in an OU has resulted in reduced 30-day readmissions and hospitalizations and decreased LOS if a subsequent hospitalization is required [38]. The Cleveland Clinic experience with OU as a venue for treatment of the ADHF patient also reported positive 90-day outcomes [39].

- Revisits were reduced by 44 %.
- ED observation discharges increased by 9 %.
- HF re-hospitalizations were reduced by 36 %.
- Observation re-hospitalizations were reduced by 39 %.

In another study, Peacock showed that institution of OU for HF showed a 56 % decrease in ED revisits, 64 % reduction in re-hospitalizations, and a slight trend in decreased mortality [40]. Limited studies on the direct cost-effectiveness of OU in ADHF treatment exist. In a study of cost-effectiveness of OU admission, a subset of low-risk ADHF patients admitted to OU demonstrated an acceptable societal marginal ratio when compared to discharge from the ED [41]. This benefit was related to the somewhat higher risk of readmission and early-after-discharge rate of death associated with ED discharge. Future cost-effectiveness studies are required to further delineate how cost-effective the OU is for ADHF.

Observation Services Reimbursement

In 2002, CMS developed a new coding and reimbursement rate specifically to cover OU services for chest pain, asthma, and heart failure. Ambulatory Patient Classification Code (APC) 0339 was designed to compensate for treating patients with these subsets of conditions aggressively on the front end versus admitting them to the acute care setting. In addition to the APC, hospitals could also bill for most diagnostic tests that were performed during the OU stay, if medically necessary. This marked a new direction in reimbursement.

Since the initiation of the OU status as venue for care, several iterations of coding and reimbursement rules have emerged and evolved. At the same time, concerns arose for use of observation status for inappropriate conditions, lengthy outpatient stays, potential inadequate care with early discharge of inpatients, unintended higher co-payments for patients, issues with the two-midnight rule, the impact on a patient's candidacy for subsequent SNF coverage, and possible improper payment for services leading to gaming the system.

In 2013, the Office of Inspector General (OIG) undertook an overall evaluation of the use and impact of the OU on Medicare patients to assess these concerns [42]. The OIG found that total hospital services for Medicare patients included 1.5 million OU stays, 1.4 long outpatient stays, and 1.1 million short inpatient stays. Most OU stays averaged one night. The use of these services was not consistent over all hospitals; so it appeared that at least some facilities could have been promoting more favorable financial reimbursements regarding OU versus inpatient level of care. From a Medicare perspective, usually a short inpatient stay is more costly than a short OU stay. The other important finding was that a significant portion of hospital stays did not qualify Medicare patients for subsequent SNF services, while in other circumstances, Medicare inappropriately paid $255 million for SNF services patients received but for which they did not qualify. This study emphasized the need for policy changes that were fair to Medicare patients, reduced inconsistencies across the country in how OU services were used, and equitable reimbursement reforms.

For 2016, the CMS OPPS Final Rule, CMS-1633-FC; CMS-1607-F2, added ten new APC s. A new code for comprehensive observation services (C-APC) was created. C-APC 8011 replaced APC 8009 with a national payment rate of $2,174.14, substantially higher than the prior extended assessment and management payments for OU care. However, a new status indicator, J2, was also created and the old J1 was deleted. This change effectively combines payments for what are considered "adjunctive" services into a single prospective payment for the total comprehensive service into C-APC 8011. This change introduces the concept of bundled payments for observation care. These new rules also capped the patient's out of pockets for observation status which was a point of contention in the prior coding scenarios. This shift to a bundled payment program is meant to promote more efficient and evidence-based protocol use in the OU.

OU services are reimbursed separately for facilities and for physician services. HCPCS observation codes (G0378, G0379, G0384, or G0463) are submitted on a UB-04 claim form by facilities. Professional observation evaluation and management services are billed as CPT codes. The requirements for coverage of OU services under C-APC 8011 are summarized in Table 2.1 [43].

For professional services the following rules apply. The physician supervising OU care can submit CPT 99218–99220 (depending on intensity of E&M service) for initial OU care. The physician must record that the member is to be in observation status, document the medical necessity for such, document the care plan, and perform regular assessment and initiate treatment. If the patient is designated to OU status and discharged from such on the same date, CPT 99234–99236 is used instead. If a patient remains in OU stays for more than two calendar days, then CPT 99224–99226 for subsequent observation care is used. OU discharge services require a minimum of 8-h stay but less than 24 h and code if 99217 is appropriate. If the patient is in a global surgical period, OU services cannot be billed.

From a Medicare perspective, OU stays are less costly than inpatient stays. Short inpatient stays result in a total cost to CMS of $5.9 billion versus $2.6 billion for observation stays. On a per-case basis, the savings are even more pronounced:

Table 2.1 Summary and requirements for the use of C-APC 8011

C-APC 8011
Claims contain eight or more units of services described by HCPCS code G0378 (observation services, per hour)
Claims contain services described by one of the following codes: HCPCS code G0379 (direct referral of patient for hospital observation care) on the same date of service as services described by HCPCS code G0378
CPT code 99284 (emergency department visit for the evaluation and management of a patient (Level 4))
CPT code 99285 (emergency department visit for the evaluation and management of a patient (Level 5)) or HCPCS code G0384 (type B emergency department visit (level 5))
CPT code 99291 (critical care, evaluation, and management of the critically ill or critically injured patient; first 30–74 min); or HCPCS code G0463 (hospital outpatient clinic visit for assessment and management of a patient) provided on the same date of service or 1 day before the date of service for services described by HCPCS code G0378
Claims do not contain include J1 service

$5,142 per short inpatient stay case versus $1,741 per observation case. From the patient perspective, co-payments for observation services are generally lower as well. The observation co-pay is less than inpatient 94 % of the time [44]. The 20 % OU copayment is usually $452 and the 2015 Inpatient co-pay was $1,260. In a 2014 analysis, 51 % of patients had to cover self-administered drug costs for an average of $528. Even considering some of the additional costs to patients, the overall financial burden is less in observation.

In order to be more transparent about the implications on an OU stay on a Medicare patient's financial responsibilities, the NOTICE act was created [45]. Effective August 6, 2016, if it is determined that a patient will be in observation for more than 24 h, the hospital must notify the patient orally and in writing of the potential consequences within 36 h. They must be informed that they are an outpatient stay and not an inpatient admission and the reasons for such. The patient must also be informed of any potential consequences of an observation stay, such as financial responsibilities (copayments, coinsurance, deductibles, etc.), services in the stay that are not covered by Medicare, and impact on possible future SMF admissions.

The data to date suggest that using the OU as a venue of care for selected patients can improve hospital efficiency, reduce inappropriate short inpatient admissions, and reduce overall costs to the system. Historically, implementation of OU has been increasing, and the model appears embedded in the evolving healthcare system. However, future changes are likely to come. While many hospitals provide observation "services" without a specific OU, it is estimated that only one-third of hospital facilities are currently using a defined OU [46]. An analysis by Baugh et al. in 2012, estimated that on a national level, cost savings from utilizing OU services would approach $3.1 billion annually [47]. Average savings per patient were estimated at $1,572. Annual savings for a hospital could range up to $4.6 million. The OU represents a viable alternative venue for appropriately selected patients and one that has a financially favorable impact on the healthcare system.

Consolidated vs. Virtual Design

Reimbursement is likely to continue to change over time, and the design of the OU with respect to the number of beds and physical layout will be impacted by these changes. The Centers for Medicare and Medicaid Services (CMS) is now targeting all diagnoses that meet medical necessity for observation services in an effort to increase quality, reduce cost, and reduce the number of inappropriate admissions. Consolidated units by design are concentrated resources in a common area designed to meet these strategic objectives. Virtual units are house wide, lacking concentric resources, and proving difficult to follow the stringent policies and procedures released in the latest Federal Registry for Observation Services. The optimal design of the OU is one that best aligns evidence-based treatment approaches with quality clinical outcomes. It is likely that there will be a continuum along which development of an OU progresses that depends on the stage of development, the average "size" of the anticipated OU population, resource investment, and total impact on the operation of the facility. However, the core of design of the OU must be optimal clinical management and provision of the "right care at the right time."

Emerging Trends

The quest for attaining quality in healthcare at reasonable costs in the United States continues to be an elusive goal. Gaps in access to healthcare, burgeoning costs, and lack of coverage for significant portions of the population plague a US healthcare system that does not claim the status of best in the world. Indeed, many Western countries have similar or better healthcare services delivered at markedly reduced costs. The US system remains predominantly fragmented with lack of true accountability to most of its stakeholders. The Affordable Care Act had a rooted mission to improve quality of care and thereby reduce overall costs. In order to achieve this challenging mission, the system must objectively define success and develop reliable metrics that reflect the status toward the ultimate goal. Health outcomes are the holy grail to determine whether patients and payers are getting the best value for their investment [48].

Despite the focus of the healthcare reform efforts, costs of healthcare continue to increase at rates above the consumer price index (CPI) [49]. The most formidable factor in today's healthcare arena involves pushback from payers that are demanding cost-efficient quality care. Payers will no longer be willing to simply reimburse for absolute units of care, even if such care is deemed medically necessary. Payers will expect value for their expenditures. Charges for care must be accompanied by measures of quality. The Centers for Medicare and Medicaid Services (CMS) is moving forward in this regard on several fronts. CMS is edging toward a customer value proposition and putting into effect its long-standing effort to link Medicare's payment system to a value-based system to improve healthcare quality. Value-based purchasing (VBP) represents the most aggressive movement for transforming the current payment system to one that rewards providers for delivering high-quality

and efficient care in an integrated delivery system. The 2016 VBP formula has multiple elements [50]. The weighted elements, patient experience of care, clinical processes of care efficiency, and outcomes, are combined to a total performance value.

Patient experience of care (25 %) + clinical processes of care (10 %) + efficiency (25 %) + outcomes (40 %) = *VBP (composite payment)*

While the VBP method may help to alter the way healthcare is provided and result in improved outcomes, additional aggressive payment models have begun to launch. In 2015 CMS began publicity reporting Medicare spending per beneficiary. The "Medicare hospital spending by claim" includes each hospital's average spending levels during a Medicare spending per beneficiary (MSPB) episode for a given period of performance. Such cost-related transparency reporting is anticipated to enhance market-driven forces that will ultimately lead to price competition that can later be tied to quality performance. The introduction of the new payment models clearly represents a continued aggressive movement in provider reimbursement in the future.

Another change is related to further bundling strategies. Bundled payments based on episodes of care will launch in April 2016. Episodes can be time based, disease based, or treatment based. Medicare has a history of traditional or fee-for-service payment models except in its managed care capitated model. Starting in 2016, HHS has set explicit goals for alternative payment models focusing on value-based payments. The innovative goal seeks to tie 30 % of traditional, or fee-for-service, Medicare payments to quality or value through alternative payment models, such as Accountable Care Organizations (ACOs) or bundled payment arrangements by the end of 2016, and 50 % of payments to these models by the end of 2018 [51]. HHS also set a goal of tying 85 % of all traditional Medicare payments to quality or value by 2016 and 90 % by 2018 through programs such as the Hospital Value-Based Purchasing and the Hospital Readmissions Reduction Programs. This effort is a radical departure from the historical approaches of Medicare [52].

Traditional insurance models have made the insurance entity bear the majority of financial risk for healthcare services. Such a model tends to reward volume and quantity over time. Emergence of the managed care model started to shift some of the burden to providers and patients. CMS is now instituting the mandatory episodes of care payment model which further shifts responsibility to include providers of care following hospital discharge through 90 days. Stakeholders at risk include the anchor hospital, physicians, and post-acute care facilities. The initial episodes of care will focus on high-profile DRGs with the anticipated goal of improving efficient and quality care. The first DRG will focus on hip and knee replacement surgeries which are the most common surgeries in the Medicare population. The Comprehensive Care for Joint Replacement (CCJR) model hopes to encourage hospitals, physicians, and post-acute care providers to collaborate and coordinate care. This model will focus on risk responsibility on the original hospital where the surgery is performed and the anchor hospital. The acute care facility will be the coordinating center to work in conjunction with post-op providers to insure quality clinical outcomes and timely care. Anticipated savings are $153 million over 5 years. While this new model is in its infancy, if such savings materialize, CMS will

likely expand to other high-profile diagnosis. And heart failure represents a logical future target [53].

CMS is also focusing efforts on reducing fraud and abuse in the healthcare system. According to CMS officials, new rules would give federal health officials more power to identify fraud early and help them reduce an estimated $55 billion in improper payments made annually through Medicare and Medicaid [54]. It is estimated that over $ 60 billion is lost annually by Medicare from fraud. The Federal Bureau of Investigation estimates that 3–10 % of the public and private healthcare dollar is lost to fraud, amounting to $75–250 billion annually [55]. Some estimates go as high as $100 billion. Current recoupments most likely only represent the surface of total fraud and abuse, and CMS will continue further aggressive efforts to stem such losses.

The hospital setting is in the midst of more intense scrutiny. In 2009, the federal RAC program (Recovery Audit Contractors) was created to recover monies related to inappropriate admissions. The third-party contractors review 1-day hospitalizations that are deemed unnecessary as services could have safely been provided in the outpatient setting [19]. Unfavorable reviews can result in significant loss of monies for hospitals. Observation services targets 24-h length of stay (LOS). 1-day stay = 24 h. What's the difference? The main difference is the ability to provide safe, cost-effective care in the most resource appropriate setting. With the LOS remaining constant in this equation, medical necessity is the deciding factor. If a patient truly meets inpatient criteria, then the inpatient setting is the appropriate environment for care. Any issues with this decision can be alleviated through proper documentation. One-day stays are not the only objective of the RAC program. Excessive readmission and several MS-DRGs known to have historical high error rates are also targets. This is best demonstrated in the Program for Evaluating Payment Patterns Electronic Report (PEPPER) developed by the Texas Medical Foundation which provides hospital-specific Medicare data statistics for discharges vulnerable to improper payments.

Readmission penalties are imposed by Medicare. Readmission of HF patients is costly and somewhat preventable. In 2010, the Patient Protection and Affordable Care Act introduced incentives to decrease readmissions. For fiscal year (FY) 2015, the Centers for Medicare and Medicaid Services (CMS) estimated that total readmissions penalties will be approximately $428 M, up from $227 M in FY 2014. For FY 2015, 2,638 facilities are being penalized. The highest penalty for a single facility is almost $3.3 M [56].

These new emerging payment models make it critical for acute care facilities to enhance relationships and data-capturing capabilities, improve coding accuracy, apply risk stratification to care pathways, and focus on clinical outcomes in order to remain financially sound. The acute care facility can survive in this ever-changing environment, but only if particular attentions to efficient processes and sound fiscal operation is maintained. For OU success in ADHF, this means creating and adhering to evidence-based guidelines, prompt and diligent physician oversight of care on an hourly basis, pristine medical record documentation, and redesign of the acute care model.

Y-Model

Not all ADHF patients are appropriate for observation status treatment, and inpatient admission may be the most appropriate. But compared to a fully staffed protocol-driven OU, the average inpatient hospital stay often utilizes outdated methods of care that are more geared toward partial workday hours of operation and less adherence to care pathway or programs designed to streamline patient evaluation and management for more routine medical conditions. Variances in care patterns also add to inefficiencies.

For the segment of the ADHF population that requires acute hospitalization, achieving efficiencies in the hospital flow is critical to resource and cost containment. The process of care in a hospital setting can be analogous to a business model in an industrial setting. Most hospital patients follow a zigzag approach when receiving care/services from the point of entry to discharge (Fig. 2.5). A patient's "flow" through the hospital care system is often not linear. The patient is shuttled through various diagnostic or therapeutic care units (e.g., radiology, laboratory, imaging department, pharmacy, etc.) in a disconnected manner. Each care unit functions more as an independent unit than as an integrated part of a cohesive strategy. Transfer between care units is not always a smooth and seamless interface. Each unit acts as a single entity from the hospital's standpoint, but should not from the patient's perspective. It is incumbent upon the physician to collate the output of the care units' results. Although the final outcome eventually is appropriate care, the zigzag process is generally an inefficient, untimely, and resource wasteful process.

Several methods have been used in process improvement approaches to enhance inpatient efficiencies and quality of care. Care maps, care pathways, critical pathways, and integrated pathways are detailed medically appropriate paths that outline daily steps to diagnostic and therapeutic interventions for a particular medical condition that are designed to organized care into an efficient process toward resolution. However, financial concerns were usually not a direct consideration in these pathways. Application of a business design model that merges quality of care and optimal financing in the process of care will insure long-term facility viability.

The Y-Model approach (Sieck Health Care Consulting) affords such a blueprint for this merger [57]. The Y-Model focuses on the desired endpoints of quality and costs. In the business environment, the key to delivering a quality end product at the maximal contribution margin is to streamline manufacturing process and reduce variances in production steps. This translates in medicine by requiring adherence to evidence-based evaluations and treatments performed expeditiously and efficiently through a streamlined process. The Y-Model involves placing proper sequencing of services "up front" at the point of entry into the medical care track. Seamless integration between operating care units is the essential core of the Y-Model (Fig. 2.6). This concept begins at the point of entry and ends at discharge and marries a clinical and financial strategy that meets quality indicators while producing desirable profit margins. Beginning in the ED, this concept emphasizes an efficient, rapid assessment and action centered on a seamless integration of ancillary services such as the

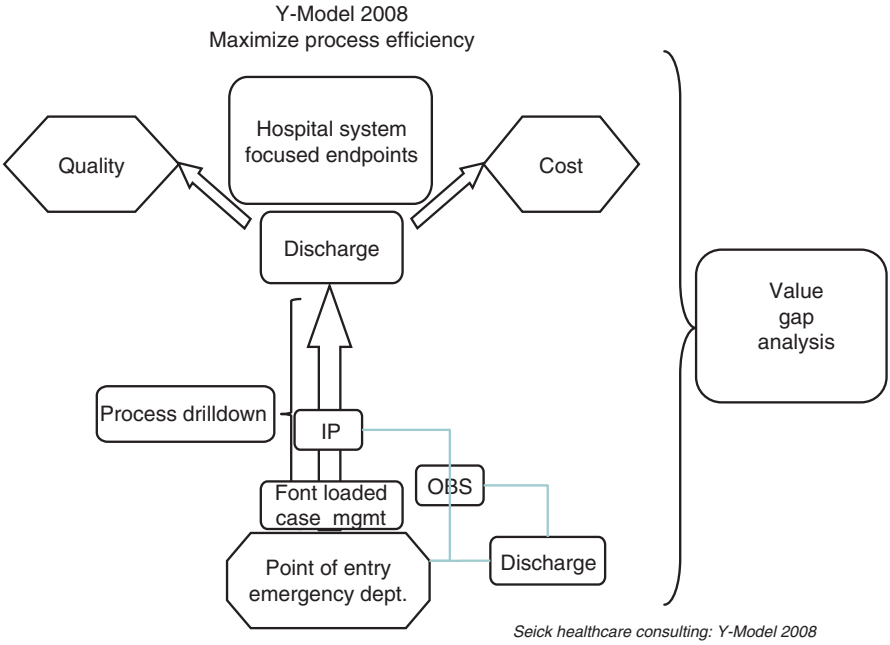

Fig. 2.5 Y-Model using risk stratification and ABC approach

laboratory, diagnostic imaging, and skilled nursing while understanding the economic impacts on decisions made as the patient is directed through the system.

This model can be similarly applied to an ADHF patient routing through the healthcare delivery setting. Patients receive services within different "care units" within the acute hospital setting. These care units are analogous to the industrial setting's business units. By understanding how each care unit's operational strategies affect each subsequent care unit from point of entry to discharge, a seamless transfer of patient care in both outpatient and inpatient settings can optimize quality improvement and positive economic value. Without each care unit providing vital information to others in this holistic approach, moving patients efficiently through the system is challenged.

Patients who require an inpatient admission are properly admitted, and those who could be effectively treated in the outpatient setting (OU) are treated and properly released. The placement of more critical patients in the inpatient acute care setting impacts the case mix index positively because the patients are simply sicker and require more resources.

Creating a care delivery system for the ADHF patient that is based on the Y-Model can positively impact the contribution margins when ADHF patients are carefully identified, risk stratified, and given appropriate early treatment during the interaction. This model emphasizes a multidisciplinary accountability model to align the "care units" that affect an ADHF patient's progress through the current system. The emphasis is on front-end compliance that sets up the pathway the

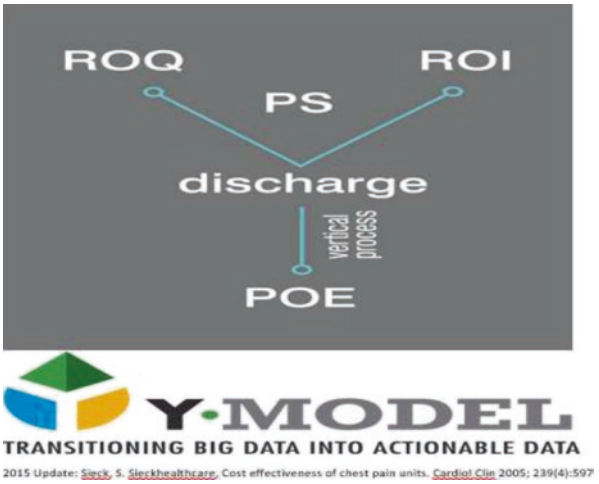

Fig. 2.6 Transformation of data, changing bedside care

patient will follow. A patient is not "arbitrarily" admitted to an inpatient bed, treated, and then discharged. A decision is made up front on the most ideal care venue for the risk-stratified patient to be admitted to and undergo tailored treatment. It also initiates the financial pathway with identified markers throughout the patient interaction that allow facilities to know the ramifications of making random decisions versus following a protocol designed to emphasize quality while optimizing economic results. The Y-Model places an emphasis on process improvement while targeting the end points of quality and contribution margin.

Instituting the Y-Model in other cardiac conditions has shown positive impact of quality parameters, reduced costs, and improved clinical outcomes. One such example is in treatment of acute coronary syndrome (ACS) [58]. Once a patient was defined as ACS in the ED, stratification was performed and appropriate therapy begun in the ED rather than waiting until ICU bed placement. Treatment was individualized and there was no gap in care services between the ED and ICU. This patient-centric analytic process resulted in identifying care gaps for optimizing outcomes, quality, cost, and patient satisfaction.

This variation of the model was recently used successfully at an 850+ bed in a medical center in Florida for an initiative on ADHF. Prior to the initiative, the hospital had a "zigzag" model of care. Patients entered through the ED, were admitted to the acute care bed, and labs completed and treatment initiated several hours into the process. With initiation of the Y-Model, a general consensus of appropriate clinical and cost-efficient processes began at the point of entry and continued through discharge. The new design resulted in improvements in turnaround time for therapy, reduced LOS, enhanced patient placement in the most appropriate bed venue (e.g., CCU, telemetry, or clinical decision unit), and improved patient satisfaction.

A well-designed process flow for inpatient ADHF care should result in cost reductions similar to that seen in the OU. The streamlined process for expeditious evaluation paralleled with initiation of monitoring and treatment from the initial

point of entry integrates a financial strategy that meets both quality metrics and evidence-based case management protocols. Beginning in the ED, this approach focuses on immediate evaluation and initiation of actions centered on seamless integration of ancillary services such as imaging studies, laboratory assessments, skilled nursing, and near continuous provider oversight and therapeutic/diagnostic adjustments.

Adapting the efficient process flow of the OU to the inpatient setting should result in overall cost efficiencies while maintaining or improving quality. The OU may represent the initial redesign in acute healthcare delivery that will ultimately transform the entire system into a more efficient process. Using this redesign with the Y-Model application overlay could result in potential significant cost savings and improved quality of care.

Conclusion

The US healthcare system is in the midst of seismic shifts. Continuing pressures to increase access to care, provide coverage to a greater portion of the population, enhance quality of care, and reduce costs will result in a healthcare delivery model that is vastly more efficient than the model seen at the end of the last century. ADHF is a condition that accounts for a significant fraction of the total costs of care for cardiovascular diseases. As such, changes in the delivery model surrounding ADHF will continue to rapidly evolve over the next decade. Payers will increasingly shift to value-based reimbursement and global episode of care reimbursement patterns. Already challenged hospital systems will need to address these financial and logistical forces if they are to survive. Financial aspects of care will impact changes in the model of care, but economics cannot overshadow clinical outcomes in overall importance. These two parameters are equally important to the successful implementation of a redesigned care process for the ADHF patient population.

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Regulatory Requirements in Acute Heart Failure

3

Nancy M. Albert

Regulatory requirements of acute heart failure services affect two areas supporting care delivery: coverage determination and performance management, both of which could affect accreditation of physicians, healthcare organizations, and healthcare plans and hospital income. The former affects reimbursement of the costs of care by third-party payors. The latter represents clinical care quality and healthcare provider conformity to national guideline-recommended acute heart failure care assessment and management services that indirectly affect accountable care organization metrics for risk-standardized acute admission rates and the ratio of observed admissions to expected admissions for heart failure. For both coverage determination and performance management regulations and indicators, some are globally applied across the environment of care settings (emergency care, short stay care, hospital care, or ambulatory care), and others are directed toward specific healthcare providers and/or care settings. The purpose of this chapter is to describe regulatory requirements for acute heart failure, many of which were designed to promote optimal use of (and minimize gaps in) evidence-based heart failure care and regulate cost of care.

Acute heart failure care regulatory requirements have developed over time for two primary reasons. First, after hospitalization for acute heart failure, patients remain at high risk for morbidity and mortality. When all-cause 30-day risk-standardized rehospitalization rates were assessed in patients discharged with decompensated heart failure, the trend from mid-2006 through mid-2009 was unchanged, at a median of 24.5 % [1]. In a study of patients using Medicare fee-for-service benefits that were hospitalized for decompensated heart failure, although mortality was on the decline over a 4- and 13-year period, respectively, 30-day rehospitalization rose over time,

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even after adjustments were made for confounding factors [2, 3]. The Patient Portability Affordable Care Act added a section to the Social Security Act that established the Hospital Readmissions Reduction Program. The program was meant to accentuate the modest decline in all-cause 30-day hospitalization rates following heart failure hospitalization, from 25.1 % in 2009 to 23.5 % in 2013, [4]. Among Centers for Medicare and Medicaid recipients, median risk-standardized unplanned readmission rates declined from 23.4 % in July 2010 to 21.9 % in June 2013 [5]. However, median risk-standardized 30-day mortality rates increased from July 2010 to June 2013 (11.8–12.0 % [5]) as have rates of 30-day emergency department (0.7 % increase) and observation unit stays (0.5 % increase) posthospitalization, offsetting reductions in cost achieved with the reduction in hospitalization rates [5]. Even with the decline in the death rate from cardiovascular diseases in recent years, one in nine deaths mentioned heart failure, and for patients who survive the acute decompensated event, 54 % of men and 40 % of women will die within 5 years [6].

Despite compelling clinical trial evidence of lower mortality when health care providers use evidence-based medications, cardiac devices and self-care strategies [7] and national evidence-based guideline-recommended management strategies [8], underutilization of evidence-based care were routinely reported. Specific gaps and disparities included core heart failure drug therapy prescriptions [9–11], cardiac device utilization [12], patient education [13, 14], self-care management behaviors [15], and collaborative care [16]. Further, lack of uniformity in heart failure care was found based on hospital size, hospital setting, and patient characteristics (including age, ethnicity, gender, and financial status) [17–21]. Attention to systems, structure, and process components of healthcare delivery and documentation during the acute hospital episode may overcome current barriers to delivery of evidence-based, individualized heart failure care. In addition, early collaborative transition care that involved a multidisciplinary team facilitated evidence-based guideline-recommended care and reduced early rehospitalization [22], and in another report, interdisciplinary communication among healthcare providers reduced hospitalization rates [23]. Regulations in acute heart failure that emerged in recent years were designed to create incentives to improve care quality and value and decrease costs of care.

Coverage Determination Regulations in Acute Heart Failure

Coverage regulations for acute heart failure are broad, as they involve Medicare patients participating in an accountable care organization and patients whose healthcare coverage involves the Centers for Medicare and Medicaid Services fee-for-service payment.

Accountable Care Organizations (*ACO*) An ACO involves a group of providers and suppliers of services who work together to deliver high-quality care for Medicare beneficiaries. To be successful, ACOs must deliver evidence-based, coordinated care and promote a patient-centric focus that ensures that multiple providers work

Table 3.1 Accountable Care Organization quality metrics that relate to acute heart failure care

Metric number and name	NQF #	Data collection method	Group overseeing the metric
ACO-8; risk-standardized all condition readmission	1789 (adapted)	Claims data	CMS
ACO-10; ambulatory sensitive conditions admission: heart failure	0277	Claims data	AHRQ
ACO-37; all-cause unplanned admissions for patients with heart failure	N/A	Claims data	CMS
ACO-38; all-cause unplanned admissions for patients with multiple chronic conditions	N/A	Claims data	CMS
ACO-31 (HF-6); heart failure: beta-blocker therapy for left ventricular systolic dysfunction	0083	GPRO WI	AMA/PCPI/ACC/AHA
ACO-33 (CAD-7); coronary artery disease: angiotensin converting enzyme inhibitor or angiotensin receptor blocker therapy – diabetes or left ventricular systolic dysfunction (left ventricular ejection fraction < 40 %)	0066	GPRO WI	AMA/PCPI/ACC/AHA

ACO Accountable Care Organization, *AHRQ* Agency for Healthcare Research and Quality, *AMA/PCPI/ACC/AHA* American Medical Association/Physician Consortium for Patient Improvement/American College of Cardiology/American Heart Association, *CAD* coronary artery disease, *CMS* Centers for Medicare and Medicaid Services, *GPRO WI* Group Practice Reporting Option Web Interface, *HF* heart failure, *N/A* not applicable

as a team. In November 2014, the Centers for Medicare and Medicaid Services published the 2015 Medicare Physician Fee Schedule Final Rule. The rule provided a revision of 33 quality measures that applied to the Shared Savings ACO program. There are four domains of quality measures: patient/caregiver experience, care coordination/patient safety, at-risk population (with seven quality measures, two of which specifically relate to patients with heart failure), and preventive care. Although metrics cover the continuum of care, there are multiple metrics that are specific to or apply to an episode of acute decompensated heart failure (Table 3.1) [24–27].

General Medicare Coverage of Heart Failure-Related Services In September 2010, Medicare published the revised national coverage determinations, and in December 2010, and thereafter new programs and program revisions became effective (Table 3.2) [28–30]. Of note, although implantable cardiac hemodynamic monitoring for heart failure has not become an approved service as of yet, cardiac rehabilitation, transitional care visit (1 claim in 30 days), and other heart failure services that apply post hospitalization were approved (with conditions) in the last

Table 3.2 Centers for Medicare and Medicaid national coverage determinations

Category and factor	Details of coverage	Date implemented
Medication: nesiritide	Must be inpatient and have a claim for acutely decompensated HF, not chronic HF and another cause of hospitalization Short-term intravenous treatment in patients with dyspnea at rest or with minimal activity	03/22/2006
Cardiac rehabilitation	Stable, chronic HF (LVEF of ≤35 % and NYHF FC II–IV symptoms despite being on optimal HF therapy for at least 6 weeks) Stable also refers to no recent (≤6 weeks) or planned (≤6 months) major CV hospitalizations or procedures	02/18/214
Cardiac devices: implantable cardioverter-defibrillator placement	Patient populations: (a) documented episode of cardiac arrest due to VF, not due to a transient or reversible cause; (b) documented sustained VT, either spontaneous or induced by an EP study, not associated with an acute MI and not due to a transient or reversible cause; (c) documented familial/inherited conditions with a high risk of life-threatening VT, such as hypertrophic cardiomyopathy; (d) prior MI with left ventricular ejection fraction ≤35 % and inducible, sustained VT or VF at EP study within 40 days of MI and did not have NYHA FC IV HF, cardiogenic shock, or symptomatic hypotension while in a stable rhythm; had CAB surgery or PCI within past 3 months; had an enzyme-positive MI within the past 40 days; had clinical symptoms or findings that would prompt candidacy for coronary revascularization or any noncardiac disease associated with <1-year survival; (e) ischemic dilated cardiomyopathy and documented prior MI, NYHA FC II and III HF, and LVEF ≤35 %; (f) nonischemic dilated cardiomyopathy >9 months, NYHA FC II and III HF and LVEF ≤35 %; (g) meet coverage requirements for CRT device and have NYHA FC IV HF Be enrolled in either a Food and Drug Administration approved Category B investigational device exemption clinical trial, a trial under the CMS Clinical Trial Policy, or a qualifying data collection system including approved clinical trials and registries Must be able to give informed consent	Version 3: 01/27/2005

Table 3.2 (continued)

Category and factor	Details of coverage	Date implemented
Wearable Automatic external Defibrillator use	Must meet the following conditions: Have a documented episode of VF or a sustained (lasting ≥ 30 s) ventricular tachyarrhythmia Dysrhythmias (listed above) may be either spontaneous or induced during an EP study but may not be due to a transient or reversible cause and not occur during the first 48 h of an acute MI May be from a familial or inherited condition with a high risk of life-threatening ventricular tachyarrhythmias such as long QT syndrome or hypertrophic cardiomyopathy Either documented prior MI or dilated cardiomyopathy and a measured LVEF ≤ 35%	January 2011
Implantable cardioverter-defibrillator interrogation (in-person and remote)	Electronic analysis (interrogation, evaluation of pulse generator status, evaluation of programmable parameters at rest/during activity, interpretation of ECG recordings at rest/exercise, and derived data elements, analysis of event markers, and device response) Reprogramming Monitoring period: in-person, 30 days; remote, 90 days Professional and technical component codes	
Wearable cardioverter-defibrillator interrogation	Electronic analysis (interrogation, evaluation of pulse generator status, evaluation of programmable parameters at rest and during activity, interpretation of ECG recordings, analysis of event markers and device response) Same as above with reprogramming Monitoring period: in-person, 30 days or 90 days Professional and technical component codes	

(continued)

Table 3.2 (continued)

Category and factor	Details of coverage	Date implemented
Cardiac output monitoring by electrical impedance	Patient populations: (a) differentiation of cardiogenic from pulmonary causes of acute dyspnea when medical history, physical examination, and standard assessment tools provide insufficient information, and the treating physician has determined that TEB hemodynamic data are necessary for appropriate management of the patient; (b) optimization of A/V interval for patients with A/V sequential cardiac pacemakers when medical history, physical examination, and standard assessment tools provide insufficient information; (c) monitoring of continuous inotropic therapy for patients with terminal congestive HF at home or for patients waiting at home for a heart transplant; (d) evaluation for acute or chronic cardiac rejection post-heart transplant as an alternative to myocardial biopsy; and (e) optimization of fluid management in patients with congestive HF when medical history, physical examination, and standard assessment tools provide insufficient information, and the treating physician has determined that TEB hemodynamic data are necessary for appropriate management Frequency: daily	Version 3: 01/06/2007
Implantable Cardiovascular monitor – in-person or remote interrogation	Interrogation device evaluation for analysis of one or more recorder physiologic CV data element from external and internal sensors Monitoring period: 30 days Professional and technical component codes	
Transtelephonic ECG transmission	Indications: (a) detect, characterize, and document symptomatic transient dysrhythmias; (b) initiate, revise, or discontinue dysrhythmic drug therapy; or (c) early (24-h coverage must be provided) monitoring of patients discharged after MI Requirements: (a) capable of transmitting ECG Leads I, II, or III; and (b) tracing must be sufficiently comparable to a conventional ECG	03/01/1980
External counterpulsation	Not covered for AHF or post-discharge after AHF episode; only disabling angina	Version 2: 04/03/2006
Telehealth monitoring	Limited set of telehealth-delivered services are covered if delivered by live video office visits and consultations that are provided using an interactive two-way telecommunications system (with real-time audio and video) by a doctor or certain other healthcare provider who is not at your location but is in specific, approved locations Store-and-forward-delivered services are not covered except in demonstration projects Home telemonitoring services are not covered	December 2015

Table 3.2 (continued)

Category and factor	Details of coverage	Date implemented
Transitional care management services	The services are required during the beneficiary's transition to the community setting following particular kinds of discharges, and the healthcare professional (a) accepts care of the beneficiary post-discharge from the facility setting without a gap and (b) takes responsibility for the beneficiary's care The patient receiving services has medical and/or psychosocial problems that require moderate or high complexity medical decision-making The transitional care period is 30 days beginning on the date the patient is discharged from the inpatient hospital setting and continues for the next 29 days Must complete a face-to-face visit for coverage; only one eligible visit claim is covered during the 30-day period If patient is readmitted to the hospital within 30 days, may still bill for previous service	January 1, 2013
Thoracic electrical impedance monitoring	Cardiac output monitoring by thoracic electrical bioimpedance is covered for six indications: noninvasive diagnosis or monitoring of hemodynamics if suspected or known CV disease, differentiation of cardiogenic from pulmonary causes of dyspnea, optimization of cardiac pacemaker refractory periods (i.e., A/V interval), assess the need for inotropic therapy, early identification of rejection post cardiac transplantation, need for fluid management (excluding patients on dialysis or with liver cirrhosis and management of drug-resistant hypertension)	January 2003
Implantable cardiac hemodynamic monitoring for heart failure	Outpatient care: has not been proven to be medically effective and is therefore considered investigational Currently, there are no specific billing codes for use	August 20, 2015

AHF acute heart failure, *A/V*, atrioventricular, *CAB* coronary artery bypass, *CMS* Centers for Medicare and Medicaid Services, *CRT* cardiac resynchronization therapy, *CV*, cardiovascular *ECG* electrocardiographic, *EP* electrophysiology, HF, heart failure, *VLEF* left ventricular ejection fraction *MI* myocardial infarction, *NYHA FC* New York Heart Association functional class, *PCI* percutaneous coronary interventions, *TEB* thoracic electrical bioimpedance, *VF* ventricular fibrillation, *VT* ventricular tachyarrhythmia

few years. Since cardiac rehabilitation programs provide medical evaluation, prescribed exercise, cardiac risk factor modification, diet education, and counseling in psychosocial, lipid, and stress management to restore active and productive lives, every patient who meets medical history qualifications should have post-discharge orders and be strongly encouraged to attend. In a Cochrane review of exercise program uptake and patient adherence, three programs developed to increase uptake of cardiac rehabilitation were effective, and two of seven programs to increase patient adherence to cardiac rehabilitation were effective [31].

Observation Unit Regulations in Acute Heart Failure

Observation care includes ongoing short-term assessment, treatment, and reassessment in order to make a decision about whether a patient will require a hospital admission or if discharge and outpatient care are feasible [32]. Regulations for observation services changed drastically after the "two-midnight" rule became effective, since the rule changed the definition of an appropriate inpatient admission under Medicare Part A [33]. Payment rates for inpatient and outpatient stays differ; inpatient stays are based on the discharge diagnosis, procedures completed, and severity of illness and require a minimum stay of two midnights. In contrast, outpatient services under Medicare Part B are a hybrid of prospective payment and a fee schedule. Observation status is often used for patients with acute heart failure who present for emergency care and who then require a significant period of monitoring or treatment before a decision concerning admission or resolution of dyspnea and other acute symptoms can be made. Generally, observation services should not exceed two calendar dates (48 h), and the majority of patients should have a decision as to whether hospital admission is needed in less than 24 h, based on the clock time documented in the medical record that coincides with the time the physician creates a written order for observation services. To receive reimbursement for observation services by Medicare, a minimum of 8 h of service is required and if over 24 h are used, Medicare will not pay separately for the excess hours used, with all costs included in a composite payment as discussed below.

Regulations specific to observation services of patients with acute heart failure include physician billing and hospital billing. Physician billing is linked to service type for initial services rendered when placing a patient in observation status and observation care following initiation of observation services. Medicare has specific documentation requirements for billing observation care services and admission to hospital service (inpatient status) following observation care. Table 3.3 provides the CPT codes used specifically for physician payment of observation services, based on the January 2010, Centers for Medicare & Medicaid Services revised consultation services payment policy for observation care, and documentation requirements [34].

Observation service coding also involves criteria hospitals must meet to receive Medicare payment, separate from physician payment. Coding for observation services is part of the Outpatient Prospective Payment System and encompasses an ambulatory payment classification (APC) composite code, labeled "extended assessment and management." This Medicare hospital outpatient *composite services* code is used in conjunction with an appropriate Type A emergency visit or critical care Healthcare Common Procedure Coding System (HCPCS) code or a G-code for direct referral to observation or from a clinic visit. Additionally, there are 16 observation, injection, and infusion services appropriate for general supervision, labeled "nonsurgical extended duration therapeutic services" that can be used. Criteria for billing include that a physician must place an order for observation status, and documentation must include admission notes, progress notes, and discharge instruction notes with time and signature. Finally, documentation must include that the healthcare provider used risk stratification criteria to determine that observation care would be beneficial [35].

Table 3.3 Medicare national coverage for medical management of heart failure in observation status

Time period	Rules	CPT codes
Following initiation of observation services	Physician coding reflects the amount of time the patient receives observation care on the same calendar day as the initial observation care If <8 h, a discharge service CPT code is not reported For all three codes, three key components are necessary: Detailed or comprehensive history Detailed or comprehensive examination Problems requiring observation unit care and medical decision-making that is straightforward or of low complexity/severity, ~30 min at bedside (code 99218); moderate complexity/severity, ~50 min at bedside (99219); or high complexity/high severity, ~70 min at bedside (99220)	99218 99219 99220
	When a patient is discharged on a different calendar day, the codes above are used to designate care received, and the discharge code is also used to designate discharge	Discharge CPT code: 99217
	When a patient receives ≥8 h of care and <24 h and is discharged on the same calendar day, codes used include admission and discharge services Requires three key components: Detailed or comprehensive history Detailed or comprehensive examination Medical decision-making that is straightforward or of low complexity/severity, ~40 min at bedside (code 99234); moderate complexity/severity, ~50 min at bedside (99235); or high complexity/high severity, ~55 min at bedside (99236)	99234 99235 99236
Subsequent observation care services	Applies when patients are held in observation care status for more than 2 calendar days For all three codes, requires two of three key components: Problem-focused interval history Problem-focused examination Medical decision-making that is straightforward or of low complexity, ~15 min at bedside (code 99224); moderate complexity, ~25 min at bedside (99225); or high complexity, ~35 min at bedside (99226)	99224 99225 99226

(continued)

Table 3.3 (continued)

Time period	Rules	CPT codes
Admission to inpatient status *following* observation care	If the same physician who ordered observation services also admits the patient for inpatient status before the end of the same calendar day observation status began, only the initial hospital visit for evaluation and management services provided on that date can be billed If the patient is admitted for inpatient status subsequent to the date of initiation of observation services, the physician must bill an initial hospital visit for the services provided on that date The physician may not bill hospital observation discharge management code The physician may not bill an outpatient/office visit for care provided while the patient received hospital outpatient observation services on the date of admission to inpatient status	NA
Documentation requirements *including* admission and discharge services	History, examination, and medical decision-making in the medical record, including: Stating the stay for observation care involves 8 h but <24 h Identification that the billing physician was present and personally performed services Identification that an order for observation services, progress notes, and discharge notes were written by the billing physician	NA

CPT Current Procedural Terminology, *NA* not applicable, *HCPCS* Healthcare Common Procedure Coding System

Quality Regulations in Acute Heart Failure Linked to Medicare Payment

The Centers for Medicare and Medicaid Services and Hospital Quality Alliance are interested in ensuring high-quality patient-centric care delivery and clinical outcomes. To that end, in June 2007, 30-day mortality for heart failure became a publically reported measure. Currently, the Centers for Medicare and Medicaid Services have publicly reported outcome measures specific to heart failure that include all-cause 30-day rehospitalization and all-cause 30-day mortality. Since publicly reported measures are available on the Hospital Compare website, hospital care is more transparent to providers and consumers. Consumers may use data to make decisions about care providers, and performance measures assist hospital leaders and providers in their quality improvement efforts. To ensure an accurate assessment form each hospital, mortality and rehospitalization measures are risk adjusted for patient age and comorbid conditions [36]. All acute care hospitals must be compliant with Centers for Medicare and Medicaid Services to receive reimbursement for hospitalizations in patients 65 years or older.

For years, the Joint Commission (JC) on accreditation of healthcare organizations, a private nonprofit organization, sets standards for healthcare delivery programs and facility requirements that involved heart failure core measures. In January 2014, the Centers for Medicare and Medicaid Services stopped their requirement for data collection of two core measures: discharge instructions (HF-1) and angiotensin converting enzyme inhibitor/angiotensin receptor blocker use for patients with left ventricular systolic dysfunction (HF-2). In January 2014, the Joint Commission also retired the discharge instruction measure and on January 1, 2015, discontinued data collection for the four-measure data set that also included evaluation of left ventricular systolic dysfunction and beta-blocker use [37].

Discontinuation of the heart failure core measure set by the Joint Commission does not negate the need for data collection on multiple performance measures. First, the Centers for Medicare and Medicaid Services and the Joint Commission have a national quality inpatient measure set for emergency departments [38] that includes multiple measures that apply to patients with heart failure, even though the measures are not specific to heart failure services or outcomes. Second, the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey solicits patients' views, comments, and ratings on their hospital experiences in 18 areas and includes the themes of medical care quality, customer service, clinician-patient interaction, cleanliness and quietness of the hospital environment, pain management, communication about medicines, and discharge information [39]. Finally, the National Quality Forum has 17 cardiovascular performance measures, 9 of which apply to acute heart failure (Table 3.4) for public reporting and quality improvement. These heart failure measures are in development and are part of an all-cause admissions and hospital rehospitalization project 2015–2017 that also includes measures of emergency department use and acute care hospitalization during home health [40]. Measures were aimed at promoting a system of patient-centered care coordination. Many measures are endorsed and funded by the Centers for Medicare and Medicaid Services, and some are new measures in the process of being vetted, using a consensus development process, by the steering committee and public. The project was initiated in November 2015 and measures are expected to be finalized in late 2016. The National Quality Forum was created in 1999 by a coalition of public and private sector leaders in response to a recommendation that an organization was needed to promote and ensure patient protections and healthcare quality through measurement and public reporting. The Department of Health and Human Services contracted the National Quality Forum in 2009 to develop a portfolio of quality and efficiency measures that will allow the federal government to determine if healthcare spending on quality initiatives achieves the best results for patients and taxpayers.

In general, performance measures for acute heart failure have undergone rigorous review by volunteer experts of many national organizations before endorsement and use in national reporting. The focus on quality of care has shifted from process metrics that reflect evidence of healthcare provider actions, toward clinical patient outcomes. Further, new attention has been placed on providers who receive patients during the transition period after hospital discharge. Over time, as new

Table 3.4 National Quality Forum measures within the all-cause admissions and readmissions project 2015–2017 that pertain to acute heart failure

NQF measure number	Measure title (details, as needed)	Steward	Status (May 2016)
0171	Acute care hospitalization during the first 60 days of home health	CMS	Endorsed
0173	Emergency department use without hospitalization during the first 60 days of home health	CMS	Endorsed
0330	Hospital 30-day, all-cause, risk-standardized readmission rate following heart failure hospitalization	CMS	Endorsed
1789	Hospital-wide all-cause unplanned readmission measure (HWR)	CMS	Endorsed
2858	Discharge to community (patients who were discharged back to the community alive and remained out of a skilled nursing facility for the next 30 days)	AHCA	New
2879	Hybrid hospital-wide readmission measure with claims and electronic health record data (risk-standardized readmission rate of unplanned, all-cause readmission after admission for any eligible condition within 30 days of hospital discharge)	CMS	New
2880	Excess days in acute care after hospitalization for heart failure (days spent in acute care within 30 days of discharge from an acute care [inpatient] hospitalization for heart failure); provides a patient-centered assessment of the post-discharge period	CMS	New
2886	Risk-standardized acute admission rates for patients with heart failure (applies to ambulatory patients receiving Medicare fee-for-service; aged 65 years and older)	CMS	New
2888	Risk-standardized acute admission rates for patients with multiple chronic conditions (must have two or more of eight conditions listed, one of which is heart failure; applies to ambulatory patients receiving Medicare fee-for-service; aged 65 years and older)	CMS	New

AHCA American Health Care Association, *CMS* Centers for Medicare and Medicaid Services, *NQF* National Quality Forum

provider groups are required to provide data on outcome measures, it is hoped that hospital and posthospital discharge providers will adhere to nationally recognized heart failure management guidelines that offer high-quality, evidence-based care recommendations.

In conclusion, regulatory requirements for acute heart failure services include those that influence coverage (and ultimately payment) and quality of care. Payment of acute heart failure care services involving diagnosis-related group payment to hospitals for inpatient care was not described; however, regulations for services provided as outpatient observational care regarding hospital and physician reimbursement, based on packaging of related services, was discussed. As newer drug,

device, and monitoring therapies become available for acute heart failure management, regulations for coverage and performance monitoring will be updated, requiring healthcare provider and administrator vigilance.

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Quality and Operational Metrics in Heart Failure

4

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Quality and Its Measurement

Quality in health care is an idealized yet elusive goal. This can, in large part, be attributed to the inherent difficulty associated with establishing a precise definition of quality—a circumstance derived from the existence of multiple stakeholders (e.g., health-care providers, local administrators, patients, community, insurers, government) each with differing perspectives on what constitutes the deliverables of "good" health care. At its core, however, quality is generally regarded as an attribute of provider care, specifically technical performance (or lack thereof) as viewed through the lens of "best-practice" medicine [1]. The latter represents the summation of those actions (or inactions) that have either proven effective or are, by virtue of consensus expert opinion, considered de facto to contribute to better outcomes (e.g., smoking cessation).

Quality is thus a comparative construct which measures variance from a benchmark set by what is considered to be best care as identified by a consensus standard. But what exactly is being measured and how can one be sure that the metric is relevant at the individual patient level and attributable to the provider (or system) in

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question? Moreover, to what standard is the assessment held: maximal, which does not consider health benefits within the context of related cost or optimal, which places a cost-effective value on care? Understanding these issues in an era of performance measures [2] and increased accountability for health outcomes is critical.

More than two decades ago, Avedis Donabedian championed the notion that quality can and should be assessed as a function of the relationship between three essential elements termed "structure," "process," and "outcome" [1]. As shown in Fig. 4.1, each can exist as both a precondition for (e.g., identification of a disparate outcome at an institution leading to a change in culture or practice) and a consequence of (e.g., inability to meet time-dependent goals for therapeutic intervention because of resource limitations) the others. These relationships, however, are far from linear and can be strongly influenced by confounding variables, especially case mix.

All of this has particular relevance to acute heart failure (HF), where, despite significant advances in medicine, postdischarge outcomes remain poor [3–5]. In the following pages, we discuss the specifics of quality as they relate to HF and highlight, using the Donabedian framework, those measures being used to differentiate performance.

Structure and Process: The Language of Operational Metrics

Structure

The definition for health-care structure is broad, including everything from geographic location and physical layout of health-care facilities, medical equipment and information technology systems, and personnel qualifications, certification, and training. This breadth leads to a lack of consensus and evidence as to what structural elements contribute to high-quality health-care process and thus high-quality outcomes. Based primarily on expert opinion, a former American College of Cardiology/American Heart Association (ACC/AHA) Heart Failure Working Group [6] recommended four structural elements be considered as indicators of quality: clinical practice guidelines, monitoring of patient care and outcomes, disease management programs, and coordinated systems of care. Initially published in 2000, excellence in these areas, particularly the latter two, has come to define centers that consistently provide high-quality HF care.

Disease Management Programs

These are multidisciplinary, patient-focused programs that cover matters such as education about the disease and its treatment, dietary counseling, efforts to improve patients' compliance with medical regimens, and interventions to help patients

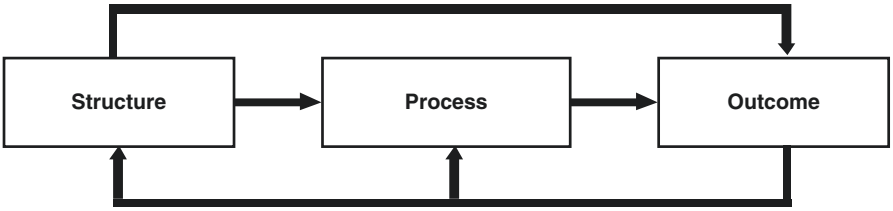

Fig. 4.1 Relationship between structure, process, and outcome in health care

achieve and maintain control of their volume status. These programs have been shown to reduce readmissions and improve functional status but not necessarily affect mortality rates [7, 8]. Further study is needed to define their overall cost-effectiveness and the optimal strategy [9, 10], as not all approaches (e.g., postdischarge telemonitoring in those recently hospitalized with acute HF) appear to provide clinical benefit [11].

Coordinated Systems of Care

As originally written by the ACC/AHA HF Working Group, this element involved the specific decision to refer medically refractory HF patients to specialty and transplant centers. It called for health-care facilities to establish a relationship with a specialty center and coordinate a plan for transfer that is predetermined and not in response to patient crisis. In such coordinated systems, patients would be referred based on their overall prognosis and response to medical care. Indeed, the literature has shown that patients with symptoms for >3 months and a more severe initial presentation are less likely to respond to therapy and may benefit from referral to specialty centers, including transplant centers [12]. Moreover, in medically refractory patients, referral to specialty centers has been reported to result in a 98 % 1-year survival rate [13, 14] and reduce readmissions by 50 %.

Though initially centered on referral, the concept of coordinated systems has morphed into one increasingly focused on greater linkage throughout the entire continuum of HF care [15, 16]. Such systems, termed accountable care organizations (ACOs), would provide continuity for patients across different institutional settings (including ambulatory and inpatient hospital visits) and, if possible, during episodes of acute decompensation. While prospective experience with structured, shared accountability, and related outcome data in HF is lacking, there is relatively strong evidence from the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure) registry which suggests a

relationship between readmission rate and early outpatient follow-up after an index HF hospitalization [17]. Among patients with acute HF who were discharged from the emergency department (ED) in the Canadian National Ambulatory Care Reporting System, an association between early collaborative HF care and increased use of drug therapies, cardiovascular diagnostic testing, and better outcomes has also been reported [18].

Process

Processes of care are the interventions made in the hospital or outpatient setting that will lead to a desired health-care outcome. They can be pharmacologic (e.g., the use of angiotensin-converting enzyme inhibitors [ACEI], beta-adrenergic blockers), diagnostic (the assessment of left ventricular dysfunction), or patient-focused (providing discharge instructions and encouraging daily weight measurement). Ideal process measures have a well-defined outcome link, are broadly applicable to a defined group of patients, and are easily measured. Adherence to such interventions serves as a marker of quality of care and forms a foundation for quality improvement.

There are several challenges in defining ideal process of care measures for HF patients. First, HF is a clinical syndrome rather than a single disease entity. Patients' symptoms and left ventricular (LV) function can vary greatly and with minimal apparent correlation. This makes it difficult to define process measures that are applicable to all HF patients. For instance, the majority of HF patients are known to have preserved systolic function; however, most diagnostic and therapeutic interventions have not been studied in this population [6]. In addition, patients at more advanced stages of disease are less likely to be receiving evidence-based therapy [19]. This is largely due to increased contraindications to therapy as mortality risk rises and decreased use of medication in eligible patients. More research is needed to define which therapies are beneficial to patients with early versus advanced stages of disease.

A second challenge is the lack of consensus as to what constitutes the ideal processes of care. A number of leading health-care organizations, including The Society of Cardiovascular Patient Care (SCPC), an institute of the American College of Cardiology, have attempted to define processes (Table 4.1) which, based on the best available evidence or, in its absence, consensus opinion should either be utilized in every patient (unless contraindicated) or at the least be tracked. While there is a considerable amount of overlap in the recommendations, there are also differences that make it difficult to set national or international goals and benchmarks for quality care. For instance, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), ACC/AHA, and SCPC each recommends ACEI or angiotensin receptor blocker (ARB) therapy for patients with LVEF <40 %, evaluation of LV function, detailed discharge instructions incorporating activity level, diet, discharge medications, follow-up appointments, weight monitoring, and what to do if symptoms worsen, and smoking cessation counseling. In addition to the

Table 4.1 Society of cardiovascular patient care heart failure accreditation calculated measures

Heart failure admission rate – observation
Heart failure admission rate – inpatient
Heart failure specific length of ED, observation, inpatient stay
Hospital 7, 15, 30, 60, 90-day HF specific readmission rate following Heart Failure hospitalization
Heart failure-specific readmission rates from a location other than home at 7, 15, 30, 60, 90 days
Heart failure-specific return to observation rates at 7, 15, 30, 60, 90 days
Heart failure-specific return to observation rates at 15 days
Proportion of heart failure patients requiring an increased level of care
Heart failure in hospital mortality rate
Evaluation of left ventricular systolic function
Median time to ECG
Proportion of patients receiving NIPPV while in the ED
Assessment of objective data – heart failure patients (process)
Proportion of patients undergoing evaluation of current level of activity and clinical symptoms (NYHA)
Proportion of patients having documented daily assessment of electrolytes and renal function
Proportion of African Americans given Hydralazine/ISDN at discharge
Proportion of heart failure appropriate patients given an approved Beta-Blocker at discharge
Proportion of heart failure appropriate patients given an ACE/ARB at discharge
Proportion of patients discharged on NSAIDS
Proportion of patients discharged on Aldosterone Antagonists
Detailed discharge instructions
Reconciled medication list received by discharged patients (Discharges from an inpatient facility to home/self care or any other site of care)
Timely transmission of transition record (Discharges from an inpatient facility to home/self care or any other site of care)
Percent of patients discharged home with written instructions or educational material given to patient or caregiver at discharge or during the hospital stay addressing all of the following: activity level, diet, discharge medications, follow-up appointment, weight monitoring, and what to do if symptoms worsen
Percentage of patients, regardless of age, discharged from an inpatient facility to ambulatory care or home health care with a principal discharge diagnosis of Heart Failure for whom a follow up appointment was scheduled and documented including location, date and time for a follow-up office visit, or home health visit (as specified)
Door to IV therapy time for nitroglycerin or other vasodilator during early stabilization
Door to IV therapy time for furosemide or other loop diuretic during early stabilization
Proportion of patients who received a Social Work Consult
Proportion of patients with diastolic dysfunction discharged with a BP >150
Proportion of patients with no past medical history of heart failure
All cause readmission rate for heart failure population
Rate of patients evaluated with NT-proBNP or BNP

*SCPC HF v2 Accreditation calculated measures, 2014 (only inclusive of those measures applicable to short stay management)

aforementioned metrics, many other metrics are tracked in the SCPC Heart Failure Accreditation tool which focuses on the daily patient level processes that apply to the management of the HF population.

These metrics along with CMS Value Based Purchasing Scores (Length of stay, 30-day readmission and inpatient mortality) give insight into the process, quality, and outcomes of a HF disease management program. Previously, there had been little to no information regarding appropriate management of the HF patient in both the Emergency Department and Observations services areas. However, recently a statement released by Collins et al. (2015) has given much improved guidance of care in these areas. Previously proposed measures, such as door-to-treatment (i.e., diuretic) time, door to provider time, make empirical sense but have been insufficiently explored. In comparison, the quality metric associated with the utilization of standardized evidence-based order sets has been proven effective in the short stay management areas as well as inpatient level of care. The ideal processes of care, and thus the markers of quality, could be substantially different for patients with acute decompensation who are treated in a short-stay setting than for patients following a prolonged hospitalization, but at present, there are simply not enough data.

A final issue is ensuring that processes of care are carried out equally across socioeconomic, racial, ethnic, and gender groups. In OPTIMIZE-HF, it was found that African American patients admitted for HF were more likely to receive evidence-based medications while in hospital but less likely to receive discharge instructions or smoking cessation counseling [20]. Disparity in care such as this across different racial, ethnic, and social groups is commonly found and is often alleviated by the involvement of the Case Manager or Social Worker. The formation and utilization of the multidisciplinary care approach can also be associated with quality indicators and improved outcomes.

Outcomes: Quality in Action

Positive outcomes are the ultimate goal of any health-care system and the true essence of quality. Ideal outcome measures should be measurable, sensitive to modifications in the structure and process of care, practical to use and should take into account patients' underlying risk for good or bad outcomes. The main challenge in using outcomes as a marker of quality is that they do not depend solely on the health care provided. Age, severity of cardiac dysfunction, presenting hemodynamic profile, degree of comorbidity, and socioeconomic status have all been shown to affect outcomes for acute HF patients [21].

An additional challenge specific to the ED setting is the relative absence of data linking ED or OU acute HF processes of care with postdischarge outcomes. Consequently, it is unknown which of the commonly used outcome measures (Table 4.2) constitute a meaningful representation of what can reasonably be attributable to ED and OU management of HF patients. Thus, while a recent review of more than 50,000 acute HF patients in Ontario, Canada, found a slightly higher 90-day mortality rate (11.9 % versus 9.5 %; log-rank $P = 0.016$) among those who

Table 4.2 Outcomes of importance in heart failure [6]

Survival
Mortality rates
Quality-adjusted life years (QALYs)
Days out of the hospital and alive[a]
Resource utilization
Index visit
Admission rate
Admission location (floor, telemetry, ICU)
Length of stay
Postdischarge
Outpatient clinic visits
Emergency department visits
Hospital readmissions
Symptom resolution
Dyspnea scores
Health status and quality of life
Short form (SF) 8, 12, or 36
Minnesota living with heart failure
Kansas City cardiomyopathy
6-min walk test
Patient knowledge and compliance
Perceived self-efficacy (diet, medications, lifestyle)
Illness-belief scales
Health literacy
Health numeracy

[a]May be considered a metric of both survival and resource utilization

were discharged from the ED versus admitted to the hospital, its interpretation within the context of health-care quality is difficult [22]. Moreover, while 90 days is a relatively short follow-up period, it is probably long enough to introduce substantial confounding. With the advent of CMS Value Based Purchasing, shorter (30-day) postdischarge event rates are now favored and may be more reflective of an ED, OU, or even inpatient treatment period. Perhaps of greater importance, 30-day mortality and readmission data for acute HF are publicly reported by the CMS as a measure of comparative hospital quality. Regardless of the sampling period, there may be added value through use of more time-sensitive metrics such as days out of hospital and alive [15], which provide a clearer signal of causality than measurement of dichotomous (and equally weighted) outcomes that occur at any point within a prespecified time frame.

The use of validated risk stratification tools within the ED and Observation services has also emerged as best practice and attribute to improved quality and outcomes. In a study done by Schrager et al. (2013) favorable outcomes were achieved

by appropriately selecting and risk stratifying acute HF patients within the ED setting and initiation of a rapid treatment protocol in the Observation Unit. Quality metrics such as favorable resource utilization decreased bed days and no significant change in recidivism rates [45].

Survival

Mortality rates are classically used for quality improvement within a health-care system. More so than other disease processes mortality in the HF population should be strongly scrutinized. Being that 50 % of HF patients suffer mortality within 5 years following an index admission, this metric is strongly correlated with not only length of stay but also rate of recidivism. Though often considered the poorest of outcomes, it should be recognized that death is most often not an unexpected event and, in some cases, particularly those with preterminal end-stage HF, may be an acceptable end point to the patient or their caregiver (ideally stipulated as such in advanced directives and advance care planning) [23–25]. This notwithstanding, mortality rate is a requisite indicator which, from a statistical perspective, should be measured from the patients' index hospitalization or at the point of initial diagnosis. Failure to do so may result in resampling of the same individual at multiple time points (i.e., episodes of recidivism) and create confounding due to competing risk for survival. Though difficult, differentiating death due to HF (i.e., sudden cardiac arrest or worsening ventricular function) from other causes is also important to provide the level of granularity needed to accurately estimate relationships within the Donabedian framework.

In terms of process to outcome link, it was found in OPTIMIZE-HF that none of the ACC/AHA performance measures resulted in reduced mortality risk and only ACEI/ARB prescription at discharge was shown to diminish the composite outcome of 60–90 days postdischarge death or rehospitalization [26]. Beta-blockade at the time of discharge on the other hand, a process not currently listed as an ACC/AHA performance measure but recommended by the GWTG-HF program, was strongly associated with a reduction in both mortality and the composite of death or rehospitalization. While the benefits of such therapy have not been specifically shown for acute HF patients treated in an ED or OU, broader utilization of ACEI/ARB and beta-blockers at discharge from either of these settings offers promise as an approach to improvement of postdischarge survival [27].

Resource Utilization

Health-care resource utilization is another important and often cited outcome measure. Because HF is a disease chronic care and recidivism with re-hospitalization rates that approach 25–30 % at 30 days [28], much of the focus on resource utilization remains appropriately fixed on postdischarge outcomes. The need to reduce postdischarge ED visits and the rate of readmission for those with acute HF is considered fundamental to both institutional quality improvement efforts and future

research endeavors [6, 16]. The avoidance of inpatient admission from short stay management can positively affect the rate of return to inpatient level of care following an index admission. Therefore, quality care provided in the ED and observation services can lend to improved outcomes such as 30-day readmission rates.

Cost is also a primary driver of the interest in terms of resource utilization, and in addition to recidivism, there is growing interest in the disposition of patients with acute HF from the ED. Currently, more than 80 % of patients presenting with symptoms of acute HF are admitted to an inpatient level of care [16]. There are little data and no clinical policies or decision rules that dictate what type of patients may go home from the ED, which can be managed in an OU setting, and who should be admitted to an inpatient unit. As of late much discussion has been had on risk stratification and appropriate decision making. Examples of these tools can be found in the SCPC Consensus White Paper: Recommendations for the evaluation and management of observation services (2014) [47].

Using decision-analytic model simulations, it has been shown that in comparison to ED discharge among low-risk ED patients, the marginal cost-effectiveness ratio is reasonable for OU admission ($44, 249 per quality-adjusted life year) but unacceptably high for hospital admission ($684,101 per quality-adjusted life year). Sensitivity analyses demonstrated that as the risk of early (within 5 days) and late (within 30 days) readmission and mortality rose, OU admission became less costly and more effective than ED discharge, and with an increase in postdischarge event rates among those discharged from the OU, hospital admission was more cost-effective [30]. As evidenced, however, by the 15-year trend toward decreasing hospital length of stay, increasing use of skilled nursing facilities at discharge, and higher rates of readmission rate among Medicare beneficiaries with acute HF [30], point-in-time decisions do not exist in isolation and may have untoward downstream consequences.

A growing area of interest with respect to resource utilization (and the potential for reduction) is variation in practice at the regional, institutional, and individual practitioner levels. Such variation contributes to de facto differences in resource consumption and may be associated with divergent outcomes [31]. Presumably, this represents a combination of over-, under-, and misuse of clinical care, each of which offers the opportunity to improve upon practice patterns. Standardization and utilization of guideline-driven medical therapy through level of care-specific order sets is proven effective and thus should be tracked [48]. For example, appropriate-use criteria have been developed to examine the rational use of radiographic testing, biomarker evaluation, and functional assessment in HF [32], such scrutiny could be (but has not been) more broadly applied to identify ineffective or wasteful processes of care.

Patient-Centered

The final three outcome measures listed are patient-centered. They involve patient perceptions of symptom severity; predominantly dyspnea and decrease in functional capacity, overall health status, quality of life, and illness beliefs/knowledge about compliance with diet and medication regimen.

During the acute phase of treatment, symptom resolution is paramount and may be the thing that matters most to patients. Though symptoms are often not measured systematically or objectively, repeat assessment of severity using validated scales if possible and identification of a differential response have emerged as an important end point for HF therapeutic trials [33–35]. However, what constitutes a meaningful change over time, and the lasting value of symptom relief as an outcome measure beyond response to ED or OU intervention, is not known.

Measures of health status and quality of life have become increasingly recognized as highly meaningful outcomes of those patients suffering from HF [36]. Those listed in Table 4.2 have been validated as tools for self-assessment of HF disease progression in chronic outpatient settings, but their direct applicability to patient care in the ED or OU is uncertain. Nonetheless, they can provide an important means to objectively compare postdischarge perceptions of wellness (or illness) which, in turn, may reflect the adequacy or inadequacy of seemingly sufficient treatment. Due to a lack of definitional standards for quality of life and variability in what may constitute a clinically significant improvement, comparative interpretation within and across scales is difficult.

Despite a rich history in the social science literature, metrics focused on disease-specific knowledge and understanding, as well as general health literacy, have achieved incomplete uptake in the world of clinical medicine. An appraisal of such aspects, however, offers the unique opportunity to evaluate often overlooked potential contributors to precipitating factors of poor disease self-management and assess the relative effectiveness of educational interventions.

Toward Quality Improvement

Clinical Practice Guidelines

Removing variation in clinical care through adherence to established, evidence-based best practices forms the basis of the contemporary quality improvement initiative. To this end, HF-specific clinical practice guidelines have been published by the ACC/AHA [13], the Heart Failure Society of America (HFSA) [37], the European Society of Cardiology (ESC) [38], and the Society of Cardiovascular Patient Care (SCPC) [39]. Individually and collectively, these represent a combination of the best available evidence and consensus expert opinion as they pertain to various aspects of the overall process of care. Clinical practice guidelines have been shown to improve health-care processes and outcomes in general as well as specifically for HF. Institutional adoption of standardized guideline-driven medical therapy has been promoted as a structural mechanism to improve the quality of care delivered to HF patients [6].

Unfortunately, many of the HF guideline-based recommendations put forth have been designed for longitudinal patient care in the clinical setting or following hospital admission. Less well-defined are the necessary process measures for

patients with acute decompensated heart failure, particularly in the ED and OU setting. With the release of the joint statement from the Heart Failure Society of America and the Society of American Emergency Medicine, there has been increased guidance in effective short stay management [46]. While the ACC/AHA has included some information on acute HF in the most recent-focused update of their 2013 Guidelines for the Diagnosis and Management of Heart Failure in Adults, and the Heart Failure Society of America (HFSA) has given recommendations for acute HF care in their 2013 Comprehensive Heart Failure Practice Guideline, only the SCPC has published clinical guidelines that are focused on the ED and OU phases of care, most recently in the Observation Services White Paper (2014) [47]. Use of the SCPC guidelines to identify acute HF patients at low risk of adverse outcomes has recently been validated using the HEARD-IT (HEart failure and Audicor Technology for Rapid Diagnosis and Initial Treatment) database [40].

Performance Measures

Whereas clinical guidelines are meant to serve as an evidentiary review of the literature and provide the scientific background for specific patient care recommendations, performance measures function as tools of accountability [2]. They focus on discrete processes of care for which there is evidence of the highest quality (class I, level A), showing unequivocal benefit and consensus that a failure to provide the therapy would meaningfully reduce the likelihood of a positive outcome. As alluded to in a preceding section, specific performance measures (Table 4.1) for HF have been developed by organizations with a vested interest in health-care quality including the JCAHO, the ACC/AHA, CMS, and, most recently, SCPC HF.

While there is evidence supporting clinical benefit from adherence to the ACC/AHA performance measures for HF [41, 42], there is also concern about the ramifications associated with utilizing performance measures to standardize quality [43]. Hospital performance regarding CMS Value Based Purchasing is now publicly reported, and increasingly, these reports are being used to distinguish providers and systems that deliver high-quality care from those who are marginal or deficient. Additionally, reimbursement and penalty at all levels are now closely tied to related, performance-based initiatives [43]. Such use of payment thresholds to incentivize performance, however, is not without consequence and may serve to reward paper compliance rather than encourage practice which results in actual substantive improvements in patient care (e.g., simple documentation of patient education on self-management versus initiation of a quantifiable, behavioral encounter) [2]. Furthermore, pay-for-performance initiatives tend to be absolute without consideration of incremental cost-effectiveness (i.e., maximal rather than optimal perspective on health care) [2, 43] and, in some instances, may even create misalignment between financial incentives for the institution itself

(i.e., by inducing performance measure achievement through relative increases in payment which are offset by declining reimbursement from reduced hospital admissions).

To ensure that relevant information is accurate, proper documentation of performance, and, perhaps more importantly, exceptions (i.e., medical, patient-level, or systematic reasons why the measure cannot or should not be performed) is needed. This may require prospective recording of additional data elements by providers during a clinical encounter or, absent this, reliance on often imperfect administrative data. Electronic medical records could facilitate data collection through exportation of quality metric information or use of provider-directed automated prompts (which may be problematic as clinicians tend to develop "alert fatigue") [2].

Accreditation

Meeting the various aspects of care stipulated by guidelines and performance measures can be a daunting task. However, cataloging, understanding, and quantifying baseline practice and outcomes are critical steps in this process and central tenets of quality and process improvement. The intensive data gathering required can be facilitated by seeking accreditation—an unbiased approach to assessment of institutional performance which serves to recognize those centers which conform to a predefined higher standard of care. Rooted in the principles of improvement science, accreditation involves a thorough review of site-specific quality elements. It is another way of replicating best practices which, at the same time, encourages institutional innovation and creativity to achieve optimal outcomes. The SCPC has been a driving force in the development of HF Accreditation, creating an "accreditation tool" that includes seven Essential Components (Table 4.3), each of which is supported by mandatory, recommended, and innovative items and processes

Purported benefits of accreditation include the introduction of critical process improvement tools, integration of care processes across departments, provision of a road map for strategic planning, enhancement of patient care, development of pathways to reduce medical errors, and streamlining of third-party analysis through use of uniform operational definitions and common language. Though experience with HF Accreditation is evolving, SCPC (Society of Cardiovascular Patient Care) has

Table 4.3 Society of cardiovascular patient care essential components for heart failure accreditation

1. Governance
2. Community
3. Pre-hospital
4. Early stabilization
5. Acute care
6. Transitions
7. Clinical quality

been associated with increased ACC/AHA evidence-based guideline adherence in the first 24 h of care [44].

Conclusions

Using the best available evidence and expert opinion, measurable quality and operational metrics for HF have been defined by a number of prominent organizations. To be in better position to achieve these metrics, health-care systems will ideally be structured around patient-focused, multidisciplinary disease management programs that focus on coordination of care across providers and institutions. Adherence to specific performance measures has been associated with improvements in patient outcomes, including increased survival and decreased recidivism, and has profound implications for reimbursement. These metrics, however, were developed for admitted patients, and whether or not they can be extended to the ED or OU is still to be determined. Rather than an impediment, this gap in knowledge provides a unique opportunity to prospectively evaluate the validity of existing practice guidelines and performance measures under differing circumstances and improve upon them in a manner that enhances their applicability to ED and OU settings.

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5 Interaction of Performance Measurements, Staffing, and Facility Requirements for the Heart Failure Observation Unit

Valorie Sweigart and Karen Krechmery

Performance Measurements

Evidence-based clinical practice guidelines for the care of heart failure patients guide providers, individual units, and hospitals in developing their own best practice measures [1]. Identifying best practice measures can integrate both administrative practices such as staffing, with clinical outcomes such as patient length of stay. Benchmarking is a method used to compare your own practice with those of like hospitals. Establishing best practice levels of performance is the goal of benchmarking.

Well-known organizations that have established guidelines also known as core measures for best practice include The Joint Commission, The American College of Cardiology, and The American Heart Association [2–4]. These organizations provide published data that can be used as a benchmark for establishing individualized patient outcome goals. The American Heart Association provides "Get with the Guidelines-Heart Failure" clinical tool-kits that are available free of charge online [5]. These guidelines are also accessible through the Quality Check website associated with The Joint Commission [6]. The Quality Check website allows public viewing of hospital outcome reporting for multiple conditions including heart failure. While some of these guidelines are intended for inpatient use, they reflect evidence-based standards of care for heart failure patients. Since these patients may become inpatient at anytime during their hospitalization, adherence to established inpatient standards is necessary. Ambulatory care guidelines can also contribute to the development of observation medicine management goals, which is considered outpatient care.

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Performance improvement measures need to be established by each institution based on the overall mission of the observation unit. These measures are used by the unit to determine the effectiveness of the heart failure protocol. Length of stay and discharge rates are common indicators of success. If the standard for the observation unit is a length of stay of less than 24 h, then length of stays greater than 24 h would indicate inefficiency either with treatment protocols, patient selection, or patient response to treatment. Discharge rates assist in identifying appropriate patient selection. The patient may have comorbidities that would have precluded effective treatment in this time frame. Therefore, exclusion criteria can be established or modified based on this data. Other data that may assist in refining protocol and patient selection may be examining time of day of admission and length of stay. Considerations such as time of discharge for elderly patients may be a factor. Based on time of admission, you may not be able to achieve the desired outcome for discharge within a 24 h time frame.

All patients admitted for heart failure must have realistic goals defined at the time of admission. Patient selection is key to the process. Placing a patient in observation must have a high probability of success within the observation time frame. Patients with multiple goals and/or comorbidities most likely will not be ready for discharge in less than 24 h.

Valuable feedback of unit/staff performance can be obtained directly from patients. Patient telephone surveys by the unit staff have been shown to provide valuable information regarding the operations of the department. A simple standardized questionnaire can be developed by the staff and physicians related to key aspects of care. Telephone calls placed at a decided interval after discharge can obtain information that can guide the department in developing their own best practices based on their patients' perspectives. This information can also be incorporated into the unit's performance improvement plan.

Health-care organizations benchmark administrative measures in which common hospital characteristics are compared to like organizations. There are many organizations or consortiums that provide these services such as Press Ganey, well known for patient satisfaction measurements. According to Press Ganey, positive patient experiences have been linked with positive clinical and financial outcomes for the organization. Therefore, measurement of patient satisfaction done with standardized methodology can be used to reflect the hospital performance and areas that can be targeted for improving patient's perception of quality [7].

Another key measure to an institution's success is staff and physician satisfaction. The Gallup Company is an organization that has demonstrated through research that organizations with a high level of staff and physician engagement or commitment report higher levels of patient satisfaction [8]. Staff that is actively engaged in the care of the patient will go above and beyond the basic standards required to provide care to the patient. One such example would be a nurse that leaves discharge materials at the bedside related to patient education vs. a nurse that reviews the materials with the patient and then assesses the patient's understanding of the information provided. Having engaged staff ultimately leads to better patient satisfaction and optimum unit level operations.

Staffing

Observation unit staffing is composed of physicians, associate providers (AP) such as nurse practitioners or physician assistants, registered nurses, support staff such as nursing assistants and unit clerks, as well as social workers. Typical models utilize an AP that is responsible for directing care during the patient visit 24 h per day 7 days per week. All patients are examined by a physician during the observation period. A physician is responsible for patient rounds during which time the plan of care for the patient is reviewed and discharge goals are defined. Registered nurses provide direct patient care and are present 24 h per day 7 days per week.

Nursing staffing models vary with the needs of each unit. All units must have a registered nurse responsible for the overall care of the patient. Typical nurse/patient ratios vary with each state/institution but generally are in the range of 4:1 or 6:1. This can be adjusted based on patient acuity or volume. The numbers of nurses required in an observation unit can be calculated using worked hours per unit of service (WHUOS). This is a common financial unit of measurement and can be benchmarked with like institutions. It is derived from the total number of hours worked by staff divided by the total number of units of service or visits. This number can then be used to more accurately predict the required budget by incorporating the number of days of the month and adjusting for seasonal or temporal fluctuating patient volumes. Many units also supplement nurses with nursing assistants. The number of nurses and support staff for each unit is dependent on the size of the unit and staffing decisions at that institution. Larger units may require clerical staff to answer phones, direct unit activities such as testing schedules, assist family members, schedule follow-up appointments for patients, etc. Nursing assistants may be required for phlebotomy, transport of patients to and from tests, and obtaining vital signs or ECGs. Finally, social services, discharge planning, nutritionists, and transplant coordinators may be on call for specialized patient needs.

As within all hospitals, basic life support (BLS) training is considered mandatory for all staff involved in patient care. Advanced life support (ALS) is also required for all registered nurses in the emergency department. Most heart failure patients go directly from the emergency department to the observation unit and will require ongoing cardiac monitoring, therefore necessitating that the RN staff in the unit to also be ACLS certified. Dysrhythmia training is also a basic competency that is a unit requirement, and other annual competencies may be needed depending on unit/hospital standards and the breadth of pathologies routinely managed in the specific OU.

Facility Requirements

Physical requirements for building a unit, or remodeling an existing area, can be found in the National Fire Protection Association 101: Life Safety Code 2009 which establishes a minimum threshold of safety for patients in new and existing structures [9]. Guidelines for building codes are also available through the American Institute of Architects (AIA). Square footage requirements, utilities requirements,

sinks, etc., for individual rooms are outlined as well as federal and state requirements for Medicare and/or Medicaid facilities.

The numbers of beds needed for an observation unit can be calculated based on the current number of emergency department beds. In a 2007 observational study by Ross et al., they were able to arrive at a common bed utilization characteristic based on emergency department observation unit (EDOU) beds per ED visit of 1 EDOU bed/7,461 ED visits or a daily number of EDOU patients per EDOU bed of 1.14 patients per bed per day [10].

Basic equipment for care of heart failure patients would include oxygen, air sources, and suction available in each room. Many of these patients receive ongoing oxygen as well as nebulizer treatments periodically. Cardiac monitoring is also required for heart failure patients. Decisions at each institution would need to include hardwire monitoring with bedside monitors or telemetry monitoring. The advantage to hardwire monitoring is having the ability to do a 12-lead ECG at the bedside at any time that a change in patient condition warrants one. ST segment monitoring capability is another advantage of bedside monitoring.

Patients in the OU will require meal services since their length of stay will be longer than an ED visit. Planning for feeding patients will need to be a consideration. Heart failure patients will most likely have specialized dietary requirements for low sodium, low cholesterol, and low fat foods. Means to provide these special needs will need to be addressed. Another consideration is the ability to feed patients at nonstandard times since these patients may be admitted at any hour of the day/night. Since the patient has been in the ED, they probably have not eaten for an extended period of time and will be hungry. Diabetes is a common co-morbidity that also requires patients to have adequate dietary services available to them.

Heart failure patients should be weighed upon admission and prior to discharge. A patient scale, preferably portable, is needed for the unit. Although scales are available to weigh up to 1,000 lb, a 600-lb scale is adequate for an OU. It should have a wide base for standing and handrails to assist the patient to stand. Further, since diuresis is a common goal with heart failure patients, toilets in each room are desirable, otherwise bedside commodes or urinals can be utilized for these patients.

Emergency equipment should be readily available if needed. This should include a defibrillator/AED and airway management equipment. A crash cart with emergency drugs and suction equipment is also necessary to perform ACLS protocols in the event of a cardiac arrest. Again, ACLS certified staff is needed to implement emergency procedures.

In summary, because of the wide variety of and unknown severity of illness of many OU heart failure patients, the OU requires staffing and physical supply needs similar to that of the ED. Furthermore, the availability of on-site expertise in cardiac monitoring and airway management is necessary to prevent complications from unexpected events. Finally, because patients may spend considerably longer periods in the OU, the dietary and bathroom needs will exceed that of the ED. Thus, the OU ultimately represents a hybrid between the ED and the inpatient environment in terms of physical plant and staffing requirements.

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Part II

Pathophysiology and Demographics

Heart Failure: Epidemiology and Demographics

6

Karina M. Soto-Ruiz

Abbreviations

ABC	Aging and body composition
ACC	American College of cardiology
ACEI	Angiotensin converting enzyme inhibitors
AHA	American Heart Association
CHD	coronary heart disease
EF	Ejection fraction
GFR	Glomerular filtration rate
HF	Heart failure
HHF	Hospitalized Heart Failure
ICD	Implantable cardioverter defibrillator
JCAHO	Joint Commission on Accreditation of Health Care Organization
LOS	Length of Stay
LVH	Left ventricular hypertrophy
MDRD	Modification of diet in renal disease
SBP	systolic blood pressure

Heart failure (HF) is defined by the American Heart Association/American College of Cardiology (AHA/ACC) as a "complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill or eject blood," and it underscores that "it is a largely clinical diagnosis that is based on a careful history and physical examination" [1]. The burden of heart failure is its enormous cost, both in human and financial measures. Heart failure affects

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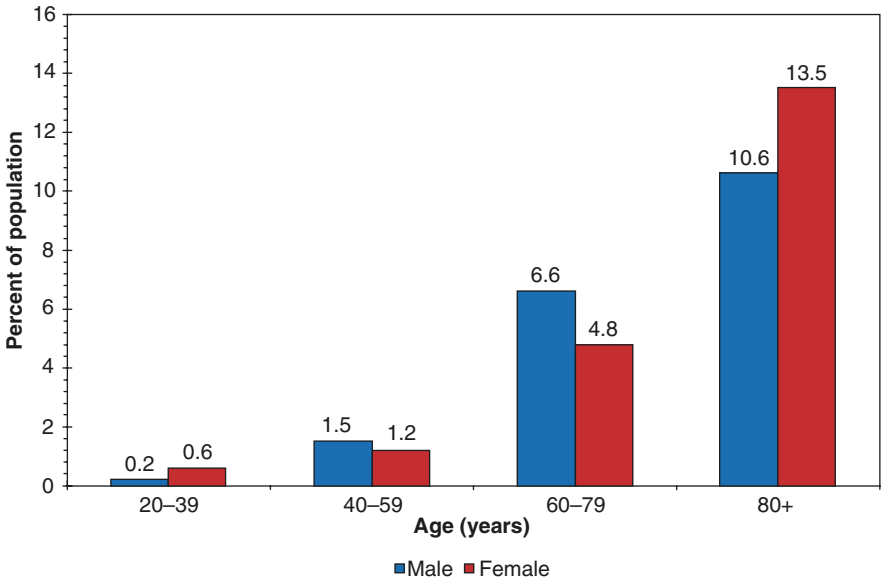

Fig. 6.1 Percentage of population with the diagnosis of heart failure according to age group (From the Heart Disease and Stroke Statistics – 2016 Update)

over 5 million people in the United States and accounts for nearly $39.2 billion annually in health care expenditures [2] . It is the most frequent cause of hospitalizations in patients 65 years of age or older. Heart failure is a disease of the elderly. It has an annual incidence of 10 cases per 1000 after age 65 (Fig. 6.1), which then doubles every decade thereafter [3]. Subjects older than 65 years represent more than 75 % of prevalent HF cases in the United States [4].

With the aging of 78 million baby boomers, 1 in 5 Americans is expected to be older than 65 years by 2050, and at risk for HF. This is projected to impact health care and health care economics [5]. It is clear that the burden of heart failure is already increasing. Projections show that by 2030, the total cost of HF will increase almost 127 to $69.7 billion from 2012. This equals ≈ $244 for every US adult [6], and prevalence will increase 46 % from 2012 to 2030, resulting in >8 million people ≥18 years of age with HF [6].

In earlier studies from Framingham, the incidence of HF diagnosed with standardized criteria was between 1.4 and 2.3 per 1000 patients annually, among people 29–79 years old [7]. Data from the Kaiser Permanent system comparing the incidence of HF in 1970–1974 and 1990–1994 in persons 65 years old or greater indicated that the age-adjusted incidence increased by 14 % over this time and was greater for older persons and for men [8]. Conversely, reports from the Framingham Heart study [9] and the Olmsted County Study [10], including outpatient heart failure data, indicate that over time the incidence remained stable [10] or even declined in women [9]. Overall, the Framingham and Olmsted County studies have shown

trends of increasing HF incidence among older persons; this pattern is important given the aging of the population.

Health care Burden

Hospitalization/Ambulatory Care

In 2012, there were 1774000 physician office visits with a primary diagnosis of HF (NAMCS, NHLBI tabulation) [11]. There are nearly 658 000 annual emergency department (ED) encounters primarily for acute HF in the USA; almost 20 % of the total HF-specific ambulatory care delivered each year [12]. Ultimately, nearly 80 % of patients treated in the ER are admitted to the hospital [13]. Heart failure is the single most frequent cause of hospitalization in persons 65 years of age or older, and hospital discharges for heart failure increased 175 % between 1979 and 2004 [3]. The annual hospitalization rate for these patients now exceeds 1 million in the United States, 80 % of whom are older than 65 years, and readmission rate as high as 50 % within 6 months of discharge has been reported [14].

National Hospital Discharge Survey data from 1979 to 2004 showed the number of hospitalizations with any mention of heart failure tripled from 1,274,000 in 1979, to 3,860,000 in 2004, and that heart failure was the first-listed diagnosis for 30–35 % of hospitalizations [15]. From 2000 to 2010, it was the first-listed discharge diagnosis of 1008000 and 1023000 patients, respectively [11]. Unfortunately, incidence cannot be obtained from these data, as the statistics were event-based (allowing multiple hospitalizations for the same individual). However, despite the large impact of HF, its burden may be inadequately assessed. In a random sample of all incident HF in Olmsted County from 1987 to 2006, hospitalizations were common after HF diagnosis, with 83 % of patients hospitalized at least once, and 43 % at least 4 times [16]. Global hospitalized heart failure (HHF) registries show that the median length of stay (LOS) ranges from 4 to 20 days and in-hospital mortality from 4 to 30 %. The data based on the American Heart Association's ongoing Get with the Guidelines – heart failure (GWTG-HF) registry revealed a median LOS of approximately 4 days and in-hospital mortality of <3 % [17]. In the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure) study follow-up cohort representing about 10 % of the overall registry, the postdischarge readmission rate was approximately 30 % within 60–90 days postdischarge, and mortality ranged from 5.4 to 14.0 % based on admission systolic blood pressure. Similarly, the ESC-HF (European Society of Cardiology-Heart Failure) Pilot survey reported 1-year mortality and readmission rates of 17.4 % and 31.9 %, respectively, at representative centers from 12 European countries [18].

Hospitalizations for HF are likely to increase due to an aging population, improved survival after myocardial infarction, and more effective therapies to prevent sudden death, such as b-blockers and implantable cardioverter-defibrillators

(ICD). Despite current management options, postdischarge mortality and rehospitalization at 60–90 days are as high as 15 % and 30 %, respectively [19]. This suggests that interventions to avoid readmissions are necessary. It has been shown that patients who have a 1-week follow-up after hospital discharge are less likely to be readmitted within 30 days than those that did not [20].

Mortality

In 2013, 1 in 9 death certificates (284388 deaths) in the United States mentioned heart failure [20]. The number of any-mention deaths attributable to heart failure was approximately as high in 1995 (287000) as it was in 2013 (284000) [11]. Heart failure prognosis is poor, with a survival rate estimated at 50 % and 10 % over 5 and 10 years [21–23]. After age adjustment, 5-year mortality was 59 % in men and 45 % in women during 1990–1999 in the Framingham data [9], and 50 % in men and 46 % in women during 1996–2000 in Olmsted County [10]. Survival improvement in the elderly population was shown in data from the Kaiser Permanent system [8]; survival after diagnosis of HF improved by 33 % in men and 24 % in women and was primarily associated with beta blocker therapy. Data suggest a relative improvement in survival after development of HF [9, 10], but others challenge this, especially in the elderly [24]. Among Medicare beneficiaries, the overall 1-year HF mortality rate declined slightly from 1998 to 2008 but remained high at 29.6 % [25].

Overall, the absolute survival rate after a heart failure diagnosis remains low, and death has increased by 20.5 % in the past decade. In patients older than 67 years old, median survival is less than 3 years after hospitalization for HF [26].

Overall, improvement in survival of the hospitalized HF population is unclear but has been reported by some [27]. In one study, the median survival increase was associated with the effectiveness of angiotensin-converting enzyme inhibitors (ACEI) therapy, increasing from 1.2 to 1.6 years in a sample size of 66,547 patients. These results have been criticized because they were measured in hospitalized patients, without validation; thus, improvement outcomes may be biased by coding trends. Administrative data from the Henry Ford Health system that included outpatient encounters reported a median survival of 4.2 years without discernible improvement over time [26]. Finally, the mortality rate after hospitalization for HF in the Health ABC (health, aging, and body composition study) was 18.0 %, similar to other studies [5, 10, 28].

Diagnosis

Clinically, the ESC guidelines define HF as a “syndrome in which patients have typical symptoms and signs resulting from an abnormality of cardiac structure of function” [29]. The ACCF/AHA Heart failure guidelines [1] described the three most common presentations of patients that healthcare providers usually encounter:

1. With a syndrome of decreased exercise tolerance: Patients that seek medical attention with complaints of reduced effort tolerance, dyspnea and/or fatigue. These symptoms that may occur at rest may be inappropriately attributed by the patients and/or healthcare provider to aging, deconditioning, or other medical disorders (e.g., pulmonary disease)
2. With a syndrome of fluid retention: patients may present complaining of leg or abdominal swelling as their primary, or only, symptom.
3. With no symptoms or symptoms of another cardiac or noncardiac disorder: during the assessment for a disorder other than HF, patients may be found to have evidence of cardiac enlargement or dysfunction

Several diagnostic criteria exist, including the Framingham criteria [7] (Table 6.1), the Boston criteria [30] (Table 6.2), the Gothenburg criteria [31], and the European Society of Cardiology criteria [32]. When the Boston and Framingham criteria were compared blindly [33], their sensitivity was 100 %; however, the specificity and positive predictive value of the Framingham criteria were lower than the Boston criteria for definite heart failure. Some authors recommend use of the Boston criteria in older adults as it has been shown to improve adverse outcome predictability [34]. The comparison of the Cardiovascular Health Study criteria and the Framingham criteria offered similar results [35]. The Framingham criteria offer good performance and are well suited for secular trends as the criteria are unaffected by time and usage of diagnostic test. In earlier Framingham and Olmstead County studies, no survival improvement was reported when heart failure was validated using the Framingham criteria [36].

Once the HF diagnosis is established, further classification is determined by the presence of preserved or reduced ejection fraction (EF). A cut-off of 50 % is recommended by the AHA and ACC, and 55 % is recommended by the American Society of Echocardiography guidelines [37]. Heart failure with an EF of 50 % or greater in

Table 6.1 Framingham criteria

Major criteria	Minor criteria
Paroxysmal nocturnal dyspnea	Bilateral ankle edema
Neck vein distention	Nocturnal cough
Rales	Dyspnea on ordinary exertion
Hepatojugular reflex	Hepatomegaly
Acute pulmonary edema	Pleural effusion
Third sound gallop	Tachycardia (≥120 beats/min)
Increased central venous pressure (>16 cm water at the right atrium)	Decrease in vital capacity by 33 % from maximal value recorded
Radiographic cardiomegaly (increasing heart size on chest X-ray film)	
Pulmonary edema, visceral congestion or cardiomegaly at autopsy	
Weight loss ≥4.5 kg in 5 days in response to treatment of CHF	

Table 6.2 Boston criteria

History	
Rest dyspnea	4
Orthopnea	4
Paroxysmal nocturnal dyspnea	3
Dyspnea on walking on level	2
Dyspnea on climbing	1
Physical examination	
Heart rate (91–110 min, 1; >110/min, 2)	1–2
Elevated jugular venous pressure (>6 cm H_2O 2; >6 cm H_2O, plus hepatomegaly or edema 3)	2–3
Rales (basilar 1; > basilar 2)	1–2
Wheezing	3
S_3 gallop	3
Chest X-ray	
Alveolar pulmonary edema	4
Interstitial pulmonary edema	3
Bilateral pleural effusion	3
Cardiothoracic ratio > 0.5	3
Upper-zone flow redistribution	2

Table 6.3 Health ABC study risk factors

1. Age	
Modifiable risk factors	*Potentially modifiable risk factors*
2. CHD	7. Heart rate (75 beats.min)
3. LVH	8. Albumin level (3.8 g/dl)
4. Smoking	9. Renal function (GFR 60 mL/min/1.73 m^2)
5. Glucose level (125 mg/dl)	
6. SBP (140 mmHg)	

ABC aging and body composition, *CHD* coronary heart disease, *LVH* left ventricular hypertrophy, *SBP* systolic blood pressure, *GFR* glomerular filtration rate

the absence of major valve disease is defined as heart failure with preserved systolic function [38]. With this threshold, ejection fraction is preserved in more than half of heart failure cases in the community [39, 40]. Assessment of diastolic function, done with two-dimensional echocardiography-Doppler, is a class I indication in the heart failure guidelines [41]. Further, left ventricular function assessment is considered a performance measure for heart failure under the Joint Commission on Accreditation of Health Care Organizations (JCAHO) [42] as left ventricular dysfunction is associated with an increase in risk of sudden death [43].

Because not all patients have volume overload at the time of initial or subsequent evaluation, the term "heart failure" is preferred over the older term "congestive heart failure" [1]. The ACC/AHA guidelines adopted the term "heart failure with preserved ejection fraction" rather than "diastolic heart failure" [1, 41]. It was found that

the prevalence of heart failure with preserved ejection fraction in patients discharged between 1987 and 2001 increased. Prevalence increased from 38 to 47 % and then to 54 % in three consecutive 5-year periods. This was more common in community patients versus referral patients (55 % vs. 45 %). Prevalence of preserved ejection fraction in patients with a discharge diagnosis of heart failure was 49 % in patients 65 years or older and 40 % among those under the age of 65 [44]. There raises concern regarding potential misdiagnosis of heart failure in patients with preserved ejection fraction and mild symptoms not requiring hospital admission [45].

Risk Factors

The risk factor profile for cardiovascular disease is changing with increasing prevalence of obesity, metabolic syndrome, and diabetes mellitus [39]. In the Health ABC study (Table 6.3), nine variables were associated with heart failure and included (1) age, (2) left ventricular hypertrophy (LVH), (3) a history of smoking (4) coronary heart disease (CHD), (5) systolic blood pressure (SBP), (6) heart rate, (7) serum glucose, (8) albumin, and (9) creatinine. SBP was dichotomized as controlled vs. uncontrolled at 140 mmHg, fasting glucose level at 125 mg/dL, resting heart rate at 75 beats/min [46] and albumin level at 3.8 g/dL [47]. Smoking and CHD status were collapsed into binary predictors. Independent risk factors were classified as modifiable (CHD, LVH, smoking, glucose level, and SBP) and potentially modifiable (heart rate, albumin level, and renal function). In this study, most modifiable risk factors were significantly more prevalent among black participants (when compared with white participants). Numeric values have been assigned to each variable (Fig. 6.2), and it has showed value in predicting 5-year risk of incident heart failure in the elderly population. It has also showed promise aiding in the identification of subclinical cardiac structural changes and elevated natriuretic peptide levels in the 30–65 years of age population, suggesting it may potentially be a tool for identifying young individuals at increased risk for HF [48].

Blood pressure and coronary heart disease remain the leading causes of HF. A substantial proportion is attributed to metabolic and cardio-renal factors, including glucose level, renal abnormalities [49], and low albumin levels. It remains unclear whether a low albumin level signifies cachexia, inflammation, or comorbidity burden, or if hypoalbuminemia precipitates symptoms due to fluid extravasation [50]. Increased heart rate has been reported as a risk factor as it may represent a surrogate of vasovagal imbalance or a physiologic response to worsening cardiac function [51].

There seems to be a higher prevalence of LVH in blacks, which is consistent with the high prevalence of uncontrolled blood pressure in this population. LVH was encountered in 8.6 % of participants with systolic blood pressure of less than 140 mmHg. A higher incidence of heart failure among black participants [5] has also been described. Patients with preserved EF were older, more likely to be female, had a higher BMI, and were more likely to be obese, and hemoglobin levels were lower than those with reduced EF [44]. Much has been talked about gender

Age	
Years	**Points**
≤71	–1
72–75	0
76–78	1
≥79	2

Heart rate	
bpm	**Points**
≤50	–2
55–60	–1
65–70	0
75–80	1
85–90	2
≥95	3

Fasting glucose	
mg/dl	**Points**
≤80	–1
85–125	0
130–170	1
175–220	2
225–265	3
≥270	5

Coronary artery disease	
Status	**Points**
No	0
Possible	2
Definite	5

Smoking	
Status	**Points**
Never	0
Past	1
Current	4

Creatinine	
mg/dl	**Points**
≤0.7	–2
0.8–0.9	–1
1.0–1.1	0
1.2–1.4	1
1.5–1.8	2
1.9–2.3	3
>2.3	6

LV hypertrophy	
Status	**Points**
No	0
Yes	2

Albumin	
g/dl	**Points**
≥4.8	–3
4.5–4.7	–2
4.2–4.4	–1
3.9–4.1	0
3.6–3.8	1
3.3–3.5	2
≤3.2	3

Systolic blood pressure	
mmHg	**Points**
≤90	–4
95–100	–3
105–115	–2
120–125	–1
130–140	0
145–150	1
155–165	2
170–175	3
180–190	4
195–200	5
>200	6

Key:

Systolic BP to nearest 5mmHg
Heart rate to nearest 5bpm
Albumin to nearest 0.1g/dl
Glucose to nearest 5mg/dl
Creatinin to nearest 0.1mg/dl
HF=Heart failure

Health ABC HF risk score	HF risk group	5-yr HF risk
≤2 points	Low	<5%
3–5 points	Average	5–10%
6–9 points	High	10–20%
≥10 points	Very high	>20%

Fig. 6.2 The health ABC heart failure score

differences in the HF population, an analysis of the ADHERE-EM registry, where women were older than men, were more likely to have hypertension, and less likely to have diabetes or a smoking history compared to men. Women were also more likely to present with a SBP >140 mmHg, less likely to present with peripheral edema, and had a lower median blood urea nitrogen (BUN), creatinine, and troponin

T values at baseline. In the unadjusted Cox proportional hazard model, women had a lower 30-day all-cause mortality compared with men (hazard ratio [HR] 0.75, $p = 0.05$), but no significant difference in in-hospital mortality, median LOS, and 180-day mortality [52].

Heart failure can be conceptualized as a chronic disease epidemic with an increase in prevalence related to the aging of the population and the improvement of survival with heart failure [26].

It is important to characterize recurrent outcomes, like hospitalizations, in chronic diseases, and these have the potential of providing new insight on the outcome of heart failure by characterizing patterns of hospitalizations and identifying subjects at risk for recurrent hospitalizations that should be offered aggressive preventive strategies [42].

Conclusion

Heart failure is a public health problem with an ever increasing incidence and prevalence. The most affected population is older than 65 years of age and male. Heart failure is the most frequent cause of hospitalizations in this population, and mortality rate increases after hospitalizations due to heart failure. Risk factors that increase probability of developing heart failure have been identified, such as hypertension and coronary heart disease. Although scientific advances have been made in identifying laboratory parameters (glucose, albumin, and creatinine levels) that aid in the risk stratification of heart failure, validated diagnostic criteria/guidelines that utilize laboratory parameters to complement the clinical picture are needed. And while the economic burden of this disease is enormous, it will only increase as population ages, life expectancy increases, and new therapeutic measures emerge improving a somewhat grim prognosis for patients already with this disease.

The diagnosis of CHF required that two major or one major and two minor criteria be present concurrently. Minor criteria were acceptable only if they could not be attributed to another medical condition.

No more than four points allowed from each of the three categories:

No, possible, or definite heart failure if score equals 0–4, 5–7, and 8–12 points, respectively.

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Pathophysiology of Acute Decompensated Heart Failure

7

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Introduction

Acute decompensated heart failure (ADHF) is a state of circulatory dysfunction that develops rapidly to fulfill the classic definition of cardiac failure: inability of the heart to provide adequate cardiac output for the needs of the body's tissues. Current refinement of this definition recognizes that the basis of this syndrome is impairment of the integrated function of the heart, peripheral vasculature, and related neurohormonal (NH) systems [1]. ADHF is an increasingly common and potentially lethal cause of acute respiratory insufficiency. It is the primary diagnosis in almost 1 million hospital admissions in this country and the secondary diagnosis in close to 2 million [2, 3]. ADHF is usually superimposed on a background of chronic heart failure (HF) but it may occur de novo. In addition, patients hospitalized for heart failure have a high prevalence of severely impaired general health status on admission, which is associated with increased short-term mortality or rehospitalization for heart failure [4]. In this regard, it has recently been reported that risk of all-cause mortality was markedly greater in patients presenting with ADHF ≥80 years old than in those aged <70 [5]. Interestingly, analysis of temporal trends in hospitalization for ADHF has shown that this rate increased from 1998–2004 and stabilized from 2005 to 2011 [6]. The number of hospitalizations for ADHF during the latter period was close to 2 million.

The clinical presentation is typically characterized by acute dyspnea resulting from pulmonary congestion due to rapid fluid accumulation in the pulmonary interstitial spaces and alveoli. Transudation of fluid into the alveoli is the basis of

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pulmonary edema, the extreme form of ADHF, which has been referred to as "flash" pulmonary edema. The pathophysiology of flash pulmonary edema is similar to that of less severe ADHF, but the physiologic derangements are more marked and the therapeutic urgency greater.

Hemodynamic Dysfunction

There is normally a modest amount of transudation of protein-poor fluid from the pulmonary microcirculation into the pulmonary interstitium. The balance of this flux is determined by the interplay of hydrostatic and oncotic forces in the pulmonary microvessels, as described by the Starling relationship [7]. These forces are normally in approximate equilibrium at pressures of – 25 mmHg. The immediate cause of pulmonary congestion is a marked elevation of pulmonary capillary hydrostatic pressure that exceeds the oncotic pressure in these vessels. Acute pulmonary congestion, the clinical hallmark of ADHF, is due to a complex sequence of pathophysiologic events that increase the rate of fluid transudation into the pulmonary interstitium and alveoli. These events are initiated by a downward spiral of left ventricular (LV) systolic function resulting in reduced stroke volume and increased LV pressure. Whereas dilation of the right ventricle may be associated with acute pressure or volume overload, LV dilation is not characteristic of ADHF.

Rapidly progressive LV diastolic dysfunction, as caused by numerous hemodynamic and metabolic factors, may also initiate markedly elevated left atrial pressure with resultant ADHF. When this occurs, NH and renal compensatory mechanisms are evoked to augment fluid retention and maintain systemic perfusion pressure and blood flow [8, 9]. The resulting increase in intravascular volume and pressure further elevates LV diastolic pressure which is transmitted to the left atrium and retrograde to the pulmonary veins and capillaries, exacerbating the initial pulmonary congestion.

Irrespective of their origin, these physiologic derangements impair gas exchange between the alveoli and pulmonary capillaries, causing hypoxemia, acidosis, and dyspnea. Additionally, the increase in lung water reduces pulmonary compliance, thereby increasing the work of breathing and worsening the clinical state. Hypoxemia and acidosis can further reduce LV contractility and further exacerbate circulatory dysfunction. Thus, a vicious cycle of progressive circulatory decompensation can ensue (Fig. 7.1).

The pulmonary lymphatics have an essential role in the removal of excess lung water, and their function is a key determinant of the rate of fluid accumulation in the pulmonary vasculature [10]. Removal of fluid by the lymphatics is slower during acute accumulation than in the basal state. Therefore, pulmonary edema can occur at less elevated pulmonary pressures that are reached acutely than at higher pressures maintained chronically. This phenomenon is important in the pathogenesis of ADHF and especially of flash pulmonary edema.

Pathophysiology of Neurohormonal Compensatory Mechanisms

Neurohormonal controls play an essential role in the integration of normal circulatory physiology through the activity of the sympathetic nervous system, renin–angiotensin–aldosterone system, arginine vasopressin, and natriuretic peptides [1, 8, 9]. Endothelium-derived vasoactive factors and other mediators also contribute to this homeostatic organization. Several of these systems augment cardiac contractility, blood volume, sodium retention, and blood pressure, while others provide a counterbalance by promoting opposite cardiocirculatory effects. Under normal physiologic conditions, these mechanisms act in concert to modulate cardiac, renal, and vascular functions to maintain appropriate blood volume, perfusion pressure, cardiac output, and its distribution. However, when impairment of myocardial function results in reduced systemic perfusion, neurohormonal activity is augmented as a compensatory response to maintain cardiac output and blood pressure. Whereas this activation may be helpful for limited periods, the deleterious effects of excessive and persistent neurohormonal activity are central to the pathophysiology of chronic HF [1, 8, 9] (Fig. 7.1).

There is less information regarding the role of maladaptive neurohormonal mechanisms in ADHF, but it appears that they are also prominent in this syndrome. In patients with ADHF, evidence of augmented neurohormonal activation and inflammatory mediator function is reflected by increases in circulating norepinephrine, renin and angiotensin II, aldosterone, arginine vasopressin, endothelin 1, and other cytokines [11–17]. In addition, it has recently been reported that ST-2, a member of the interleukin family, is associated with increased cardiac structural abnormalities and is a powerful prognostic indicator in patients with ADHF [18].

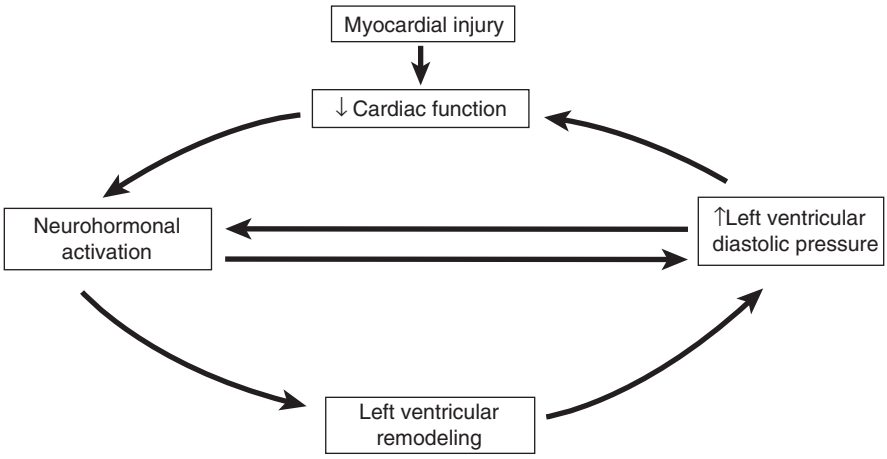

Fig. 7.1 Cardiac dysfunction in heart failure can be exacerbated by overactivation of initially compensatory neurohormonal systems

Excessive levels of these mediators have extensive pathophysiologic effects, including direct myocardial and vascular toxicity, decreased contractility, arrhythmias, vasoconstriction, increased cardiac afterload, renal sodium and water retention, and pulmonary congestion [9]. In addition, augmented activity of these mediators correlates with prognosis in patients with ADHF [18, 19]. These findings support the role of neurohormonal activation and increased cytokine activity in the pathogenesis of ADHF and have important implications for diagnosis, prognosis, and treatment.

The natriuretic peptides, of which B-type natriuretic peptide (BNP) is the most important, normally provide a counterbalance to the foregoing neurohormonal systems. BNP promotes natriuresis, reduces activity of the sympathetic nervous and rennin–angiotensin–aldosterone systems, inhibits vasopressin and endothelin, decreases systemic vascular resistance, and induces venodilation [20]. Thus far, the endogenous natriuretic peptides appear to have a relatively small role in the amelioration of ADHF. The clinical importance of BNP is in its use as a diagnostic tool and its therapeutic potential when applied in pharmacologic doses. BNP has assumed important diagnostic, therapeutic, and prognostic roles for managing patients with ADHF [21, 22]. In this regard, delayed measurement of BNP in patients with ADHF, which was accompanied by delayed treatment, was associated with increased mortality [23]. Further, it was recently reported that in patients admitted with ADHF, addition of NT-proBNP-guided therapy to multidisciplinary care improved clinical outcomes compared to multidisciplinary care alone, including mortality and rehospitalization [24].

As is clear from the foregoing, activation of the sympathetic nervous system, renin–angiotensin–aldosterone systems, vasopressin, and inflammatory markers in patients with HF has a profound and adverse effect on cardiac and renal function. The combination of this dual organ malfunction, which has been termed the cardiorenal syndrome [25], is associated with diuretic resistance and is common in ADHF. The pathophysiology of the syndrome appears to be related to a complex interplay of neurohormonal and hemodynamic mechanisms. It has important therapeutic and prognostic implications because conventional therapy is limited and clinical outcomes are poor. Whether worsening renal function specifically contributes to the progression of circulatory derangement or is a marker of advanced cardiac and kidney impairment is unclear [26].

Clinical Presentation

The demarcation between ADHF and chronic HF is not always clear. Three types of presentations of ADHF have been described [2]: (1) progressive worsening of chronic HF into decompensation, which comprises a majority of admissions; (2) de novo ADHF, comprising ~20% of patients; and (3) acute ADHF superimposed on the stable chronic HF state. The usual sequence of events, as previously described, is acute LV failure causing abrupt increase in LV pressure and pulmonary congestion/edema. These are followed by the compensatory mechanisms that can produce

further deterioration, which, if they persist, can progress to chronic HF. The ultimate clinical outcome is determined by the reversibility of ADHF, the underlying chronic pathophysiology, the triggers of ADHF, and the interplay of these variables.

In a typical clinical scenario, a patient with chronic HF will maintain stability unless there is a circulatory disruption that requires physiologic adjustment. Activation of the latter mechanisms to restore stable cardiac output and filling pressures can ultimately overwhelm homeostatic controls and result in the development of ADHF. When a patient arrives in the ED with ADHF, the critical efforts in the therapeutic process are rapid relief of pulmonary edema and improvement in oxygenation. This goal requires prompt relief of hemodynamic dysfunction to reduce left atrial pressure and alleviate pulmonary congestion [18]. Although it is common to observe rapid resolution of the acutely decompensated state by rapid reduction of preload and/or afterload, the hemodynamic adjustments initiated by most conventional acute therapies do not provide long-term circulatory stability [18, 19]. The derangements in the neurohormonal axis and other chronic control mechanisms that led to the decompensated state usually persist after the primary therapeutic interventions. Therefore, it is essential to immediately address these factors in the secondary phase of management.

Precipitating Factors and Clinical Outcome

Numerous clinical factors can provoke ADHF, and one or more precipitating factors or comorbidities have been identified in a majority of patients presenting with ADHF [2, 3, 27, 28]. Among the most frequent are myocardial ischemia, respiratory pathology, arrhythmias, uncontrolled hypertension, and dietary and medication noncompliance. Any of these factors singly or in combination can initiate the pathophysiologic processes resulting in acute circulatory decompensation when superimposed on chronic HF, or this may occur in the absence of the latter if the provocation is severe enough. Although average left ventricular ejection fraction is moderately reduced (35–40 %) in patients with ADHF, it is preserved in a large minority of this population. Mortality in patients with ADHF has been reported to be 3–4 % in hospitalized patients and 8–10 % at 60–90-day follow-up, which is higher than for patients presenting with acute myocardial infarction without HF [2, 29]. Unfavorable clinical outcome in ADHF is associated with advanced age, acute coronary syndrome, renal insufficiency, respiratory processes, and hyponatremia.

Therapeutic Implications of Excessive Neurohormonal Activation

Identifying precipitating factors, relieving symptoms, directly improving short- and long-term outcomes, and initiation and optimization of long-term therapies are the overall goals of therapy in ADHF. Based on the neurohormonal model of heart

failure and the pharmacologic actions of current therapeutic modalities, the limitations and potentially deleterious role of some of these approaches can be appreciated. Thus, although diuretics, vasodilators, and positive inotropic agents may afford symptomatic relief and important therapeutic benefits acutely, their excessive use can exacerbate underlying detrimental neurohormonal overactivity on the myocardium, vasculature, kidney, and fluid and electrolyte balance (Fig. 7.1). Diuretics and vasodilators stimulate further activation of the sympathetic nervous system, renin–angiotensin–aldosterone system, vasopressin, and endothelin, as do direct vasodilators [9]. Additionally, the unfavorable myocardial effects of positive inotropic agents are similar to those of the endogenous catecholamines described previously [28]. In addition, inotropic agents can increase atrial and ventricular arrhythmias [29]. These considerations have stimulated concern for judicious and physiologically rational application of these therapeutic approaches based on underlying pathophysiology to mitigate their undesirable effects. Novel neurohormonal antagonists have been investigated for ADHF. The oral direct renin inhibitor, aliskiren, recently demonstrated no beneficial effect on cardiovascular death or HF rehospitalization but increased adverse effects [30]. Serelaxin is a recombinant form of human relaxin-2 found to significantly improve HF signs and symptoms and markers of congestion and end organ damage [31].

Summary

ADHF is an increasingly common and potentially lethal form of heart failure. It is usually superimposed on a background of chronic HF, but it may occur de novo. Numerous provoking factors have been identified, and most patients with ADHF have important comorbidities. Early repeat hospitalizations are common in this patient population, which has a high short-term posthospital mortality. The maladaptive compensatory neurohormonal mechanisms that contribute to chronic HF are also operative in ADHF. Although conventional therapy with diuretics and positive inotropic agents may yield early salutary clinical results, caution must be exercised with these methods because they have the potential to further augment adverse neurohormonal activation. The cardiorenal syndrome is a particularly challenging complication, the precise mechanisms of which have not been clarified. It is anticipated that current investigation of ADHF will afford enhanced approaches to its management.

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Part III

Emergency Medical Services and Emergency Department Assessment and Treatment of Acute Heart Failure

The Out-of-Hospital Management of Acute Heart Failure

8

Andrew M. McCoy, Richard B. Utarnachitt, and Marvin A. Wayne

Introduction

Emergency medical services (EMS) personnel frequently encounter patients with acute heart failure (AHF). Nearly one million hospitalizations annually are for AHF [1], and many of these patients are initially cared for by EMS in the prehospital setting. AHF is one of only two cardiovascular diseases with an increasing prevalence; the other is atrial fibrillation. Five million Americans have the disease, and more than 500,000 are newly diagnosed each year. AHF is a major disease of our aging population [2] as most hospitalizations for AHF involve patients older than 65 years [3]. AHF is not only very prevalent, but also very deadly. The mortality rate for AHF has been reported to range from 8 to 25 % [4]. Favorable outcome for AHF is dependent on rapid assessment and treatment initiated in the out-of-hospital setting [5–10].

Acute heart failure is defined as the abrupt onset or the rapidly progressive development of significant symptoms related to inadequate myocardial pumping function. Most commonly, AHF presents as respiratory distress due to pulmonary congestion but can also present as poor systemic perfusion with or without pulmonary congestion. Some cardiology organizations have classified the variety of AHF

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presentations into these syndromes: acute decompensated heart failure (new or acute on chronic), hypertensive AHF, acute pulmonary edema, cardiogenic shock, high-output failure, and right heart failure [11].

Heart failure represents a significant percentage of the patients treated in the prehospital environment for shortness of breath. Of all patients transported by advanced providers for shortness of breath over a period of 4 years in a single county, 15 % were found to have a hospital discharge diagnosis of heart failure. Many of these were misdiagnosed by the prehospital providers as COPD, asthma, and other diagnoses [12].

However, these are not distinct categories clinically, and during initial assessment and management, it is often difficult to clearly distinguish. Therefore, we prefer classifying AHF patients more in the manner of Mebazaa and colleagues [13], who suggested the following clinical scenarios:

1. Dyspnea with high SBP >140 mmHg
2. Dyspnea with normal SBP 100–140 mmHg
3. Dyspnea with low SBP <100 mmHg
4. Dyspnea with sign of acute coronary syndrome
5. Isolated right ventricular failure

Pathogenesis of Acute Heart Failure

Understanding the pathophysiology of AHF is helpful for appreciating the clinical presentation and for classifying patients into the above categories. This will lead to more specific and patient-tailored therapy.

AHF has a number of underlying etiologies as listed in Table 8.1. Nearly half of these cases are due to acute coronary syndrome, and another quarter are related to acute worsening of myocardial function (either systolic or diastolic). Please refer to Chap. 7 for full discussion of the pathophysiology of AHF.

Table 8.1 Precipitating causes of acute cardiogenic pulmonary

Edema (APE)	
Cause	Incidence (%)
Worsening heart failure	26
Coronary insufficiency	21
Subendocardial infarction	16
Transmural infarction	10
Acute dysrhythmia	9
Medication noncompliance	7
Dietary indiscretion	3
Valvular insufficiency	3
Other	5

From Marx et al. [44], with permission

It is important to appreciate that the pulmonary congestion is a reflection of increased volume and pressures in the left ventricle and left atrium and that often these patients are not volume overloaded. Rather the insufficient pumping of the heart leads to a redistribution of body water [14]. Over time and left untreated, most patients will also develop excess total body water, but this is not typically the case with acute exacerbations, particularly new onset heart failure (e.g., due to large myocardial infarction or acute value dysfunction) or exacerbations of heart failure under effective long-term therapy.

Field Assessment

Assessment begins with a rapid, focused history and physical examination of the patient. This includes acute symptoms, recent illness, past history and prescribed medications, medication compliance, and diet. Together, this constitutes an important first step in the field diagnosis of AHF (Table 8.2). Critical elements of the physical examination include accurate determination of vital signs. Prehospital providers, even in the absence of peripheral edema, should strongly consider cardiogenic pulmonary edema in patients presenting with acute respiratory distress, hypoxemia, tachypnea, rales or wheezing, and marked hypertension. Such patients often have histories of poorly controlled hypertension and/or prior cardiac disease.

Table 8.2 Diagnosis of congestive heart failure

Prior history and comorbid states
Chronic heart failure
Hypertension
Ischemic heart disease
Valvular heart disease
Anemia
Dysrhythmias
Thyroid disease
Current situation
Medications (prescribed regimen and current compliance, other drug use)
Symptoms of acute coronary syndromes
Diet or exercise indiscretions in patients with known heart failure
Signs of pulmonary edema such as tachypnea, low oxygen saturation, rales, and peripheral edema
Lack of signs of chronic obstructive pulmonary disease, asthma, or airway obstruction
Lack of signs of pneumonia or sepsis, such as fever and purulent sputum
Tools
Pulse oximetry
End-tidal carbon dioxide waveform morphology and trending
12-lead ECG and continuous rhythm monitoring

Blood pressure of greater than 180/120 mmHg is common in this setting and is a good sign of reversibility. In these patients, a rapid reduction in blood pressure often produces prompt relief of respiratory distress. Marked hypertension associated with acute respiratory distress and wheezing, particularly in elderly patients without a history of asthma or pulmonary infection, is strongly suggestive of AHF. Such a presumptive diagnosis may be supported by the presence of cardiovascular medications and the absence of respiratory medications, such as metered-dose inhalers. Even when these facts are present, out-of-hospital personnel should always consider alternate etiologies such as pulmonary embolism, pneumonia, COPD and asthma, and drug overdose before diagnosing patients as having APE. Cardiac rhythm monitoring and 12-lead electrocardiograms (ECGs) are essential in patients suspected of AHF, particularly for identifying arrhythmia and/or acute coronary syndrome that may be the inciting event, and should be placed on the patient shortly after arrival on the scene.

Electrocardiogram

A 12-lead ECG should be obtained on all patients to ascertain the presence of acute and/or chronic cardiac changes that may be creating or contributing to the current episode.

In addition to the ECG, a number of other diagnostic aids have been developed to improve accuracy in the evaluation and diagnosis of AHF. Although not currently used in the prehospital environment, a rapid bedside assay of blood levels of B-type natriuretic peptide (BNP) is now available. BNP is a neurohormone secreted mainly by the cardiac ventricles in response to volume expansion and pressure overload which rises in the setting of acute heart failure [15–20]. Application of such testing in the out-of-hospital environment may be a logical extension and further aid in diagnosis. Noninvasive cardiac output (NICO) devices, such as impedance cardiography [21, 22], have also been suggested as diagnostic tools, but their complexities and cost have to date precluded their out-of-hospital use.

APE is often difficult to distinguish clinically from an exacerbation of chronic obstructive pulmonary disease (COPD) or other acute pulmonary disorders. The misdiagnosis of AHF in the out-of-hospital setting has been documented to be 23 % in one study [23] and 32 % in another [24]. The need for the correct identification of precipitating events, and the rapid initiation of appropriate treatment, is critical to achieve a positive outcome. Inappropriate therapy, as a result of misdiagnosis, may result in harm to the patient. Hoffman and Reynolds reported that adverse effects were more common in misdiagnosed patients. Untoward effects included (a) respiratory depression in patients receiving morphine, (b) hypotension and bradycardia in patients receiving both morphine and nitroglycerin, and (c) hypotension and arrhythmias associated with hypokalemia in patients receiving furosemide.

Emergency Medical Services Scope of Practice

An understanding of the scope of practice of EMS providers is critical to the discussion of the interventions that might be utilized in the prehospital care of AHF. While some countries, primarily European, staff their EMS with physicians and nurses, the majority of countries use individuals with limited and specific training in out-of-hospital care of the acutely ill and injured.

Although there is some degree of variability in differentiation, most of the western hemisphere and Australia utilize a tiered level of providers who at entry have the training and equipment to provide basic life support care for cardiac arrest and provide first aid care to victims of trauma and those complaining of chest pain and respiratory distress. The highest qualification of training includes the ability to administer drug therapy and utilize advanced airway techniques. For purposes of illustration, the US EMS scope of practice will be presented.

The United States has adopted the National Scope of Practice for EMS providers, a document created by the National Highway and Traffic Safety Administration in 2007. This describes four levels of prehospital providers. The first level, the emergency medical responder (EMR), was previously titled the first responder. This provider is trained in CPR and the use of the automatic external defibrillator (AED), as well as basic first aid, including oxygen administration and care of simple trauma. They are not associated with transportation of the patient by ambulance.

The following are the minimum psychomotor skills of the EMR:

- Airway and breathing
  - Insertion of airway adjuncts intended to go into the oropharynx
  - Use of positive pressure ventilation devices such as the bag valve mask (BVM)
  - Suction of the upper airway
  - Supplemental oxygen therapy
- Pharmacological interventions
  - Use of unit-dose auto-injectors for the administration of life-saving medications intended for self- or peer rescue in hazardous materials situations (e.g., MARK I, etc.)
- Medical/cardiac care
  - Use of an automated external defibrillator
- Trauma care
  - Manual stabilization of suspected cervical spine injuries
  - Manual stabilization of extremity fractures
  - Bleeding control

The next level is the emergency medical technician (EMT). This provider has the capabilities of the EMR, in addition to noninvasive monitoring and assisting the patient with the administration of their own medications. This level of provider is given minimal education in pathophysiology, and their treatments are primarily

driven by patient complaint and symptoms. As for airway management, some states currently allow this level to place blind insertion airway devices (BIAD) such as the King LT or Combitube. This level of provider is the minimum allowed to transport the patient in an ambulance.

The following are the minimum psychomotor skills of the EMT:

- Airway and breathing
  - Insertion of airway adjuncts intended to go into the oropharynx or nasopharynx
  - Use of positive pressure ventilation devices such as manually triggered ventilators and automatic transport ventilators
- Pharmacological interventions
  - Assist patients in taking their own prescribed medications, such as inhaled bronchodilators
  - Administration of the following medications with appropriate medical oversight:
    - Oral glucose for suspected hypoglycemia
    - Aspirin for chest pain of suspected ischemic origin

The next level, the advanced EMT (AEMT), is able to establish an intravenous line and administer a limited list of medications. Many states currently allow the EMT to administer many of the medications listed only for the advanced EMT.

The following are the minimum psychomotor skills of the AEMT:

- Airway and breathing
  - Insertion of airways that are NOT intended to be placed into the trachea
  - Tracheobronchial suctioning of an already intubated patient
- Assessment
- Pharmacological interventions
  - Establish and maintain peripheral intravenous access.
  - Establish and maintain intraosseous access in a pediatric patient.
  - Administer (non-medicated) intravenous fluid therapy.
  - Administer sublingual nitroglycerin to a patient experiencing chest pain of suspected ischemic origin.
  - Administer subcutaneous or intramuscular epinephrine to a patient in anaphylaxis.
  - Administer glucagon to a hypoglycemic patient.
  - Administer intravenous dextrose to a hypoglycemic patient.
  - Administer inhaled beta-agonists to a patient experiencing difficulty breathing and wheezing.
  - Administer an opioid antagonist to a patient suspected of opioid overdose.
  - Administer nitrous oxide for pain relief.

The highest defined prehospital provider level is the paramedic. This level is permitted to administer the widest range of medications and procedures which are

usually limited only by medical director authorization and in some instances state rule.

The following are the minimum psychomotor skills of the paramedic:

- Airway and breathing
  - Perform endotracheal intubation (ETI).
  - Perform percutaneous cricothyrotomy.
  - Decompress the pleural space.
  - Perform gastric decompression.
- Pharmacological interventions
  - Insert an intraosseous cannula.
  - Enteral and parenteral administration of approved prescription medications.
  - Access indwelling catheters and implanted central intravenous (IV) ports for fluid and medication administration.
  - Administer medications by IV infusion.
  - Maintain an infusion of blood or blood products.
- Medical/cardiac care
  - Perform cardioversion, manual defibrillation, and transcutaneous pacing.

The Emergency Medical Services Challenge

Due to the significant variability in scope of practice by the four EMS levels of training, the ability to provide care for the patient with AHF is limited by state or local implementation of this scope of practice model and the willingness of an EMS medical director to authorize various treatment modalities.

At first blush, the National Scope of Practice model would appear to limit the administration of nitroglycerin for AHF only to paramedics. This would limit care for many persons living in areas with only basic life support EMS response, which is often the case outside urban areas. However, since the EMT may assist the patient with administration of their own medications, and it is reasonable to assume that a large number of AHF patients would have NTG prescribed by their physician, EMS personnel will be able to help assure properly aggressive treatment with NTG.

Continuous positive airway pressure (CPAP) ventilation involves the administration of oxygen via a positive pressure device for spontaneously breathing patients. The EMT is allowed to assist a patient's ventilations with a BVM and to provide positive pressure ventilation to the cardiac arrest victim. The application of CPAP has proven clinical benefit, is arguably easier than ventilating with a BVM, and has a similar or lower risk of adverse effects, so an increasing number of areas do allow EMTS to utilize this modality.

For the medical director of a paramedic service, the greatest challenge has been to adopt treatment protocols based on the current understanding of the pathophysiology of AHF. Traditionally, the use of diuretics by EMS has been commonplace, and the role of nitroglycerin has not been well accepted. Many service protocols include the administration of morphine for AHF despite no data to

support its use. Further, some services that include NTG in their protocols are extremely conservative, allowing paramedics to administer NTG in a manner more appropriate for angina than the high adrenergic state of AHF. Some also rely too heavily on the transdermal route of NTG despite the poor pharmacodynamic properties of this route.

Prehospital Management of Acute Pulmonary Edema

The prehospital management of AHF must be tempered by the inherent limitations of assessment modalities, diagnostic testing, and personnel expertise in this setting. The focus should be on therapies that will most likely lead to immediate benefit with low risk of harm should the working diagnosis of AHF be incorrect. Even in the emergency department, the primary condition causing the patient's dyspnea and other symptoms may not be clear. Primary objectives for the treatment of AHF are to reduce pulmonary capillary hydrostatic pressure, to redistribute pulmonary fluid, and to improve forward blood flow. These goals may be achieved by reducing LV preload and afterload, providing ventilatory and inotropic supports, and identifying and treating the underlying etiology of the syndrome (Table 8.3).

Notwithstanding the inherent limitations of blood pressure as a reflection of perfusion, from a practical standpoint, it is perhaps the best initial gauge for directing therapy of AHF. Table 8.4 presents an approach to therapy based on blood pressure. As blood pressure changes, then therapies should change accordingly. While clinical judgment and consideration of patient-specific factors must impact treatment decisions, this table should provide a useful conceptual guide to serve as a starting point.

General therapy in addition to above specific measures:

1. IV access.
2. 12-lead ECG and monitor cardiac rhythm (rate and rhythm management as indicated).
3. ASA (chewed) and transport to PCI-capable facility, if concern for ACS.
4. Bronchodilator (nebulized) if wheezing.
5. Waveform capnography if available to monitor ETCO2; waveform may help in diagnosis.

Table 8.3 Management of acute congestive heart failure: overview

Identify CHF
Identify and treat specific etiology when possible
Provide oxygen and ventilatory support when needed
Reduce LV preload
Reduce LV afterload
Provide inotropic support when needed
Select receiving facility based on needed resources

Table 8.4 Hemodynamic approach to AHF treatment

Systolic blood pressure	Hemodynamic management Goal is normalizing systemic perfusion and cardiac preload/afterload	Oxygenation and ventilation Goals are O_2 sat 94–99 %, adequate air exchange and relief of dyspnea	Volume management Goal is appropriate amount of intravascular and total body water
>150	Aggressive use of vasodilators (high-dose nitrates, consider ACE inhibitors)	High-flow oxygen, strongly consider CPAP	Diuresis if evidence of peripheral edema
90–150	Careful use of vasodilators (low-dose nitrates)	Oxygen as needed to maintain sat, consider CPAP if significant respiratory distress	Diuresis if evidence of peripheral edema
70–89	Inotropic agents (dobutamine)	Oxygen to maintain sat, CPAP with extreme caution (hypotension, AMS)	Avoid diuresis and consider need for careful IV fluid administration
<70	Dual inotropes/vasopressors (dopamine, norepinephrine), mechanical assist (aortic balloon pump)	Oxygen to maintain sat, consider intubation and mechanical ventilation	Avoid diuresis Administer IV fluids unless clear pulmonary congestion, especially if using PPV

CPAP continuous positive airway pressure, *AMS* altered mental status, *IV* intravenous, *PPV* positive pressure ventilation

Reduction of Left Ventricular Preload

The initial effort to reduce the pulmonary congestion in patients presenting with APE should be to reduce the pressure and volume of blood flow to the pulmonary vasculature. This may be accomplished by dilating the venous capacitance system. This will result in decreased blood return to the right ventricle (preload), hence reducing blood flow to the pulmonary vascular bed. The net result is a reduction in LV preload, which then allows the LV output to more closely match inflow from the pulmonary system. Pharmacologic therapy to reduce LV preload includes the use of nitrates primarily. Loop diuretics such as furosemide should only be used in the prehospital setting when there is clear evidence of total volume overload, such as worsening peripheral edema or known acute weight gain. Morphine and other opioids should be avoided.

Nitrates

Nitroglycerin and related drugs at low dosages are primarily venodilators but also cause arterial vasodilation at higher doses. Intracellularly, they react with and convert sulfhydryl groups to S-nitrosothiols and nitric oxide. These reactive groups

then activate the enzyme guanylate cyclase which catalyzes the formation of cyclic guanosine monophosphate (cGMP). This nucleotide induces the reentry of calcium back into the sarcoplasmic reticulum of vascular smooth muscle, thereby causing its relaxation.

Nitroglycerin is currently the vasodilator agent of choice for the reduction of LV preload in the field setting. It is fast acting, efficient, and easy to administer [25]. Nitroglycerin's effectiveness in reducing mortality in patients with APE in the prehospital setting has been demonstrated by Bertini [26]. In this study, even hypotensive patients (systolic blood pressure <100 mmHg) were found to respond positively to nitroglycerin. Likewise, Hoffman and Reynolds compared a number of prehospital management protocols for APE and concluded that nitroglycerin was beneficial, whereas morphine and furosemide had no additive effect when combined with nitroglycerin and were occasionally deleterious. Higher than conventional doses of sublingual nitroglycerin (0.8 mg and 1.2 mg vs. 0.4 mg) have been recently studied and found to be safe [27]. The beneficial vasodilation effect of nitroglycerin must be closely monitored to avoid excessive reduction in blood pressure, which may occur from both the decrease in venous return and arterial vasodilation. Thus, a potential disadvantage of nitroglycerin is that it can lead to excessive hypotension, particularly in patients without adequate preload (e.g., hypovolemia and inferior wall myocardial infarction (MI) with significant right ventricular (RV) involvement). Note that nitrates should be avoided in patients who recently took a phosphodiesterase inhibitor [these are drugs used for pulmonary hypertension and erectile dysfunction, such as Viagra (sildenafil), Levitra (vardenafil), and Cialis (tadalafil)].

Morphine

Although morphine has been used for decades to treat acute MI, unstable angina, and AHF, few clinical trials have demonstrated its effectiveness for these conditions. Its popularity in treating pulmonary edema arose because of its vasodilatory and antianxiety effects. However, morphine's vasodilatory effects are transient and are the result of histamine release. Recently, concerns have been raised over the use of morphine in treating AHF in the ED. A retrospective study of the ED management of APE and intensive care unit (ICU) admissions showed that morphine administered in the ED was associated with significant increases in ICU admissions and the need for ETIs when compared with treatment with sublingual captopril [28].

A prospective study of morphine use in prehospital APE treatment showed that the drug was minimally effective as single therapy or in combination with nitrates [23]. Furthermore, the effects of morphine in depressing respiration and the central nervous system may be particularly deleterious in misdiagnosed patients. The authors strongly recommended against using morphine for routine treatment of acute heart failure.

Furosemide

Furosemide has been a mainstay of treatment for APE since the 1960s although its effectiveness has been examined in only a few studies. Its primary mechanism of action involves the inhibition of sodium reabsorption in the ascending limb of Henle's loop in the renal medulla. This results in an increased excretion of salt and water in urine. The net effect of this action is a lowering of plasma volume, a decrease in LV preload, and a decrease in pulmonary congestion. These effects are beneficial in patients presenting with cardiovascular volume overload. In addition to its diuretic effects, furosemide also induces neurohumoral changes. These include both vasodilatation (by promoting renal prostaglandin E2 and atrial natriuretic peptide secretion) and vasoconstricting effects. The latter, via the feedback loop, can result in peripheral elevation of mean arterial pressure, LV pressure, heart rate, and systemic vascular resistance through enhancement of the renin–angiotensin system (RAS). Stroke volume index and pulmonary capillary wedge pressure initially decrease but subsequently increase after the RAS enhancement (usually within 15 min). The latter effects are not beneficial in the treatment of AHF particularly in the absence of volume overload [29]. Furthermore, misdiagnosis of AHF and subsequent inducement of inappropriate diuresis can lead to increased morbidity and mortality in patients with other conditions such as pneumonia, sepsis, or COPD. Thus, while furosemide is still an important and beneficial component of medical therapy for chronic heart failure, it should be used very judiciously for the initial treatment of AHF. There has been some evidence that administration of furosemide is safe in acute decompensated heart failure in the prehospital setting [30, 31]. Because of the limited patient information and evaluation capabilities inherent in the prehospital environment, furosemide should be reserved for selected cases when it will be clearly safe to administer [32].

Combined Drug Therapies with Nitroglycerin, Furosemide, and Morphine

Nitrates are frequently combined with loop diuretics in treating pulmonary edema. A complex, randomized, prospective clinical study from Israel investigated the efficacy and safety of these drugs in treating patients presenting with severe pulmonary edema in the prehospital setting [33]. This study concluded that intravenous (IV) nitrates administered as repeated high-dose boluses (3 mg every 5 min) after a low dose (40 mg) of furosemide were associated with lower ETI and MI rates than the administration of low-dose nitrates (1 mg/h, increased by 1 mg/h every 10 min) and high-dose furosemide (80 mg every 15 min). A prospective observational study on the use of sublingual nitroglycerin in the prehospital setting in 300 patients with presumed MI or CHF analyzed treatment-related adverse events. Only four patients experienced adverse events, most of which were bradycardic–hypotensive reactions, and all recovered subsequently [34].

A retrospective case review evaluated outcomes of 57 patients presumed to have prehospital APE who were treated in the field with combinations of nitroglycerin, furosemide, and/or morphine [11]. Although only a small study, any combination treatment including nitroglycerin was associated with both subjective and objective (respiratory and heart rates, blood pressure, respiratory distress, mental status) improvement. Combination treatment with furosemide and morphine without nitroglycerin, on the other hand, resulted in a substantial number of patients not responding to treatment and some actually deteriorating. Ultimately, 23 of 57 (47 %) patients in this study were found not to have pulmonary edema. A larger retrospective case series evaluated outcomes in 493 patients receiving prehospital nitroglycerin, furosemide, and/or morphine versus no treatment for CHF. Mortality was significantly reduced in those receiving any prehospital drug treatment but especially in the subset of critical patients (5 % vs. 33 %, $p < 0.01$) [35].

Reduction of Left Ventricular Afterload

A variety of pharmacologic agents, including nitroglycerin at higher doses, angiotensin-converting enzyme (ACE) inhibitors, nitroprusside, dobutamine, and dopamine, may be useful in the reduction of LV afterload. Most of these are not commonly used in the prehospital environment.

Nitrates at Higher Doses

High-dose nitrates can reduce both preload and afterload.

CHF patients present with very elevated arterial and venous pressures; frequent doses of nitrates may be required to control blood pressure and afterload. Some patients develop tolerance to nitroglycerin, but this is not of concern in the prehospital environment. Another concern with high-dose nitrates is that certain patients are very sensitive to even normal doses and may experience marked hypotension. These are typically patients with tenuous preload status (e.g., preexisting hypovolemia or significant RV infarction in the setting of inferior wall MI). It is therefore critical to monitor blood pressure during high-dose nitrate therapy [27].

Ventilatory Support

Patients with acute CHF may be treated with a spectrum of ventilatory support modalities based on the patient's clinical condition and comorbid factors. Initial treatment includes oxygen therapy to maintain oxygen saturation of at least 93–94 %. Current guidelines recommend oxygen administration only as needed and to the extent needed to maintain this level of saturation. Inhaled bronchodilators should be administered when bronchospasm is evident. True bronchospasm may be triggered

by interstitial edema, especially in patients with underlying reactive airway disease. Initial concerns that the beta-agonist effect of bronchodilators such as albuterol could result in injury to the myocardium were dispelled by a study that found no rise in cardiac necrosis markers in AHF patients receiving bronchodilators [38].

In cases of severe respiratory distress or impending respiratory failure (ineffective respiratory effort, hypoxemia, hypercarbia), assisted ventilation is needed. Traditionally, this has been accomplished in tandem with ETI. However, ETI is a challenge to accomplish effectively in noncomatose, nonparalyzed patients with the limited resources and personnel usually available in the field setting. Further, ETI is associated with various infectious (e.g., nosocomial pneumonia, sinusitis) and noninfectious complications (e.g., barotrauma; oral, nasal, or laryngeal trauma; respiratory muscle weakness; prolonged weaning). To avoid these complications and lengthy ICU stays, noninvasive ventilatory support is being increasingly used. ETI remains necessary when altered mental status requires airway protection or when other patient characteristics prevent the successful application of noninvasive positive pressure ventilation.

Noninvasive Positive Pressure Ventilation

Noninvasive positive pressure ventilation (NIPPV) is now considered an effective adjunctive treatment of AHF/APE [37–39]. NIPPV improves ventilation and oxygenation in the patient with APE by several mechanisms. Its ability to increase intra-alveolar air pressure shifts the flow of fluid back into the pulmonary capillaries and thereby reduces pulmonary congestion and opens more alveolar for effective gas exchange. NIPPV decreases the mechanical work of breathing and thereby decreases myocardial demand. Two different methods of providing NIPPV are used: continuous positive airway pressure (CPAP), which provides a constant level of positive pressure applied throughout inspiration and exhalation, and bi-level positive airway pressure (BiPAP), which allows provision of higher pressure during inspiration than expiration.

The concept of prehospital CPAP administration was examined by Kosowsky and found safe and practical [24]. In this study, trained paramedics applied CPAP in 19 patients with cardiogenic pulmonary edema and showed that none required field intubation and that hemoglobin oxygen saturation increased from a mean of 83.3–95.4 % after CPAP administration via a face mask. Two patients intolerant of CPAP required ETI on ED arrival, and an additional five patients required ETI within 24 h. There were no adverse events related to CPAP therapy. Since then, there have been several prehospital studies to examine the value of prehospital CPAP.

Hubble and Richards [4] examined the impact of CPAP by EMS when they implemented it in one of two adjoining counties. Care in both county systems was the same except for the addition of CPAP by one. In the county without CPAP, 25 % of the AHF patients required intubation, while in those receiving CPAP, only 9 % required intubation. Those without CPAP were also more likely to die (odds ratio 7.4).

Another prehospital study [40] found a 30 % reduction in the need for intubation and a 21 % absolute reduction in mortality following application of CPAP by paramedics.

BiPAP has been investigated as an alternative to CPAP in a number of conditions but has shown a significant advantage over CPAP only in patients whose respiratory failure is due to COPD exacerbation [41]. A number of individual studies reported some success with BiPAP, and some problems, including increased rates of MI [42], associated with its use in treating acute CHF.

In an out-of-hospital study of patients with presumed CHF, EMS personnel considered the use of BiPAP to be safe and judged this method to improve dyspnea and respiratory distress in their patients [42]. Although oxygen saturation was significantly greater for the BiPAP plus conventional treatment group, compared with the conventional treatment group, treatment times, length of hospital stay, intubation rate, and death rates were not significantly different between the groups. Of the two types of noninvasive ventilatory support, there is good supporting evidence for the effectiveness of CPAP. The technology is reasonable for field implementation, but there is room for further refinement, especially regarding the volume of oxygen required. Greater experience of field providers should also lead to better outcomes because this therapy is not only patient dependent but operator dependent as well. In the case of BiPAP, the risk–benefit ratio is conflicting in the literature. In addition, the existing technology for BiPAP is suboptimal for out-of-hospital use. However, this too may show greater field use in the future.

This review focuses on the importance of understanding that the pathogenesis of AHF is usually related to intravascular fluid redistribution rather than to primary volume overload. Management of suspected AHF begins with correct assessment and management of underlying causes of elevated ventricular filling pressures and continues by improving oxygenation with the application of ventilatory support, reduction of LV preload and afterload with nitroglycerin, and inotropic support in the setting of symptomatic hypotension.

The EMS scope of practice places both limitations as well as unique opportunities for the implementation of appropriate prehospital treatment of AHF. The EMS medical director must understand the national, state, and local scope of EMS practice to determine the best method to implement the following therapies.

Finally, EMS personnel should choose an appropriate receiving facility for the patient with moderate or severe AHF. In particular, this decision should be guided by concern for ACS, particularly STEMI, and by the potential needed for advanced invasive therapies such as aortic balloon pump. Transport time and distance considerations and the level of providers are also important considerations.

Nonacute Prehospital Management of Heart Failure

The increasing use of community paramedicine in various incarnations throughout the country has often involved assessment of heart failure patients in their home-living situation on non-emergency days. This may include routine weight assessments, peripheral edema assessment, and other measures of chronic illness. These

programs often partner with local hospitals to reduce readmissions that would otherwise not be compensated per Center for Medicare and Medicaid Services rules. Some of these programs also result in triage of patients to destinations other than emergency departments. Data regarding the effectiveness of these programs is not yet available, but will be forthcoming in the near future [43]

Conclusion

AHF is a common and often life-threatening condition encountered by prehospital emergency medical personnel. Patients with this condition must receive rapid, accurate assessment and aggressive treatment. For patients with elevated blood pressure, high-dose nitrates represent the out-of-hospital treatment of choice, whereas diuretics and morphine should be reserved for select patient groups. More data are needed on the efficacy and safety of ACE inhibitors to justify their use in the field. CPAP has been shown to be effective, and the growing clinical experience in the prehospital setting has been strongly positive. Emerging diagnostic assays and tools offer promise of fast and accurate diagnosis of CHF. Finally, transport of APE patients should be matched with the cardiovascular care resources of receiving facilities to optimize chances of survival.

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Dyspnea Assessment and Airway Management in Acute Heart Failure Patients

9

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Dyspnea is the most common presenting symptom in patients with acute heart failure (AHF) [1–4]. Alleviating breathlessness is a critical goal of early AHF management. For the vast majority of patients, traditional AHF therapies such as intravenous (IV) loop diuretics, vasodilators such as nitroglycerin or ACE inhibitors, and supplemental oxygen are able to improve dyspnea [5]. For other patients, the severity of their respiratory distress requires the use of additional treatment modalities, such as noninvasive positive pressure ventilation or rarely endotracheal intubation, to ensure adequate oxygenation and ventilation. In this chapter, we review the assessment of dyspnea followed by airway management in AHF.

Assessment of Dyspnea

Despite the importance of dyspnea relief to patients and caregivers, as well as its use as an endpoint in clinical trials, no validated dyspnea assessment tool currently exists [6]. Measurement scales such as Likert or visual analog scales are commonly utilized instruments used to assess dyspnea in nearly every large pharmacologic clinical trial to date [6–8]. From a clinical perspective, however, the severity of dyspnea is rarely quantitatively assessed; rather, its presence or absence combined with a clinical impression regarding its severity guides immediate management. Furthermore, the exact pathophysiologic mechanisms by which AHF patients experience the sensation of dyspnea are not fully known [9]. Thus, targeting another parameter, for example, high blood pressure, with the goal of alleviating dyspnea has been proposed, but this relationship has yet to be conclusively defined [10–12]. Retrospective analyses demonstrate an association between dyspnea and hard outcomes (i.e., death, rehospitalization). While these findings require prospective

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confirmation, intuitively, patients with persistent symptoms despite treatment likely predict a worse outcome [13].

Guidelines on assessment of dyspnea in AHF or dyspnea-guided therapy do not exist, alluding to the lack of evidence in this area. Alternatively, current therapy appears to improve but not completely resolve dyspnea in many patients. A commonly used classification scheme used in chronic HF is the New York Heart Association (NYHA) classification, where the presence or absence of dyspnea is a dominant classification characteristic (see Table 9.1). As patients commonly complain of dyspnea at time of arrival to the hospital, this is not as useful in AHF; most patients would be categorized as Class III or IV.

At the present time, we suggest the following: (see Table 9.2) [1] All patients who present with AHF should be asked if they feel short of breath, or have a sensation of breathlessness. Determining the impact of breathlessness on a patient's daily living may also provide a reference point for severity. For example, a patient who normally walks three blocks without dyspnea can now walk only five steps. Another example would be the patient who has dyspnea with any movement but is not dyspneic at rest and whether this represents a change from the patient's baseline functional status. In addition, whether the patient experiences orthopnea or paroxysmal nocturnal dyspnea should also be determined. If a change from baseline is noted, suspicion for worsening volume overload is increased [2]. After treatment, patients should be frequently reassessed to determine response to therapy. Caution is warranted for patients in whom the clinical exam and physician impression show marked improvement, yet patient-reported symptoms are unchanged. While undertreatment is one possibility, other causes of dyspnea (e.g., pulmonary embolism, emphysema) should be considered.

There are additional clinical diagnostic tools that can aid in making the diagnosis of AHF that should be combined with the patient's history and physical exam. Most, if not all, patients complaining of dyspnea in the emergency department will get a chest X-ray (CXR) performed. Pulmonary edema, Kerley B-lines, pulmonary vascular congestion, and pleural effusion(s) are various findings evident in a patient

Table 9.1 The New York Heart Association functional classification [14]

Class I	Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.
Class II	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
Class III	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.
Class IV	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort increases.

Adapted from: The Criteria Committee of the New York Heart Association [14].

Table 9.2 Key points in the evaluation of the dyspneic patient with concern for AHF

Assess if patient's dyspnea is different from their baseline functional respiratory status or if orthopnea or PND are present.
CXR findings that indicate AHF may include pulmonary edema, Kerley B-lines, pulmonary vascular congestion, and pleural effusions.
BNP < 100 pg/ml is highly sensitive to rule out AHF as cause of dyspnea.
Lung ultrasound showing B-lines is highly sensitive and specific for AHF.
Patients with hypoxia require supplemental oxygen via nasal cannula or facemask.
If hypoxia or work of breathing is not improved with supplemental oxygen only, noninvasive positive pressure ventilation with CPAP or BPAP should be initiated.
Endotracheal intubation should be performed in obtunded patients on arrival or patients who do not improve with CPAP/BPAP.

with AHF with fluid overload; while these CXR findings are quite specific with specificities greater than 90 %, they are poorly sensitive [15].

Natriuretic Peptides

Natriuretic peptides (NP), like BNP (brain natriuretic peptide) or NT-proBNP, are produced in the myocardium *by* myocytes secondary to increased ventricular filling pressure. Elevated NP levels are associated with AHF, although it can also be elevated in other diseases like pulmonary embolism and end-stage renal disease. The common cutoff used to exclude the presence of AHF is 100 pg/ml – at this cutoff level, BNP is highly sensitive with a negative likelihood ratio of less than 0.2 [15]. American College of Emergency Physician's (ACEP) clinical policy guideline on the management of acute heart failure in the emergency department gives a level B recommendation for the use of BNP to improve diagnostic accuracy with the following guidelines: if BNP < 100 pg/dL, AHF is unlikely (negative likelihood ratio 0.1); if BNP > 500 pg/dL, AHF is likely (positive likelihood ratio 6) [16].

Lung Ultrasound

Lung ultrasound has emerged as a new modality to assist in the diagnosis of patients with dyspnea. Patients with AHF have pulmonary edema, or extravascular fluid in the lung interstitium and alveoli, which appears on lung ultrasound as B-lines. B-lines are reverberation artifacts that start at the pleural line, radiate down through the lung, and move with pleural sliding with respirations (see Fig. 9.1). A positive lung ultrasound of interstitial edema requires 3 or more B-lines in at least 2 intercostal spaces bilaterally. A recent meta-analysis by Al Deeb et al. evaluated the accuracy of lung ultrasound B-lines in the clinical diagnosis of acute cardiogenic pulmonary edema (ACPE) [18]. Seven studies were used in the final analysis, and the summed sensitivity and specificity of using lung ultrasound B-lines to diagnose ACPE are 94.1 % and 92.4 %, respectively. The positive likelihood ratio was 12.4 and the

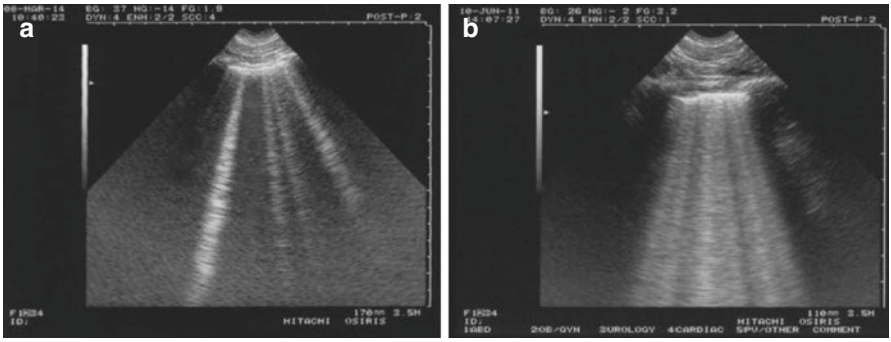

Fig. 9.1 Lung ultrasound and B-lines (**a**, **b** – B-lines [17])

negative likelihood ratio was 0.06 [18]. Given these results, in patients with a moderate to high pretest probability of ACPE, the presence of B-lines significantly strengthens the diagnosis, whereas the lack of B-lines in a patient with low pretest probability of ACPE strongly supports an alternative cause of the patient's dyspnea.

Airway Management

While most AHF patients do not require definitive airway control, those with severe respiratory distress require emergent and decisive management. Even those with only mild to moderate respiratory distress should be carefully assessed to determine the need for supplemental oxygen. This includes a thorough history, as clinical conditions permit, to assess for other causes or historical features contributing to dyspnea (e.g., fever and cough suggesting pneumonia, history of chronic obstructive pulmonary disease) as well as review of a complete set of vital signs, including oxygen saturation, and assessment of volume status in conjunction with a careful cardiovascular-pulmonary exam.

For patients who require supplemental oxygen, determining whether it is delivered via nasal cannula, varying oxygen-delivering masks or a ventilator after endotracheal intubation depends on the condition in which the patient presents as well as response to initial therapy. Moribund patients require definitive airway control with endotracheal intubation, whereas those whose clinical condition can be stabilized or rapidly reversed may be managed with alternative methods such as noninvasive ventilation (NIV) with bi-level positive airway pressure, BPAP, versus continuous positive airway pressure, CPAP. Unfortunately, no quick, simple, and universal method exists to determine which patients will turn around with NIV from those who require definitive airway control. At the present time, this continues to be a primarily clinical decision with experience demonstrating that patients who appear in the greatest distress often recover without intubation if initial therapy is begun rapidly (e.g., NIV in patients with flash pulmonary edema).

For those who require definitive airway management, rapid sequence intubation (RSI) is the preferred method. This involves the simultaneous administration of a

sedative along with a paralytic without bag-valve mask ventilation. A key step in RSI is preoxygenation to minimize the risk of hypoxia after the patient is paralyzed. Patients who present with pulmonary edema will not be able to tolerate prolonged periods of apnea compared to healthy adults and will experience oxygen desaturation more rapidly [19]. The risk of aspiration versus hypoxia needs to be carefully considered for these patients as preoxygenation with BVM may be necessary. RSI has been the preferred mode of intubation in the emergency department for years and is both safe and effective [19].

Rapid Sequence Intubation

In RSI, unconsciousness is achieved using a fast-acting sedative agent. Etomidate is one of the most common induction agents used in RSI and is preferred because of its rapid onset and offset of action [19]. The induction dose of etomidate is 0.3 mg/kg IV. Benzodiazepines should be used with caution in patients with cardiovascular disorders. The most commonly used benzodiazepine in RSI is midazolam at a dose of 0.3 mg/kg IV. Midazolam has some negative inotropic effects, however, and should generally be avoided to prevent further cardiovascular decompensation in AHF patients requiring intubation [19].

Paralysis during RSI completely relaxes the patient's musculature and thereby allows for better first-pass success [19]. Succinylcholine is the most commonly used paralytic agent owing to it s rapid onset of action and relatively brief half-life. Succinylcholine is a depolarizing neuromuscular blocking agent and binds to acetylcholine receptors systemically, but the desired effect of paralysis occurs through its action at the motor end plates. Succinylcholine also stimulates muscarinic receptors on the myocardium and can be a negative chronotrope [19]. This is important to recognize as sinus bradycardia may occur, but is uncommon with single doses. If clinically indicated, atropine rapidly reverses the bradycardia. When succinylcholine is contraindicated, there are other alternatives available such as vecuronium and rocuronium-both of which are non-depolarizing paralytics and have been used successfully in RSI.

Endotracheal intubation generally has few immediate side effects for otherwise healthy individuals but may pose substantial risk for those with underlying cardiovascular disease. Intubation induces catecholamine release that can lead to an increase in heart rate and blood pressure resulting in an overall increase in myocardial oxygen demand. Fentanyl, a synthetic opioid, can be used to attenuate this increase myocardial oxygen demand. The dose of fentanyl is 3 μg/Kg and is given over 60 s prior to intubation [19].

Noninvasive Ventilation

Noninvasive ventilation (NIV) is an important maneuver for both symptomatic and therapeutic management. It is generally applied using a tight fitting facemask but can also be provided with a nasal mask. Facemask is preferred in patients presenting with respiratory distress if the patient will tolerate it. The benefits of noninvasive

ventilation include absence of the risks associated with endotracheal intubation, preservation of speech and swallowing along with patient comfort [20]. Appropriate patient selection is key to implementing noninvasive ventilation. Those unable to protect their airway (e.g., patients with altered mental status) are not candidates for noninvasive ventilation.

There are two primary NIV modalities, continuous positive airway pressure (CPAP) and bi-level positive airway pressure (BPAP). Continuous positive airway pressure differs from bi-level positive airway pressure in that it provides a fixed level of positive pressure throughout the respiratory cycle. Bi-level positive airway pressure, as the name implies, provides two levels of support during the respiratory cycle, once during the inspiratory phase and then again during expiration. Continuous positive airway pressure is similar to positive end expiratory pressure, PEEP, which is used in traditional mechanical ventilation. The purpose of CPAP (and PEEP) is to increase the functional residual capacity of the lungs by prevention of alveolar collapse that would occur secondary to injury or pulmonary edema [20]. In addition to end expiratory pressure, bi-level positive airway pressure provides inspiratory pressure and is thus preferred in patient with hypercarbia and increased work of breathing [20].

A Cochrane Review published by Vital et al. in 2013 evaluated the role of NIV for acute cardiogenic pulmonary edema [21]. The primary objective was to determine the effectiveness and safety of NIV in the treatment of adult patients with acute cardiogenic pulmonary edema. This meta-analysis included 32 studies comparing outcome differences with standard medical care alone to standard medical care combined with NIV, either CPAP or BPAP.

When compared to standard medical care alone, NIV reduced hospital mortality (relative risk 0.66) and endotracheal intubation (relative risk 0.52). There was no difference in hospital length of stay with the addition of NIV but intensive care unit stay was found to be decreased by 1 day with NIV. The incidence of acute myocardial infarction was not significantly increased with the use of NIV compared to standard medical care alone, and fewer adverse events like worsening respiratory failure and decline in mental status were seen with the use of NIV. The author's overall conclusion was that the use of NIV in conjunction with standard medical care is effective and safe for the treatment of acute cardiogenic pulmonary edema [21].

American College of Emergency Physician's (ACEP) clinical policy guideline on the management of acute heart failure syndromes in the ED gives a level B recommendation for the use of CPAP and level C recommendation for the use of BPAP [16]. The level C recommendation for BPAP was a result of a single study suggesting a higher incidence of myocardial infarction with the use of BPAP, although follow-up studies and the aforementioned 2013 Cochrane Review have not shown such an association [21, 22].

When initiating CPAP, it should be started at 5–10 cm H_2O and should be titrated in 2 cm H_2O increments based on the patient's clinical status and degree of hypoxemia. Close interval assessments are needed on any patient who is placed on noninvasive ventilation to ensure compliance and to assess improvement or worsening in clinical status. Although arterial blood gases are rarely performed in the ED setting, patients who are failing to improve with CPAP may be retaining CO_2, which is an

indication to switch to BPAP to improve ventilatory support. Some patients may find the tight fitting mask to be claustrophobic or painful and low doses of morphine or fentanyl, used with caution, may be utilized to ensure compliance.

Conclusion

Assessing breathlessness and ensuring its relief is a major goal of initial AHF management. For patients who present moribund or with altered mental status and respiratory distress, immediate endotracheal intubation with RSI is recommended, recognizing that hypoxia may worsen rapidly secondary to paralysis in patients with cardiogenic pulmonary edema. For patients with moderate to severe respiratory distress, immediate use of NIV may rapidly improve patient's signs and symptoms.

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Volume Assessment in Heart Failure

10

Anna Marie Chang and Alfred B. Cheng

Background

In the out-of-hospital (or prehospital) realm, early treatment of patients suspected of suffering from ADHF improves mortality [1]. However, patients that did not have heart failure but received empiric treatment with medications targeting heart failure (furosemide, nitroglycerin, and morphine) had a higher mortality than patients who remained untreated. Those patients ultimately found to not have heart failure who received bronchodilators had a mortality rate of 3.6 %. Patients ultimately found not to have heart failure but who received heart failure therapy had an increased mortality to 13.6 %. The non-HF group that received no therapy had a mortality of only 8.2 %, highlighting the importance of having a correct diagnosis and volume assessment prior to treatment [1].

The main reason for hospitalization for ADHF is related to the symptoms of shortness of breath, potentially signifying congestion, rather than low cardiac output [2]. In addition, patients with signs of congestion had increases in the risk of mortality and hospitalization [2]. Hemodynamic profiles have been used to stratify patients presenting with acute heart failure. In 1978, Forrester et al. demonstrated four patient profiles after acute myocardial infarction that predicted outcomes [3]. These profiles were based on the presence or absence of congestion (pulmonary capillary wedge pressure (PCWP) > or ≤18 mmHg) and adequacy of perfusion (cardiac index >2.2 l/min/m [3]) which could be ascertained by Swan-Ganz catheter readings. The findings were extended to patients with acute heart failure by Stevenson [4]. For example, indications of congestion included a recent history of

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orthopnea and/or physical examination with evidence of jugular venous distention, rales, hepatojugular reflux, ascites, peripheral edema, leftward radiation of the pulmonic heart sound, or a square wave blood pressure response to the Valsalva maneuver. Compromised perfusion was defined by presence of a narrow proportional pulse pressure pulsus alternans, symptomatic hypotension (without orthostasis), cool extremities, or impaired mentation. Physicians synthesized the presence or absence of any or all of these signs to make a subjective assessment of the patients' volume and perfusion status when wedge pressures or cardiac index measures were not available. Profile I represents no congestion or hypoperfusion (dry-warm); profile II, congestion without hypoperfusion (wet-warm); profile III, hypoperfusion without congestion (dry-cold); and profile IV, both congestion and hypoperfusion (wet-cold) [5]. These clinical profiles predict short-term survival, with patients fitting profile II and IV having twice the mortality rate compared to profile I. It appears that increased volume and congestion (wet) predict a worse prognosis, and perhaps these patients need to be more aggressively treated. The rest of this chapter will discuss methods to help assess volume overload.

The Gold Standard

The gold standard for determining congestion in ADHF is performed by measuring right atrial pressure and PWCP via cardiac catheterization [2]. In addition to pressure, one needs to assess blood volume. The gold standard determining blood volume is radioisotopic measurement. It is generally held that a reliable blood volume analysis can be provided by the dual-labeling radioisotope technique, which includes red cell volume measurement using 51-Cr or 99-mTc as a label and a separate plasma volume assessment using 125-I- or 131-I-tagged human serum albumin (International Committee for Standardization in Hematology). More recently, it has been suggested that blood volumes can be estimated from a single 125-I- or 131-I-HSA assessment effectively, rapidly, and at a lower cost [6]. However, the definition of rapid from these studies is 1.5 h. Although radioisotope blood volume analysis may be useful in ideal conditions, there are no ED-based clinical studies that show effectiveness. In the ED, we need to rely on tools that are faster and more widely available.

History and Physical Examination

The 2009 American College of Cardiology/American Heart Association Revised Guidelines recommend volume assessment for all patients with heart failure during the initial evaluation and with follow-up examinations [7]. Physicians should begin their evaluation of a patient with a history and physical examination. The guidelines recommend measurement of body weight, sitting and standing blood pressures, jugular venous distension, and hepatojugular reflux, as well as edema in the legs and

abdomen. It also recommends evaluation for pulmonary rales and hepatomegaly [7]. These are the factors that have been the standards of hemodynamic profiling. However, Stevenson and Perloff demonstrated that physical signs have limited accuracy in estimating hemodynamics in chronic HF [8]. Furthermore, the inter-rater reliability for hemodynamic profiling among emergency physicians was poor to fair at best, with observers agreeing on the hemodynamic profile only 64 % of the time [9]. Despite the lack of data on the reliability of physical examination findings, practice guidelines emphasize their importance in the evaluation of patients with HF, and they should be determined [7].

In nondifferentiated dyspneic patients in the ED, the diagnosis is even more difficult. In a meta-analysis of 18 studies by Wang et al., a history of congestive heart failure or myocardial infarction were the most helpful features to identify patients with potential heart failure [10]. Risk factors for HF that were also helpful included hypertension, diabetes, valvular heart disease, older age, male sex, and obesity. Those who reported symptoms of paroxysmal nocturnal dyspnea, orthopnea, or dyspnea on exertion were also more likely to have HF; however, these were less reliable than past medical history. This is true in many patients with chronic HF, who have elevated intravascular volume without overt peripheral edema or rales. However, depending on the study, signs and symptoms have varying sensitivity and specificity. Butman et al. reported that JVD was both specific and sensitive for an increased PCWP [11], while another study, defining volume overload as a PCWP > 18 mmHg, concluded that JVD and HJR had a predictive accuracy of only 81 % [12]. The presence of rales has a sensitivity and specificity as low as the 50 % range [8]. Further information about sensitivity and specificity of history and physical examination findings can be found in Table 10.1.

In physical examination teachings, the S3 is highly specific for ventricular dysfunction and elevated left ventricular filling pressures. In fact, the presence of an S3 has the highest positive likelihood ratio (LR 11.0) for volume overload [9]. However, the inter-rater reliability of this physical exam finding is very low [12], and it is often difficult to auscultate in patients with confounding diseases (e.g., COPD and obesity) and in noisy environments such as the emergency department. In fact, the 2009 updated guidelines do not list heart sounds as a method to assess volume status or the diagnosis of heart failure [7].

Another confounding factor to the diagnosis of volume overload may be the presence of hypoperfusion. Although the majority of patients with HF do not present with hypoperfusion, their cardiac function may be severely depressed. Conversely, patients with hypoperfusion may have a concurrent illness, or be suffering from hypovolemia rather than pump failure, or have excessive vasodilation from their heart failure; this must be considered when taking the history. When patients present with more severe volume deficits, orthostatic symptoms and hypotension may suggest hypovolemia and not necessarily hypoperfusion. Orthostatic symptoms may include dizziness upon standing, shortness of breath with exertion or at rest, weakness, malaise, and syncope if the deficit is severe. However, the utility of orthostatic vital signs in the emergency department has

Table 10.1 History and physical examination findings and their association with volume overload and heart failure diagnosis

			Summary LR (95 % CI)	
Finding	Sensitivity	Specificity	Positive	Negative
Initial clinical judgment	0.61	0.86	4.4 (1.8–10.0)	0.45 (0.28–0.73)
History				
Heart failure	0.60	0.90	5.8 (4.1–8.0)	0.45 (0.38–0.53)
Myocardial infarction	0.40	0.87	3.1 (2.0–4.9)	0.69 (0.58–0.82)
Coronary artery disease	0.52	0.70	1.8 (1.1–2.8)	0.68 (0.48–0.96)
Diabetes mellitus	0.28	0.83	1.7 (1.0–2.7)	0.86 (0.73–1.0)
Hypertension	0.60	0.56	1.4 (1.1–1.7)	0.71 (0.55–0.93)
Smoking	0.62	0.27	0.84 (0.58–1.2)	1.4 (0.58–3.8)
COPD	0.34	0.57	0.81 (0.60–1.1)	1.1 (0.95–1.4)
Symptoms				
PND	0.41	0.84	2.6 (1.5–4.5)	0.70 (0.54–0.91)
Orthopnea	0.50	0.77	2.2 (1.2–3.9)	0.65 (0.45–0.92)
Edema	0.51	0.76	2.1 (0.92–5.0)	0.64 (0.39–1.1)
Dyspnea on exertion	0.84	0.34	1.3 (1.2–1.4)	0.48 (0.35–0.67)
Cough	0.36	0.61	0.93 (0.70–1.2)	1.0 (0.87–1.3)
Physical examination				
Third heart sound	0.13	0.99	11 (4.9–25.0)	0.88 (0.83–0.94)
Abdominojugular reflux	0.24	0.96	6.4 (0.81–51.0)	0.79 (0.62–1.0)
Jugular venous distension	0.39	0.92	5.1 (3.2–7.9)	0.66 (0.57–0.77)
Rales	0.60	0.78	2.8 (1.9–4.1)	0.51 (0.37–0.70)
Any murmur	0.27	0.90	2.6 (1.7–4.1)	0.81 (0.73–0.90)
Lower extremity edema	0.50	0.78	2.3 (1.5–3.7)	0.64 (0.47–0.87)
Valsalva maneuver	0.73	0.65	2.1 (1.0–4.2)	0.41 (0.17–1.0)
SBP < 100 mmHg	0.06	0.97	2.0 (0.60–6.6)	0.97 (0.91–1.0)
Fourth heart sound	0.05	0.97	1.6 (0.47–5.5)	0.98 (0.93–1.0)
SBP > 150 mmHg	0.28	0.73	1.0 (0.69–1.6)	0.99 (0.84–1.2)
Wheezing	0.22	0.58	0.52 (0.38–0.71)	1.3 (1.1–1.7)
Ascites	0.01	0.97	0.33 (0.04–2.9)	1.0 (0.99–1.1)

Abbreviations: LR likelihood ratio, *CI* confidence interval, *PND* paroxysmal nocturnal dyspnea, *SBP* systolic blood pressure, *COPD* chronic obstructive pulmonary disease

been questioned. In a sample of 132 presumed euvolemic patients, 43 % had "positive" orthostatic vital signs [13]. In a comparison of over 200 ill patients and 20 control patients, orthostatic changes in systolic blood pressure and diastolic blood pressure demonstrated no statistically significant association with level of dehydration, and it was impossible to define a group of patients who had a "positive" tilt-table test [14].

The combination of history and physical examination findings may aid the physician in diagnosing volume overload. However, diagnostic imaging, natriuretic peptides, and other noninvasive techniques are also available to address the issue.

Chest Radiography

Chest radiographs may aid in the diagnosis of volume overload or may help guide the differential diagnosis of the acutely dyspneic patient in the emergency department. In the presence of heart failure, one may find pulmonary venous congestion, cardiomegaly, and interstitial edema. However, the absence of radiography findings does not exclude heart failure [7]. Collins et al. found that up to 20 % of patients who were eventually diagnosed with heart failure had negative chest radiographs at the time of evaluation in the emergency department [15]. Furthermore, in late-stage heart failure patients, chest radiography has unreliable sensitivity, specificity, and predictive value for identifying individuals with high PCWP.

Natriuretic Peptides

The natriuretic peptides (NP) are hemodynamically active neurohormones that are released into the bloodstream when there is increased myocardial pressure and stretching, so that they can enable vasodilation and natriuresis. It is released as a prohormone and cleaved into the biologically active BNP and NT-proBNP. Assays for BNP and its synthetic by-product NT-proBNP are commercially available.

Compared with BNP, NT-proBNP has a longer plasma half-life [16]. There is ample evidence that both BNP and NT-proBNP are useful in diagnosing and predicting prognosis in heart failure, including the Breathing Not Properly Multinational Trial (BNP Trial) [17], the Rapid Emergency Department Heart Failure Outpatient Trial (REDHOT) [18], PRIDE (pro-BNP Investigation of Dyspnea in the Emergency Department) [16], and the ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness) Trial [19]. These molecules behave similarly and are elevated in the setting of heart failure. These studies demonstrated that BNP and NT-proBNP are useful in the diagnosis and risk stratification of patients with heart failure.

Furthermore, the natriuretic peptides also provide an overall assessment of volume status. In studies of patients on hemodialysis, plasma BNP levels before and after hemodialysis correlate with the degree of body fluid and volume retention [20, 21] and with inferior vena cava diameter measurements that are reflective of hydration status.

However, because the NPs can be elevated with any type of myocardial stress, independent of volume status (e.g., myocardial infarction, pulmonary embolus), physician judgment must also be used. Both BNP and NT-proBNP interpretation must be used carefully in obese individuals [22], older patients, and those with renal disease or on hemodialysis [21]; all these factors affect the sensitivity and specificity of the test. Knowledge of the patient's baseline levels and any associated change may also be useful.

For more detailed information regarding the diagnostic and prognostic utility of natriuretic peptides, please refer to Chap. 12.

Phonocardiography

Auscultation of an S3 heart sound is difficult in the emergency department setting, and as mentioned previously, interobserver concordance is low [23]. Phonoelectrocardiographic devices have been developed in order to improve detection of abnormal heart sounds, specifically an S3 or S4. The Audicor system is an acoustic cardiogram that collects both sound and electrical data. Earlier studies showed that it has increased the likelihood of the diagnosis of HF and left ventricular dysfunction [24, 25]. However, in a multinational study of over 990 patients, although the system was specific for the diagnosis of acute decompensated heart failure and affected physician confidence, its lack of sensitivity did not improve diagnostic rates [26]. Furthermore, the test did not have any independent prognostic information.

Ultrasonography

Ultrasound has become increasingly available at the bedside. It has been shown to be useful in a myriad of conditions and has been helpful in the assessment of volume status in the critically ill patient [27] including septic shock and trauma [28].

The inferior vena cava diameter (IVCd) has been shown to indicate volume status and blood loss. In a study of 31 healthy male volunteers who were donating 450 ml of blood, IVCd measured both during inspiration (IVCi) and during expiration (IVCe) showed a decrease of 5 mm after blood loss [29]. The wide variation between individuals of IVC diameter makes isolated measurements difficult to interpret for volume status (Fig. 10.1).

Studies have addressed using respiratory variation in IVCd as a marker for the diagnosis of HF. IVCd is dynamic and changes with changes in intrathoracic pressure. During inspiration, intrathoracic pressure decreases thereby increasing venous return and causing distention of the IVC. During expiration, an increase in

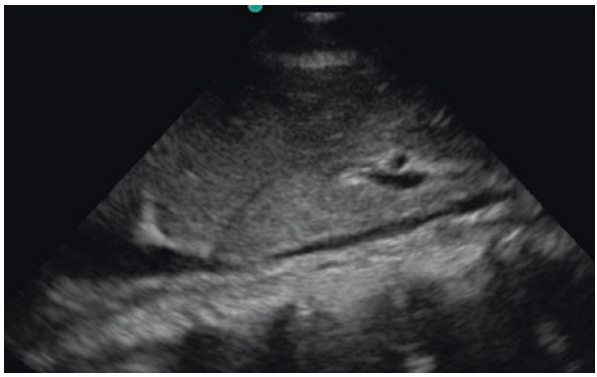

Fig. 10.1 Over 75 % collapse of IVC, seen on long axis view (Image reproduced with the permission of Dr Alfred Cheng)

intrathoracic pressure causes a collapse of the IVC [27, 29]. A measurement for this variation in IVC diameter is the IVC collapse index (IVC-CI). The IVC-CI is equal to the difference between the IVCDe and the IVC diameter in inspiration (IVCi) divided by the IVCe. Absolute values for a normal IVC-CI do not exist; however, the IVC-CI in normal healthy subjects is typically between 0.25 and 0.75 (see Fig. 10.1). In HF, volume overload dilates the IVC to the point that decreased intrathoracic pressure does not change the resulting diameter and thus the IVC-CI remains close to 1 (Fig. 10.2). In patients who are intubated, a similar measure can be used known as distensibility index (dIVC), which instead uses the maximum and minimum diameter of the IVC rather than the IVCi and IVCe. dIVC is equal to the (maximum diameter – minimum diameter)/minimum diameter. If the value is greater than 18 %, it suggests the patient is fluid responsive and may not be volume overloaded [30, 31].

Another diagnostic use of point-of-care ultrasound is the assessment of the lungs for pulmonary water by the identification of the presence of sonographic artifacts, known as B-lines, lung comets, or comet tails. These imply thickened interstitial or fluid-filled alveoli. B-lines occur most commonly in patients with HF and correlate with elevated PCWP and extravascular pulmonary water [32]. Clinical studies using these ultrasound findings have shown good sensitivity and specificity for distinguishing between congestive heart failure and COPD (sensitivity range, 85.7–100 %; specificity range, 92–97.7 %) [33]. In a study of 94 patients presenting to the ED with acute shortness of breath, an US that showed comet tails had a positive likelihood ratio (LR+) of 3.88 and a negative likelihood ratio (LR−) of 0.5 [34]. Consensus guidelines for point-of-care lung ultrasound by an expert panel were released in 2012 stating that two or more positive regions bilaterally constitute a scan positive for increased interstitial lung water. A positive region was defined as three or more B-lines in a longitudinal plane between two ribs [35]. With these emerging noninvasive modalities in ultrasound, the bedside clinician has never had more tools at their disposal to assess for heart failure.

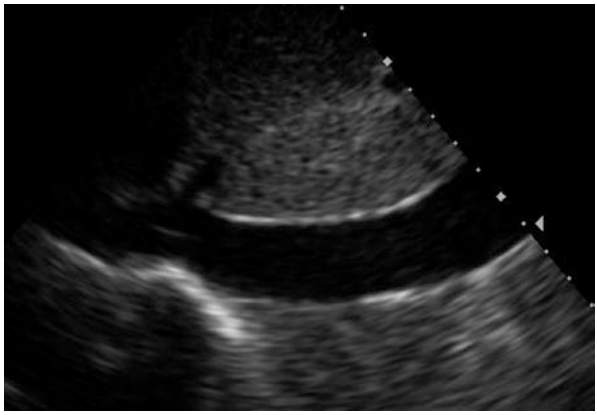

Fig. 10.2 Plethoric IVC, a sign of volume overload, seen on long axis view (Image reproduced with the permission of Dr Alfred Cheng)

Impedance Monitors

Impedance cardiography (ICG) is a noninvasive measurement of cardiac output, cardiac index, and thoracic fluid content. Electrical impedance is the resistance to flow of an electrical alternating current, and the human thorax is an inhomogeneous electrical conductor. Bone and tissue are poor conductors, while blood and fluids are good conductors and decrease impedance. When a high-frequency electrical current is injected across the thorax, paired electrodes can be used to measure impedance reflected as voltage changes. The changes in thoracic voltage result from changes that occur from blood volumetric and velocity alterations related to the cardiac cycle. By analyzing these changes and their relation with ECG-derived timing measures, variations in blood flow through the great vessels result in estimates of stroke volume [36].

ICG directly measures certain parameters including heart rate, thoracic fluid content (1/baseline impedance [per k ohm]), velocity index (first time derivative/baseline impedance [per 1000 s]), acceleration index (second time derivative/baseline impedance [per 100 s]), and pre-ejection period (time from EKG Q wave to aortic valve opening [ms]) [37]. It would make sense that by measuring the thoracic fluid content, one can estimate the hemodynamics and fluid profile of a patient.

In the outpatient setting, Packer et al. [38] followed 212 stable HF patients who underwent serial clinical and ICG evaluation every 2 weeks for 26 weeks and who were followed up for the occurrence of death or worsening of HF requiring hospitalization or emergent care. Those with a higher thoracic fluid content (TFC) were at an increased risk for hospitalization and emergent care [38].

The bioimpedance cardiography in advanced heart failure (BIG) substudy was conducted within the ESCAPE Trial and was designed to determine the utility of bioimpedance cardiography as an adjunct tool for HF monitoring in hospitalized patients with advanced HF [36]. TFC was not predictive of poor outcomes, as it had been in the outpatient setting. In patients with systolic HF, TFC was poorly correlated with invasively measured RAP and PCWP. It can be inferred from the poor correlation between the pulmonary artery catheter (PAC)-derived and ICG-derived clinical profiles that in general that ICG is a poor surrogate for PAC-derived data in chronic heart failure patients who are readmitted to the hospital and should not be used as an alternative.

Bioimpedance Vector Analysis

A further use of bioimpedance is known is BIVA, or bioelectrical impedance vector analysis, which is a noninvasive technique to estimate body mass and water composition by bioelectrical impedance measurements, resistance, and reactance [39]. To measure BIVA, the patient lies supine on a nonconductive surface, without metal contacts, with straddle inferior limbs at 45° and superior limbs abducted at 30° to avoid skin contacts with the trunk. Two skin electrodes are applied, one on the right hand and the other on the right foot. These measures are then compared to the

normal distribution adjusted by patient's height and weight, age, and sex. This is plotted within ellipses, and measurements of vectors measured in degrees of elevation from the *x*-axis are termed the phase angle (PA), and it has prognostic value in many clinical situations. Short vectors are associated with edema, whereas long vectors indicate dehydration [40].

In disease entities where volume assessment is crucial, there appears to be a correlation between BIVA values and hydration status. BIVA was useful in predicting fluid overload in critically ill patients. In a cohort of 121 patients in an intensive care unit, central venous pressure values >12 mmHg were associated with shorter impedance vectors in 93 % of patients, indicating fluid overload [41]. In 22 HF patients, using deuterium dilution as the standard for total body water evaluation, BIVA measurements had excellent correlation with total body water content ($r = 0.93$, $p = 0.01$) [38]. Di Somma et al. enrolled 51 patients in an ED, half of whom were ultimately diagnosed with ADHF based on clinical and laboratory findings. BIVA of ADHF patients was compared with BIVA of controls, and the difference was statistically significant ($P < 0.007$); the numbers reported in ADHF patients had greater hydration (76.7 ± 4.0 %) compared with controls (73.1 ± 1.9 %). In patients with average hydration values >80.5 %, there was a correlation with events at 3 months (death or rehospitalization for cardiogenic event) with a sensitivity of 22 % and specificity of 94.2 % (positive likelihood ratio 4.6, positive predictive value 66.7, negative predictive value 74.1) [39]. More recently, a study of 77 patients found that BIVA measurements did not improve diagnosis of ADHF in this population [42]. However, there are many limitations to this type of procedure in the ED. It is still a new technology that has not gained widespread use; the utility of the tool above and beyond what are already available has not been proven in an undifferentiated ED population, and it cannot be used on uncooperative patients.

Conclusion

It is difficult to accurately assess volume status on patients in the ED. Only through careful history taking, physical examination, and the assortment of the tools and diagnostic tests that are available in the ED can physicians put together a profile of the patient. Ultrasound skills such as measurement of IVC show promise; more training is needed for most practitioners to make it useful. New technologies such as BIVA show promise; however, future studies need to address its utility in the diverse patient population seen in the ED.

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Emergency Department Ultrasound as a Diagnostic and Therapeutic Guide

11

Jennifer Carnell, Reeva Patel

The clinical role of ultrasound (US) has changed rapidly over the past few decades. As technology has improved, it has allowed US machines to become portable with improving quality of images. The most dramatic change has been in the emergency and critical care settings where it provides immediately interpretable and reproducible images at bedside, allowing answers to time-sensitive questions [1]. As the use of ultrasound expands, it is likely that it will be used at bedside throughout hospitals to perform rapid evaluations and monitor response to treatment. Its advantages include its noninvasive nature, lack of ionizing radiation, and cost-effectiveness [2].

Point of care ultrasound (POCUS) is becoming a tool to rapidly diagnose patients in the emergency department (ED) and other hospital settings who present with undifferentiated dyspnea. In many situations, POCUS is able to rapidly distinguish ADHF from other common causes of dyspnea leading to appropriate management and risk stratification of heart failure patients [3].

Cardiac Ultrasound

In 2008 the American College of Emergency Physicians (ACEP) published emergency ultrasound guidelines that defined emergency providers' (EP) scope of practice in limited cardiac US as an ability to evaluate general cardiac contractility and central venous volume [4]. The American Society of Echocardiography subsequently supported these ACEP guidelines [5].

The use of cardiac POCUS to evaluate dyspnea in the ED setting was first introduced by Kimura in 2001 [6]. Cardiac ultrasound facilitates clinical decision-making by identifying impaired systolic contractility in patients with acute shortness

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of breath or chest pain, consequently directing pharmacologic treatment or other interventions toward treatment of heart failure [7].

Cardiac POCUS can be used for global assessment of left ventricular (LV) systolic function. Evaluation of LV systolic function includes an overall assessment of endocardial excursion and myocardial thickening, using multiple windows that include the parasternal long and short, subxiphoid, and apical views. It is performed to assess global function of the heart by assessing LV function to help differentiate between diastolic and systolic heart failure. Visual estimation, E-point septal separation (EPSS), and fractional shortening are established methods that ED physicians have used to place LV ejection fraction (LVEF) into broad categories of normal, moderately reduced, and severely reduced [5, 8, 9]. Studies show that global systolic function can be assessed accurately by POCUS and correlates well with echocardiographer interpretations (Figs. 11.1, 11.2, 11.3, 11.4, 11.5, and 11.6) [7, 9].

Visual estimation of ejection fraction (EF) is widely used and considered comparable to calculated EF when performed by providers experienced in POCUS [10].

Visual estimation of EF by both cardiologists and EPs has been shown to correlate well with quantitative assessments of EF [11, 12]. A recent study demonstrated a sensitivity of 98.7 % and a specificity of 86.2–87.9 % for low EF when two EPs used visual estimation to evaluate EF when compared to a gold standard of cardiologists using the modified Simpson method of EF calculation [12]. Randazzo et al. used a subjective visual estimation technique of LVEF in patients who were scheduled to receive a formal echocardiogram (echo) from the ED. A diverse group of providers that included attendings, residents, and a physician assistant used visual estimation to classify EF as poor, moderate, or normal. The overall agreement in estimation of function between the EPs and cardiologists was good ($r = 0.712$) [13]. Fractional shortening and the Teichholz method for estimation of EF in M-mode imaging are alternative methods of measuring EF [1].

While detection of reduced EF is extremely helpful, use of reduced EF alone as an echo variable for predicting AHF would result in failure to detect the nearly half of all HF patients with preserved EF [14]. The diagnosis of heart failure with preserved EF, previously referred to as diastolic heart failure, is complex and incompletely agreed upon by experts [15]. The use of tissue and flow Doppler in the diagnosis of heart failure with preserved EF is not an expected EP skill. However, the scope of POCUS is always expanding as providers attain mastery of additional ultrasound exams. One recent publication detailed a focused protocol for diagnosis of heart failure with preserved EF that could be performed in the emergency department [16]. One study found EP-performed echocardiograms to have a high sensitivity (92, 95 % confidence interval, 60–100) but moderate specificity of 69 % (95 % CI, 50–83) in identifying clinically significant diastolic function [17]. Another study found the evaluation could be performed by EPs in under 10 min and yield a sensitivity of 89 % and a specificity of 80 % for diastolic dysfunction [10, 18].

A few studies have employed echo to evaluate the acute impact of HF treatment on structural and functional changes. Some studies found changes in invasive hemodynamics correlated with changes in echo parameters during treatment of HF, specifically change in right atrial (RA) pressure with change in inferior vena cava diameter (IVCd) and change in pulmonary capillary wedge pressure (PCWP) with change in IVCd and IVC collapsibility [19]. Several early studies of HF

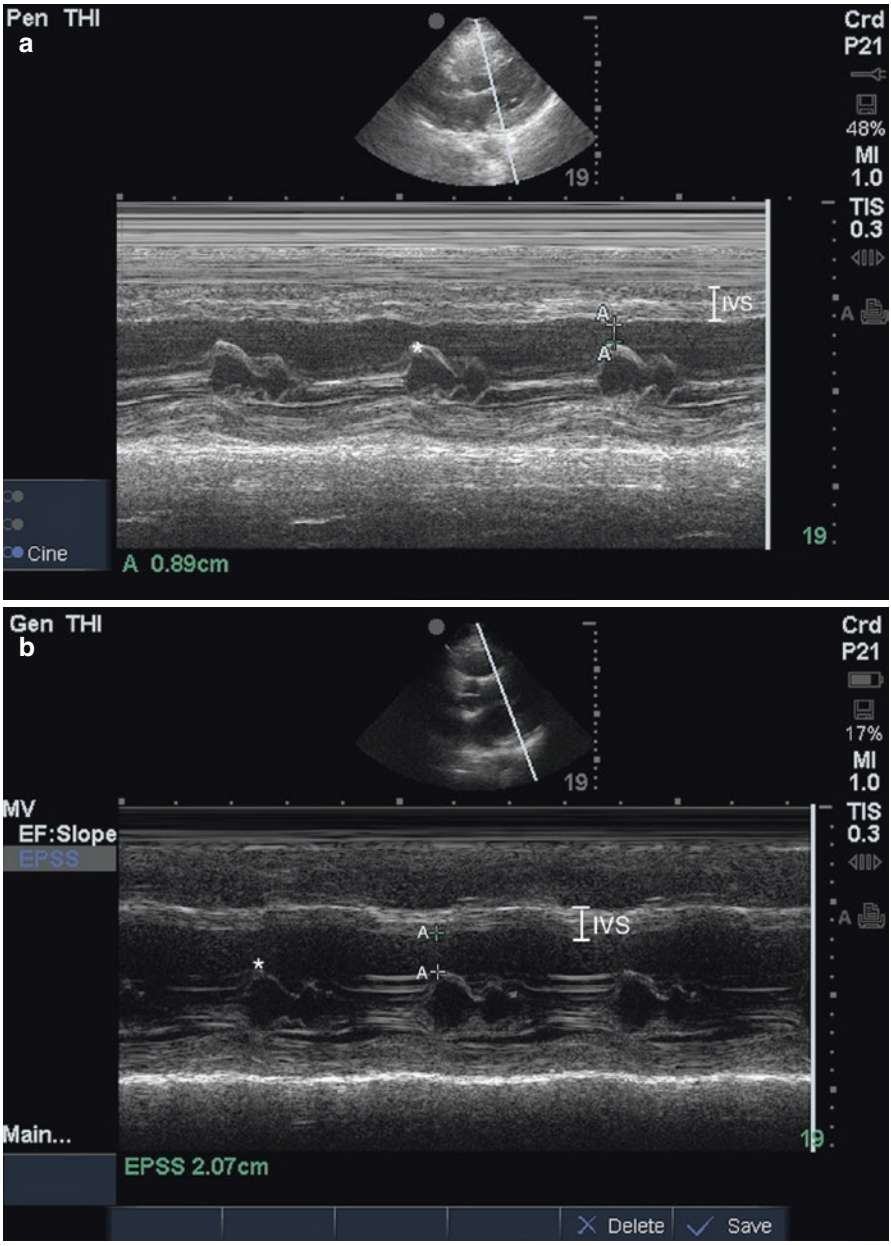

Fig. 11.1 (**a**, **b**) (EPSS normal, abnml). End point septal separation (EPSS) is the use of M-mode in the parasternal long cardiac window to evaluate the distance between the anterior leaflet of the mitral valve and the interventricular septum in end diastole. EPSS >1.2 cm is considered abnormal and is associated with poor ejection fraction. *IVS* interventricular septum, * Anterior mitral valve leaflet, *A-A* EPSS

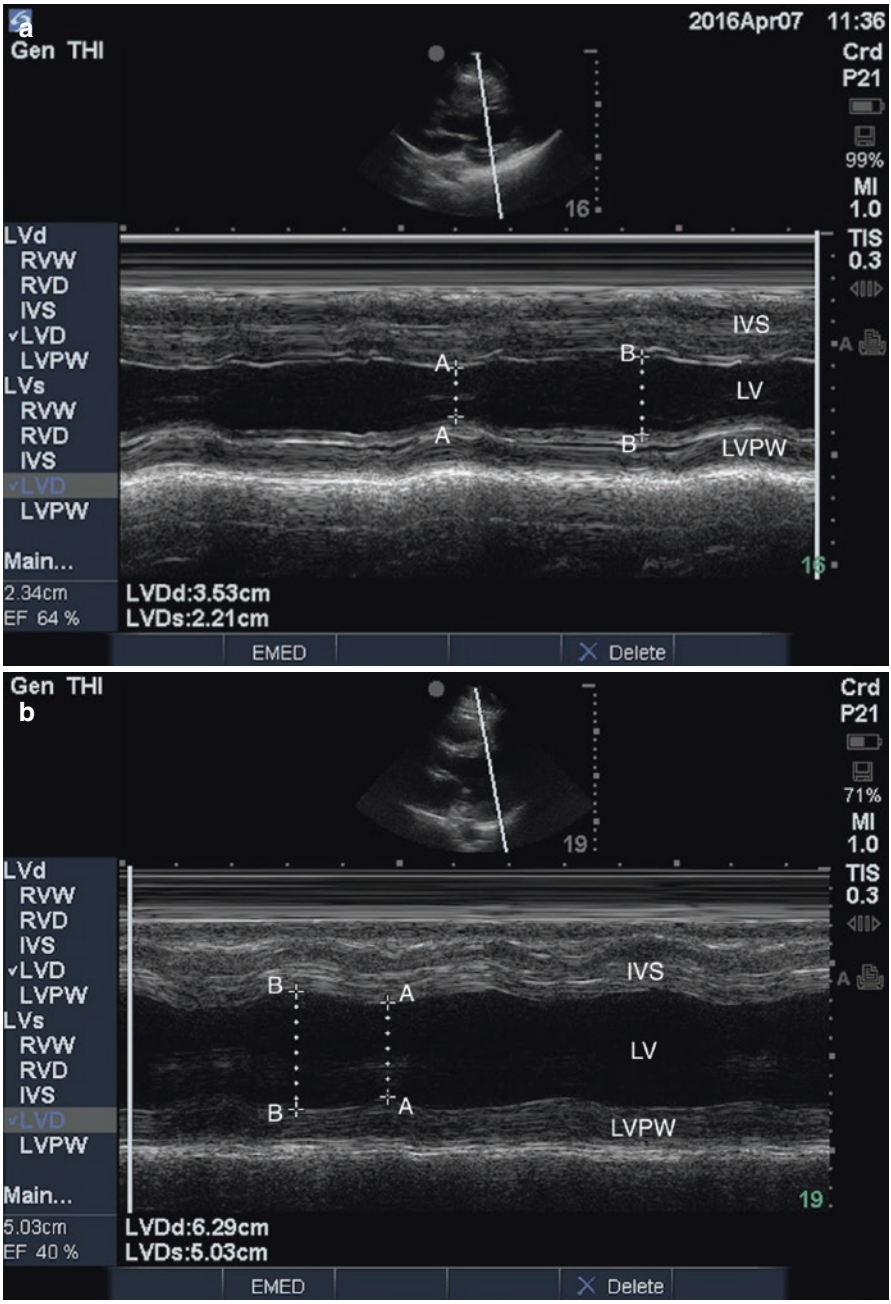

Fig. 11.2 (**a**, **b**) (FS nml, abnml). Fractional shortening (FS) is the use of M-mode in the parasternal long cardiac window to measure the degree of left ventricle (LV) chamber shortening between diastole and systole. FS is expressed as a percentage by calculating the difference between end-diastolic LV diameter and end-systolic LV diameter. The difference is then divided by the end-diastolic LV diameter and multiplied by 100. Some ultrasound machines possess software that will convert FS% into EF as is recorded in this image. *IVS* interventricular septum, *LV* left ventricle, *LVPW* left ventricle posterior wall, *A to A* LV end-systolic diameter, *B to B* left ventricle end-diastolic diameter

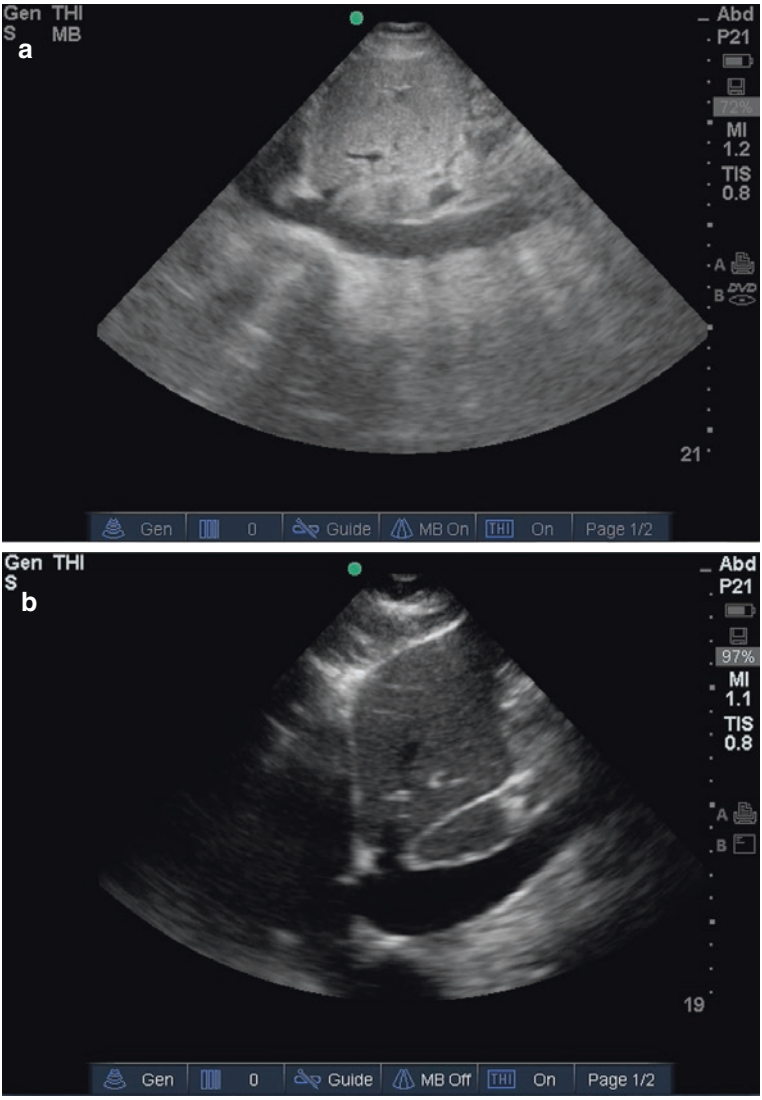

Fig. 11.3 (**a**, **b**) (nml, plethoric). A longitudinal view of the inferior vena cava (IVC). A plethoric IVC shows limited to no respiratory variation and is associated with AHF

demonstrated acute reduction in LV size with concomitant decrease in left-sided filling pressures [20–24] although others did not confirm this finding [25, 26].

Ultrasound of the Inferior Vena Cava

If bedside assessment of the inferior vena cava (IVC) functions as a rapid noninvasive means for clinicians to determine a patient's right atrial pressures, it may be a tool to help differentiate decompensated from compensated HF in the absence of other conditions that raise RA pressure [27].

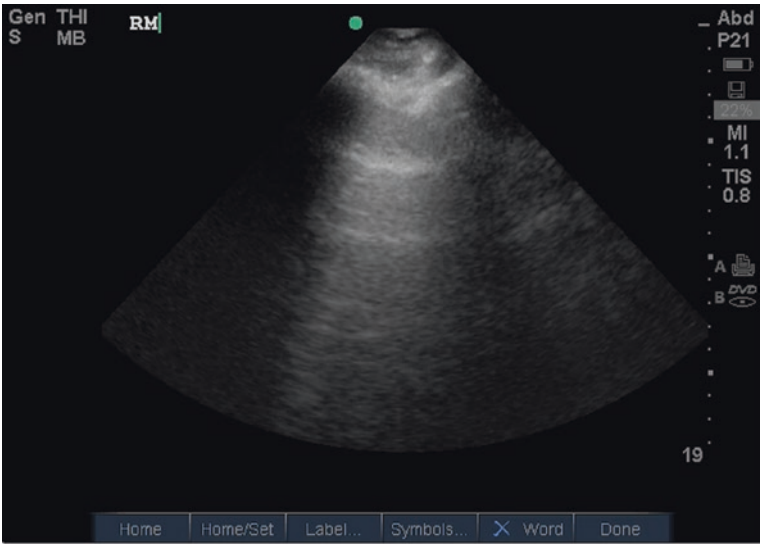

Fig. 11.4 (A lines). A lines. The hyperechoic pleural line with reverberation artifact of the pleura producing equally spaced, repeating hyperechoic horizontal lines referred to as A lines may be seen in normal lung or in pathologic conditions such as chronic obstructive pulmonary disease (COPD) or pneumothorax. A lines are not seen well in acute exacerbations of heart failure as B lines (see Fig 11.5) erase or obscure A lines.

Evaluation of the IVC is routinely performed with the patient supine or minimally inclined [28]. A subxiphoid or right lateral view of the IVC approximately 2–4 cm proximal to the entrance of the IVC into the RA is assessed for changes in diameter as the patient breathes.

IVCd is thought to be easy to measure in patients with HF and has low interobserver variation [22]. Studies in patients without HF have shown a moderate to high degree of inter-rater reliability for IVCd measurement [29, 30]. One issue that arises when discussing IVC imaging is the significant heterogeneity in how IVC measurements are made. One study evaluated the inter-rater reliability of several methods of IVCd measurement and found the best inter-rater reliability using the anterior midaxillary longitudinal approach with the liver as an acoustic window as compared to both longitudinal and transverse subxiphoid IVC measurements [31].

The IVC collapsibility index (CI) is calculated by determining the difference between the maximum (IVCdmax) and minimum IVC diameter (IVCdmin) via the following formula CI = (IVCdmax-IVCdmin)/IVCdmax. At the extremes, a low collapsibility index indicates that there is very little change in the IVC diameter with respirations, while a high CI occurs when there is significant respirophasic change in the IVC diameter [32].

The IVC diameter changes in response to both intrathoracic and intra-abdominal pressure variations and right atrial (RA) volume. Generally, in the spontaneously breathing patient, the negative intrathoracic pressure produced by inspiration increases venous return to the right atrium, producing a transient decrease in IVC

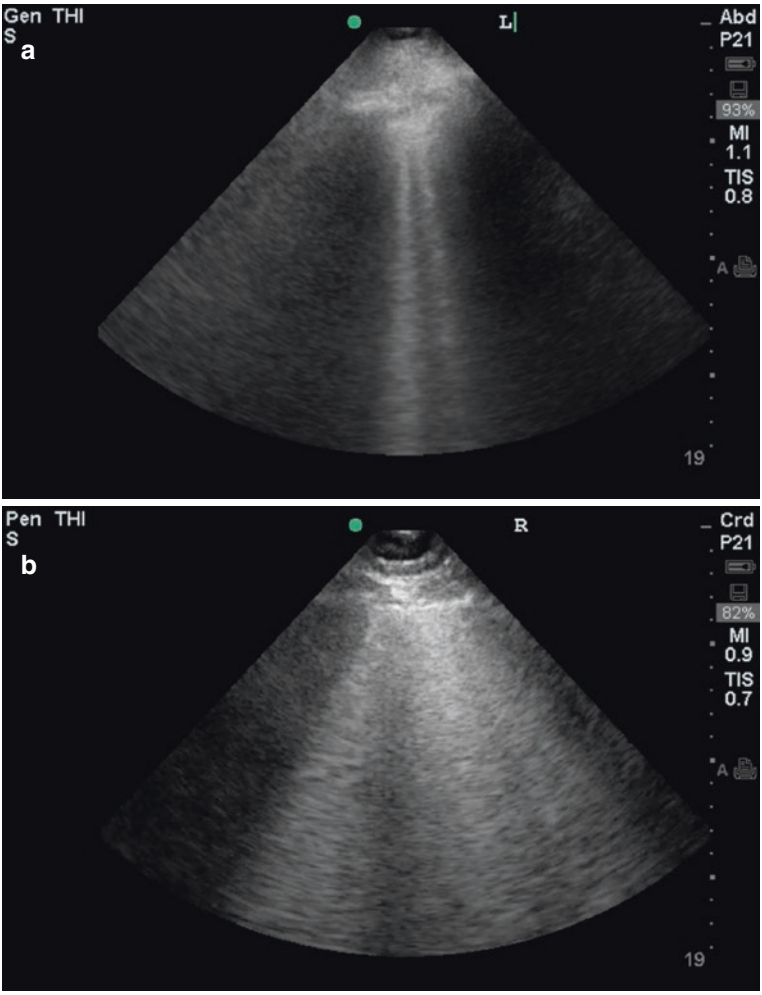

Fig. 11.5 (B lines). B lines are vertical hyperechoic lines arising from the pleural line and extending to a depth of at least 18 cm. Greater than three B lines in a single intercostal space is considered abnormal: Image "a" shows two prominent B lines extending down from the pleural line. Image "b" shows confluent B lines extending down from the pleural line, appearing more as a hyperechoic or bright white sheet than as individual B lines. The confluent B lines (or B lines that merge into one another) are indicative of more significant interstitial fluid than is present when individual B lines can be identified.

diameter that reverses as the positive intrathoracic pressure associated with expiration limits venous return to the heart.

In patients with left heart failure or other obstructive conditions (cardiac tamponade, massive pulmonary embolism, right heart failure, tension pneumothorax), poor forward movement of blood leads to rising RA pressures. With elevation of RA pressures, the diameter of the IVC increases and respirophasic changes in the IVC

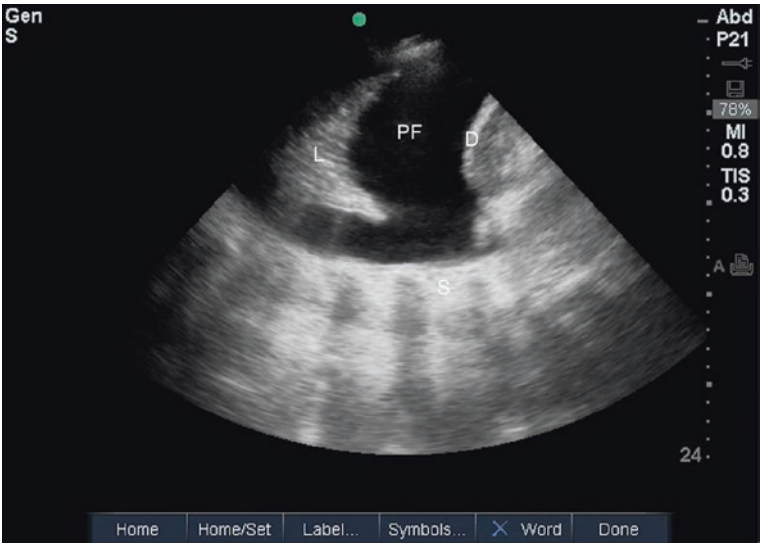

Fig. 11.6 The spine can been seen superior or cephalad to the diaphragm (in this image, to the left of the diaphragm is superior/cephalad in the body) due to the presence of significant pleural fluid that provides an excellent acoustic window for viewing deeper structures such as the spine. When aerated lung alone is present and there is no pleural fluid, the spine is not visible superior to the diaphragm because the air within the lung scatters the sound waves, not allowing the sound waves to reach the deeper spine.

diameter become limited. At the extreme, heart failure results in a plethoric IVC that is dilated and has minimal to no change in diameter with respirations.

Consequently, ultrasound imaging of the IVC may offer noninvasive information regarding RA pressure [33–41]. Kircher et al. reported that CI >50 % was indicative of right atrial (RA) pressures <10 mmHg, whereas CI <50 % indicated RA pressures >10 mmHg [33]. In another study, CI <20 % during passive respiration and CI <40 % during forceful inhalation were both predictive of RA pressures >10 mmHg as measured during right heart catheterization. The IVC has been shown in a number of studies to also correlate to PCWP as well [38].

Besli found that mean IVC diameter is significantly greater in patients with systolic HF than those without HF. Additionally, IVCd was significantly greater in patients with decompensated systolic HF when compared to those with compensated HF. Likewise, the percentage of patients with no IVC diameter variability with respirations was 36 % in patients with decompensated HF versus 5 % in those with compensated HF [42]. Thus IVC imaging may help differentiate between patients with decompensated and compensated HF [42].

IVC imaging has also been employed to help elucidate the cause of dyspnea in patients presenting to the ED. Miller et al. evaluated patients with undifferentiated dyspnea using IVC measurements [43]. They used the caval index which is similar to the CI and is expressed as a percentage via the formula (IVCe – IVCi)/IVCe × 100 %

where IVCe and IVCi are the diameters of the IVC in expiration and inspiration, respectively. His group found that a caval index of less than 33 % yielded a sensitivity of 80 % and a specificity of 81 % for the detection of AHF in patients with dyspnea. Furthermore, extremely low caval indices of less than 15 % carried a high likelihood ratio (LR) of greater than ten that the patient's dyspnea was due to AHF.

Another ED-based study of undifferentiated dyspnea had very similar results. A low IVC variability (15 % or less) in patients with dyspnea predicted a causative etiology of AHF with 92 % sensitivity and 84 % specificity. The static measure of absolute IVC diameter did not differentiate dyspnea due to AHF from other causes [27]. In both of these studies, as IVC diameter variability decreased, the likelihood increased that a patient's dyspnea was due to AHF [27, 43].

Evaluation of the IVC may be prognostic as well as diagnostic. Pellicori et al. suggest that increasing IVCd is associated with worse prognosis in patients with HF regardless of their LVEF [44]. Patients in the highest tertile of IVC diameter had approximately a 40 % risk of an adverse event within the first year and patients with HF in the lowest tertile of IVC diameter had a similar outcome to subjects without HF [44].

US exam of IVCd and collapsibility has been used in diagnosis and therapy of chronic HF with the assumption that IVCd reflects RA pressure [33, 45–47]. Yavasi et al. [48] found that the mean IVC-CI increased significantly with treatment of HF. After the therapy, there was no significant difference between the IVC-CI of the HF patients and controls. The study suggested that treatment response could be better monitored via serial measurements of IVC-CI than serial NT-proBNP levels as there was no significant change in BNP after the therapy.

The IVC-CI shows promise as a diagnostic aid in identifying decompensated heart failure as the cause of dyspnea in patients presenting to the ED and monitoring treatment of ADHF [27, 43, 48]. Standardization of the exact part of the IVC chosen for measurement and patient position at the time of measurement would help produce results that are more easily compared and grouped for analysis.

Lung Ultrasound

Air scatters sound waves. Consequently, air-containing structures such as the lungs were not considered to be amenable to evaluation with ultrasound. Lung ultrasound (LUS) has gained broader application due to a greater understanding of the artifacts generated by the interaction of the US and lung structures and content [28].

Lung ultrasound can be done with the standard cardiac probe or any other low-frequency probe, along the intercostal spaces. Additionally, a high frequency probe can also be used to visualize the pleura but will not provide the necessary depth to evaluate for certain diagnostic artifacts such as B lines. Bilateral hemithoraces are scanned along the anterior chest upper and lower halves as well as laterally superior to the diaphragm [49].

In ultrasound images, the pleural line is represented as a hyperechoic line just deep to the soft tissue of the thoracic wall. In normal conditions, sliding of the parietal and visceral pleura against one another can be seen with respirations.

A lines are produced by a reverberation artifact and appear as multiple, relatively evenly spaced horizontal lines that are parallel to the pleural line [50].

When interstitial fluid is present, the increased alveolar edema produces characteristic artifacts known as B lines that consist of hyperechoic vertical lines which arise from the visceral-parietal lung interface, extend to a depth of at least 18 cm, move with respiration, and erase A lines. Isolated B lines can be found in normal lung, especially in the more dependent regions. On the contrary, three or more B lines per intercostal space are considered abnormal and consistent with the diagnosis of alveolar interstitial syndrome (AIS). AIS can be focal and unilateral, as in pneumonia or pulmonary contusion, or diffuse and bilateral as in pulmonary edema or acute respiratory distress syndrome (ARDS) [41, 49].

LUS easily detects pleural effusion, a pathologic finding frequently present in ADHF. A pleural effusion appears as an anechoic area in the dependent area of the thorax, delimited inferiorly by the diaphragmatic dome and superiorly by the aerated lung [41, 50, 51].

LUS may be used to distinguish between AHF and other noncardiac causes of dyspnea, particularly the COPD exacerbation [28, 41, 52–54].

Evaluation for both B lines and pleural fluid facilitates that differentiation. B lines are strongly associated with other indices of congestion (i.e., radiographic, measurement of extravascular lung water by the dilution technique, PCWP, echocardiographic, and intrathoracic impedance monitoring) [55–58]. Consequently, lung ultrasound can provide direct insight into the pulmonary interstitium [58–62].

A meta-analysis of seven studies, the majority conducted in the ED or ICU, showed that, in patients with acute dyspnea, lung ultrasound for B lines has a sensitivity of 94.1 % and specificity of 92.4 % for the diagnosis of acute cardiogenic pulmonary edema [53]. Another study in the ED population showed a sensitivity of 86 % and specificity of 98 % for lung US in diagnosis of diffuse AIS [60].

Lung US also detects and quantifies pleural effusion with a higher sensitivity and specificity than plain radiographs. Finding a pleural effusion in a patient with multiple and bilateral B lines can significantly increase the probability of a cardiogenic cause of dyspnea [41].

A multicenter prospective trial was conducted in seven EDs to evaluate the diagnostic accuracy of different approaches to evaluation of the dyspneic patient [54]. Specifically, they hypothesized that adding LUS to routine clinical assessment and chest radiography would increase EPs' ability to distinguish ADHF from noncardiogenic dyspnea. It was a robust study that included over 1000 patients who were evaluated and scanned by 62 EPs in both community and academic hospitals with each EP enrolling a median of 42 patients. Each patient was scanned in six thoracic zones (three per hemithorax): the second intercostal space at the midclavicular line, the fourth intercostal space at the anterior axillary line, and the fifth intercostal space at the posterior axillary line. LUS was considered positive for diffuse interstitial syndrome if two or more zones bilaterally showed the presence of at least three B lines. The LUS-implemented approach had a significantly higher accuracy (sensitivity 97 %, specificity 97.4 %) in differentiating ADHF from noncardiac causes of acute dyspnea than the initial clinical workup (sensitivity 85.3 %, specificity 90 %) and also greatly outperformed chest radiography alone (sensitivity 69.5 %, specificity 82.1 %)

and natriuretic peptides (sensitivity 85%, specificity 61.7%, $n=486$). One in five patients was reclassified into the correct diagnosis after LUS was performed (net reclassification index of LUS compared with standard workup = 19.1%).

The Pivetta study is among several that show that LUS can be implemented by nonexperts and, consequently, that the diagnostic results achieved in these studies can be generalized to other settings [52, 54, 63]. It has been shown that LUS can easily be learned through short didactic sessions [63]. Even in the hands of novice sonographers, LUS can be a reliable tool to predict cardiogenic dyspnea [52, 63]. Furthermore, these studies demonstrate a high interobserver agreement between inexperienced and expert sonographers when interpreting LUS images. One of the studies also suggests that an abbreviated two-zone scan of the lateral and inferior lung zones bilaterally has similar sensitivity and specificity to the eight-zone scan detailed by Volpicelli and generally accepted as the standard in LUS [52, 60].

Missed or delayed diagnosis of ADHF in the ED is associated with prolonged hospital stay, higher rates of ICU admission, higher mortality, and increased costs [64–66]. In patients with heart disease, lung US may provide information about prognosis. Frassi et al. [67] reported that B lines were associated with a twofold increase in the rate of death, myocardial infarction, or HF hospitalization (HR 1.9, 95% CI 1.1–3.4) at follow-up. In an outpatient study of HF patients, a higher number of B lines on LUS identified patients with a fourfold risk of death or HF hospitalizations and a greater than threefold risk of urgent HF visits, HF hospitalizations, or death from any cause over 6 months, independent of risk factors such as age, sex, NYHA class, and clinical congestion score [68]. Furthermore, this study found that only one in five patients had crackles on exam despite being in the group with the greatest number of B lines. This finding supports the use of LUS as a sensitive predictor of subclinical pulmonary congestion in HF. In both studies, lung US predicted relevant clinical outcomes, including death and incident cardiovascular events [67, 68].

Finally, because of the ability of LUS to show rapid extravascular water variation [69], it is a precious aid in assessing the extent of pulmonary congestion and may be used not only in the diagnosis of ADHF but also in monitoring the response to diuretic treatment. Lung US is able to capture changes in congestion status after intravenous diuretic therapy in decompensated HF [70]. Additionally, lung imaging enables a more direct assessment of extravascular lung water than indirect measures. Coiro et al. [71] evaluated the prognostic significance of quantification of B lines in patients discharged after acute HF compared with other classical congestion markers. The major finding of this study is that residual pulmonary congestion, as easily assessed by lung ultrasound (quantified as greater than 30 B lines), at discharge is an independent predictor of both short-term mortality and hospitalization for worsening HF.

Multisystem Ultrasound

The prior studies looked at each organ individually and reported various specificities in differentiating ADHF from other causes of dyspnea [1, 72–74].

Recent research has investigated multisystem imaging by combining components that had previously been used in isolation to diagnose or evaluate heart failure. Mantuani published the use of a "triple scan" (TS) of the heart, lungs, and IVC to differentiate between a cardiogenic and non-cardiogenic cause of pulmonary edema in an acutely dyspneic patient [74]. Subsequently, multiple multi-organ ultrasound studies evaluating dyspneic patients have been published.

In a direct comparison of integrated lung-cardiac-IVC (LCI) US versus lung US alone, Kajimoto et al. demonstrated the strength of a multisystem approach to ultrasound in undifferentiated dyspnea. Cardiologist-performed LCI US had a sensitivity of 94 % and specificity of 91 %, while lung US alone had a sensitivity of 96 % and specificity of 54 % for differentiating AHF from primary pulmonary disease in acutely dyspneic ED patients [72].

Anderson et al. [1] evaluated a combination of LVEF less than 45 %, IVC-CI less than 20 %, and B lines of at least 10 total in eight lung regions and found a low sensitivity of 36 % and a high specificity of 100 % for ADHF. Russell et al. [75] reported a sensitivity and specificity of 83 and 83 % for ADHF with an US evaluation that included LVEF, B lines, IVC-CI plus pleural effusion, and diastolic dysfunction. Interestingly, the presence of a pleural effusion combined with an ejection fraction <45 % was 98 % specific for ADHF, with an LR of 51. Their study also found that the specificity of treating EP diagnosis for ADHF improved from 44 to 83 % when POCUS was used.

Two studies have specifically assessed the impact of multi-organ POCUS in addition to history and physical exam on the accuracy of the treating EPs' initial diagnosis [76, 77].

Pirozzi et al. used a protocol that evaluated the heart, lungs, and IVC, adding a lower extremity venous compression study in patients with dyspnea. Diagnostic accuracy was significantly better in the group that received immediate POCUS (5 % incorrect initial diagnosis) rather than an exam within 1 h of ED arrival (50 % incorrect initial diagnosis). The study did not find a difference in hospital length of stay or mortality between the two groups.

Mantuani's follow-up study in 2016 showed that the TS improves diagnostic accuracy when performed after the initial history and physical exam. Overall accuracy of the treating physician's impression significantly increased from 53 % before TS to 77 % after the EPs interpreted images from a study investigator who performed TS on their patient. The TS increased treating EP sensitivity for ADHF to 100 %, enabling them to pick up subtle ADHF cases initially misdiagnosed as COPD or other diagnoses. Additionally, the TS was associated with a 95 % specificity for the diagnosis of ADHF, allowing the EPs to reliably exclude this diagnosis. Notably all TS were performed nearly immediately in this population with respiratory distress, allowing EPs to tailor therapeutics appropriately for the disease process [76].

In severe undifferentiated dyspnea, immediate TS resulted in a statistically significant improvement in treating EPs' overall diagnostic accuracy. Its primary utility was to rapidly diagnose or exclude ADHF. Astute clinicians should incorporate multisystem US into their ED evaluation of acute dyspnea. Future studies investigating whether early multi-organ ultrasound results in improved outcomes in heart failure would be impactful.

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Diagnostic and Prognostic Biomarkers in Emergency Department Heart Failure

12

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Introduction

In the USA, there are over one million heart failure admissions per year, with 35 % of cases progressing to death or readmissions within 60 days. In spite of major advances in therapy, prognosis for heart failure remains poor. Challenges still remain in timely diagnosis of acute heart failure and accurate risk stratification of patients with heart failure. Biomarkers, with their objectivity and widespread availability, have an indispensible role in improving heart failure management. Among the biomarkers available today, natriuretic peptides are the most validated and accepted for acute heart failure diagnosis. For prognostic evaluation of heart failure, natriuretic peptides, troponin, creatinine, blood urea nitrogen (BUN), serum sodium, and novel biomarkers such as mid-region proadrenomedullin (MR-proADM), C-terminal pre-pro-vasopressin (copeptin), and ST2 have all been shown to be effective in identifying high-risk patients who are more likely to have adverse clinical outcomes.

It is important to note that heart failure is a complicated disease, involving dysfunctions in multiple physiological processes. A biomarker representing a single pathophysiological process is unlikely to be sufficient for the evaluation of heart failure patients. A multimarker approach utilizing biomarkers representing different pathophysiological processes is required to adequately assess the risk profile of a given heart failure patient. As a result, significant effort has been placed on biomarker research, leading to the emergence of several promising novel biomarkers for heart failure diagnosis and risk stratification.

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Table 12.1 Characteristics of BNP and NT-proBNP

	BNP	NT-proBNP
Components	BNP molecule	NT fragments (1–76) NT-proBNP (1–108)
Molecular weight	4 kDa	8.5 kDa
Genesis	Cleavage from NT-proBNP	Release from ventricular myocytes
Half-life	20 min	120 min
Clearance mechanism	Neutral endopeptidase clearance receptors	Renal clearance
Increase with normal aging	+	++++
Correlation with estimated glomerular filtration rate	−0.20	−0.60
Approved cutoff(s) for CHF diagnosis	100 pg/mL	Age <50: 450 pg/mL Age >50, <75: 900 pg/ml Age >75: 1800 pg/mL
Entry on US market	Nov 2000	Dec 2002

Natriuretic Peptides

Natriuretic peptides have become a staple in assisting the clinical diagnosis of acute heart failure. The most relevant biomarkers in this peptide family are B-type natriuretic peptide (BNP), N-terminal prohormone BNP (NT-proBNP), and atrial natriuretic peptide (ANP). BNP was originally isolated from the porcine brain, leading to its original name "brain natriuretic peptide," although it is made predominantly in the cardiac ventricles in humans. BNP is a 32-amino acid peptide hormone with an in vivo half-life of 20 min. BNP is a cleavage product of NT-proBNP, which itself is a cleavage product of prohormone BNP, a 134-amino acid peptide. NT-proBNP is a 76-amino acid peptide with an in vivo half-life of 120 min. ANP is a 28-amino acid peptide hormone first isolated from the atrial tissue of rats. Among the three, BNP and NT-proBNP are more validated by clinical trials and more widely used in today's clinical practice (Table 12.1). Natriuretic peptides are released by the cardiac ventricles in response to increased wall stress caused by the volume expansion and pressure overload that accompanies heart failure. They are protective hormones that serve to counteract the physiological abnormalities of heart failure. Their functions include increasing glomerular filtration rate (GFR), increasing sodium and water excretion, increasing vasodilation by relaxing arterioles and venules, inhibiting cardiac hypertrophy, and inhibiting renin and aldosterone secretion [1].

The need for biomarkers in diagnosing acute heart failure stemmed from the fact that differentiating between pulmonary and cardiac causes of acute dyspnea has traditionally been a challenge as the physical exam, laboratory, and radiographical finding between the two conditions have significant overlap. Delayed diagnosis and

therapy for acute heart failure not only increases morbidity and cost but also leads to increased mortality, making accurate diagnosis of heart failure in the emergency department imperative. A quick, simple, and objective test can greatly aid in the diagnostic workup of patients with acute dyspnea. BNP and NT-proBNP have emerged to fill in the role of this much-needed supplement to history and physical exam. Over the years, the use of natriuretic peptides has expanded into prognostic evaluation of heart failure patients.

Natriuretic Peptides in the Diagnosis of Acute Heart Failure

Although BNP was first isolated by Sudoh et al. in 1988, its role as a biomarker in acute heart failure was not established until 2002. The multicenter Breathing Not Properly trial, by Maisel et al., was the first study to validate the effectiveness of BNP in the diagnostic workup of patients presenting to the emergency department (ED) with acute dyspnea. In this study, a BNP > 100 pg/mL was shown to be 73 % specific and 90 % sensitive for the diagnosis of acute heart failure with a diagnostic accuracy of 83.4 %. The negative predictive value of BNP < 50 pg/mL for acute heart failure was 96 % [2]. Besides BNP, NT-proBNP has also been studied extensively for the diagnostic evaluation of patients with acute dyspnea. In the PRIDE (Pro-Brain Natriuretic Peptide Investigation of Dyspnea in the Emergency Department) study by Januzzi et al., NT-proBNP was shown to have comparable sensitivity and slightly higher specificity (90 % sensitive and 85 % specificity) for the diagnosis of acute heart failure [3]. Natriuretic peptide levels are highly reproducible and can be checked with ease in a typical clinical laboratory. Adding natriuretic peptide levels to the standard diagnostic evaluation of acutely dyspneic patients can significantly reduce clinical indecision and diagnostic lag time, leading to their widespread acceptance (Fig. 12.1). ANP, although discovered around the same time as BNP, suffers from in vitro instability, which has limited its use in routine clinical practice. Recently, biochemical assays targeting a stable fragment of the ANP prohormone, mid-region proANP (MR-proANP), became available, leading to the emergence of ANP as a diagnostic in acute heart failure. The diagnostic utility of MR-proANP was examined in a large-scale multinational study, Biomarker in Acute Heart Failure (BACH) trial by Maisel et al. in 2008. In the BACH trial, 1641 patients with acute dyspnea were studied for the diagnostic accuracy of MR-proANP for acute heart failure. This study demonstrated that MR-proANP ≥ 120 pmol/L was non-inferior to BNP > 100 pg/L for the diagnosis of acute heart failure (Table 12.2). Requiring both BNP and MR-proANP to be elevated increased the diagnostic accuracy of acute heart failure to 76.6 % compared to 73.6 % for BNP elevation alone. In addition, MR-proANP measurements added to the diagnostic accuracy of BNP in patients with intermediate BNP value and obesity, but not in renal insufficiency, elderly patients, and patients with edema [4].

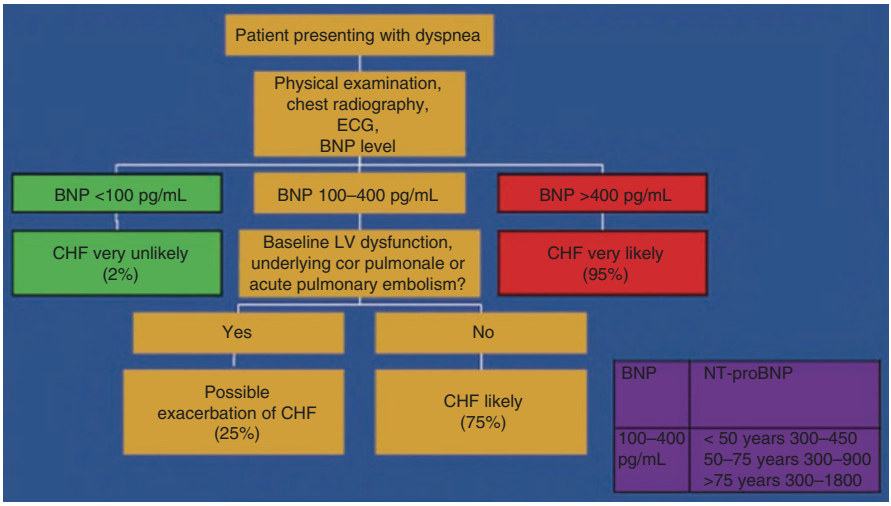

Fig. 12.1 Algorithm using B-type natriuretic peptide (BNP) and N-terminal prohormone B-type natriuretic peptide (NT-proBNP) levels to rule in and rule out congestive heart failure (CHF). ECG indicates electrocardiography; *LV* left ventricular (Copyright MedReviews, LLC. Reprinted with permission of MedReviews, LLC. Maisel [50]. Reviews in cardiovascular medicine is a copyrighted publication of MedReviews, LLC. All rights reserved)

Table 12.2 MR-proANP vs. BNP for diagnosis of acute heart failure

Measure	Sensitivity	Specificity	Accuracy
MR-proANP 120 pmol/L	95.56	59.85	72.64
BNP 100 pg/Ml	96.98	61.90	73.50
Difference	1.42	2.05	0.86
Upper 95 % limit	2.82	3.84	2.10
Non-inferiority *p*	<0.0001	<0.0001	<0.0001

MR-proANP mid-regional pro-atrial natriuretic peptide, *BNP* B-type natriuretic peptide

Natriuretic Peptides in the Prognostic Evaluation of Heart Failure

Another important function of natriuretic peptides is their use in the risk stratification of heart failure patients. The ability to accurately risk stratify patients can allow clinicians to tailor therapy to fit each patient's needs. These individualized treatments will not only decrease morbidity and mortality but also reduce cost to the overall health system. Both BNP and NT-proBNP have been studied with promising results in the prognostic evaluation of heart failure patients.

Multiple natriuretic peptide studies have been performed in the ED setting, mostly in patients presenting with acute dyspnea. While the majority of these studies focused on the diagnostic utility of natriuretic peptides, major prognostic

evidence had arisen as well. For example, the ADHERE (Acute Decompensated Heart Failure National Registry) database of 65,275 acute heart failure patients showed that BNP level at the time of admission had a nearly linear relationship with the risk for in-hospital mortality. The adjusted odds ratio for mortality between BNP quartile 4 (BNP > 1730 pg/mL) and BNP quartile 1 (BNP < 430 pg/mL) was 2.23 with $p < 0.0001$. In addition, initial ED BNP levels can identify patients at high risk for 30-day mortality or readmission [5]. These findings were confirmed and expanded upon later in an analysis of the Get With The Guidelines Heart Failure registry. In this study, the admission BNP of 99,930 acute heart failure patients was analyzed by gender and categories of ejection fraction including reduced (<40 %), borderline (40–49 %), and preserved (≥50 %). Though there were differences in BNP values between genders and ejection fraction categories, in all categories and genders, patients with a BNP above the median had higher mortality than those below. BNP remained predictive of in-hospital mortality after adjusting for over 20 variables [6]. These two large registry studies highlight BNP's prognostic ability for mortality.

NT-proBNP is also highly prognostic in patients with acute heart failure. Januzzi et al. demonstrated that an ED NT-proBNP level greater than 1000 pg/mL is indicative of severe heart failure and is associated with adverse prognosis [7]. Furthermore, the IMPROVE-CHF (Canadian Multicenter Improved Management of Patients with Congestive Heart Failure) study showed that knowing a patient's NT-proBNP level during ED evaluation can decrease the duration of the ED visit by 21 % and reduce 60-day rehospitalization rate by 35 % in addition to reducing overall medical costs [8].

The prognostic value of natriuretic peptides can play an important role in guiding treatment strategies. Having a baseline natriuretic peptide level when a patient's heart failure is stable can go a long way to assist with prognostic evaluation when he/she goes into acute heart failure. Acute heart failure patients whose natriuretic peptide levels remain elevated despite appropriate inpatient therapy often have a poorer prognosis and require closer follow-up in the outpatient setting. For example, Bettencourt et al. showed that among 182 patients admitted to the hospital for acute heart failure, discharge NT-proBNP above the median (>4137 pg/mL) was associated with increased post-discharge adverse outcomes. He also showed that the change in NT-proBNP values with treatment is highly prognostic. Patients with NT-proBNP increase greater than 30 % from admission to discharge had the worse outcome, followed by patients with less than 30 % change in NT-proBNP levels. Patients with more than a 30 % decrease in NT-proBNP levels had the best outcome. The single best predictor of mortality and readmission in this study was the change in NT-proBNP levels from admission to discharge [9]. Within the hospital setting, the current general consensus is to obtain a natriuretic peptide value at admission and again prior to discharge when the patient is deemed to be clinically optivolemic. Repeat natriuretic peptide levels are suggested if there is clinical deterioration. While some trials have shown that the lower the natriuretic peptide level at discharge, the lower the risk of death and readmission, overall, the literature has been inconsistent. Still, an as-low-as-possible natriuretic peptide level is a reasonable goal for clinicians to aim for while treating a patient for acute heart failure. In fact, a BNP level of <350 pg/mL or NT-proBNP level <4000 pg/mL at discharge is

generally linked to a stable post-hospital course, which is especially true if the patient is clinically optivolemic.

As to why a patient's natriuretic peptide level can remain elevated despite recommended in-hospital treatment, the answer may be multifactorial. First, the high natriuretic peptide level could reflect the severity of patient's baseline heart failure, which may result in persistently elevated ventricular wall stress. Second, excessive treatment with diuretics may cause the patient to enter a prerenal state leading to a decreased GFR. Because natriuretic peptides are partly cleared by the kidneys, a decreased GFR can lead to inappropriately elevated natriuretic peptide levels due to poor clearance. In patients with concurrent right heart failure leading to edema and ascites, significant diuresis can occur prior to any effects on ventricular preload, resulting in persistent elevation of ventricular wall stress despite diuresis. Finally, there is the possibility that the treatment was inadequate and ventricular wall stress remains elevated despite treatment [3].

Perhaps the most exciting and rapidly expanding use of natriuretic peptides is in the outpatient setting, where natriuretic peptides can help to identify patients who are at high risk for future adverse events. For example, the Framingham Offspring Study, which evaluated 3346 asymptomatic outpatients, demonstrated that elevated natriuretic peptide levels were predictive of future adverse cardiovascular events and mortality. In this particular cohort, BNP values above the 80th percentile were associated with increased risk for death (hazard ratio = 1.62, $p = 0.02$), first major cardiovascular event (hazard ratio = 1.76, $p = 0.03$), atrial fibrillation (hazard ratio = 1.91, $p = 0.02$), stroke or transient ischemic attack (hazard ratio = 1.99, $p = 0.02$), and heart failure (hazard ratio = 3.07, $p = 0.002$) [10]. These natriuretic peptide elevations in asymptomatic patients may reflect a change in cardiac or renal function that has not yet manifested as clinical deterioration. Measuring natriuretic peptides in these patients can help to identify clinical deteriorations early on and assist with therapeutic interventions to prevent the development of significant symptoms.

In outpatient management of heart failure, it is very important to know each patient's optivolemic natriuretic peptide level, which can serve as a baseline for comparison during subsequent evaluations. This is especially true in cases where symptoms have not yet appeared. A greater than 50 % rise of natriuretic peptide levels from baseline is associated with high risk for impending heart failure decompensation. The clinician must also keep in mind that small changes in natriuretic peptide levels (<50 % of baseline levels) could reflect biological variability in some patients and may not represent a forthcoming clinical event. Therefore, a detailed history, physical exam, and standard laboratory values are still very important in heart failure management.

Natriuretic Peptide-Guided Heart Failure Therapy

With increasing data supporting the prognostic utility of natriuretic peptide, there have been several attempts to use natriuretic peptides to guide outpatient heart failure therapy with relative success. The first large-scale natriuretic peptide-guided

therapy study was the STAR-BNP study by Jourdain et al. STAR-BNP was a multicenter study comparing the outcomes of BNP-guided therapy against standard clinical therapy. A total of 220 NYHA class II and III patients optimally managed with ACE inhibitors, beta-blockers, and diuretics were involved in the study. These patients were randomized to receive either BNP-guided therapy with a goal BNP of <100 pg/mL or standard clinical therapy according to guidelines at the time. The patients were followed for up to 15 months for a primary end point of heart failure-related death or admission. By the end of the study, the BNP-guided arm had significantly fewer patients reaching primary end point than the standard clinical therapy arm (24 % vs. 52 %, $p<0.001$) [11]. The STAR-BNP study was followed by the BATTLESCARRED study, which was a large-scale study comparing NT-proBNP-guided therapy, intensive clinical management (treatment by a heart failure management team led by heart failure specialists), and usual care (treatment at the discretion of a primary care physician). A total of 366 patients were enrolled and followed for up to 3 years. The study found that 1-year mortality was significantly less in both the NT-proBNP-guided therapy arm (9.1 %) and the intensive clinical management arm (9.1 %) when compared to the usual care arm (18.9 %; $p=0.03$). In addition, the study found that in patients less than 75 years of age, the 3-year mortality was significantly lower in the NT-proBNP-guided arm (15.5 %) when compared to both the intensive clinical management arm (30.9 %, $p=0.048$) and the usual care arm (31.3 % and $p=0.021$), highlighting the long-term benefit of natriuretic peptide-guided therapy [12]. The largest natriuretic peptide-guided heart failure therapy trial was the TIME-CHF trial, which was a prospective randomized study evaluating the effectiveness of NT-proBNP-guided therapy versus symptom-guided therapy with a total of 499 chronic heart failure patients followed for up to 18 months. This study found similar rates of survival free of all-cause hospitalizations between the NT-proBNP-guided therapy arm and symptom-guided therapy arm (41 % vs. 40 %, respectively; $p=0.39$). Additionally, NT-proBNP-guided heart failure therapy led to higher rates of survival free of all-cause hospitalizations in patients aged 60–75 years ($p<0.02$) [13]. A meta-analysis of natriuretic peptide-guided therapy confirmed that natriuretic peptide-guided therapy reduced all-cause mortality in patients <75 years old and reduced heart failure and cardiovascular hospitalization in all patients [14]. These studies have consistently shown the long-term effectiveness of natriuretic peptide-guided heart failure therapy, highlighting the potential benefit of adding natriuretic peptides to future heart failure treatment algorithms. This is reflected in the 2013 ACCF/AHA Guideline for the Management of Heart Failure, which gives a Class IIa level of evidence B recommendation to using natriuretic peptide-guided therapy [15].

Natriuretic Peptides for Heart Failure Screening

Finally, using natriuretic peptides in screening for asymptomatic heart failure patients is also a possibility in the future, as many patients with left ventricular dysfunction would have elevations in natriuretic peptide levels prior to developing symptoms of

heart failure. This would be a far more convenient and cost-effective method than the current gold standard for left ventricular dysfunction detection, the echocardiogram. There are many reasons why screening with natriuretic peptides would be beneficial. First of all, cardiac disorders are common and are a source of considerable morbidity and mortality. Additionally, natriuretic peptides are elevated early in the disease process, often before symptoms develop and thus can allow for early treatment. Finally, early treatment in heart failure is associated with better outcomes and is more cost-effective than delayed action. The future of natriuretic peptide use in the outpatient setting, whether it be managing chronic heart failure or screening for new cases, is bright, and the utility of natriuretic peptides is only going to increase with time.

Caveats of Natriuretic Peptide Use

In order to optimally use natriuretic peptides in clinical practice, the clinician must be aware of important caveats and limitations of their use:

- Obesity: Natriuretic peptide levels are generally lower in obese patients both with and without heart failure. The reason for this is currently not completely understood. It may have to do with increased natriuretic peptide receptor-C clearance receptors on adipocytes. This is supported by the fact that obese patients still have elevated levels of precursor hormones despite having low BNP and NT-proBNP levels. Measured natriuretic peptide levels in obese patients should be multiplied by a factor of two to three to account for this discrepancy.
- Gray zone: In relation to diagnosis, moderate increases in natriuretic peptides fall into the "gray zone" where the evidence is not as strong in supporting an acute heart failure diagnosis. In these cases, clinical acumen is especially important, and other causes of myocardial stress should be considered, such as pulmonary hypertension, pulmonary embolism, arrhythmias, acute coronary syndrome, pneumonia, or COPD with cor pulmonale.
- Renal disease: As mentioned above, renal disease can influence natriuretic peptide levels through several mechanisms including decreased clearance of natriuretic peptides and counter-regulatory responses from cardiorenal syndrome. It has been suggested that natriuretic peptide cutoffs for patients with a GFR <60 mL/min may need to be raised. Detailed knowledge of a patient's renal function is important when natriuretic peptides are used for clinical assessment.
- Shock: Natriuretic peptide values have been shown to be unreliable in cases of shock and therefore should be avoided in hemodynamically unstable patients.

Blood Urea Nitrogen

BUN is a serum by-product of protein metabolism. It is probably one of the oldest prognostic biomarkers in heart failure. Urea is formed by the liver and carried by the blood to the kidneys for excretion. Diseased or damaged kidneys cause BUN to

accumulate in the blood as the GFR goes down. Conditions such as hypovolemic shock, congestive heart failure, high-protein diet, and bleeding into the gastrointestinal tract will also cause BUN elevations. BUN plays a unique role as a short-term as well as long-term prognostic marker in patients with heart failure. In 2005, Fonarow et al. analyzed the ADHERE database for predictors of in-hospital mortality among 65,275 acute heart failure admissions. Of the 39 variables evaluated in this database, BUN ≥ 43 mg/dL was the single best predictor of mortality, followed by admission systolic blood pressure <115 mmHg and serum creatinine ≥2.75 mg/dL (243.1 μmol/L) [16]. Another study done by Aronson et al. in 2004, which involved 541 patients with acute heart failure, examined the prognostic utility of BUN, serum creatinine, BUN/creatinine ratio, and estimated creatinine clearance. There were 177 mortalities in this cohort and the mean follow-up period was 343 ± 185 days. The risk of all-cause mortality increased significantly with each quartile of BUN, with an adjusted relative risk of 2.3 in patients in the upper quartiles ($p = 0.005$). Creatinine and estimated creatinine clearance were not statistically significant predictors of mortality after adjustment for other covariates. BUN/creatinine ratio yielded similar prognostic information as BUN (adjusted relative risk = 2.3; $p = 0.0007$ for patients in the upper quartiles) [17]. As seen in these studies, elevated BUN levels are strongly associated with adverse outcomes in patients hospitalized for acute heart failure. Therefore, BUN levels should be considered in the routine prognostic evaluation of patients with acute heart failure.

Creatinine

Creatinine is a breakdown product of creatine phosphate in muscle tissue. It is usually produced at a fairly constant rate. Creatinine is cleared by the kidneys with little-to-no tubular reabsorption. Creatinine accumulates in the blood when GFR decreases in the setting of renal dysfunction. As a result, serum creatinine levels are commonly used to calculate the creatinine clearance, which is a surrogate for GFR and renal function. Since renal dysfunction is a negative prognostic factor in patients with heart failure, elevations of creatinine are associated with poor outcomes in heart failure patients. This was shown in a study by Vaz Perez et al. in 2009, involving 128 patients who were hospitalized for acute heart failure. In this study, elevated admission creatinine level was a strong predictor of both 1-year and 5-year mortality. For 1-year mortality, creatinine and ejection fracture were both independent predictors of mortality in multivariable analysis ($p < 0.001$), whereas body mass index and NYHA class did not reach statistical significance. In the multivariate analysis for 5-year mortality, creatinine and NYHA class were independent predictors of all-cause mortality ($p < 0.001$), whereas body mass index and age did not reach statistical significance [18]. In another study by Aronson et al. involving 467 patients with acute heart failure, persistent creatinine elevation above baseline was associated with significantly worse outcomes. Persistent creatinine elevation in this study was defined as ≥0.5 mg/dL increase in serum creatinine above baseline for more than 30 days. Transient creatinine elevation was defined as creatinine elevation ≥0.5 mg/dL above

baseline that subsequently decreased to <0.5 mg/dL above baseline within 30 days. Persistent creatinine elevation was seen in 115 patients and transient creatinine elevation was seen in 39 patients. The 6-month mortality rates were 17.3 % in patients without creatinine elevation, 20.5 % in patients with transient creatinine elevation, and 46.1 % in patients with persistent creatinine elevation. Compared to patients' stable creatinine (<0.5 mg/dL increase from baseline), the adjusted hazard ratio for mortality was 3.2 ($p<0.0001$) in patients with persistent creatinine elevation [19]. These studies highlighted the fact that elevated creatinine level is a strong predictor of medium- and long-term mortality in patients with heart failure and can serve as a fast and inexpensive biomarker to help identify patients at high risk for mortality.

Troponin

Troponin, a biomarker widely used for the diagnosis of myocardial infarction, is increasingly being recognized as a valuable biomarker for risk stratification of heart failure patients. Elevated troponin levels have long been associated with increased in-hospital and long-term mortality, as shown by Peacock et al. in an analysis of the ADHERE database. In this analysis, patients admitted for acute heart failure were risk stratified by admission troponin levels. Positive troponin was defined as troponin I greater than 1000 ng/L and troponin T greater than 100 ng/L. From this database, 4240 patients had a positive troponin by this definition. Patients with a positive troponin had significantly increased risk for in-hospital mortality when compared to patients with negative troponin (odds ratio = 2.55; $p<0.001$) [20]. These findings have also been shown in the recently published BACH trial where acute heart failure patients with an elevated troponin had significantly increased mortality [8].

Further refinement of the troponin assay has led to high-sensitivity troponin assays capable of measuring troponin I in the ng/L range. This has made it possible to detect troponin levels in virtually all patients with heart failure. In a study by our group, we examined 144 patients hospitalized for acute heart failure with serial measurements of troponin I. Using a high-sensitivity troponin I assay, troponin levels were detectable in every patient in the study. We found that patients with small troponin elevations at discharge (troponin I > 23.25 ng/L) have significantly higher risk for 90-day mortality and readmission than patients with troponin I less than 23.25 ng/L (hazard ratio = 3.547; $p=0.003$). Patients with small troponin elevations and BNP elevations are at even higher risk for mortality and readmission comparing to patients without elevations in troponin and BNP (hazard ratio = 15.972; $p=0.007$). In addition, we found that patients with increasing troponin levels during hospitalization have significantly increased risk for 90-day mortality than those with stable or decreasing troponin levels (hazard ratio = 4.520; $p=0.047$) [21]. The significance of our findings lies in the fact that every patient included in the analysis had measurable troponin levels, thus extending the prognostic value of troponin to the entire acute heart failure population. Furthermore, since the trend of troponin levels during acute heart failure treatment is prognostic of adverse events, serial measurements of troponin levels should be considered during hospitalization for acute heart failure.

The findings of this study are confirmed and supported by other cohort studies showing increased mortality with elevated troponin levels measured with high-sensitivity assays [22, 23]. A large trial is needed to further confirm these findings, as surely, high-sensitivity troponin measurements are likely to become a routine part of the evaluation and treatment of acute heart failure patients.

Sodium

It is well known that hyponatremia is a common consequence of heart failure and is associated with worse outcomes. The cause of hyponatremia in heart failure is complex and involves several pathophysiological processes. Decreased cardiac output due to heart failure leads to activation of the renin–angiotensin–aldosterone system (RAAS), increased sympathetic discharge, and the release of vasopressin from the posterior pituitary gland. The RAAS decreases sodium and water delivery to the collecting duct by increasing tubular reabsorption while further stimulating the sympathetic nervous system and increasing vasopressin release. The sympathetic nervous system also stimulates RAAS and further potentiates sodium and water conservation via renal afferent vasoconstriction and direct action on the proximal tubules. Finally, vasopressin upregulates aquaporin channels in the collecting ducts, leading to increased water reabsorption. The combined effect of these pathophysiological pathways forms a vicious cycle of sodium and free water retention, leading to hyponatremia, worse heart failure symptoms, and increased mortality [24].

As a result, serum sodium measurements could help to give clinicians a glimpse of the prognosis of a patient. In a trial by Kearney et al. involving 553 outpatients, serum sodium was shown to be an independent predictor of all-cause mortality during their 5-year follow-up period. In fact, for a 2 mmol/L decrease in serum sodium, the calculated hazard ratio was 1.22 ($p<0.01$) [25]. Furthermore, in a retrospective study of 4031 outpatients with heart failure by Lee et al., serum sodium <136 mmol/L was associated with a 50% increased risk of mortality at both 30 days and 1 year [20]. Finally, Klein et al. reported from the OPTIME-CHF study that serum sodium is a significant predictor of increased 60-day mortality with a hazard ratio of 1.18 per 3 mEq/dL decrease in serum sodium ($p=0.018$). Hyponatremic patients also had longer hospital stays and higher 60-day rehospitalization rates in this study [19]. Although hyponatremia is associated with worse outcomes in heart failure patients, one must keep in mind that multiple factors influence serum sodium levels, including both pathophysiological processes and medications, which must be taken into consideration when serum sodium is used for the prognostic evaluation of heart failure patients.

Emerging Biomarkers of Heart Failure

Over the past decade, significant progress has been made in the discovery of new biomarkers representing different physiological processes with the potential to improve the accuracy of diagnostic and prognostic evaluation of heart failure patients.

The biomarkers worth mentioning are mid-region proadrenomedullin (MR-proADM), C-terminal pre-pro-vasopressin (copeptin), ST2, and procalcitonin.

Mid-region Proadrenomedullin and Bioactive Adrenomedullin

Adrenomedullin (ADM) is a 52-amino acid ringed peptide with C-terminal amidation. It was first isolated from human pheochromocytoma cells. Since its first report, studies examining the effects of ADM have increased exponentially, highlighting its important role in physiology. ADM is a peptide hormone with natriuretic, vasodilatory, and hypotensive effects mediated by cyclic adenosine monophosphate (cAMP), nitric oxide, and renal prostaglandin systems. ADM expression is seen in many tissues and organ systems, including cardiovascular, renal, pulmonary, cerebrovascular, gastrointestinal, and endocrine tissues. ADM acts as both a circulating hormone and a local autocrine and paracrine hormone. ADM plasma concentrations are increased in hypertension, chronic renal disease, and heart failure [26]. Despite its important role in many disease processes, for many years, the clinical application of ADM was limited by its in vitro instability. This problem has been solved by the emergence of the mid-region (MR) biomarkers, which are stable fragments of prohormones. One of these mid-region markers is MR-proADM, which is a stable fragment of proadrenomedullin. MR-proADM is released in a one-to-one fashion with the inactive precursor of the biologically active ADM, and its serum levels reflect the degree of activation of the ADM system [27].

The prognostic potential of MR-proADM was demonstrated in the BACH trial. Among the 1641 patients enrolled in the study, 568 patients were diagnosed with acute heart failure. In this acute heart failure population, MR-proADM not only carried independent prognostic value but was also found to be superior to both BNP and NT-proBNP in predicting mortality within 14 days. MR-proADM also provided significant additive incremental predictive value for 90-day mortality when added to BNP and NT-proBNP [4]. Despite the promising results in the BACH trial, MR-proADM is still a very nascent biomarker as there are few other studies exploring its use. One other analysis is from the PRIDE trial where MR-proADM was assessed in 560 patients presenting with acute dyspnea of which 180 had acute heart failure. In the whole population, MR-proADM was the best at discriminating mortality at 1 year compared to mid-regional pro-atrial natriuretic peptide, NT-proBNP, eGFR, and Galectin-3. The addition of MR-proADM to a model predicting 1-year mortality significantly increased the C-index from 0.760 to 0.792 and had a hazard ratio of 2.7 ($p < 0.001$). Findings were similar when patients with acute heart failure were only analyzed [28]. These studies provide compelling evidence to further pursue MR-proADM as a biomarker for early mortality risk.

While these studies show the promise of MR-proADM, one potential limitation of the assay is that though the assay reflects the activity of the ADM system (reflecting more chronic underlying physiologic changes), it does not reflect the amount of the biologically active ADM and the active physiology at the time of assessment. MR-proADM is released in a one-to-one fashion with the inactive ADM precursor;

however, only a small fraction of the inactive ADM precursor undergoes further processing to biologically active ADM [29]. Recently, an assay has been developed to specifically measure the biologically active form of ADM or bioactive adrenomedullin (bio-ADM). As bio-ADM has a very short half-life (22 min), this assay allows for short-term monitoring of a patient's current physiologic state [30]. This assay was recently evaluated in 246 patients with suspected acute heart failure using plasma samples collected upon presentation to the ED. The primary 30-day outcome consisted of two components: (1) severe clinical outcomes consisting of death, cardiac arrest with return of spontaneous circulation, respiratory failure with intubation, emergency dialysis, and acute coronary syndrome and (2) health-care utilization outcomes consisting of length of stay greater than 5 days, return ED visit in 30 days, and readmission within 30 days. In total, 85 subjects (36.4 %) had the primary outcome. The concentration of bio-ADM was significantly higher in patients with the primary outcome compared to those without and bio-ADM had an AUC of 0.70 for the primary outcome. Findings were similar when only severe clinical outcomes were analyzed and in the 124 patients with confirmed acute heart failure. In a multivariate model with other biomarkers, bio-ADM remained significant with an adjusted odds ratio of 2.68 ($p<0.001$) [31]. Research with bio-ADM is at its very beginning, but given the prior findings with MR-proADM, bio-ADM has promising potential.

Copeptin

Copeptin is a powerful new mid-region biomarker discovered in recent years. It is a fragment of the vasopressin prohormone pre-pro-vasopressin. Pre-pro-vasopressin is cleaved into copeptin and vasopressin inside the posterior pituitary gland. Post-cleavage, both copeptin and vasopressin are released in equimolar amounts into circulation and cleared by the kidneys. It is well known that vasopressin is a major contributor to hyponatremia. In addition, elevated vasopressin is consistently seen in patients with severe heart failure, highlighting vasopressin's potential as a prognostic biomarker. However, vasopressin has not been widely used in clinical practice due to its rapid clearance and in vitro instability. Unlike vasopressin, copeptin is very stable in vitro, making it an ideal surrogate biomarker for vasopressin. In the BACH trial, which is the largest trial examining copeptin in patients with acute heart failure, elevated copeptin levels were associated with increased 90-day mortality, heart failure-related readmissions, and heart failure-related emergency department visits. Patients in the highest quartile had an increased 90-day mortality with a hazard ratio of 3.85 ($p<0.001$) compared to the lowest quartile. In addition, mortality was significantly increased in patients with elevated copeptin (above median) and low sodium (<135 mEq/L) with a hazard ratio of 7.36 ($p<0.001$) [32]. No other studies have evaluated copeptin in acute heart failure patients, but in other studies of chronic heart failure patients, copeptin continues to display a prognostic ability for mortality [33, 34]. These findings highlight the prognostic utility of copeptin in patients with acute heart failure and have opened the door to future copeptin-guided vasopressin antagonist therapy in acute heart failure patients.

ST2

ST2 is cardiac biomarker that has recently gained increasing interest in heart failure and will likely have wide uptake as a new point of care assay has been approved in Europe and Asia. ST2 is a member of the interleukin-1 receptor family of proteins and acts as the receptor to IL-33. First identified in cultured cardiac myocytes, the ST2 gene was found to be highly upregulated when mechanical strain was applied to myocytes [35]. Mice with ST2 gene knockout can develop severe cardiac hypertrophy, fibrosis, and heart failure, suggesting that ST2 may have a cardioprotective effect in response to myocyte strain and injury. There are two transcripts of the ST2 gene, soluble and the membrane-bound IL-33 receptors. The interactions between IL-33 and the two ST2 forms are complex and currently incompletely understood, but some light has been shed on their functions. The IL-33/ST2 complex is believed to be protective to the myocardium under strain by acting as an activated fibroblast–cardiomyocyte paracrine system that works to prevent hypertrophy and fibrosis. The soluble ST2 receptor is believed to play a modulating role in the interaction between IL-33 and the membrane-bound ST2 receptor. Over the long term, the IL-33/ST2 complex may have a role in the inflammatory and remodeling processes of the myocardium in heart failure patients [36].

Despite some of the lingering questions about the exact physiological functions of ST2, the fact that it is significantly upregulated during myocyte strain has spawned several studies to assess its role as a biomarker in heart failure. In a trial of 139 patients with severe (NYHA III–IV) heart failure, Weinberg et al. found that baseline ST2 levels correlated very well with baseline BNP and proANP levels. Furthermore, a change in the ST2 value at 2 weeks (when compared to baseline values) was predictive of mortality or heart transplantation in both univariate and multivariate analyses [37]. Another trial by Bayes-Genis et al. found a similar benefit in using a change in ST2 to risk stratify heart failure patients. They found that if the ratio of ST2 at 14 days, compared to baseline ST2, was greater than 0.75, it had an AUC of 0.772 for predicting 1-year cardiac events [38]. When applied to patients presenting to the ED with dyspnea, ST2 also had promising results. A post hoc analysis of the PRIDE study found that ST2 levels were higher in patients with acute heart failure than those without, but ST2 was inferior to NT-proBNP for diagnosing acute heart failure. Additionally, a ST2 value of 0.20 ng/mL or higher predicted 1-year mortality with hazard ratios of 5.6 ($p<0.001$) for all patients with dyspnea and 9.3 ($p=0.03$) for patients with acute heart failure (note – this value was obtained using an older ST2 assay). Furthermore, an ST2 value of 0.29 ng/mL or higher is predictive of 1-year mortality with an AUC of 0.80 ($p<0.001$) [39]. Another study of 346 patients presenting with acute heart failure found similar findings. In this study, ST2 was found to correlate with BNP, NT-proBNP, CRP, severity of heart failure, left ventricular ejection fraction, and creatinine clearance. ST2 levels were significantly higher in patients who died at one year with a graded response seen with rising concentration. The AUC for ST2 was 0.71, which was similar to BNP (AUC 0.66) and NT-proBNP (AUC 0.68). ST2 remained a significant predictor of mortality in multivariate analysis with a hazard ratio of 1.82 ($p=0.01$) [40].

These trials mount to considerable evidence of ST2's powerful predictive ability for mortality.

ST2 may not only predict mortality, but mode of death. There has been work on ST2's ability to predict sudden cardiac death. One small study involving 99 patients showed that the combination of ST2 and NT-proBNP could help to identify patients at high risk for sudden cardiac death [41]. ST2 has also been shown to be predictive of adverse outcomes in stable outpatients. In a study by Daniels et al., which examined 558 stable patients who were referred for outpatient echocardiogram, elevated ST2 levels were associated with increased right atrial size, right ventricular dysfunction, and increased 1-year mortality. In this study, patients with increased BNP and ST2 levels were at even higher risk for mortality when compared to patients with normal BNP and ST2 levels [42]. Lastly, ST2 has repeatedly been tested against other biomarkers and been shown to be a significant, if not the most significant, biomarker predicting mortality. ST2 beat Galectin-3 (another biomarker of fibrosis), it beat high-sensitivity troponin and growth differentiation factor-15 (though with added benefit from the other biomarkers), and it remained one of the strongest predictors in a panel of six biomarkers [43–45]. Overall, the evidence strongly supports ST2 as a powerful predictor of mortality and clinical use of this biomarker is now more widespread. It is likely the next biomarker to be incorporated into heart failure management. As a marker of myocardial inflammation, remodeling, and strain, ST2 is an exciting new addition to the biomarker arsenal for the evaluation of heart failure patients.

Procalcitonin

Procalcitonin (PCT) is a biomarker unlike the others presented above, as it does not help diagnose heart failure or provide prognostic value. However, it is surely to become a vital tool in ED for the evaluation of patients with acute dyspnea and guide management as it helps predict which patients likely have a bacterial pneumonia and warrant antibiotics. PCT is a 116-amino acid protein produced by C cells in the thyroid. It is the precursor protein of calcitonin, a hormone involved in calcium homeostasis. Under normal physiologic conditions, PCT is only produced in the thyroid gland and is minimally detectable in blood. However, in pathological states, PCT is produced by extra-thyroidal tissues such as the liver and intestines. Notably, PCT rises in bacterial infections but does not in viral infections [46]. This latter quality makes it a valuable tool in the ED as it can help guide whether to give or withhold antibiotics in a patient with suspected pneumonia.

In the BACH trial, Maisel et al. evaluated the utility of PCT for diagnosing pneumonia. One hundred and 55 patients had a primary or secondary diagnosis of pneumonia of which 29 had concurrent acute heart failure. PCT strongly predicted pneumonia with an AUC 0.72 in the entire cohort, though this was lower in the subjects with concurrent acute heart failure (AUC 0.64). When PCT and antibiotic use was evaluated in the 560 patients with acute heart failure, there was a notable increased mortality in patients treated with antibiotics whose PCT was less than

0.05 ng/ml and in patients not treated with antibiotics whose PCT was greater than 0.21 ng/ml [47]. This finding highlights the importance of appropriate antibiotic use and the potential for PCT to direct antibiotic therapy. The use of PCT will become clearer upon completion of the Improve Management of Heart Failure with Procalcitonin (IMPACT-EU) study, a trial where antibiotic therapy is guided by PCT values in patients with acute heart failure. While not performed with an emphasis on heart failure patients, other studies have similarly shown that a PCT less than 0.1 ng/ml helps exclude pneumonia [48, 49]. If further trials confirm these findings, PCT is poised to become a routine biomarker for use in patients with dyspnea in the ED.

Conclusion

Although significant work is still needed to further define their role in the overall management of heart failure patients, biomarkers with their objectivity, reproducibility, and accessibility are excellent adjuncts to physical examination and imaging studies in heart failure diagnosis and risk stratification. With advances in basic science, new biomarkers representing different physiological processes continue to emerge. Along with traditional predictors of prognosis, biomarkers can help to identify high-risk patients who need closer monitoring and more aggressive therapy. By continually enhancing our understanding of the underlying pathophysiology and improving our ability to identify high-risk individuals, biomarkers will undoubtedly improve the effectiveness of heart failure diagnosis and risk stratification, leading to better patient outcomes.

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Emergency Department Therapy of Acute Heart Failure

13

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Overview

Acute heart failure syndrome (AHF) is the leading reason for hospitalization and readmission in North America [1, 2] and is the leading discharge diagnosis among elderly Americans [3]. It is a disorder of heterogeneous etiology that is largely defined by a single, homogenous symptom: dyspnea [4]. Other findings, including signs of systemic venous congestion and/or hypoperfusion, fatigue, weakness, and chest pain, may accompany breathlessness, but the degree to which they are present varies greatly between patients. Conventional therapy is most often directed toward alleviation of dyspnea, and need for additional intervention is dependent on the presence of other clinical abnormalities [5].

While most instances (80%) of AHF occur in patients with a history of chronic disease, a de novo presentation is not uncommon. Therefore, AHF is often more than simple exacerbations of underlying chronic disease, and effective management requires an approach that considers the complex nature of this disorder. Often presumed to be a direct consequence of volume overload, AHF is more accurately depicted by a model that considers the superimposition of potentially divergent precipitants on underlying systolic, diastolic, or mixed cardiac dysfunction [4, 6]. Effective treatment of AHF requires an understanding of the interplay between basal cardiovascular pathophysiology and those factors that specifically contribute to the decompensated state.

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General Approach to Treatment

Treatment of AHF can be broadly divided into two distinct phases. In the *stabilization phase*, initial intervention directed toward immediate life-threatening conditions is followed by subsequent efforts to alleviate symptoms through targeted management of acute precipitants. This is followed by the *in-hospital phase* where continued remediation of residual signs and symptoms and ongoing surveillance for interval development of renal or cardiac injury occur [4]. The latter also includes initiation or up-titration of chronic guideline-directed medical therapy that is in accordance with existing recommendations from the Heart Failure Society of America [5] and the American College of Cardiology/American Heart Association [7] and discharge planning with an eye toward linkage to care in the early postdischarge period.

The focus of this chapter will be on the stabilization phase of AHF treatment, which generally occurs in the first 24–48 h of care. Initiation of this phase usually takes place (~80 % of the time) in the emergency department (ED). In the United States, nearly 668,000 annual ED visits for AHF have been reported [8], representing 20 % of the total heart failure ambulatory care delivered every year [9]. For most ED patients, depending on severity, the care continues in an inpatient (85 %) or observation unit (OU) setting.

The primary goal of treatment during this early phase is symptom reduction, which is often achieved by rebalancing hemodynamics and volume status [4]. The need to prevent myocardial or renal injury during this phase has gained increasing prominence with evolving data that show worse outcomes when these develop in the hospital [10]. Cognizance of this is especially important because, in some cases, such myocardial and renal injury may be iatrogenically mediated through inappropriate or excessive medication administration (especially diuretics) [11], underscoring the need to deliver patient appropriate, targeted therapy.

Precipitants and Targeted Therapy

The goal of targeted therapy is to deliver the right medication to the right patient at the right time [12]. Doing so enables, at least in the acute phase of management, mitigation of the physiological perturbation that is most directly causing or contributing to cardiac decompensation. Common precipitants of AHF (and resulting consequences) include:

- *Acute hypertension*—an abrupt rise in blood pressure which causes impedance to forward flow by a structurally and/or functionally compromised left ventricle; the net effect is a mismatch between necessary and achievable stroke volume resulting in a backflow of fluid from systemic to pulmonary vasculature ("vascular failure"); typically occurs in a patient with chronic hypertension.
- *Excess fluid accumulation*—neurohormonal activation (principally aldosterone and arginine vasopressin), worsening renal function, high dietary sodium

consumption, excess fluid intake (or intravenous administration if AHF develops in the hospital), or medication noncompliance, either singularly or in combination, leads to fluid accumulation and increased preload; the net effect is the presentation of excess volume to a left ventricle which is incapable of responding by the Frank–Starling mechanism; the consequence is a buildup of fluid in the lungs and onset of clinical pulmonary congestion ("congestive failure").

- *Acute or subacute myocardial dysfunction*—onset of ischemic, inflammatory (from infectious and noninfectious causes), or idiopathic myocardial damage that results in rapid development of cardiac dysfunction (either regionally or globally); the net effect is to limit the heart's pumping ability which produces a precipitous decline in cardiac output ("pump failure").
- *Deterioration of advanced chronic heart failure*—overexertion, medication-related (under-, over-, or inappropriate use), worsening renal function, or indolent (i.e., "smoldering") myocardial necrosis; the net effect is a progression of underlying advanced disease and an intolerable acute or subacute increase in baseline symptoms.
- *Dysrhythmia*—development of tachycardia (often atrial fibrillation) or, less commonly, bradycardia (often medication related), which reduces the time spent in systole and/or diastole; the net effect is to limit cardiac output through a decrease in ventricular filling and stroke volume.
- *Aortic or mitral valve dysfunction*—stenotic, regurgitant, or mechanical valve abnormality which develops acutely (often from infection or, in the case of mitral regurgitation, from ischemic complications such as left ventricular dilation with leaflet tethering or papillary muscle rupture) or subacutely (typically from worsening of underlying chronic valve disease); the net effect is an increase in end-diastolic volume with consequent backflow into the pulmonary vasculature.

Identifying the specific precipitant (and, hence, the acute pathophysiology to be targeted) can be facilitated by consideration of clinical variables. To make rapid but precise treatment decisions during the stabilization phase, such variables should be readily identifiable on presentation or available shortly after arrival. These variables can then be combined to yield clinical profiles that are more (or less) amenable to certain therapies.

Clinical Profiles

Clinical profiles in AHF are defined by the presence (or absence) of relatively consistent features within important variable categories including presenting signs and symptoms (pulmonary congestion with or without systemic edema and evidence of hypoperfusion), hemodynamic parameters (primarily blood pressure and heart rate), and rapidly available diagnostic test results (electrocardiographic changes consistent with ischemia or infarct, biomarker indicators of acute renal and myocardial stress or injury, and findings consistent with heart failure on chest radiography)

[4, 6, 13]. This approach incorporates important aspects of prior conceptual models of AHF (e.g., the "quadrants" of HF [14]), but is more treatment facing in its perspective.

In deriving clinical profiles (Table 13.1), blood pressure serves as a critical branch point [4, 6, 13]. Reasons for this relate to its clear importance as a precipitating factor (more than 50 % of all AHF episodes are associated with a systolic blood pressure >140 mmHg) [15] and its role as the principal determinant of in-hospital morbidity and mortality [16]. While interpretation of these profiles within the context of echocardiographically determined cardiac function may be useful for de novo cases where the underlying physiology is not known or in patients with refractory symptoms, in most circumstances, such information will not dramatically impact intervention during the stabilization phase. Moreover, for some patients with decompensated chronic disease, the presenting clinical profile may be more dependent on acute, precipitating factors than previously established echocardiographic abnormalities or underlying etiology (i.e., ischemic or nonischemic), and overreliance on the latter information may preclude application of situation-appropriate therapeutic intervention. An example of this would be the administration of aggressive diuresis to an established HF patient with reduced ejection fraction and systemic edema when in fact their acute decompensation was triggered by an episode of atrial fibrillation with rapid ventricular rate.

Specific Targets of Therapy

The importance of appropriate ED treatment of acute HF cannot be sufficiently underscored. Data from Acute Decompensated Heart Failure National Registry (ADHERE) show that when intravenous (IV) vasoactive medications are started early by ED physicians rather than waiting for the inpatient service, outcomes such as mortality rate (4.3 % vs. 10.9 %), intensive care unit admission rate (4 % vs. 20 %), and total hospital length of stay (3 days vs. 7 days) are dramatically improved [17]. Therefore, knowing which agents to administer and the correct circumstance in which to administer them is critical. An overview of therapeutic targets within the context of clinical profiles. These targets are discussed in greater detail in the following sections with increased emphasis placed on those that are particularly relevant to management of the short-stay HF patient. While each is presented in isolation, there may be some overlap of targets in an individual patient.

Acute Hypertension (Afterload)

As noted, elevated BP (systolic BP > 140 mmHg) is present in more than half of all patients with Acute Heart Failure Syndrome (AHFS), and for those with substantial dyspnea, appropriate, early vasodilatation can lead to substantial improvement in symptoms [18]. A number of agents can produce afterload reduction, yet only a handful have been rigorously tested in the management of AHFS, and head-to-head

Table 13.1 Clinical profiles of acute heart failure

Profile	Common precipitants	Signs and symptoms	Hemodynamics on presentation
Profoundly hypertensive	Abrupt rise in BP	Rapid onset of dyspnea ("flash pulmonary edema"); systemic edema may be absent; diaphoresis with adequate perfusion typical	Systolic BP > 160 mmHg; sinus tachycardia and hypoxia common
Normal to moderately hypertensive	Progressive fluid accumulation	Gradual or subacute worsening of dyspnea; moderate to severe systemic edema; minimal distress with adequate perfusion	Systolic BP > 100 mmHg but <160 mmHg; tachycardia and hypoxia uncommon
Hypotensive	Deterioration of advanced, chronic disease; excessive diuresis	Mild dyspnea; often with cool, edematous extremities	Systolic BP < 90 mmHg; HR often normal but may be <60 beats per min if on baseline medications with rate control effects
Cardiogenic shock	Myocardial injury, valve dysfunction	Rapid onset of dyspnea with evidence of profound hypoperfusion	Systolic BP < 90 mmHg; tachycardia common (unless on rate control agents)—may be ventricular in origin
Arrhythmogenic	Ventricular or supraventricular dysrhythmia	"Palpitations" and "dizziness"; mild to moderate dyspnea (often secondary feature); systemic edema may be present or absent	Systolic BP variable; HR < 60 or >120 beats per min; hypoxia
Acute coronary syndrome	Acute myocardial ischemia or infarct	Chest pain with dyspnea	Systolic BP > 100 mmHg; HR variable; hypoxia less common
Isolated right heart failure	Right ventricular ischemia or infarct (right coronary or left circumflex); pulmonary hypertension; tricuspid or pulmonary valve dysfunction; pulmonary artery obstruction (embolism)	Dyspnea without rales; systemic edema if subacute or long standing	BP variable; tachycardia and hypoxia often present

BP blood pressure, *HR* heart rate

comparison trials are sorely lacking. Regardless, it has been postulated that in patients with hypertensive AHF, the decision to implement therapy focused primarily on BP control (rather than volume reduction) may be more important than actual agent used [12]. Though such a hypothesis has not been tested in clinical trials, as shown in Studying the Treatment of Acute Hypertension (STAT), the degree of BP reduction has critical bearing on outcomes, with an increase in adverse event rates when the systolic BP declines to less than 120 mmHg [19]. Thus, when managing acute hypertension with any agent, close monitoring and frequent BP measurement is essential.

Nitrovasodilators

Nitrates have long been considered the first-line agents for AHF associated with elevated blood pressure. With varying strengths of recommendation, guidelines endorse the use of nitrate therapy in AHF. The use of nitrates is recommended by the Canadian Cardiovascular Society, the European Society of Cardiology (class IIa), and the American Heart Association (class IIb) [1, 20, 21].

As a class, nitrates work by providing an exogenous source of nitric oxide that is then available to bind to soluble guanylate cyclase, thereby producing vascular smooth muscle relaxation [22]. Combined effects on venous capacitance and arterial resistance lead to a decrease in pulmonary capillary wedge pressure (PCWP) [23, 24]. At higher doses (i.e., $\geq$ 150–250 mcg/min), arteriolar dilation predominates, helping to improve cardiac output through a reduction in afterload [25–27]. This effect may be more pronounced when systemic vascular resistance is severely elevated [28] and may be mediated through a dose-dependent, differential effect on the augmentation index—a measure of the amplified pressure wave that is reflected back to the central circulation from the periphery (i.e., a ratio of central/peripheral pulse pressure) during each cardiac cycle [29]. Nitrate tolerance is a common but poorly understood phenomenon thought to involve O_2 free radical formation and nitric oxide (NO) synthase inhibition which can decrease the hemodynamic response to ongoing administration despite up-titration [30, 31].

Nitroglycerin (glyceryl trinitrate) is the most common nitrate used in the United States and is typically given as an initial sublingual tablet or spray (400 mcg/dose) to enable quick absorption and rapid onset of action. For persistent symptoms, transdermal application (1–2 in. of 2% ointment) or, for more severe cases, IV administration may be required. Because the half-life of nitroglycerin (NTG) is short (<5 min), a continuous infusion (rate, 20–400 mcg/min) may be needed to maintain the effect. Higher doses of IV NTG (or its relative, isosorbide dinitrate [ISDN]) may be particularly useful in patients with profound BP elevations and respiratory distress (i.e., hypertensive cardiogenic pulmonary edema). Intravenous nitrovasodilators, when used in the treatment of AHF in the ED, have been shown to be effective in improving blood pressure and dyspnea in the short term [32]. Repeat IV bolus (every 3–5 min) of both high-dose NTG (2 mg) [33] and ISDN (4 mg) [34, 35] has been associated with a reduction in the need for mechanical

ventilation and intensive care unit admission, a lower incidence of cardiac injury (as evidenced by biomarkers), and a shorter total hospital length of stay. In studies to date, substantial doses of NTG (mean [SD] = 6.50 [±3.47 mg]) and ISDN (mean [SD] = 11.4 mg [±6.8 mg]) have been given with a low incidence of hypotension (<4 %) and no report of adverse neurologic, renal, or cardiac events.

While sustained administration of such aggressive therapy may not be appropriate for the OU, most patients who respond do so quickly, often circumventing the need for continued IV nitrate therapy. Results of a topical high-dose nitrate strategy (two sublingual NTG tablets followed by application of ten NitroDerm TTS patches) have been reported with demonstration of a reduced intensive care unit admission rate and greater improvement in cardiac stress in the high-dose nitrate arm [36]. Importantly, this strategy was implemented in a nonmonitored setting (general medical ward), thus enabling possible extrapolation to the OU. Preload-dependent conditions, such as right heart ischemia, pericardial effusion/pericarditis, or restrictive cardiomyopathy, should be considered a contraindication to nitrate therapy (regardless of dose).

Even though the use of nitrates has been shown to be safe and effective in the stabilization phase of AHF, a recent large retrospective cohort study of over 11,000 patients did not show an improvement in short-term or near-term survival. In comparing patient groups receiving nitrates to non-nitrate groups, Edwin et al. found mortality rates of 1.8 % vs. 1.5 % ($p = 0.151$) at 7 days and 10.55 % vs. 10.1 % at 30 days ($p = 0.540$) [1].

Sodium nitroprusside (NTP) is another nitric oxide donor that can be used in profoundly hypertensive and dyspneic patients. The administration of NTP results in both preload and afterload reductions even at lower doses and has been shown to be effective for patients with refractory elevations in systemic vascular resistance [37]. However, controlled trials of NTP in AHF are lacking. Because of potential significant and prolonged hypotension as well as reflex tachycardia, invasive arterial monitoring and close supervision are recommended [38]. Furthermore, NTP may increase the risk of coronary steal syndrome and cyanide toxicity. Suffice to say, if used to treat AHF, NTP should be considered a contraindication to short-stay management in an OU setting.

Natriuretic Peptides

Since its approval by the Food and Drug Administration in 2001, nesiritide, a recombinant form of brain natriuretic peptide (BNP), has been widely studied as an alternative to existing vasodilator therapy with early trials suggesting benefit with its use [39–42]. However, Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF), a large ($n = 7141$) definitive trial of nesiritide, was completed in 2010 finding a statistically significant but clinically irrelevant difference in dyspnea with the use of nesiritide, without any benefit on hard end points such as mortality and readmission. Additionally, an increased risk of asymptomatic hypotension with the use of nesiritide was seen (21.4 % vs.

placebo 12.4 %) [43], though no other signals of potential harm were noted. Offering no specific advantage over existing therapy, nesiritide has fallen out of favor and is rarely used in the management of AHF today.

Other natriuretic peptide compounds, including ularitide (a synthetic analog of urodilatin, an atrial-NP derivative) and cenderitide (a chimer of c-type and d-type NP) [44], have been developed and are currently subject to preliminary investigation. Phase I and II studies of ularitide have shown favorable hemodynamic effects in reducing dyspnea without inducing renal dysfunction in AHF patients [45]. Ularitide is currently being tested in the phase III TRUE-AHF clinical study [46]. Cenderitide is being evaluated as a continuous subcutaneous infusion for use after the stabilization and in-hospital phase for systolic blood pressure reduction [45]. Further research is needed to determine what role, if any, these drugs will have in the ER and OU management of AHF.

Angiotensin-Converting Enzyme Inhibitors

Angiotensin-converting enzyme (ACE) inhibitors have been used in the setting of acute HF with hypertension. As a class, they are effective antihypertensives and provide antagonism of the renin–angiotensin–aldosterone system, making them ideal agents for HF treatment. Abundant data show substantial benefit from the use of oral ACE inhibitors in chronic HF (i.e., disease regression, symptom improvement, decreased mortality) [47–49]. Based on this, the American College of Cardiology/American Heart Association guidelines recommend ACE inhibitor therapy, absent contraindications, for all patients with symptomatic left ventricular dysfunction (< 40 % ejection fraction) [21]. Data abounds showing substantial benefits in disease regression, symptom improvement, and decreased mortality [50]. The timing of initiation of oral ACE inhibitor therapy has been recommended to be within the first 24–48 h after hemodynamic stabilization. There is limited data on the safety of ACE inhibitors in the early phase of therapy (first 12–24 h) [32, 51]. Major concerns include sustained hypotension due to their relatively longer half-lives, renal dysfunction, and hyperkalemia. Therefore, absent further safety data, ACE inhibitors should be used with caution during the stabilization phase of AHF care.

Calcium Channel Blockers

Due to their negative inotropic effects, beta-blocking agents and nondihydropyridine calcium channel blockers (CCBs) are considered contraindicated in the initial management of AHF [52]. It has also been recommended to avoid rapid-onset dihydropyridine CCBs, such as sublingual nifedipine, as they produce unpredictable effects on peripheral resistance and have been correlated with an increased risk of coronary and cerebral hypoperfusion [50, 53]. However, fourth-generation short-acting IV dihydropyridine CCBs (i.e., nicardipine and clevidipine) have shown

promise [54]. As shown in the PRONTO trial, clevidipine works to rapidly and safely reduce blood pressure and dyspnea in patients with hypertensive AHF. Compared with standard of care ($n=53$), more patients in the clevidipine group ($n=51$) reached target blood pressure range within 30 min (71 % vs. 37 %, $p=0.002$); dyspnea improvement within 45 min (−37 vs. 28 on a visual analog scale, $p=0.02$) was also greater in the clevidipine group [55] suggesting a potential future role for this class of agents in AHF.

Investigational Therapy

Relaxin is a peptide hormone released in pregnancy that helps regulate hemodynamic function and renovascular blood flow. Specific effects of relaxin include production of nitric oxide, vascular endothelial growth factor, and matrix metalloproteinases as well as inhibition of endothelin and angiotensin II. Such effects result in a number of vascular changes (especially systemic and renal vasodilation) that may be beneficial in acute hypertensive HF [56].

The RELAX-AHF trial, a multicenter international randomized control trial of 1161 patients with AHF, was published in 2013 and suggests the drug serelaxin improved dyspnea in the visual analog scale through day five and reduced average length of stay. However, the proportion of patients with significant improvement in dyspnea measured by the Likert scale during the first 24 h was not improved. While 60-day readmission was also not significantly improved, all-cause mortality and cardiovascular death at 180 days were significantly decreased [57, 58]. Based on the latter, a large-scale trial powered for mortality and worsening in-hospital HF has been initiated, results of which will determine the future role of serelaxin in the management of AHF.

Other drugs including TRV-027, a novel beta-arrestin biased ligand of the angiotensin II type 1 receptor, are currently being studied for use in AHF as well.

Excess Volume (Preload)

Volume overload is another common feature in patients presenting with AHF, and the relief of congestion through removal of excess fluid is an important goal of therapy [59]. The 2013 American College of Cardiology Foundation/American Heart Association Heart Failure Guidelines recommends diuretic therapy without delay in the emergency department in patients with significant fluid overload [21]. Despite a lack of prospective, randomized trials, diuretics have remained the mainstay of therapy for decades and are used in the vast majority (∼90 %) of patients with acute HF symptoms. Several alternatives have been recently investigated, but none has been found to be superior in terms of safety or efficacy. Consequently, diuretics remain the de facto “standard” of care for AHF in those with (and often without) hypervolemia.

Loop Diuretics

Intravenous loop diuretics (furosemide, bumetanide, torsemide, and ethacrynic acid) work by inhibiting the Na^+–K^+–2Cl− cotransport channel in epithelial cells which line the thick ascending limb of the loop of Henle [60] and are the most common class of medication used in the treatment of AHFS. They work to produce an osmotic diuresis and have an onset of action of approximately 30 min postadministration with a peak effect at 2–4 h. Furosemide is the agent used most frequently in the United States, and with typical dosing (40–80 mg IV every 8–12 h), in-hospital fluid losses can approach 4 L [61]. Furosemide has been noted to have hemodynamic effects as well, with nonsustained vasodilation occurring 5–15 min after administration [62]. Latent vasoconstriction has also been reported and appears to be related, at least in part, to activation of neurohormonal factors [63]. Despite this potential disadvantage, loop diuretics do effectively reduce filling pressures and induce symptomatic improvement [64], making them widely accepted for acute HF treatment.

The optimal approach to diuretic dosing and administration has been a source of ongoing controversy. Higher cumulative doses of furosemide have been associated with an increased risk of in-hospital death in one study [11], and in a Cochrane Collaborative review, continuous infusion was found to be more effective than repeat bolusing, particularly for those patients with refractory edema or congestion [65]. The best evidence to date, however, has come from the recently completed diuretic optimization strategies evaluation (DOSE) study, which prospectively compared approaches to IV furosemide administration [66, 67]. Using a 2 × 2 factorial design, patients (n = 308) were randomized to receive high (2.5 times daily oral) vs. low (daily oral) dosing and intermittent bolus (every 12 h) vs. continuous infusion for a period of at least 48 h. No statistical difference in global symptom relief or absolute change in renal function at 72 h was found for either level of comparison (i.e., low vs. high dose and intermittent bolus vs. continuous infusion) [67]. However, there was a signal of greater improvement with use of a high-dose strategy in several secondary end points including dyspnea relief, weight loss and net volume loss, proportion free from signs of congestion, and reduction in biomarkers of myocardial stress (i.e., NT-proBNP) suggesting some clinical benefit with a high-dose diuretic approach.

Some patients are found to be less responsive to even high-dose loop diuretics, and they have shown to have poorer outcomes and increased mortality [68]. Though such resistance is more common in those on long-term therapy, on occasion, it may be seen in diuretic-naïve patients with profound volume depletion and decreased renal perfusion. In such patients, an enhanced effect may be achieved through combining loop and thiazide diuretics [69, 70]. Adding a thiazide leads to what has been called "sequential nephron blockade" based on the portion of the nephron where the two classes of drugs exert their effect. In patients undergoing continuous furosemide infusion and intact renal function (GFR > 75 mL/min), adding a thiazide potentiates the diuretic effect [7] but requires close monitoring for hypokalemia as both loop and thiazide diuretics are known to decrease hemoconcentration of potassium. The ongoing Combination of Loop with Thiazide-type Diuretics in Patients

with Decompensated Heart Failure (CLOTRIC) is the first large-scale trial to evaluate the safety and efficacy of adding thiazide to loop diuretic therapy [71].

Vasopressin Antagonists (Vaptans)

Arginine vasopressin, also known as antidiuretic hormone, triggers manufacture and cell membrane insertion of aquaporin-2 molecules in renal collecting ducts and thus serves as a potent stimulus for free water reuptake by the kidneys. Vasopressin release is upregulated in HF, and its appearance contributes greatly to dysregulated fluid accumulation. While V1 receptors primarily regulate the effect of vasopressin in the vasculature (where it produces vasoconstriction), V2 receptors function in the kidney. Antagonists of vasopressin (conivaptan [a dual V1/V2 receptor antagonist], tolvaptan [a V2 ≫ V1 receptor antagonist], and lixivaptan [a V2 ≫ V1 receptor antagonist]) block this pathway, resulting in increased excretion of low-solute fluid, enabling reversal of hyponatremia (a known risk factor in acute HF) without adversely affecting glomerular filtration rate or renal blood flow [72]. This class of medications, therefore, has broad theoretical appeal for use in AHFS, offering a pharmacological approach to volume reduction that lacks the drawbacks of loop diuretics. Despite such potential, utility of the "vaptans" in Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan (EVEREST), a two-part investigation that enrolled over 4,000 patients with acute HF, was less than ideal offering a statistically significant (though clinically marginal) improvement in dyspnea, edema, serum sodium, and renal function without any long-term effect on mortality or HF-related morbidity [73, 74]. More recent studies have found tolvaptan use to be an independent and powerful predictor of improving sodium levels in hyponatremic AHF, an independent predictor of survival, but did not show improvement in outcome [75]. Consequently, there is no indication for use of vasopressin antagonism in AHF at present.

Ultrafiltration

Mechanical fluid removal using ultrafiltration is an alternative to pharmacological diuresis and a viable option for the management of AHF with volume overload, particularly in those with diuretic resistance or the cardiorenal syndrome. Ultrafiltration is an efficient yet costly (~$19,500 for device acquisition and $950 per filter, with 1–2 filters required per treatment) mechanism which uses venovenous hemoconcentration to extract up to 500 mL of isotonic fluid per hour. While early trials such as Ultrafiltration Versus Intravenous Diuretics for Patients Hospitalized for Acute Decompensated Heart Failure (UNLOAD) suggested a reduction in readmissions with the use of ultrafiltration [76], the recently completed Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARRESS-HF) found no beneficial effects on fluid removal or renal function and no difference in mortality or rehospitalization through 60 days with ultrafiltration compared to a stepped diuretic approach [77]. As a result, the role of ultrafiltration is limited in the management of AHF.

Diminished Cardiac Function

Cardiac output can be acutely reduced for a number of reasons, but ischemia, valvular dysfunction, and arrhythmia are among the most common. Each of these has inherent therapy that warrants a discussion that is beyond the scope of this chapter. It is important to remember, however, that when treating HF related to such causes, the primary intervention should be directed toward the inciting factor (i.e., reperfusion for ischemia, surgery for critical valve dysfunction, or rate control for atrial fibrillation) rather than the end manifestation.

On occasion (<5 % of the time), reduced cardiac output with hypoperfusion will result from a simple, subacute progression of underlying, advanced HF, and intervention to improve pump function (i.e., inotropes) may be needed. In general, such patients are poor candidates for short-stay management of AHF, but some, especially those with end-stage disease, may benefit from a brief "tune-up" with medications that augment cardiac function. For those without evidence of pulmonary congestion, a small bolus of isotonic normal saline (250–500 cc) may be attempted first, as these individuals frequently suffer from intravascular depletion as a result of chronic overdiuresis. It is important to remember that while inotropic agents can effectively transiently improve cardiac function, they should be used cautiously, especially in patients with coronary artery disease, as they increase myocardial oxygen demand and enhance the potential for arrhythmia development [38, 78–80].

The most commonly used inotropes are norepinephrine, dobutamine, and milrinone. Norepinephrine is an alpha- and beta-adrenergic agonist that combines cardiac chronotropic and ionotropic response (and, consequently, cardiac output) with peripheral vasoconstriction [81]. Dobutamine acts through β_1- and β_2-adrenergic receptor stimulation to increase inotropy and chronotropy [82]. Vascular effects include vasodilatation at low doses and vasoconstriction at higher doses. Patients with a history of beta-blocker usage at baseline may require increased dosing to achieve therapeutic effect [83]. Milrinone is a type III phosphodiesterase inhibitor (PDEI) which also improves hemodynamic function (i.e., stroke volume and cardiac output) but does so by preventing intracellular breakdown of cyclic adenosine monophosphate (cAMP) [84]. Though this activity is independent of adrenergic receptor stimulation, it produces similar net effects on the heart (i.e., inotropy, chronotropy, and lusitropy) [85]. In the peripheral circulation, however, vasodilatory effects predominate resulting in significant preload and afterload reduction. This latter response may cause a worsening of hypotension, particularly in patients with intravascular volume depletion [86]. Concurrent administration of dobutamine and milrinone (or an alternative PDEI such as amrinone or enoximone) yields an additive effect on cardiac function and may be a useful approach for those on chronic beta-blocker therapy [87, 88].

Positive inotropic effects can also be accomplished by targeting the myocardial contractile apparatus itself. Traditionally, this has been achieved through the use of cardiac glycosides (i.e., digoxin) which produce their desired effect by inhibition of Na^+–K^+ ATPase. Mediated through an increase in intracellular sodium, this works to establish a gradient that promotes intracellular calcium ion accumulation, which

subsequently enhances myocyte contractility, resulting in an incremental improvement in cardiac output. Digoxin was commonly used for management of AHF two to three decades ago but has since fallen out of favor [89]. Digoxin, however, is one of the few medications which, when used in the ambulatory setting, has actually been shown to reduce rehospitalization for HF [90], and there is resurgent interest potential utility for patients with acute symptoms [91].

Other agents that enhance myocyte contractility include levosimendan (a calcium sensitizer that functions through K^+–ATP channels) [92], istaroxime (a concurrent inhibitor of Na^+–K^+ ATPase and stimulator of sarco-endoplasmic reticulum calcium ATPase) [93], and omecamtiv mecarbil (a direct-acting cardiac myosin activator) [94]. Of these, levosimendan has been most extensively studied, but in Survival of Patients With Acute Heart Failure in Need of Intravenous Inotropic Support (SURVIVE), the largest trial of the medication to date, no clinical benefit over dobutamine was found [95]. A recent double-blind randomized control study of 606 AHF patients found omecamtiv mecarbil to be associated with no improvement in dyspnea in all but the highest doses when compared to placebo [96].

Is There a Role for Morphine Sulfate?

Perhaps the most common other medication used in the treatment of AHF is morphine sulfate. Morphine is thought to produce mild vasodilatation (venous ≫ arterial) with a reduction in preload and, to a lesser extent, afterload. In addition, morphine may induce respiratory relaxation and exert a calming effect on those with agitated dyspnea. The evidence in support of morphine use for acute HF is limited with few if any trials demonstrating benefit and several actually showing potential harm with an increased risk of endotracheal intubation, need for intensive care unit admission, and prolonged hospital length of stay [97, 98]. Moreover, in ADHERE, morphine use was found to be an independent predictor of in-hospital mortality [adjusted odds ratio (95% CI) = 4.84 (4.52, 5.18)] [99]. Thus at best, morphine appears to be of marginal utility and, at worst, a possible contributor to suboptimal outcomes.

Oxygen Therapy and Ventilatory Support

Virtually, all AHF patients will receive supplemental oxygen therapy. Nasal cannula delivery for mild dyspnea and a nonrebreather face mask for moderate dyspnea will generally be sufficient. For patients with profound dyspnea, early initiation of noninvasive positive airway pressure ventilation (NIPPV; either continuous [CPAP] of bilevel [BiPAP]) can dramatically reduce symptom severity and may decrease the need for endotracheal intubation. Though prior studies suggested a relative increase in the rate of myocardial infarction with the use of BiPAP (vs. CPAP), several reviews [100, 101] and the recently completed prospective Three Interventions in Cardiogenic Pulmonary Oedema (3CPO) trial showed equivalence with regard to safety and efficacy (though neither appears to provide a mortality benefit when compared to face

mask oxygen therapy) [102]. When using noninvasive ventilation, initial CPAP is typically set at 5–7 cm H_2O with BiPAP starting at 8–10 cm H_2O inspiratory and 4–5 cm H_2O expiratory with up- (or down)-titration as needed (max = 15 cm H_2O for CPAP and 20/10 cm H_2O for BiPAP). In addition to reducing the work of breathing, NIPPV decreases preload helping to offset pulmonary congestion.

Approximately 5 % of acute HF patients overall and up to 40 % of those with cardiogenic pulmonary edema will require endotracheal intubation (ETI) [98, 103, 104]. For most of these individuals, signs of impending respiratory failure such as severe dyspnea, tachypnea, diaphoresis, muscle fatigue, and confusion will be readily apparent on arrival to the ED. In others, however, findings may be more subtle. Parameters that indicate potential need for ETI include persistent hypoxia ($SaO_2 < 80$) or hypoxemia ($PaO_2/FiO_2 < 200$) despite supplemental oxygen, hypercarbia ($PaCO_2 > 55$ mmHg), and acidosis (pH < 7.25) [105]. The requirement for endotracheal intubation is associated with poor outcome [106] and decreases the risk of neurologically intact survival in patients with acute HF who suffer in-hospital cardiac arrest [107]. Such patients are clearly poor candidates for short-stay management of AHF.

Conclusions

The management of AHF has evolved from an approach that is focused predominantly on diuresis for all to one that responds more directly to the complex interplay of underlying disease and acute precipitants. Recognition of divergent clinical profiles, despite homogeneity in presentation, will help ensure delivery of the most appropriate therapy for an individual patient and improve the likelihood of optimal outcome. Such therapy may involve a mixture of interventions, each ideally targeting a specific contributor to the acute decompensated state and administered during the appropriate phase of treatment. Despite the need for potentially differing specific therapy, the goals of intervention remain consistent: acute symptom relief without induction of cardiac or renal dysfunction.

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Part IV

Observation Unit Treatment and Disposition

Observation Unit Admission Inclusion and Exclusion Criteria

14

Jason M. Hogan, Sean Collins, and Gregory J. Fermann

Emergency department (ED) observation units (OUs) represent an emerging cost-effective treatment option for low-risk acute heart failure (AHF) patients. After initial evaluation and treatment in the ED, AHF patients can be discharged, admitted to the hospital, or undergo further management as observation patients. Observation status is independent of the actual location of care delivery and can therefore occur in beds anywhere in a hospital or in dedicated OUs. Likewise, this short-stay population can be managed by inpatient specialists, hospitalists, or emergency providers. Observation is fundamentally a billing status defined by the Center for Medicare and Medicaid Services (CMS) as care spanning typically less than 24 h but no more than 48 h. As such, the objective ED evaluation in conjunction with provider intuition, response to treatment, and assessment of self-care barriers represents an important factor in risk stratification for AHF patients and subsequent inclusion or exclusion from an OU stay.

Background

Nearly 75% of ED visits for AHF ultimately lead to hospitalization, and this high proportion of ED visits with resultant inpatient admission has not changed over the last decade [1, 2]. The costs and morbidity associated with these hospitalizations have generated increased pressure to manage these patients more efficiently in the

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Table 14.1 Recommended inclusion and exclusion criteria for OU entry

	Recommended	Comments
Inclusion criteria		
Blood pressure	SBP > 100 mmHg	
Respiratory rate	<32 breaths/min	
Heart rate	Less than 110 bpm	Consider atrial fibrillation if the rate can be controlled with oral meds
Renal function	BUN < 40	Consideration should be given for relative changes from baseline
	Creatinine < 3.0	
ECG findings	No acute ischemic changes	Consider not normal but unchanged to be eligible for OU
Natriuretic peptides	BNP < 1,000 pg/mL	Consider in context of clinical scenario
	NT-proBNP < 5,000 pg/mL	
Respiratory	On O_2 per NC	Consider after weaned off BiPAP/CPAP
Troponin	Nondetectable troponin	Consider low, detectable, and non-rising elevations as OU eligible
Social support	Ability to establish	
Exclusion criteria		
Mechanical ventilation	BiPAP/CPAP	
Vasoactive medications	No active titration	

SBP systolic blood pressure, *BUN* blood urea nitrogen, *ECG* electrocardiogram, *BNP* B-type natriuretic peptide, *NT-proBNP* N-terminal pro-B-type natriuretic peptide

acute care environment [2–7]. Such inpatient admissions could possibly be avoided in a large proportion of patients, as relatively few ultimately receive intensive acute care, mechanical ventilation, and circulatory support or undergo invasive diagnostic or therapeutic interventions [8, 9]. After appropriate risk stratification, selected AHF patients may be safely and effectively managed in an OU at a lower cost compared to an inpatient stay [10–12]. In a relatively short period of time, an OU can provide frequent reassessment in a monitored setting, IV diuretics, afterload reduction, targeted patient education, and coordination with outpatient providers regarding medication regimens and close follow-up. Despite the fact that prospective, randomized, controlled trials evaluating this strategy are lacking, preliminary evidence suggests that AHF patients managed in an OU setting have similar outcomes and improved resource utilization compared to a risk-matched group of admitted patients [11, 12].

Risk Stratification on Emergency Department Presentation

The Society for Cardiovascular Patient Care (SCPC, formerly the Society of Chest Pain Centers) has published several recommendations for patient selection and management in the observation setting. Generated from existing evidence on AHF risk stratification and later externally tested in an independent data set, these recommendations can serve as a guide to identify patients who may benefit from an OU

stay rather than an inpatient admission [13, 14]. Table 14.1 outlines recommended inclusion and exclusion criteria for OU entry based on the SCPC recommendations that have been updated to reflect current evidence and emerging practice patterns.

Initial risk stratification has typically focused on the prediction of acute inpatient mortality as the primary endpoint. Further, the majority of studies have focused on identifying high-risk, rather than low-risk, physiologic markers in ED patients with AHF and have been limited by using retrospective design in hospitalized patients. ED patients have traditionally not been enrolled; thus, those patients discharged from the ED are rarely included. Despite these and other limitations, low blood pressure, renal dysfunction, low serum sodium, and elevated cardiac biomarkers (troponin [Tn] or natriuretic peptides [NP]) have been repeatedly shown to be increased risk factors for morbidity and mortality [15].

However, a recent prospective cohort study conducted at four hospitals enrolled 1,033 ED patients with AHF, including 7.7 % that were discharged from the ED, to evaluate the incidence of severe adverse events (SAE) within 30 days of ED evaluation (ACS, coronary revascularization, emergent dialysis, intubation, mechanical cardiac support, CPR, and death). The study assessed readily identifiable ED variables to select a cohort of patients who may be eligible for ED discharge, and the resultant decision tool was highly sensitive for a 30-day mortality and SAE [16]. Similarly, a prospective observational cohort study enrolled 559 AHF patients at six Canadian EDs to assess for a 30-day death and a 14-day SAE. Their Ottawa Heart Failure Risk Scale identified prior intubation for respiratory distress, vital sign abnormalities, ECG changes, laboratory findings, and history of stroke/TIA as important variables in their final risk prediction model [17].

Overall, clinical variables for risk stratification of AHF patients are often categorized broadly into demographics, cognitive/functional status, comorbidities, hemodynamics, cardiac ischemia markers, electrolytes, and heart failure biomarkers.

Demographics

The current recommendations published by the SCPC do not specifically refer to age, sex, or race as inclusion or exclusion criteria. Lee and colleagues looked at over 12,000 ED patients with AHF to derive and validate a prediction rule for a 7-day mortality. Among several other variables further outlined below, their retrospective analysis found age to be an independent predictor of a 7-day mortality risk (adjusted odds ratio [OR], 1.40 (95 % CI, 1.16–1.69), $p < 0.001$) [18].

Hemodynamics

As more studies have attempted to delineate high-risk versus low-risk cohorts using simple, rapidly available data points, systolic blood pressure (SBP), heart rate, and oxygen requirement have proven to be important markers for rapid assessment and disposition. In the Emergency Heart Failure Mortality Risk Grade (EHMRG) 7-day mortality risk score, mortality risk increased with higher triage heart rate (OR, 1.15 [CI, 1.02–1.30]), lower triage SBP (OR, 1.52 [CI, 1.31–1.77] per 20 mmHg), and

lower initial oxygen saturation (OR, 1.16 [CI, 1.01–1.33] per 5 %) [18]. However, this study had several limitations including a retrospective patient identification, an exclusion of early readmission for AHF as an outcome, and a practice environment not reflective of the United States. Stiell and colleagues found that both heart rate >110 beats/min and oxygen saturation less than 90 % at ED arrival were independent predictors of SAE [17]. In AHF patients who are ultimately admitted, those with SBP of less than 120 mmHg had threefold higher inpatient mortality than those with SBP greater than 140 mmHg (7.2 % vs 2.5 %, $p<0.001$) [19]. In the HF patient who presents in acute distress, a lower initial SBP may reflect left ventricular contractile dysfunction while a higher initial heart rate suggests the need for increased chronotropy to maintain cardiac output and increased sympathoadrenergic response. A lower initial oxygen saturation demonstrates increased pulmonary congestion and underlying respiratory compromise and therefore places the patient at increased risk for mortality [18].

Although a majority of patients who present with AHF will require oxygen supplementation, most patients can be titrated down to a nasal cannula after initial steps targeting decongestion and symptom relief, and these individuals can be easily managed in an OU. Patients requiring acute critical care interventions such as active titration of parenteral vasoactive medications, intubation, or ongoing noninvasive positive pressure ventilation (NIPPV) meet ICU-level criteria and may need to be excluded from OU stay. However, some patients who are initially supported with NIPPV may be quickly weaned from this and could be eligible for OU management. Many of these patients are hypertensive and do well with aggressive blood pressure control and may improve rapidly and avoid intubation [20–22]. If a patient can be weaned off NIPPV in the ED after initial stabilization, transitioning their care to an OU may be considered if other criteria are met.

Renal Function and Electrolytes

Elevated creatinine (SCr > 3.0 mg/dL) and blood urea nitrogen ([BUN] > 40 mg/dL) on hospital admission are strongly correlated with increased in-hospital and post-discharge mortality, and this is reflected in the SCPC recommendations [23]. In the aforementioned prospective cohort study, an elevated BUN represented one of the primary predictors of adverse events ($p=0.01$), while the use of dialysis trended toward significance [16]. Two other ED-based studies similarly found an elevated BUN and creatinine to be independent predictors of SAE and mortality, respectively [17, 18].

Hyponatremia, as defined by a serum sodium <135 mmol/L, is associated with increased in-hospital mortality, post-discharge mortality, and readmission rates [24]. Hyperkalemia that may accompany renal insufficiency, resulting from excess repletion in the setting of diuretic use or from potassium-sparing diuretic use, can complicate OU management [25]. Conversely, the large prevalence of loop diuretic use can frequently lead to hypokalemia. An abnormal potassium level (<4.0 mmol/L or >4.5 mmol/L) functions as one of the elements of the EHMRG 7-day mortality

risk score, with an increased mortality risk seen in those with hyperkalemia compared to hypokalemia [18].

Cardiac Ischemia and Myocardial Necrosis Markers

Evidence of ongoing ischemia, as demonstrated by ECG changes and elevated troponin, continues to be strongly associated with increased acute mortality, post-discharge mortality, and increased readmission rates. The presence of ST depression on the ECG provided improved recognition of those patients with AHF at higher risk of a 30-day mortality [26]. Peacock illustrated that AHF patients with elevated cTn (and SCr < 2.0) had higher in-hospital mortality. However, this study utilized first-generation troponin assays, and many patients who would have elevated troponin levels utilizing the contemporary assays in place today may have been in the "normal troponin" group in this study. Diercks showed that a small OU cohort with a SBP > 160 mmHg and a normal cTn suffered no 30-day adverse events (death, readmission, myocardial infarction, or arrhythmias) [27]. The recently derived risk prediction tools outlined above have likewise identified an elevated troponin level as an independent predictor of both SAE and mortality [16–18]. Despite the above findings identifying a higher-risk cohort, patients with minimally elevated troponin levels may still be candidates for observation management, especially if serial troponin measurements are followed to exclude acute coronary syndrome (ACS). Troponin elevation in patients with AHF is not uncommon, though the majority is not due to ACS [28]. Many patients may have low, but detectable, troponin levels that may not confer an elevated risk of cardiac events when compared to those with ACS or significant troponin elevation. Further, with the anticipated introduction of high-sensitive troponin assays, it is imperative to identify a level of troponin elevation that differentiates low-risk from non-low-risk patients with AHF.

Biomarkers

The natriuretic peptides B-type natriuretic peptide (BNP) and its N-terminal precursor fragment (NT-proBNP) stand as the most established AHF biomarkers for evaluating undifferentiated dyspnea and assessing for worsening HF. Patients with a BNP level less than 100 pg/mL are unlikely to have AHF, and multiple studies have shown that rising BNP and NT-proBNP levels are associated with increased disease severity as well as increased risk for mortality in AHF [29–31]. Nonetheless, there remains no absolute cutoff for these markers in regard to evaluating OU eligibility. The SCPC guidelines suggest a BNP level less than 1,000 pg/mL or an NT-proBNP level less than 5,000 pg/mL as good candidates for an OU stay. However, patients with levels above these ranges may still be appropriate OU candidates depending on the overall clinical scenario. Clinical trials have shown limited effect of routine

BNP measurement on patient outcomes, and the following BNP levels to indicate response to therapy or "safe" discharge level have revealed mixed results [32–35]. Additionally, the growing emphasis on novel blood-based biomarkers and their ability to risk stratify patients with AHF has produced an abundance of different assays. A large, multicenter, prospective study evaluated several biomarkers in hospitalized AHF patients and found that novel markers such as mid-regional adrenomedullin (MR-proADM) and soluble (s)ST2 improved prediction of individual patient risk at 30 days and 1 year when added to a model using established clinical variables [36].

Cognitive and Functional Status

While the objective ED evaluation and provider intuition play important roles in determining safe disposition, all patients with AHF should undergo a self-care evaluation to determine the safety of potential outpatient management. A variety of social, behavioral, and environmental factors often contribute to a patient's acute presentation, and these same factors continue to form barriers to optimal outpatient management and goals of reducing readmissions [37, 38]. Certain social barriers such as medication availability, lack of follow-up care, or patient education are opportunities for meeting these goals and can be addressed in an observation setting [39, 40]. On the other hand, patients with complex psychosocial needs, such as end-stage HF or lack of social support leading to consideration of skilled nursing facility placement, frequently require inpatient resources. Ultimately, the institutional resources and policies should dictate whether a patient's broader needs represent inclusion or exclusion criteria [41].

Summary

We suggest ED patients with AHF be divided into three broad categories (Fig. 14.1). Those at high risk for mortality or serious adverse events based on initial ED evaluation should be admitted to the hospital, with an ICU admission needed in those who require invasive monitoring, ventilatory support, or other ICU-level treatment. Those without high-risk features should be further risk stratified based on their active comorbidities, response to initial therapy, and ability to manage their illness as an outpatient. Those with active comorbidities or significant self-care barriers may be better suited for inpatient management. Those without active comorbidities who have an incomplete response to initial therapy may be ideal candidates for an OU. Candidates for ED discharge are those with adequate response to ED therapy and no high-risk markers, significant comorbidities, or self-care barriers.

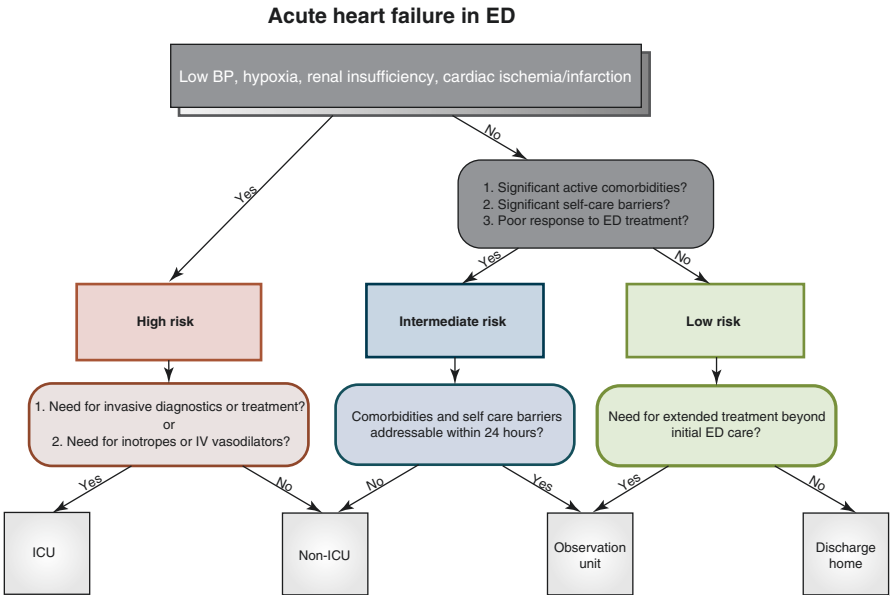

Fig. 14.1 A conceptual model of acute heart failure risk stratification in the ED based on known predictors of the risk for mortality or serious adverse events, presence of absence of comorbidities, and self-care issues. Such an algorithm may augment clinical judgment in disposition decisions (*ICU* intensive care unit)

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Acute Decompensated Heart Failure in the Observation Unit: Treatment Protocols

15

John Pease

Introduction

Treatment of acute decompensated heart failure (ADHF) patients remains challenging. There is limited data from randomized controlled trials of these patients in the emergency department (ED), much less the observation unit (OU). As a result, there has been little consensus regarding their management, adding to the inconsistent care these patients receive. Only recently have guidelines emerged to provide clinicians a framework from which to work [1]. This chapter will focus on therapeutic management, with respect to general supportive measures and pharmacologic therapy, and most importantly, specific treatment protocols that can be implemented in the OU.

Initial ED Management of Acute Decompensated Heart Failure

The majority of patients who present to the ED with ADHF have a chief complaint of dyspnea, and they are often hypoxic with increased work of breathing. Supplemental oxygen should be reflexively administered in essentially all patients with a target of maintaining an oxygen saturation $\geq 92\%$. This may require high flow oxygen by face mask in some patients, while others may only need oxygen by nasal cannula.

In cases of flash pulmonary edema, often associated with severe hypertension and diastolic dysfunction, more aggressive airway management may be necessary.

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In some cases, endotracheal intubation may be warranted or inevitable, but every attempt should be made to avoid this because of the transient nature of the requirement for positive pressure and the associated morbidity with mechanical ventilation. Obviously, patients requiring invasive ventilation are not good candidates for OU care. However, the use of aggressive airway adjuncts such as noninvasive ventilation (NIV), consisting of either continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP), may assist in avoiding the need for intubation while maintaining adequate oxygenation and ventilation. NIV should not be considered a substitute for intubation, but rather as a bridge to allow therapies directed at reducing filling pressures and pulmonary congestion to become efficacious. Further, brief periods of NIV should not exclude patients from the OU by default especially in patients with acute pulmonary edema, as these patients may rapidly improve with the combination of NIV and pharmacologic therapy.

While both methods of NIV appear to offer benefit, controversy exists regarding the relative superiority of either method. Both interventions produce similar reductions in cardiac filling pressures and improve respiratory status, but a recent meta-analysis found a significant reduction in mortality for patients treated with CPAP, but not BiPAP, and no overall difference on intubation rates [2]. However, more recent data from a large, multicenter, randomized controlled trial demonstrated no significant outcome differences between the two methods, as well as no mortality benefit of NIV in general [3]. Based on the available evidence, it is difficult to distinguish either method as superior, and there is likely to be general equivalence in clinical practice. Despite the conflicting evidence, expert opinion still recommends that NIV be considered as a useful adjunct in the management of patients with ADHF.

Although many patients with acute pulmonary edema are too complex for subsequent OU management, a significant number will turn around quickly with aggressive ED treatment, particularly those with acute uncontrolled hypertension. Concurrent with the aforementioned airway management, all efforts should be directed at reducing pulmonary congestion and preload. The most rapid improvement will be achieved with potent vasodilators such as nitroglycerin, nesiritide, or nitroprusside. Although they are quite effective, their immediate intravenous use often requires significant time to initiate a luxury these patients may not have on initial presentation. Sublingual nitroglycerin therapy, in doses larger than those typically used for chest pain (as many as twenty 0.4 mg tablets or sprays), can be quite effective [4]. One can achieve significant reductions in preload and afterload (blood pressure) with a marked improvement in respiratory symptoms, often within minutes of initiation of sublingual therapy [4]. Patients can then be transitioned to other formulations of a vasodilator (e.g., topical or oral) and can become reasonable candidates for the OU.

The addition of an intravenous diuretic to this strategy is common and makes practical sense as it will result in significant diuresis and eventual drop in preload. However, a minority of patients, usually those that present with acute pulmonary edema from severe hypertension, do not suffer from total fluid overload but rather a maldistribution of fluid into the pulmonary bed. Therefore, overall diuresis will

result in little improvement in this patient population. In summary, there appears to be an immediate benefit from rapid administration of sublingual nitroglycerin with or without an intravenous loop diuretic.

Observation Unit Management

The mainstays of treatment in the OU can be separated into two areas, (1) supportive care with correction of hypoxia and (2) pharmacologic therapies. A continuation of the supportive care initiated in the ED with supplemental oxygen is typically required in order to allow time for more permanent measures to take effect.

These more permanent measures are achieved via pharmacologic therapies. Pharmacologic therapies are usually twofold, diuretics used to reduce edema by reduction of blood volume and venous pressures and vasodilators that improve afterload and diastolic filling time and aid with LV remodeling.

Pharmacologic Therapy

The mainstay of therapy for ADHF is pharmacologic especially in the setting of hypertension and pulmonary edema, and the primary goal is to rapidly decrease filling pressures. Additional important goals include improving cardiac output through a reduction in afterload and/or improvement in contractility. Furthermore, given the large percentage of ADHF patients with underlying diastolic dysfunction, improving the ventricle's ability to fill with blood through efforts to improve myocardial relaxation is crucial.

Diuretics

Diuretics are often the first-line therapy in the ED management of patients with ADHF and have also become a mainstay of many OU treatment protocols. Diuretics reduce the total volume overload which, more importantly, decreases central venous pressures, right and left heart filling pressures, and pulmonary vascular pressures. This decrease in venous congestion allows intrapulmonary fluid to return to the circulation and improves pulmonary edema and, therefore, dyspnea and hypoxia. The loop diuretic furosemide is most commonly used although other loop diuretics are equally effective. Expert opinion suggests the initial following dosing strategies: 20 mg of intravenous furosemide in diuretic-naïve patients or an amount equivalent to the patient's total usual daily oral dose given via an intravenous formulation. Peak diuresis should occur within 30–60 min, and urinary output should be monitored closely. Repeat doses, in some instances double the first dose, are often effective in patients who fail to respond initially. The most recent practice guidelines for ADHF from the Heart Failure Society of America recommend loop diuretics at "doses needed to produce a rate of diuresis sufficient to achieve an optimal volume status" [5]. While

diuretics have demonstrated substantial clinical utility, the potential for harmful side effects is significant and must not be lost on the treating physician. In addition to electrolyte depletion (e.g., K^+, Mg^+) and potentially inducing a metabolic alkalosis, diuretics result in decreased renal perfusion and neurohormonal activation by increasing renin and norepinephrine [6, 7]. Historically, the use of continuous dose loop diuretic (e.g., furosemide 5–10 mg/h) has been advocated to temper the deleterious effects of intermittent boluses of higher doses. Although inconclusive, a Cochrane Review suggested greater diuresis and a better safety profile when loop diuretics were given as continuous infusion [8]. The most up-to-date available data suggests that intravenous continuous infusion and bolus loop diuretic therapy have similar efficacy in patients with ADHF [9]. In patients with diuretic resistance, the use of an additional diuretic that works on the proximal tubule, e.g., metolazone, may produce effective diuresis. Although large clinical trials evaluating timing and routes have not been performed, the use of diuretics remains a mainstay in the treatment of ADHF.

Vasodilators

Oxygen therapy and loop diuretics may be sufficient therapy for mild ADHF exacerbations, especially if their visit is due to brief periods of medical or dietary noncompliance. However, this frequently is not adequate and the addition of vasodilators becomes necessary, particularly in patients with severe hypertension and/or diastolic dysfunction. Most hypertensive patients are well perfused and hence are best treated with vasodilators such as nitroglycerin, nesiritide, or nitroprusside. Some patients with mild ADHF may respond to sublingual, oral, or topical nitrates and several reports advocate this approach [4, 10]. Others have promoted the use of sublingual angiotensin-converting enzyme inhibitors in this setting, based largely on a small trial of 21 patients who showed symptomatic improvement after treatment with sublingual captopril [11]. Data from ADHERE, a multicenter heart failure registry, suggests that patients treated early (<6 h) with an intravenous vasodilator had lower 48-h in-hospital adjusted mortality [12]. This data generates enthusiasm that early goal-directed blood pressure control initiated in the ED or OU may hold promise and further study is warranted.

Despite their widespread acceptance as standard therapy, surprisingly, little clinical outcome data exist for nitroglycerin and nitroprusside to support their use in ADHF. Physician familiarity with nitroglycerin use in patients with chest pain may contribute to its use in conjunction with diuretics as frequent first-line therapy in ADHF. The relatively predictable effect on the reduction of preload and blood pressure makes nitroglycerin an attractive choice. In this setting, dosing of intravenous nitroglycerin is typically higher than with chest pain, with usual starting doses of 50 mcg/min, depending upon initial blood pressure. It is not uncommon to need doses in excess of 200 mcg/min, with frequent (e.g., as often as every minute) titration. Nitroprusside can also be particularly useful in patients with acute pulmonary edema associated with severe hypertension, but its use has fallen out of favor and is usually reserved for those failing nitroglycerin.

There are several limitations to both of these therapies, including the deleterious effects of neurohormonal activation and the need for titration and hemodynamic monitoring. The latter two characteristics make these agents ill-suited for use in the OU. When employed in the OU, nitroglycerin's use is typically limited to a fixed, non-titratable dose. These drawbacks have led to a search for better therapeutic agents, ideally ones that improve acute symptoms and hemodynamics as well as mortality.

Nesiritide

Nesiritide is identical to human endogenous B-type natriuretic peptide (BNP) and is the first commercially available natriuretic peptide used for the treatment of ADHF. It serves as an antagonist to pathologic vasoconstrictive neurohormonal activation that occurs in ADHF. A pivotal, randomized, controlled trial demonstrated nesiritide decreased pulmonary capillary wedge pressure more than either nitroglycerin or placebo at 3 h and more than nitroglycerin at 24 h [13]. In addition, nesiritide's hemodynamic effects were longer lasting, without a need for up-titration, which was frequently necessary in the nitroglycerin group to maintain adequate reduction in wedge pressure [14]. Several characteristics emerged that suggested it was quite suitable for the ED or OU population, including a lack of proarrhythmic effect, no tachyphylaxis, and no need for titration [15]. Of all the vasodilators, only nesiritide has been specifically studied in the ED OU. The PROACTION study was a blinded, randomized, controlled trial of standard therapy versus nesiritide for OU heart failure management. It reported that the addition to nesiritide to standard therapy resulted in a significant decrease in the rate of "days in hospital" over the subsequent 30 days post-discharge [16].

However, the safety of nesiritide has been called into question as two meta-analyses suggested significant impairment of renal function and a trend toward increased risk of 30-day mortality which severely curtailed its use [17, 18]. More recent data from a large, randomized, placebo-controlled study reveals that nesiritide is not associated with an increase in serum creatinine or 30-day mortality; unfortunately, statistically significant improvements in dyspnea compared to standard therapy were also not found in this inpatient study [19]. Future research will be needed to further define the role of nesiritide in ADHF.

Inotropes

The use of inotropes has essentially no role in the OU management of patients with ADHF. While agents such as dobutamine and milrinone are effective at improving cardiac output and tissue perfusion, both cause neurohormonal activation and an increase in ventricular ectopy and appear to be associated with an increase in long-term mortality [20, 21]. Patients exhibiting clear signs of decreased perfusion or overt cardiogenic shock should be managed in an intensive care unit with appropriate hemodynamic monitoring.

Management Algorithms in the Observation Unit

A number of management algorithms for ED or OU care have recently appeared in the literature. Conclusive evidence identifying suitable patients who clearly benefit from a particular strategy are lacking, and only recently have specific recommendations to drive management been published [1]. It does appear, however, that patient risk stratification and initiation of aggressive treatment in the ED may limit potentially irreversible myocardial toxicity, especially in those with moderate to severe ADHF [12, 22]. The algorithm depicted in Fig. 15.1 attempts to provide some guidance for the diagnostic and prognostic evaluation of the suspected ADHF patient, in addition to recommendations for level of care and disposition decisions.

Using typical historical, physical examination and key diagnostic test features, a clinical profile of ADHF is defined. An assessment of initial severity is determined, based primarily upon level of respiratory distress and evidence of hypoperfusion. Further risk stratification is then derived after the initial work-up is completed which includes tests that demonstrate important prognostic information such as serum sodium, renal function, troponin, BNP, and the initial systolic blood pressure [22–25]. For the purposes of this chapter's focus on OU care, sections pertaining to the potentially life-threatening complications of respiratory failure or cardiogenic shock will not be discussed.

Figure 15.2 provides further management strategies in patients with ADHF who have a predominance of symptoms due to pulmonary congestion [26]. This algorithm divides patients into two clinical groups based upon the initial presenting blood pressure. Patients who are initially hypertensive may benefit more from aggressive vasodilator therapy and a modest dose of diuretics, while those who are initially normotensive are often substantially volume overloaded and require more aggressive diuretic therapy. Both groups may be candidates to undergo protocolized care and OU monitoring. In the OU, responses to treatment and achieving therapeutic targets determine disposition, whether to be discharged to home or admitted for inpatient care.

Another algorithm with more patient-specific treatment recommendations for management of ADHF in the OU is described in Fig. 15.3 [27]. In this strategy, treatment of ADHF is generally based on the presence or absence of volume overload and an assessment of the patient's cardiac output. On the left side of Fig. 15.3 [A, C, D, E, F], treatment recommendations are given for patients with ADHF experiencing signs and symptoms of volume overload, manifested by pulmonary congestion [27]. One of the limitations of this algorithm is grouping all patients with pulmonary congestion together, regardless of the etiology. There is no consideration of the patient's blood pressure or whether systolic or diastolic dysfunction is present. Nonetheless, it is quite helpful with general management principles. The right side of the algorithm provides treatment recommendations for patients with low cardiac output, and since most OUs exclude these patients, little discussion of this component of the algorithm is warranted.

Volume overload is divided into mild and moderate-severe groups; patients with mild volume overload (Fig. 15.3 [C]) are treated with intravenous diuretic therapy,

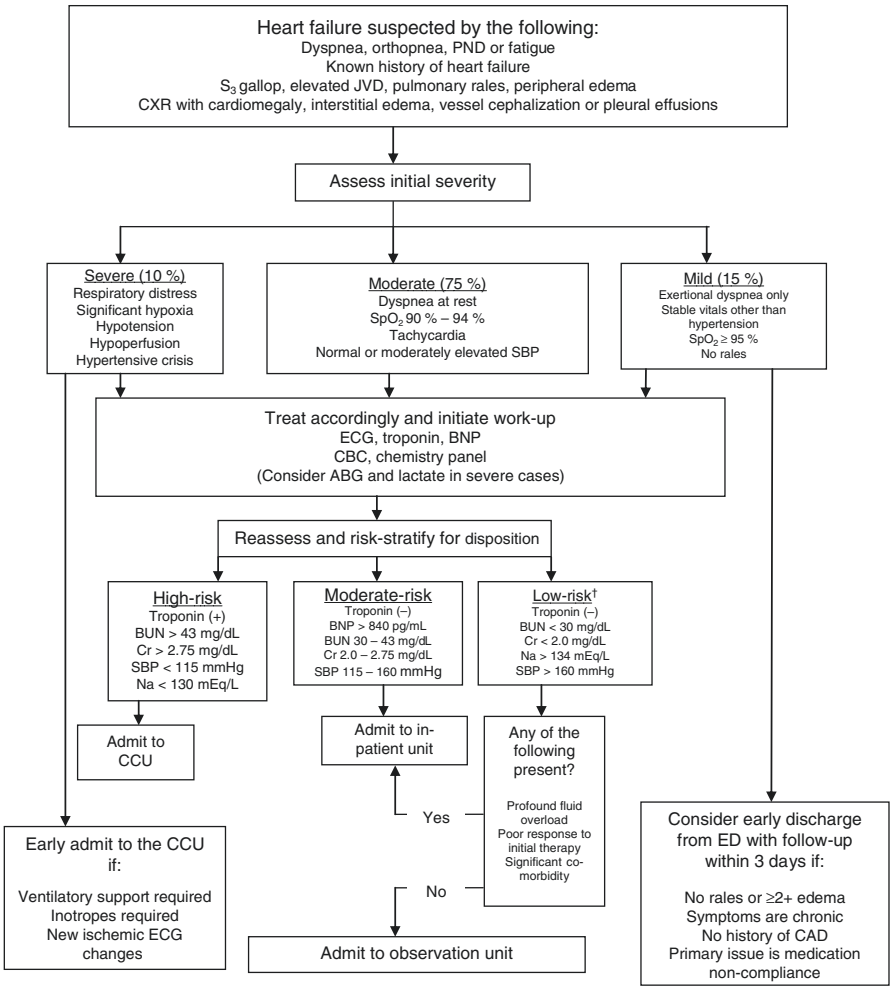


Fig. 15.1 Management algorithm developed by Phillip Levy, MD, MPH, and Jalal Ghali, MD, for use at Detroit Receiving Hospital. *ABG* arterial blood gas, *BNP* B-type natriuretic peptide, *BUN* blood urea nitrogen, *CAD* coronary artery disease, *CCU* cardiac care unit, *CBC* complete blood count, *Cr* creatinine, *CXR* chest radiograph, *ECG* electrocardiogram, *JVD* jugular venous distention, *PND* paroxysmal nocturnal dyspnea, *SBP* systolic blood pressure, *SpO2* saturation of peripheral oxygen. †To meet this classification, all 5 criteria should be present

typically loop diuretics [D]. Dosages in patients previously taking diuretics are guided by the total home daily dose, given as an intravenous bolus. Therapy for patients not taking oral diuretics at home is based upon renal function, and clinicians should exercise caution with diuretic therapy in such patients to avoid further renal injury. Success of diuretic therapy is driven by urine output goals, and recommendations for repeat diuretic dosing are described in the algorithm [27]. Again, caution should be exercised with extremely high doses of loop diuretics; prerenal

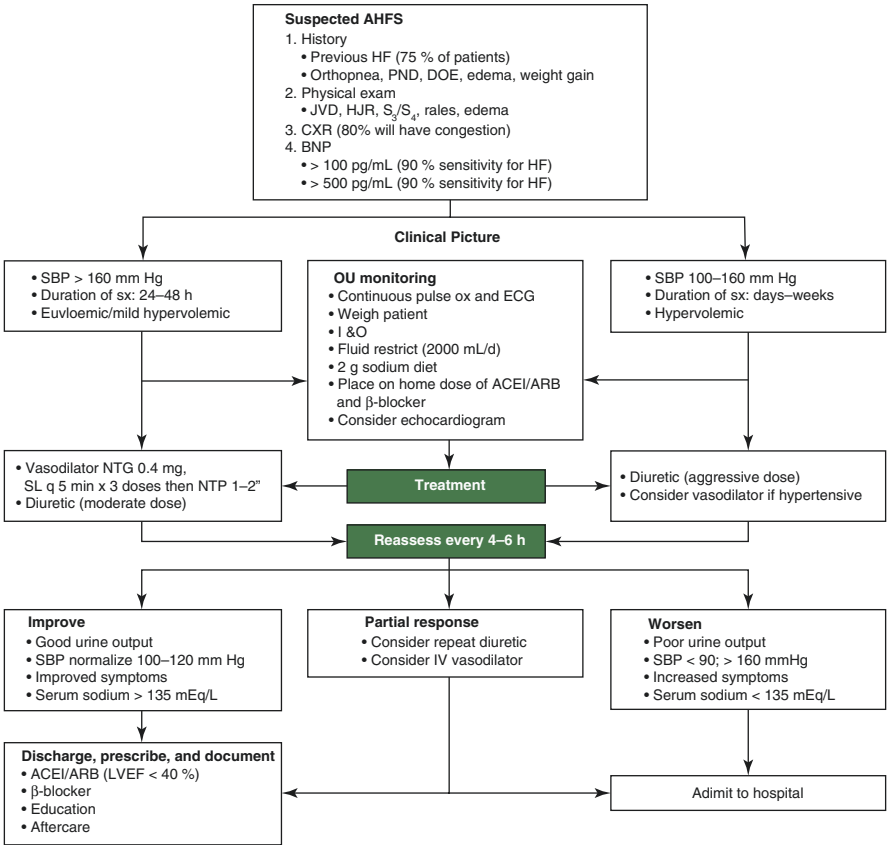


Fig. 15.2 Observation unit algorithm. *ACEI* angiotensin-converting enzyme inhibitor, *AHFS* acute heart failure syndrome, *ARB* angiotensin receptor blocker, *BNP* B-type natriuretic peptide, *CXR* chest radiograph, *DOE* dyspnea on exertion, *ECG* electrocardiogram, *HF* heart failure, *HJR* hepatojugular reflux, *I&O* intake and output, *IV* intravenous, *JVD* jugular venous distention, *LVEF* left ventricular ejection fraction, *NTG* nitroglycerin, *NTP* nitropaste, *OU* observation unit, *PND* paroxysmal nocturnal dyspnea, *SBP* systolic blood pressure, *SL* sublingual, *SX* symptoms (Adapted from Fermann and Collins [26])

azotemia and electrolyte abnormalities are common and should be recognized and treated quickly. A management strategy for electrolyte disturbances in this setting is included in the accompanying standing orders (Fig. 15.4) [27].

The authors recognize that patients with more severe pulmonary congestion, which typically include those with severe hypertension and resultant acute pulmonary edema, are likely to have an inadequate response to intravenous diuretic therapy alone. In these patients, the initial pharmacologic regimen should be more aggressive and include both an intravenous diuretic and a parenteral vasodilator (Fig. 15.3 [F]) if the blood pressure allows [27]. Intravenous nitroglycerin or nesiritide may be used to produce a more rapid response and more effectively relieve the signs and symptoms of congestion in these patients. No specific recommendations

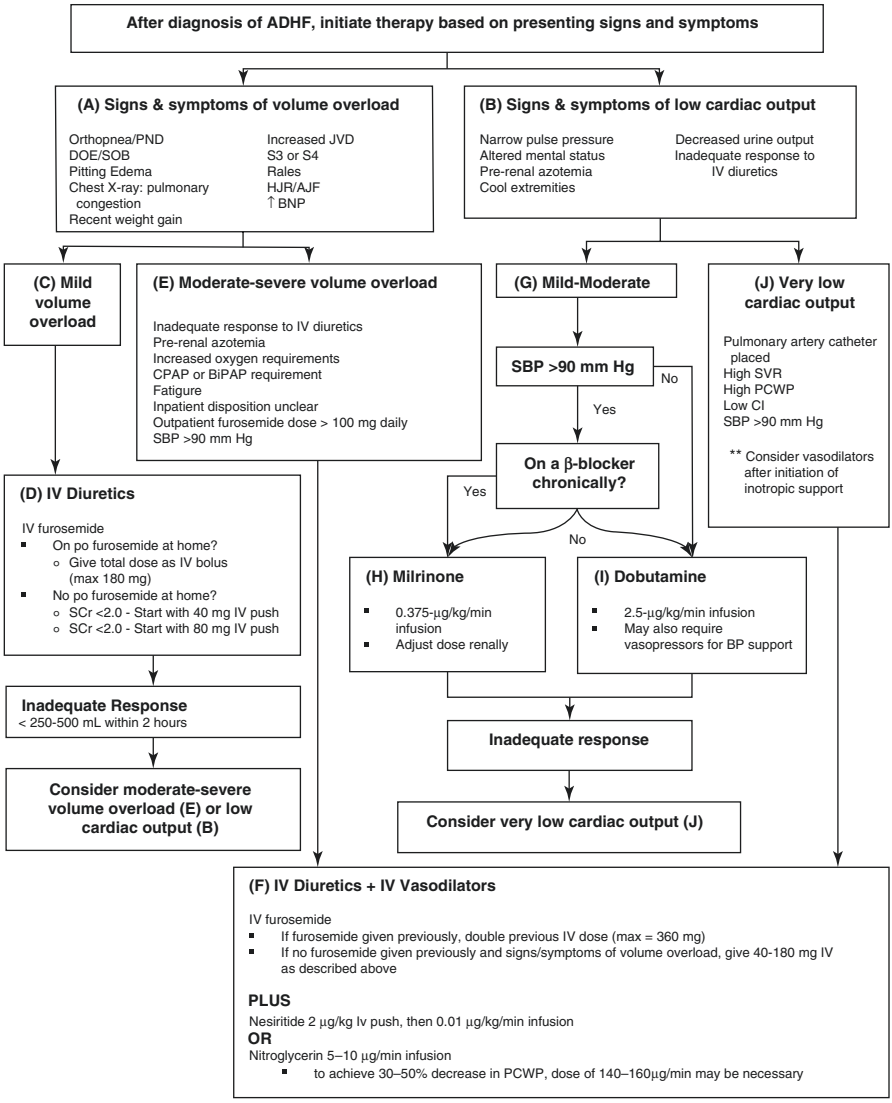


Fig. 15.3 Acute decompensated heart failure (ADHF) treatment algorithm. *AJR* abdominal jugular reflex, *BiPAP* bilevel positive airway pressure, *BNP* B-type natriuretic peptide, *BP* blood pressure, *CI* cardiac index, *CPAP* continuous positive airway pressure, *DOE* dyspnea on exertion, *HJR* hepatojugular reflex, *IV* intravenous, *JVD* jugular venous distention, *PCWP* pulmonary capillary wedge pressure, *PND* paroxysmal nocturnal dyspnea, *PO* by mouth, *SBP* systolic blood pressure, *SCr* serum creatinine, *SOB* shortness of breath, *SVR* systemic vascular resistance (Adapted from DiDomenico et al. [27])

are provided as to which vasodilator should be used. Of note, the suggested starting dose of nitroglycerin (5–10 mcg/min) described in Fig. 15.3 [F] should be considerably higher [27].

Congestive Heart Failure Order Set
For Acute Decompensated Congestive Heart Failure Patients
Emergency Department Order Sheet

Date Time Primary Diagnosis: Acute Decompensated Congestive Heart Failure
Secondary Diagnosis: _____
Vital signs q4h and as directed by medications (see individual medications)

- ❑ Labs: Basic metabolic panel, calcium, magnesium, phosphorus, CBC, PT/INR, PTT, BNP, CK, CK-MB, Troponin, O_2 saturation
- ❑ Digoxin level (if outpatient medication)
- ❑ Patient Weight: _____
- ❑ Ins and Outs
- ❑ 12 Lead ECG
- ❑ AP and lateral
- ❑ Foley catheter prn heavy diuresis
- ❑ Diet: <2.4g Na, low fat
- ❑ Fluid restriction: 1800 mL/24h; if Na <131 mg/dL, restrict fluid to 1500 mL/24h

Intravenous Furosemide
- ❑ If furosemide naïve, furosemide 40 mg IVP x 1 dose
- ❑ If on furosemide as outpatient
  Total daily dose as IV _____ mg: maximum 180 mg
  - Goal: >500 mL urine output within 2 hours for normal renal function
    >250 mL urine output within 2 hours if renal insufficiency
  - If goal urine output not met within 2 hours, double the furosemide dose to a maximum of 360 mg IV
  - Monitor symptom relief, vital signs, BUN, SCr, electrolytes

Nesiritide
- ❑ 2 µg IV push followed by 0.01 µg/kg/min IV infusion
- ❑ If symptomatic hypotention during infusion, discontinue nesiritide
  - Monitor symptom relief, vital signs q15m × 1 hour, then q30min × 1 hour, then q4h, urine output, electrolytes, BUN, SCr, magnesium, calcium, phosphorus
- ❑ If poor symptom relief or diuretic response ≥3 hours after nesiritide therapy initiation AND SBP ≥90 mm Hg, may consider titration of nesiritide
  - Nesiritide 1 µg/kg IVP and increase infusion by 0.005 µg/kg/min
  - May increase infusion rate q1h after first dosage, increase to a maximum dose of 0.03 µg/kg/min

Nitroglycerin 50 mg/250 mL
- ❑ 5 µg/min IV infusion; titrate dose q5min by 10–20 µg/min to achieve symptom relief
  - Monitor symptom relief, vital signs q15min until stable dose, then q30min × 1 hour, then q4h, ECG, urine output

Dobutamine 500 mg/250 mL
- ❑ 2.5 µg/kg/min IV infusion and titrate dose every 5 minutes to desired response to a maximum dose of 20 µg/kg/min
  - Monitor symptom relief, vital signs q15min until stable dose, then q30min × 1 hour, then q4h; ECG; urine output

Milrinone 20 mg/100 mL
- ❑ 0.375 µg/kg/min
  - Monitor symptom relief, vital signs q15min until stable dose, then q30min × 1 hour, then q4h; ECG; urine output

Fig. 15.4 Physician order set for the initial management of acute decompensated heart failure in the emergency department/observation unit. *AP* anterior/posterior, *BNP* B-natriuretic peptide, *BUN* blood urea nitrogen, *CBC* complete blood count, *CK* creatine kinase, *CK-MB* creatine kinase MB isoenzyme, *ECG* electrocardiogram, *INR* international normalized ratio, *IV* intravenous, *IVP* intravenous push, *PO* by mouth, *PRN* as needed, *PT* prothrombin time, *PTT* partial thromboplastin time, *SBP* systolic blood pressure, *SCr* serum creatinine, *Clcr* creatinine clearance (Adapted from DiDomenico et al. [27])

❑ Digoxin _____
Dose Route Frequency

❑ Lisinopril PO _____
Dose Frequency

❑ Losartan PO _____
Dose Frequency

❑ Metoprolol PO _____
Dose Frequency

❑ Spironolactone PO _____
Dose Frequency

Electrolyte Replacement

❑ Potassium

level (mEq/L)	IV dose (over 1 h)	PO dose	When to recheck potassium
3.7–3.9	20 mEq	40 mEq	12 hours or next morning
3.4–3.6	20 mEq × 2 doses	40 mEq × 2 doses	6 hours or next morning
3.0–3.3	20 mEq × 4 doses	40 mEq × 3 doses	4 hours after last dose
<3.0	20 mEq × 6 doses	Give IV only	1 hour after last dose

• If Clcr <30 mL/min, reduce dose by 50%

❑ Magnesium

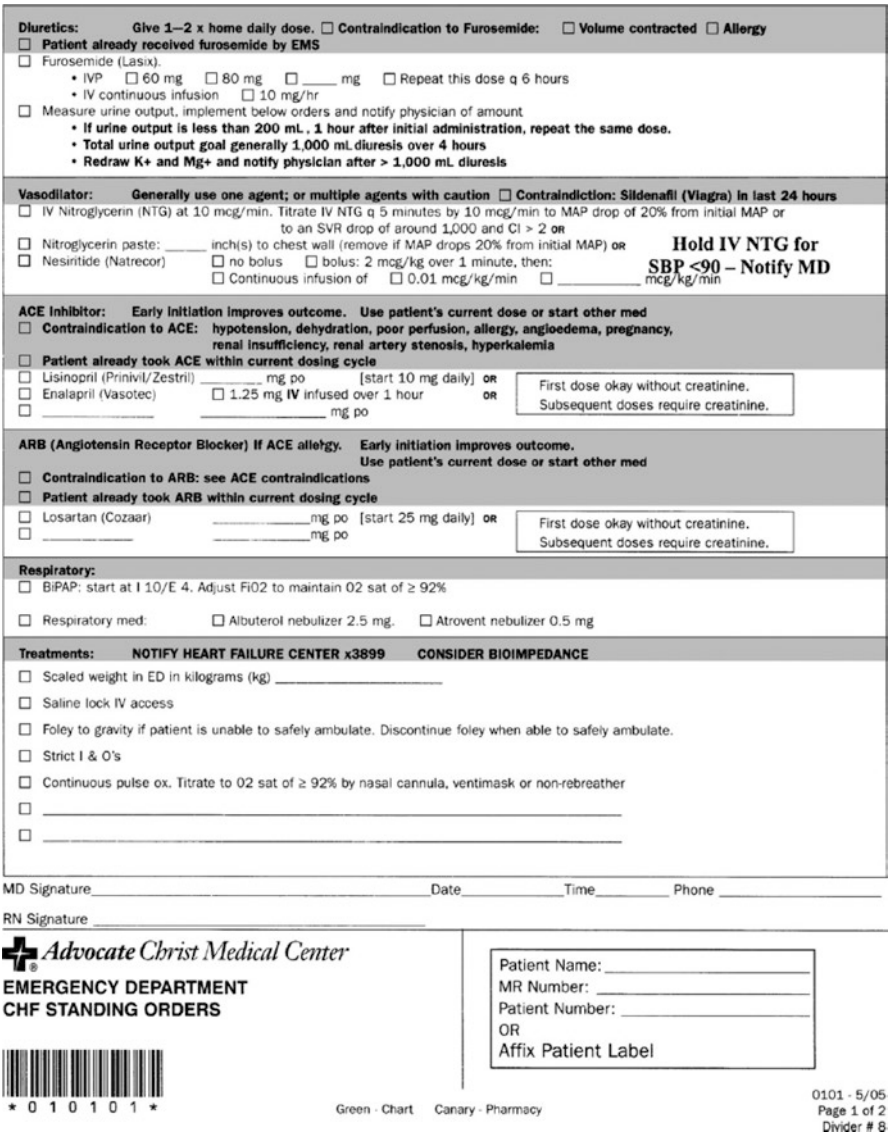
level (mEq/L)	IV dose	PO dose (Mg oxide)	When to recheck magnesium
1.9	Give PO only	140 mg	Next morning
1.3–1.8	1 g $MgSO_4$ for every 0.1 below 1.9 (max 6 g)	Give IV only	Next morning
<1.3	8 g $MgSO_4$	Give IV only	6 hours after last dose or next morning

• $MgSO_4$ 1–2 g, infuse over 1 hour
• $MgSO_4$ 3–6 g, infuse ≤2 g/hour

_____ _____
Physician Signature Date

Fig. 15.4 (continued)

Physician order sets for OU management of ADHF are typically necessary to standardize the evaluation and treatment of these patients. Figures 15.4 and 15.5 represent two example order sets with slightly different components [27, 28]. While the former represents a more exhaustive compilation, the latter illustrates a comparatively abbreviated order set, limited to one page, that was developed to maximize ease of use, minimize errors, and meet key ADHF clinical practice guidelines [28]. These orders are for sample purposes only and should be modified accordingly to accommodate institutional variations in practice. Again, the inclusion of orders for inotropic therapy in Fig. 15.4 is not typically indicated in OU patients.



Diuretics: **Give 1–2 x home daily dose.** ☐ **Contraindication to Furosemide:** ☐ **Volume contracted** ☐ **Allergy**
☐ **Patient already received furosemide by EMS**
☐ Furosemide (Lasix).
- IVP ☐ 60 mg ☐ 80 mg ☐ ____ mg ☐ Repeat this dose q 6 hours
- IV continuous infusion ☐ 10 mg/hr

☐ Measure urine output, implement below orders and notify physician of amount
- **If urine output is less than 200 mL , 1 hour after initial administration, repeat the same dose.**
- **Total urine output goal generally 1,000 mL diuresis over 4 hours**
- **Redraw K+ and Mg+ and notify physician after > 1,000 mL diuresis**

Vasodilator: **Generally use one agent; or multiple agents with caution** ☐ **Contraindiction: Sildenafil (Viagra) in last 24 hours**
☐ IV Nitroglycerin (NTG) at 10 mcg/min. Titrate IV NTG q 5 minutes by 10 mcg/min to MAP drop of 20% from initial MAP or to an SVR drop of around 1,000 and CI > 2 **OR**
☐ Nitroglycerin paste: _____ inch(s) to chest wall (remove if MAP drops 20% from initial MAP) **OR**
☐ Nesiritide (Natrecor) ☐ no bolus ☐ bolus: 2 mcg/kg over 1 minute, then: ☐ Continuous infusion of ☐ 0.01 mcg/kg/min ☐ _____ mcg/kg/min

Hold IV NTG for SBP <90 – Notify MD

ACE Inhibitor: **Early initiation improves outcome. Use patient's current dose or start other med**
☐ **Contraindication to ACE: hypotension, dehydration, poor perfusion, allergy, angioedema, pregnancy, renal insufficiency, renal artery stenosis, hyperkalemia**
☐ **Patient already took ACE within current dosing cycle**
☐ Lisinopril (Prinivil/Zestril) _____ mg po [start 10 mg daily] **OR**
☐ Enalapril (Vasotec) ☐ 1.25 mg **IV** infused over 1 hour **OR**
☐ _____ _____ mg po

First dose okay without creatinine.
Subsequent doses require creatinine.

ARB (Angiotensin Receptor Blocker) If ACE allergy. **Early initiation improves outcome. Use patient's current dose or start other med**
☐ **Contraindication to ARB: see ACE contraindications**
☐ **Patient already took ARB within current dosing cycle**
☐ Losartan (Cozaar) _____mg po [start 25 mg daily] **OR**
☐ _____ _____mg po

First dose okay without creatinine.
Subsequent doses require creatinine.

Respiratory:
☐ BiPAP: start at I 10/E 4. Adjust Fi02 to maintain 02 sat of ≥ 92%
☐ Respiratory med: ☐ Albuterol nebulizer 2.5 mg. ☐ Atrovent nebulizer 0.5 mg

Treatments: **NOTIFY HEART FAILURE CENTER x3899** **CONSIDER BIOIMPEDANCE**
☐ Scaled weight in ED in kilograms (kg) _____
☐ Saline lock IV access
☐ Foley to gravity if patient is unable to safely ambulate. Discontinue foley when able to safely ambulate.
☐ Strict I & O's
☐ Continuous pulse ox. Titrate to 02 sat of ≥ 92% by nasal cannula, ventimask or non-rebreather
☐ _____
☐ _____

MD Signature_____Date_____Time_____ Phone _____
RN Signature _____

Advocate Christ Medical Center
EMERGENCY DEPARTMENT
CHF STANDING ORDERS

Patient Name: _____
MR Number: _____
Patient Number: _____
OR
Affix Patient Label

* 0 1 0 1 0 1 *

Green - Chart Canary - Pharmacy

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Fig. 15.5 New congestive heart failure emergency department order set. *ACE* angiotensin-converting enzyme, *ARB* angiotensin receptor blocker, *EMS* emergency medical services, *IV* intravenous, *IVP* intravenous push, *MAP* mean arterial pressure, *NTG* nitroglycerin, *PO* by mouth, *SBP* systolic blood pressure, *SVR* systemic vascular resistance, *BiPAP* bilevel positive airway pressure, *I/E* inspiratory/expiratory, *I* intake, *O* output (Adapted from Reingold and Kulstad [28])

Conclusions

Evidenced-based guidelines for the management of ADHF patients in the ED and OU are just now emerging [1]. While treatment protocols and management algorithms appear vital to the success of any OU strategy, they are currently

based largely on anecdotal experience or, at best, data from small trials. Cornerstones of these algorithms are appropriate patient risk stratification and recognition of those primarily with pulmonary congestion versus those with cardiogenic shock. Further delineation based upon (1) severity of volume overload, (2) associated renal insufficiency, and (3) relationship to presenting blood pressure appears to aid with management decisions. Unfortunately, there is little consensus among authors regarding an overall approach. Suffice it to say, the systematic use of therapeutic agents (intravenous diuretics and vasodilators) with a priori clinical target is paramount. Further, in appropriate patients, data appears to support the early use of vasodilators [13]. Additional recommendations await publication of institutional experience with algorithms such as those presented here.

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Education Elements in the Observation Unit for Heart Failure Patients

16

Brad P. Mayeux and Robin J. Trupp

Introduction

Heart failure (HF) is a complex clinical syndrome associated with great morbidity, mortality, and economic burden in the United States [1]. The vast majority of healthcare expenses for HF result from hospitalizations and rehospitalizations for the management of the decompensation events [1]. The American College of Cardiology Foundation and American Heart Association (ACCF/AHA) 2013 HF guidelines include several recommendations to address the post-discharge needs of patients [2]. Included is the recommendation to provide specific education on facilitating self-care (IB recommendation). Implicit is that self-care education be given regardless of the site of care (admission versus ED or observation unit (OU) care).

Prompt identification of the precipitant for the decompensation, such as tachyarrhythmias, sodium indiscretion, or ischemia, drives the treatment plan. Yet the precipitant is frequently unclear or may be multifactorial, requiring significant investigation. It has been estimated that the majority of hospitalizations could be avoided with improved adherence to medication and dietary regimens and careful monitoring of changes in signs and symptoms of HF [3–5]. Although educational needs for the patient with HF are vast, in an OU given the short-term nature of the interaction, education must be directed and succinct. In fact, HF education has been identified as a key task of OU care that is associated with decreased readmissions [6]. Once the precipitant is identified, it should become the focus of patient education, as nonadherence to prescribed pharmacologic and nonpharmacologic interventions significantly impacts both the short- and long-term management of HF.

Not unexpectedly, during times of stress, as seen in patients presenting to an emergency department (ED) with acute dyspnea, retention of any information given is limited [7]. If the patient is ultimately hospitalized, the time urgency for providing

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Table 16.1 Self-care behaviors recommended for all patients with HF

Maintain current immunizations, especially influenza and *Streptococcus pneumoniae*
Develop a system for taking all medications as prescribed
Monitor for changes in weight, increase or decrease
Monitor for changes in signs/symptoms of shortness of breath, swelling, fatigue, and other indicators of worsening HF
Restrict dietary sodium intake to 2,000 mg per day; learn to read labels
Restrict alcohol intake
Avoid other recreational toxins, especially cocaine
Cease all tobacco use and avoid exposure to secondhand smoke
Do not ignore emotional distress, especially depression and anxiety. Seek treatment early
Tell your provider about sleep disturbances, especially snoring, witnessed apnea, excessive daytime sleepiness
Achieve and maintain physical fitness
Visit your provider at regular intervals
Do not take over-the-counter medicines or herbal supplements without consulting with a provider
If diabetic, achieve diabetes mellitus treatment goals

Adapted from Riegel et al. [9]

information is lessened somewhat, as the inpatient environment offers additional opportunity for, and reinforcement of, education. Therefore, patient and family education should take advantage of the "teachable moments" that occur across the spectrum of inpatient care, beginning in the ED and ending at discharge [8].

Self-Care

On a near daily basis, patients have variability in symptoms producing differing impacts on daily activities and quality of life. Adequate self-care reflects actions taken by the patient to maintain well-being and/or reduced HF symptoms. However, it is fair to presume that patients presenting to the ED experienced some level of self-care inadequacy.

HF self-care starts with understanding HF and its treatment and involves patients' decisions about behaviors intended to maintain physiological stability and about changes in their HF status [9]. Self-care maintenance behavior involves decisions made about following the therapeutic regimen, including taking medications as directed, eating a low-sodium diet, exercising, engaging in preventive behaviors, and actively monitoring their signs and symptoms. On the other hand, self-care management refers to the decisions made in response to changes in HF signs and symptoms, such as calling a healthcare provider, taking an extra diuretic, or going to the ED. Table 16.1 lists self-care behaviors recommended for patients with HF.

Viewing the patient as the "essential member" of the healthcare team shifts the focus to providing them with education and skills necessary to successfully integrate self-care practices into their normal daily life. As previously stated, the

majority of decompensation is directly attributable to nonadherence to therapeutic regimens, and adherence is closely connected to self-care, making this a great educational partnership. In the haste to shorten length of stay and meet facility and national goals for care, clinicians may simply treat patients' symptoms, thus failing to identify the cause for the decompensation. By conducting a thorough assessment to identify the precipitating event, clinicians can also identify self-care needs. Acknowledging any barriers to and consequences for nonadherence to the therapeutic regimen and actionable items could enhance self-care behavior.

Causes for Decompensation

Nonadherence to the medication schedule and volume overload, directly related to sodium indiscretion (willful or inadvertent) and excess fluid intake, are the major causes for decompensation or worsening HF [4, 10]. To reduce post-discharge morbidity and mortality, a thorough evaluation and consideration of precipitating factors is encouraged [2]. Education and close outpatient surveillance by the patient and family can reduce nonadherence and lead to the detection of early changes in clinical status so that interventions to prevent further clinical deterioration and ultimately ED care and hospitalization can be implemented [2].

Medication and Dietary Adherence

Dietary and medication adherence has profound implications for the management of HF. Lack of adherence as a contributor to decompensation and hospitalization has been well documented [4]. Poor adherence also has significant economic repercussions for individuals and for hospitals. For example, if insufficient medication is taken for the treatment to be fully effective, as when patients "ration" diuretics to extend the life of a prescription, ED care or hospitalization may be necessary. In today's healthcare environment, financial penalties are also issued to institutions with excessive HF readmission rates. Therefore, strategies targeting improved adherence to diet and medication must be individualized. One size does not fit all here.

Dietary Instructions

The American Heart Association, the Institute of Medicine, and the US Department of Agriculture all advocate for Americans to restrict sodium intake to 2,300 mg per day [11–13]. For African Americans, those with heart disease or those over the age of 40, this restriction drops to 1,500 mg per day. However, given American's consumption of processed products and fast food, this degree of sodium restriction is challenging for even the most dedicated individual. Since diuretics act by increasing sodium excretion in the urinary filtrate, which is followed by increased water

excretion, a diet high in sodium makes diuretics essentially ineffective in controlling volume and symptoms. Patients must be taught and understand the relationship between fluid and sodium for managing volume and for controlling HF symptoms. Counseling should include repeated in-depth instruction on the components of a 2-g sodium diet, involving family members and caregivers as well. Having the patient complete a food diary over the course of several days will yield important insights into dietary habits, food preferences, and average fluid consumption. Reading food labels, low-sodium food choices when dining out, and cooking with herbs and spices to improve palatability are important aspects that should be included. Providing written materials or useful websites for low-sodium food choices and recipes is essential for success at home. As a note, salt substitutes should be used with caution, as many replace sodium chloride with potassium chloride, thus increasing the potential risk of hyperkalemia.

In advanced HF, further dietary sodium restriction may be necessary to attenuate the expansion of extracellular fluid volume and the development of edema. Although sodium restriction may mitigate the development of edema, it cannot totally prevent it because the kidneys are capable of reducing urinary sodium excretion to less than 10 mmol per day. Hyponatremia should not be treated with sodium liberalization because this hyponatremia is typically dilutional in nature and occurs in the setting of free water excess. Liberalized sodium intake or replacement should be reserved for overt cases of severe excessive diuresis and dehydration.

Within the ED and OU, simple questions about recent dietary intake may yield the cause of decompensation. Accompanying family members are also good sources of information regarding food or fluid ingestion. As discussed above, patients should understand that dietary indiscretion produces fluid retention and worsening symptoms. Thus, efforts should focus on helping patients make the association between behavior and symptoms. The challenge lies in doing this without preaching or condemning. Learning will not occur within that scenario. If a connection between a particular behavior and its negative consequences can be made, lifestyle changes are more likely to take place. However, behavioral changes do not happen overnight, and those who view the recommended changes as personal choices, rather than as edicts imposed by others, are more likely to make permanent lifestyle modifications [2].

Recognizing obvious sources of sodium, such as a saltshaker or potato chips, is evident for most patients, but in a typical diet, they constitute less than 25 % of total sodium intake. Hidden sources of sodium play a greater role in dietary intake and yet are often unrecognized. Good HF clinicians are also good detectives. Common high-sodium content items include, but are not limited to, canned soups and vegetables, pickles, cheeses, softened water, tomato juice, antacids, and processed foods. As discussed above, a food diary provides important information on food choices and eating patterns. Having the patient start this diary after treatment in the emergency department affords the clinician next evaluating the patient much-needed information and the ability to discuss alternative lower-sodium choices. The ED and OU should be stocked with printed materials for patients and families to use at home.

Medications

Pharmacologic interventions are vital to managing symptoms and halting disease progression in HF. Yet, medications for heart failure are both complex in their administration and costly. Polypharmacy, or the need for multiple medications, is a normal consequence of an evidence-based approach to managing HF because beta-blockers, angiotensin-converting enzyme (ACE) inhibitors and/or angiotensin receptor blockers, aldosterone inhibitors, electrolyte supplements, and diuretics must all be taken at different times throughout the day. New medications for HF, such as ivabradine or sacubitril/valsartan, or medications for comorbidities, infections, or other needs are prescribed, have dose changes, or are discontinued. No wonder patients become confused and fail to take as directed.

Potential barriers to medication adherence should be identified and addressed. Besides financial barriers, other frequently missed obstacles include real or perceived side effects, depression, forgetfulness, and understanding the importance of and need for the medication [7, 8]. To improve self-care and adherence, ongoing discussions must occur between clinicians and patients to reach understanding and agreement on the necessity for medications and the appropriate regimen [8]. Rather than mandated or imposed views, this discussion may require some compromise from both parties, as a patient may agree to take more medications than initially desired or a clinician acknowledges the patient may be taking less than is ideal. What is most important is that healthcare providers know *all* medications being taken.

Medication reconciliation is the process of comparing medication orders to all of the medications the patient has been taking. This reconciliation is done to avoid medication errors such as omissions, duplications, dosing errors, or drug interactions. More than half of patients have at least one medication discrepancy on admission to a hospital [14]. In addition, there is an increased risk for discrepancy at every transition point: from home to ED, ED to admission, one unit to another, and inpatient to discharge. Recognizing that medication errors put patients at risk and are largely preventable, the Joint Commission named medication reconciliation as the 2005 National Patient Safety Goal #8. The first step in medication reconciliation is to obtain the most accurate list of current medications prior to giving any medications in the ED (except in emergency or urgent scenarios). This includes prescription and over-the-counter medications, vitamins, and supplements, noting the dose, route, frequency, indication, and time of the last dose for each. Each facility likely has a specific form and process for documenting medication history and adherence. Besides the patient and family, the patient's pharmacy and previous medical records may be reliable sources of information. Patients should be instructed to bring all of their medications whenever seeking or receiving healthcare.

To assist with adherence, a variety of aids are available and may be helpful to some. These aids include pill boxes, medication trackers, timers, or interactive websites, to name few. For those with financial constraints, most major pharmaceutical companies offer assistance programs for individuals unable to afford medications. Many require documentation of medical necessity from the prescriber, and patients

may need to submit documentation of financial need as well. Although this process is unlikely to be initiated in the ED, it is important to recognize resource options and to make the necessary referrals. Access to social worker or case management staff can be quite valuable in addressing these concerns.

Worsening Signs and Symptoms

Despite advanced warning signs and symptoms of decompensation, many patients either fail to recognize or fail to react to them. For example, Friedman reported that 90 % of patients hospitalized due to worsening HF experienced dyspnea 3 days prior to hospitalization [15]. Additionally, 35 % reported edema, and 33 % had cough 1 week prior to admission [16]. This delay may be a failure to routinely monitor symptoms or an inability to recognize and interpret symptoms when they occur. Thus, when patients cannot recognize or acknowledge worsening signs and symptoms, clinicians lose the chance to intervene and potentially avert hospitalization. Therefore, educating patients and their families on both the signs and symptoms associated with worsening HF, and actions to take, provides an excellent opportunity to reduce hospitalizations and healthcare expenditures.

Unfortunately, there is no one single sign or symptom indicative of worsening HF. Rather, patients experience a constellation of signs and symptoms, including increased dyspnea and/or fatigue, weight gain, orthopnea, and paroxysmal nocturnal dyspnea. Efforts to improve patients' abilities to recognize, interpret, and act on the early signs and symptoms may be facilitated when patients receive simple consistent advice on what changes in symptoms are important and clear endpoints that should prompt them to seek help. Essential aspects of education are presented in Table 16.2.

Respiratory Symptoms

As mentioned above, the majority of patients with decompensated HF have evidence of excess extracellular volume or congestive signs and symptoms. However, typical respiratory complaints, such as dyspnea, have poor sensitivity and are nonspecific to HF [17]. In addition, many patients with HF also have significant comorbidities that may further limit respiratory function, such as chronic pulmonary disease or obesity. When such comorbidities are present, the clinical importance of alterations from everyday respiratory limitations becomes the measure for pending decompensation. For example, using three pillows to sleep may be a normal sleep pattern for some and would not be considered as evidence of orthopnea, but for others, a change from one to two pillows may be indicative of congestion. Patients may report sleeping on one pillow but fail to mention that pillow is used in their recliner because they cannot tolerate lying flat in bed without severe respiratory distress. Additionally, emergency room clinicians may ask about sleep

Table 16.2 Essentials of heart failure patient education

Daily weights every day of your life
Use the same scale at the same time of the day wearing comparable clothing
Weigh first thing in the morning after going to the bathroom
Notify your healthcare provider if you gain 3 or more pounds overnight or 5 pounds over 3 days OR if you lose weight and experience dizziness on standing up
Maintain a low-sodium diet to help avoid fluid retention
A dietary intake of 2,000 mg of sodium per day is recommended
Ask for written materials that can help you make healthier choices
Salt is everywhere. Learn to read labels
Be conscious of fluid intake
Do not drink eight glasses of water per day if taking a diuretic (water pill). This defeats the purpose of the medication
Drink small sips when thirsty or when taking medications
Do not carry liquids with you
Fluid comes in a variety of formats: soup, Jell-O, ice, watermelon
Be as active as possible
Engage in physical activity at least three to four times per week
Appropriate activities include walking or biking
Avoid any form of heavy lifting or isometric exercises
(Isometric exercises are those in which a force is applied to a resistant object, such as pushing against a brick wall)
Treatment of heart failure is directed at reducing the workload in your heart, not straining it. Do not lift anything heavier than 10 pounds
Notify your healthcare provider of changes in your symptoms or weight
This includes weight gain of 3 or more pounds overnight or 5 pounds over 3 days, increased fatigue or shortness of breath, dizziness, or fever, to name a few
Your physician or nurse will give you additional, specific instructions to follow
Keep their emergency number readily available in case of need
Bring all of your medications with you whenever you are seeking or receiving healthcare
This includes both prescription medications and those purchased without a prescription, such as vitamins, pain medicines, or nutritional supplements

patterns, including hours of sleep, daytime sleepiness, the presence of snoring, witnessed apnea, and nocturia, to discover other possible sleep disturbances that impact HF [18].

Patients with chronic HF live with dyspnea, and breathlessness becomes "normal" or a part of everyday life [19]. Adjustments to constant dyspnea usually center on reducing physical activities to decrease breathlessness. In that scenario, seeking treatment occurs only when the usual strategies, such as rest or fresh air, fail to relieve symptoms and the patient becomes anxious or frightened. Initial treatment is aimed at rapidly alleviating air hunger and hypoxia. It is important to remember that substantial pulmonary congestion can occur without rales or jugular venous pressure being evident [19].

Changes in Weight

Just as diabetics monitor glucose levels to better manage their disease, so should patients with HF monitor their weight. While neither precise nor totally reflective of volume status, daily weights comprise the gold standard for the outpatient care and management of HF. However, less than half of HF patients report weighing themselves daily, even in the first week following a hospitalization for decompensation [21]. As previously discussed, daily weights will not occur or be accurate if the patient does not own a scale, devalues the necessity of performing the task, or fails to do so consistently and appropriately. Although the focus of weight monitoring is to detect weight gain, indicating fluid retention, patients should also pay attention to weight loss. Excessive weight loss can be the consequence of dehydration, result in electrolyte imbalances or worsening renal function, and produce symptoms of dizziness, fatigue, and shortness of breath. In advanced HF, when the patient's appetite and caloric intake decline, excess volume may take place in the absence of any apparent weight gain, as true body mass is lost through muscle and fat catabolism.

Fatigue

Patients with HF experience chronic fatigue and reduce their physical activity accordingly to mitigate exhaustion. However, worsening or increasing fatigue, in the absence of increased physical activity, can be an early indicator of decompensation. Any increased fatigue that lasts longer than 2–3 days should be a source of concern for the patient and should prompt closer attention to sodium and medication adherence. Should additional symptoms develop or the fatigue continues or worsens, patients should notify their clinician immediately so that treatment interventions can be initiated and hospitalization possibly avoided. However, as with dyspnea, fatigue is a vague, nonspecific symptom that is difficult to quantify and can be included in the differential diagnosis for many other conditions and diseases.

Nocturia

One of the earliest symptoms of excess extracellular fluid is nocturia. To maintain homeostasis, the heart attempts to eliminate excess volume through the secretion of natriuretic peptides from atrial and ventricular myocytes. These endogenous peptides act by dilating the renal afferent arteriole, preventing sodium reabsorption, and counteracting neurohormonal vasoconstriction effects. Atrial natriuretic peptide is secreted primarily at night, when right atrial pressures are highest as a result of supine positioning. Consequently, urinary volume is increased, and the patient is awakened to void. Patients should pay attention to new-onset or increasing nocturia that occurs in the absence of changes in the medication, especially increased diuretics or dietary regimen.

Reinforcement of Education

Information can be presented in different formats. Accordingly, a variety of educational materials must be accessible within the ED. Some examples of materials available include videotapes or CDs, pamphlets, or printed pages specifically distributed by the institution. Such materials should also be consistent with educational information given by other departments or community agencies. It is not unusual for patients to be given conflicting instructions on weight changes, such as call if you gain 2 pounds overnight, 3 pounds overnight, 5 pounds in 2–3 days, or 5 pounds in a week. When faced with conflicting advice, many simply opt to do nothing. Having these materials at hand provides patients and families the opportunity to read and have questions answered, resulting in an expedited education process.

Because high levels of relapse are likely to occur after short-term behavioral interventions, plans for reinforcement of the education must be established to improve long-term adherence and to prevent additional decompensation events [22]. Patients should be scheduled for a follow-up visit with the primary care physician or other clinicians managing HF within days of discharge [19]. This quick appointment serves many purposes. The first is to ensure that treatment has been adequate in resolving the congestion and that no new issues have developed. The second is to closely compare the medications prescribed at discharge with the previous regimen to identify and correct any discrepancies. Finally, reinforcement of education can be provided, especially education specific to the precipitant of the exacerbation. If the cause was not identified, healthcare providers more familiar with the patient may be able to discern it at this appointment and provide the requisite education.

Summary

For many, episodes of decompensated HF may be largely avoidable through self-care through sign and symptom monitoring and enhanced adherence to treatment regimens. Unfortunately, during incidents of worsening HF, it can be difficult to provide education to patients on better managing their disease. A better plan in the ED is to begin by treating the excess volume and alleviating the symptoms. Once stabilized and in the OU, there are ample opportunity and teachable moments when educational content is likely to be better received and understood. Education and counseling that address specific concerns may provide knowledge, support, and self-care behaviors. Importantly, discharge instructions should include prompt follow-up with the established primary care physician or cardiologist within days of ED treatment or hospital discharge [9]. Sending patients home with a wallet-sized card detailing these salient points further reinforces their importance (Table 16.3). Finally, in advanced or complex cases, referral to a HF specialist may be warranted [2].

Table 16.3 Example of wallet-sized patient reminder card

	Medications			Medications		
	Medications	Strength	Dosing	Medication	Strength	Dosing
Call	———	———	———	———	———	———
	———	———	———	———	———	———
Dr.—–at (—–)—–	———	———	———	———	———	———
If you have signs or symptoms of worsening CHF	———	———	———	———	———	———
	———	———	———	———	———	———
	———	———	———	———	———	———
	———	———	———	———	———	———
	———	———	———	———	———	———
	From the ADHERE® Scientific Advisory Committee					
				Appointments		
		Increase in shortness of breath		Date	Time	
Reminder *Always maintain a low-salt diet*		Swelling in the legs or ankles		———	———	Patient
		Weight gain ≥3 lbs within a few days		———	———	Reminder
		Difficulty breathing when lying down		———	———	Card
		Worsening tiredness		———	———	
		Stomach bloating/ fullness and loss of appetite		———	———	
		Dry cough, especially when lying down		———	———	
Adhere Acute Decompensated Heart Failure National Registry						Patient name
				ADHERE is a registered trademark of Scios Inc. and pending before the USPTO ©2004 Scios Inc. All rights reserved		
				Back	Front	

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Emergency Department and Observation Unit Discharge Criteria

17

Kevan E. Meadors and Deborah B. Diercks

Appropriate discharge and disposition from the emergency department and observation unit has the potential to lead to major changes in the long-term care for patients with heart failure (HF). Today, HF affects nearly six million Americans, thus causing substantial morbidity and mortality. Due to the ever-aging population and increased survival from cardiovascular diseases, the HF prevalence is expected to continue growing [1]. This results in one million ED visits and more than one million annual hospital discharges, making HF the most common principal discharge diagnosis in adults ≥65 years old [1–3]. The past several years have consistently shown that more than 80 % of these ED visits for acute HF result in admission compared to only 13 % of the total 136 million annual ED visits in the United States [4]. Moreover, HF is the most expensive admission or readmission reason for the elderly population in our nation [5].

While we search for ways to improve these shocking statistics, we must take into consideration that HF is still a complicated disease to manage and its progressive nature remains unchanged. An estimated one-third of patients hospitalized for acute HF will be readmitted or will have expired within 3 months of discharge, and within 1 year, up to half of the patients will have expired [5]. As it is a chronic disease, the patient's baseline status must be considered in all disposition decisions. This chapter will review how patient-centered measures, physical exam findings, and changes in laboratory parameters and imaging can be utilized in the decision to discharge heart failure patients from an observation unit or the emergency department.

Accurate disposition is a challenge and perhaps more daunting than the management of these patients to emergency physicians. ED doctors tend to have a low-risk tolerance when it comes to discharging a HF patient due to the lack of directive national guidelines or a validated decision tool to identify those patients that are low

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risk for adverse events after discharge [6]. Also, there is pressure on ED physicians to make timely dispositions due to the large volume of undifferentiated patients waiting for assessment [5]. This may result in inappropriate admissions and premature ED discharges with resultant increased cost and morbidity, respectively [7]. Although the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) guidelines on the management of heart failure suggest that patients with mild to moderate symptoms generally do not require admission, risk assessment solely based on symptoms is often difficult [8]. In order to increase the number of patients discharged to home, effective treatment must be initiated in the ED as part of patient management or as an OU protocol. This early intervention and avoidance of hospital admission can result in significant cost savings. This saving benefit is particularly evident if patients with heart failure are at low risk for adverse events [9].

Success of any protocol is dependent on accurate identification of patients suitable for an early discharge plan. Variables that are routinely measured during an ED workup, including renal function, B-type natriuretic peptide (BNP), respiratory rate, and a history of dialysis, can be used to help identify HF patients who are at low risk for adverse events if discharged [6]. Measures that have consistently been associated with patients who are at an increased risk for morbidity and mortality are renal dysfunction, low blood pressure, low serum sodium, and elevated cardiac biomarkers [1]. Multiple studies recommend dividing HF patients who present to the ED into three broad categories in order to anticipate their disposition and expedite their treatment plan: patients at high risk for serious adverse events, patients with active comorbidities, and patients with neither high-risk features nor active comorbidities. Patients with high risk for serious adverse events should be admitted to the hospital without delay, and ICU admission should be considered for those with highly unstable vital signs, concern for airway instability, inadequate systemic perfusion, or cardiac arrhythmias requiring continuous IV intervention. This group is estimated to represent about 20 % of all HF patients presenting to the ED. Patients lacking high-risk features but with active comorbidities and self-care barriers for discharge are appropriate for inpatient management or the observation unit, based on their response to the initial ED therapy and predicted length of stay. Finally, those who have no high-risk features for adverse events after discharge and no active comorbidities can be considered for observation unit versus discharge, also based on how quickly they respond to therapy and return to their baseline [1, 10]. An estimated 50 % of HF patients could be safely discharged home from the ED after a brief period of observation, and strategies such as this could help us identify such patients [4, 10].

The observation unit (OU) is an ideal disposition for patients on the border of discharge and admission. Observation is technically a billing status indicating that, while a patient is receiving care in the hospital or ED setting, they are still considered to be an outpatient. The unit is not meant to keep patients for greater than 48 h, but it can serve as a place to treat and risk-stratify patients while determining whether they need to be officially admitted for further management [1, 10]. Interventions in the OU are not costly or complex. They consist mostly of diuresis, afterload reduction, frequent reassessment, and patient education. The use of the OU is very efficient and

conserves significant resources when compared with a full admission. Some OUs are not a distinct location in the hospital, but consist of a mixture of observation patients among the admitted patients in the hospital. This is less efficient for the observation providers but requires the least amount of hospital resources to create the OU. The more efficient model is to cluster OU patients into a specific area of the hospital designed to deliver observation appropriate care [1, 10].

Early evaluation and management of HF in the ED or OU setting are poorly defined by the ACCF/AHA guidelines or the Heart Failure Society of America (HFSA). The majority of HF patients require IV diuresis upon presentation until their symptoms subjectively improve [1]. Patients may also benefit from the addition of topical or sublingual nitroglycerin or supplemental oxygen, but most do not require any additional intervention [10]. The ED and OU can easily provide this level of management. Early and frequent assessment of response to treatment and the ability to discharge home are integral to observation unit management.

Consensus guidelines for discharge from the ED and OU have been developed [10]. These guidelines are based on the presence of factors associated with increased risk for adverse events. Although the lack of these parameters does not ensure a patient is ready for discharge, they are useful in identifying those with persistent decompensated heart failure who would benefit from additional treatment. Discharge criteria can be divided into three separate categories: patient-centered measures, hemodynamic and clinical parameters, and laboratory measurements and imaging (Table 17.1).

Table 17.1 Discharge criteria: ideally, a candidate for discharge would make all of these criteria

Criteria
Patient-centered measures
Improvement in dyspnea
No chest pain that would raise concern for acute coronary syndrome (ACS)
Ability to ambulate without dyspnea above the baseline
Free of symptoms of congestion
Self-care barriers resolved
Hemodynamic/clinical parameters
Systolic blood pressure <160 mmHg, >90 mmHg
S_3 resolution
Oxygen saturation >90 %
Urine output >1 L
Decrease in weight/return to dry weight
Laboratory measurements and imaging
B-type natriuretic peptide levels
Stable blood urea nitrogen (BUN)
Stable or declining troponin level
Return to normal or baseline of electrolytes
CXR changes
US evaluation

Patient-Centered Measures

It has been well established that the change in patient-centered outcome measures such as dyspnea can be utilized to assess therapeutic success and improvement in symptoms. Dyspnea is the most common symptom in patients with HF that present to the ED [1, 5], and resolution of dyspnea remains the most common goal of treatment [1]. A high proportion of patients have improvement in their dyspnea during the ED stay due to standard therapy, and many have complete resolution of their dyspnea within their 24-h OU stay [10]. However, the subjective nature of this patient-centered measure had made it challenging to standardize. Furthermore, dyspnea has not been shown to correlate well with worsening HF during hospital admission or post-discharge events. Maneuvers that illicit cardiac stress such as changing patient's position from sitting to supine or ambulation tests may help to identify the more subtle effects of HF on dyspnea and may serve as more definitive measures of clinical improvement. Other symptoms related to HF such as fatigue and body swelling may become equally important to explore as patient-centered outcomes [1]. Assessment of dyspnea is an integral component of disposition assessment.

Patients also should be able to ambulate without an increase in dyspnea from the baseline. Although there is no trial that has assessed this measure in an observation unit setting, it is effectively an inexpensive 6-min exercise test. The distance that a patient can ambulate in a 6-min period without excessive dyspnea and fatigue has been shown to correlate with long-term mortality [11, 12]. Unfortunately, many comorbid illnesses, such as obesity and lung disease, affect this outcome measure. It is important to assess a change from the baseline.

While the prior studies did not specifically evaluate the ED, one investigation tested the feasibility of a 3-min walk in the emergency department and found that 85 % of all patients were able to complete the walk and the ability to walk 3 min was associated with outcomes [13]. In addition, freedom from symptoms of congestion has also been associated with improved long-term outcomes, although orthopnea can persist even after subjective improvement in dyspnea [14, 15].

Another patient-centered measure that should be present at the time of discharge is the lack of ongoing chest pain. It has been reported that acute coronary syndrome (ACS) is a trigger for up to 25 % of patients with heart failure decompensation. Therefore, patients should be pain-free or have undergone an evaluation for ACS prior to discharge [16].

Finally, self-care barriers must be overcome in order to be able to discharge HF patients safely. Patients and/or family members must feel confident in caring for themselves at home and express full understanding of medication changes and follow-up appointments. Moreover, patients must not be at a high risk of falling at home and must have dependable transportation.

Hemodynamic/Clinical Parameters

Hemodynamic and clinical parameters can be a part of the data used to assess suitability for discharge. These comprise measures of perfusion, volume status, and oxygenation-based physical exam findings, as well as automated measures. Systolic

blood pressure (SBP) is a useful predictor of adverse events at the time of presentation and discharge [17]. In the initial presentation of patients with decompensated HF, a hypertensive response is adaptive, although persistent elevation of SBP can correlate with increased risk of worsening renal function. In HF, any deterioration of renal function clearly correlates with morbidity and mortality; therefore, adjustment of medications to prevent hypertension is essential prior to discharge. While the ideal blood pressure at the time of hospital discharge is not clearly elucidated, patients should at least have a SBP <160 mmHg [17]. Conversely, as medications are titrated, patients must be able to ambulate without symptoms of dizziness; therefore, the SBP should exceed 90 mmHg [18].

Clinical findings can also be used to assess adequacy of acute interventions. These include a combination of changes in physical exam and easily obtained values such as pulse oximetry, urine output, and weight. Of all the clinical examination findings, the presence of an S_3 is most suggestive of acute decompensation [19]. Serial exams that document the resolution of an S_3 by auscultation can be used as a discharge criterion [19]. However, the presence of a digitally recorded S_3 has not been shown to be associated with prognosis or improved diagnostic accuracy in one large clinical trial [20]. This physical exam finding, like an improvement in jugular venous distention, is dependent of physical attributes of the patient and careful physical exam assessment by the physician.

Another criterion, noted as part of the evaluation, is oxygen saturation. Patients should have an oxygen saturation greater than 90 % [18]. No data exist to support this value; however, it is reasonable to only discharge patients who are able to maintain their oxygen saturation. Transient nighttime drops in oxygen saturations are common because HF is associated with an increased prevalence of obstructive sleep apnea. Therefore, pulse oximetry as a discharge criterion should be assessed when the patient is awake.

Urine output assessment is another parameter that can be used as a surrogate to assess treatment efficacy. Although there are no studies that compare the amount of urine output with outcomes, intuitively, this makes sense. Clinically, 1 L appears to be a significant amount. Closely linked to urine output is the patient's weight [18, 34]. Dry weight is often one of the only baseline parameters that is known in the ED. Theoretically, a decline in the patient's weight can represent a resolution of the acute progression of the disease process; however, "overshooting" this parameter can lead to hypotension, hypoperfusion, and worsening renal function. Although not supported by clinical trials, it is reasonable to suggest that a patient's weight should be declining at the time of discharge; however, additional assessment may be warranted in patients who are below their dry weight at the time of discharge assessment.

Laboratory Measurements and Imaging

Improvement in laboratory parameters may also be used to assess patients at the time of discharge. B-type natriuretic peptide (BNP) levels are the most established diagnostic biomarkers for HF [1]. BNP levels have been associated with a decrease in hospitalization, intensive care unit utilization, hospital length of stay, and cost of treatment when used as a diagnostic strategy. The Rapid ED Heart Failure Outpatient

Trial (REDHOT) results showed that BNP levels predicted early outcomes more accurately than physician's impression. Patients in this study with BNP levels less than 200 pg/mL had 0 % mortality at 30 days, regardless of EF [4]. Another study involving Veterans Administration patients found that patients with BNP level less than 230 pg/mL demonstrate a very low risk of recidivism to the ED, readmission, and even death [4]. However, BNP levels can be affected by age, sex, weight, and renal function and can thus be misleading [1]. BNP levels are found to be lower in obese patients with HF and are higher in patients with renal dysfunction. For these reasons, comparing the ED BNP level to the patient's baseline is of more value than standardizing the normal limits for all HF patients [4]. BNP levels that are more than 50 % changed from the baseline generally represent worsening HF [1]. Newer markers are also available, such as ST2 and galectin-3, and may aid with the prognostic assessment and diagnosis of HF [1].

Collins et al. comprised a STRATIFY decision tool to help identify HF patients in the ED who were at low risk for 30-day adverse events and could thus be safely discharged home. The decision tool included 13 variables that are readily available in the ED, including age, body mass index (BMI), BNP, diastolic blood pressure (DBP), blood urea nitrogen (BUN), serum sodium level, respiratory rate, oxygen saturation, troponin level, the use of dialysis, the outpatient use of supplemental O_2, the outpatient use of an ACEI, and QRS duration. While an elevated BNP was not shown to be a significant predictor of serious adverse events or death, its elevation did show a trend toward an association with adverse events [6].

Elevated troponin levels have been shown to be predictive of long-term prognosis in HF patients [21–23]. Patients with severe HF may have chronically elevated levels. The STRATIFY decision tool constructed by Collins et al. found that an elevated troponin level in the ED was found to be one of the two significant predictors of adverse events. The study also found that 13 % of patients with HF in the ED had a less than 5 % risk of death or serious complications in the first 30 days after ED presentation. Of note, adverse events related to ACS were most commonly seen in the first 5 days after ED presentation and were detected using troponin testing in the ED [6]. It is recommended that HF patients have no ischemic changes or elevated troponin in order to be candidates for the OU. However, patients with only minimally elevated troponin levels may still be appropriate for observation management if the levels are trended to rule out acute coronary syndrome. These patients are at risk for failing observation care and may need to be moved to inpatient management [1]. Therefore, patients with an elevated initial troponin level are probably not ideal candidates for an early discharge strategy.

Traditional chemistry labs that are routinely assessed daily in patients with decompensated heart failure can also be used in the assessment at the time of discharge. The ED measured BUN level is the other variable measured in the STRATIFY decision tool found to be a significant predictor of adverse events [6]. Appropriate candidates for the OU include patients whose BUN levels are less than 40 mg/dL and whose creatinine levels are less than 3.0 mg/dL [10]. Improvement in the BUN and serum creatinine in patients with initially abnormal values is a potential marker of treatment success and may be useful in determining disposition [24].

Attention has been placed on the significance of worsening serum creatinine in the setting of treatment for decompensated heart failure [17, 26, 35]. An increase in creatinine level of >0.3 mg/dL from hospital admission correlates with in-hospital death, complications, and length of stay. The presence of worsening renal insufficiency, as defined by a creatinine change of >0.3 mg/dL from prior values, is concerning, and patients may warrant further treatment until the creatinine improves or stabilizes [17]. Extrapolation from these studies suggests that an increase in serum creatinine identifies a high-risk group of patients.

In addition, studies have shown an association between worsening renal function after discharge and poor prognosis [25]. Gotsman et al. studied the significance of serum urea and renal function in patients with heart failure. They found that serum urea may independently have prognostic importance for patients beyond renal function [26]. It may be a more comprehensive data point to measure the clinical status because it encompasses parameters such as renal function, fluid volume balance, hemodynamics, and neurohormonal axis. Since serum admission and discharge urea are predictors of 1-year survival, admission serum urea may be used as possible data point for admission given its probable prognosis for both short-term and long-term survival.

Another laboratory parameter associated with prognosis is the sodium level [27]. A sodium level of <136 mEq/L has been shown to correlate with 30-day and 1-year mortality [11, 24]. In patients with normal serum sodium and BUN at the baseline, a decrease in sodium may be an indicator for the need of admission [11, 24]. In addition, an improvement in serum sodium during hospitalization is associated with reduced mortality [28, 29].

Chest radiography is another tool to evaluate HF patients in the ED and can give the physician insight into the degree of pulmonary venous congestion, cardiomegaly, and interstitial edema. While CXR is specific for these findings, their absence cannot rule out acute HF. Many patients, especially those in late-stage HF, have few radiographic signs despite their classic HF exacerbation symptoms [1]. Improvements on CXR after response to treatment may lag behind clinical findings, and therefore the CXR may not be the ideal imaging modality to assess suitability for discharge. Ultrasound is another imaging modality that can help the ED physician assess for left ventricular function, volume status, and pericardial effusion. Studies have shown that bedside ultrasound is (sensitivity, 97 % [95 % CI, 95–98.3 %]; specificity, 97.4 % [95 % CI, 95.7–98.6 %]) specific for detecting acute HF in the ED setting [29]. Residual pulmonary congestion identified by lung ultrasound at the time of discharge has been associated with a higher risk of rehospitalization and death [30].

Independent of the clinical presentation, the success of early discharge is related to the adequacy of outpatient follow-up and appropriate medication adjustment at the time of discharge. The initial improvements gained in the ED or observation unit can be quickly negated if the patient is discharged without suitable outpatient management plans. Key components include close follow-up to ensure adequate medication adjustment, dietary education, and a management plan (Table 17.2). This can be achieved by collaboration with the entire healthcare team to ensure appropriate follow-up and communication between providers, including the ED physician, the

Table 17.2 Outpatient key components

Nursing case management
Physician follow-up (primary care coordinated with cardiology)
Optimization of medication regimen
Patient education
Social support (home health assessment)

patient's primary care provider, and the cardiologist. The providers must engage in structured communication and participation in the management of the patient [4]. Also very crucial is a concept known as shared decision-making (SDM). This involves an agreement and detailed understanding of the plan of care between the provider and the patient [6]. There have been several recent studies analyzing patients' understanding of their discharge instructions, one of which showed that only 10% of patients understood all of the topics on their discharge instructions immediately after they were explained to the patient. The discharge instructions did adhere to Joint Commission guidelines, but follow-up appointments and discharge medications were still very poorly understood by the patient [31]. This presents the healthcare team with an opportunity to not only cover all of the discharge instructions appropriately but adapt to the patients' level of understanding and employ closed-loop communication or other family members that are reliable and willing to help with the outpatient care.

Another opportunity for improvement lies in the timeliness of discharge summaries after patients leave an inpatient visit. They typically describe the treatment given during the visit and the laboratory results but sometimes fail to accurately relay the transition of care information, including changes made in medications, pending studies, or follow-up recommendations or appointments. The untimeliness of these summaries makes them to the primary care provider or the cardiologist in the early follow-up period [32]. Improving the quality of the transition of care information and making them easily and immediately accessible to the primary care providers can reduce the risk of readmission for these patients [33].

It should also be noted that every patient will not fit every criteria and that all recommendations must be interpreted in consideration of the patient's baseline status and follow-up care. The best recommendations contain a combination of these parameters adjusted for the individual patient. Utilizing a combination of patient-centered outcomes and more objective measures provides ample evidence that can help drive the disposition decision. Appropriate discharge from the emergency department or OU must be accompanied with adequate follow-up. Patient education is also extremely important on dietary recommendations, medication schedules, and tracking body weight to help prevent need for further emergency room visits or hospital admissions.

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Effective Discharge Planning

18

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Discharge planning is the process of evaluating and planning for the patient's needs post discharge. An effective discharge plan begins with the first encounter in the emergency department (ED), regardless of the disposition, and must be evaluated every step of the way during the treatment period [1–3]. The discharge period has been identified as an opportunity to have a positive impact on patient outcomes and needs to be a priority for the health-care team. An in-depth look into the causes of readmissions must influence discharge planning and drive a strategical approach to improve current methods.

Many studies focus on the clinicians' impressions of readmissions, but few incorporate the patient and caregiver's perspective [4]. Focusing on both and collaborating with all members of the health-care team at every level of the treatment period can give us the most effective results [4–7]. The majority of research has been in the area of discharge planning from the inpatient setting [8, 9]. Although limited, there is emerging data on improved patient outcomes and better allocation of health-care resources with targeted post-discharge interventions in the ED [10]. This is especially true in high-risk groups such as the elderly and those with inadequate support structure [10].

Nearly all patients with heart failure will experience acute symptoms at least once, necessitating evaluation in the ED [9]. With ED visits and hospital admissions

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being scrutinized at every level, hemodynamically stable heart failure patients will be stabilized in the ED and discharged home adding to the burden of the ED staff to provide a comprehensive discharge plan [11]. Failure to meet this responsibility results in repeated admissions.

Why Is Discharge Planning So Important for Heart Failure Patients?

Utilization of ED services is growing approximately twice the rate of population growth, and reimbursement penalties for readmissions force close attention on "preventable" admissions [10]. As a result, research is being conducted to identify gaps in the transition of care as well as to identify possible errors or mismanagement in a patient's care [5, 12, 13]. Heart failure is the cause of nearly one million hospitalizations annually and accounts for over one million ED visits per annum [14–18]. In the last decade, hospitalization for heart failure has significantly increased for people <65 years of age and >85 years of age [5]. Approximately 20 % of heart failure patients are readmitted within 1 month of discharge and 50 % within 6 months [16, 19–21]. These readmissions also account for 70 % of the costs [6]. According to the Medicare database from 2003 to 2004, heart failure was the leading cause of recurrent hospitalizations [13]. These points reiterate the importance of exploring areas of improvement in the discharge process and coordination of care.

Patients with heart failure often have a high prevalence of comorbid conditions which may lead to polypharmacy and multiple health-care providers [22–24]. This, in combination with low health-care literacy and other barriers to self-care [23], can make management of heart failure difficult and often necessitates a patient-specific discharge plan. Individualized discharge plans improve adherence and outcomes by empowering patients to manage their health problems [4, 5, 7, 8]. Fortunately, with the advent of electronic medical records (EMR) and health information exchange (HIE), most communication failures can be analyzed and addressed [25]. The increase in post-discharge health-care services alone may not be the only answer in decreasing readmissions [5]. The quality of the services as well as monitoring the delivery of best practices may be more important to the overall picture [5].

Effective Discharge Planning

The effective discharge plan starts with identifying the links between the cause of the current admission and what may lead to readmissions. It should start with the first encounter in the ED, regardless of the final disposition of the patient [2, 3]. Recent research focuses on patient engagement in delivery of high-quality care and encourages patients to engage in self-care after discharge as opposed to focusing on the provider's perspective [7]. Frequent evaluation of the discharge plan throughout the treatment period will allow for revisions as needed. Annema et al. illustrated that health-care providers and patients along with their caregivers agreed on the reason

for readmission a third of the time [6]. Overall, nonadherence to diet, fluid restriction, and medication were the most important factors related to a preventable HF readmission [6].

Contents of the Effective Discharge Plan

Assessment

Patients and their caregivers are often unprepared to care for themselves in the next care setting [25]. Causes for readmissions are multifactorial and include issues such as lack of adherence, inadequate discharge preparation, and education [3]. With the development of patient-reported measures to reflect the patient's perceived needs at discharge, health-care providers can assess a patient's "readiness" for discharge and concentrate efforts on quality improvements in discharge planning [12]. Tools such as brief prescriptions, ready to reenter community, education, placement, assurance of safety, realistic expectations, empowerment, and directed to appropriate services (B-PREPARED) and Care Transitions Measure 3 (CTM-3) can be used to assess a patient's readiness [12].

Inadequate patient education and nonadherence to the medical plan alone may account for as many as 40 % of the readmissions [26]. Assessing a patient's characteristics such as functional, cultural, and psychosocial aspects is also an important part of the transition of care process [5]. Most programs use eight specific characteristics in their post-discharge disease management, which are patient education; early assessment after hospital admission, including caregivers in the care plan; medication review; early post-discharge follow-up; telephone follow-up; home visits; medication review; and post-discharge handoff to outpatient providers [5]. It is difficult to identify which specific intervention carries the most weight since many institutions use the "bundled intervention approach," but institutions most successful in reducing rehospitalizations were the ones that included home visits and/or follow-up telephone calls [5].

Barriers such as low health literacy, lack of preparedness on discharge, and a paucity of social support might be addressed with a more structured and individualized patient-centered education program and an increased awareness of outpatient resource availability [7]. As many as 90 million Americans have poor health literacy, and as many as 62 % of patients treated in the ED for heart failure are unable to read the label on a prescription bottle [23]. A more formal and detailed education on disease progression might alleviate anxiety and fear [7, 27, 28]. Discharge instructions should be legibly written and in a patient-friendly format [29]. It is recommended that they are written at the sixth grade reading level; however, most are written at a ninth to tenth grade level [8]. Older individuals may need materials that are written in larger print. In heart failure, teach-back methods were associated with increased patient compliance and knowledge retention as well as decreased hospital readmissions [5]. This method should be employed in all aspects of patient education.

Early identification of patient's caregivers and their specific roles as well as the patient's social support system is imperative. Adequate support has been shown to have a positive impact on the patient's ability to adhere to a self-care program and increased capability of symptom management [5]. Assessing the need for a formal support system such as home care, nursing home, and hospice/palliative care might break several barriers to self-care [5, 30]. Particular attention should be paid to groups of individuals with a greater need for transition of care such as those with increased frailty, those who are non-English speakers, and those with cognitive deficits [5]. A better system for coordination of care in the form of EMR and HIE as well as addressing medication discrepancies and using a low-literacy friendly approach to medication understanding and symptom management are all areas needing improvement [7, 25, 27, 28].

Socioeconomic status is an independent risk factor for readmission with the highest risk for readmission being associated with the lowest income [31, 32]. The average number of medications taken by a patient is 10.5 and increases as the severity of symptoms increase [33]. With the implementation of the Affordable Care Act, health system outcome improvements have been established such as better coordination of care and post-discharge follow-up. Ongoing research focuses on patient-centered outcome interventions on functionality, symptoms, and quality of life (QOL) [5].

Medications

It is important that the discharge plan includes medications that are evidence based [34]. The preadmission medication list must be reconciled with the discharge list, and clear written instructions should be given to the patient about what to stop and what to continue or add. The medication plan for the treatment of heart failure can be challenging and complex which may lead to discrepancies, unwarranted side effects, and nonadherence, all of which may contribute to hospital readmissions. Patients with low health literacy and impaired cognition are at highest risk [27].

Loop diuretics were commonly cited as problematic and difficult to adhere to because of disturbing side effects and fear of adverse effects to other organs. New research suggests that a tailored, pharmacist-delivered intervention on medication reconciliation might have a positive impact especially for high-risk individuals [27]. This approach consists of patient-specific counseling specifically assessing the patient's barriers to understanding and compliance, an illustrated medication schedule, and a pillbox to assist the patient at home [27]. The intervention would conclude with a follow-up telephone call after discharge, and if problems were detected, pharmacists would provide the needed assistance [27].

Another concern is the interaction between over-the-counter medications and herbal products. Patients seldom tell the health-care provider about the over-the-counter medications and herbal therapies they are taking. Because there are many possible drug-to-drug interactions, it is best to encourage patients to discuss all medications and supplements that they are taking and to maintain a written record of all.

Diet

Nonadherence to dietary restrictions can lead to worsening symptoms and subsequent readmissions [22, 34, 35]. Few patients have the knowledge of how to follow a low-sodium diet, and only 36 % report following dietary recommendations [23, 36]. New guidelines from the American Heart Association recommend limiting sodium to 1500 mg/day for patients with stages A and B heart failure because of the data linking its intake to heart failure risk factors such as hypertension, left ventricular hypertrophy, and other cardiovascular diseases. Currently, there is insufficient data to support definitive sodium restrictions in those with stages C and D heart failure [37]. Discharge instructions for the patient with heart failure should include a clear diet plan with examples of foods to avoid and how to read a food label. It has been reported that up to 42 % of patients with heart failure are poor at reading food labels [23].

Some patients also need to restrict fluids. Alarmingly, 38 % of patients with heart failure report thinking they are required to drink large quantities of fluids [38]. Those with persistent fluid retention or severe hyponatremia, despite a low-sodium diet and diuretics, may benefit from a fluid restriction [23]. These individuals will need instructions on how to measure fluid intake and ways to address the sensation of thirst.

Activity

The activity plan should be tailored to the individual [23]. Patients need to be reassured that activity is beneficial and receive instructions on how to monitor their tolerance and symptoms. Exercise has been shown to improve oxygen delivery, decrease inflammation, increase peak oxygen uptake, and decrease depression [23].

Signs and Symptoms

Many patients delay seeking help for an extended period, possibly due to failure to routinely monitor symptoms and/or failure to recognize and identify the symptom as related to heart failure [23]. Delays in seeking medical care may result in unnecessary readmissions [35]. Fewer than 50 % of patients weigh themselves daily, and those that do only do so intermittently [23]. Patients who weigh themselves are more likely to make appropriate adjustments in sodium intake and diuretic dosing [23]. Thus, the best discharge plans include written guidance on how, why, and when to weigh and when to notify a health-care provider of a change in weight.

Follow-Up Care

Patients and their caregivers are at times the only common thread moving through the health-care system and often have to navigate their own way [25, 39]. An early assessment of patient's understanding of his condition and his needs in the home

setting needs to be started soon after admission. Identifying caregiver(s) early on can incorporate them into the care plan [5].

Telephone follow-up in high-risk patients might help improve self-care and symptom recognition and management [5]. Evaluation of newer strategies such as telemedicine might show improvement in quality of life measures as well as lead to earlier detection of nonadherence and clinical deterioration allowing for earlier intervention [8, 40].

The time immediately following discharge is a particularly vulnerable period, especially with changes to the previous medical therapy [24, 39]. Early follow-up after discharge is imperative, and ideally, it is scheduled prior to the patient being discharged [5]. Early follow-up results in lower readmission rates [24]. Most patients need an outpatient follow-up visit within 1 week of discharge [9, 24]. The goal for high-risk patients, those with two admissions in the past year, is to be seen in 48 h and those at moderate risk to be called within 48 h and have an office visit with within 5 days [2]. The bulk of the interventions are usually carried out by a single clinical leader such as a nurse or an advanced practice nurse (APN) [5]. Frequently the burden of the caseload can be daunting [5]. A collaborative approach using a multidisciplinary team might be better to carry out these interventions [5]. The utilization of both primary care providers (PCP) and cardiologists can be beneficial and may lead to improved adherence to evidence-based care [39]. The PCP may be able to see the patient earlier than the cardiologist and can provide care for noncardiac concerns [39]. Ultimately, members of a team with specific training in the management of heart failure will carry more weight in making a change [5]. A detailed handoff to outpatient providers should include information about hospital events, procedures, pertinent lab and imaging tests, medications and therapies implemented [4, 5], as well as information concerning the patient's functional status, learning needs, and care plan for follow-up care [2].

Regional barriers to care including transportation, access to meals, weather, economy, and the availability of affordable health care must be recognized and addressed [41]. Solutions such as better care coordination and improved communication between health-care team member and patients can be implemented. Each institution must assess the needs of their community and develop plans to ease the impact of these barriers for their patients.

How to Get It All Done

Discharge planning begins with the very first encounter between the patient and the health-care system regardless of the final disposition of the patient [42]. All members of the health-care team including physicians, nurses, pharmacists, social workers, as well as patients and their caregivers must be involved in assessing the needs of the patient and their ability to meet them [42, 43]. Goals include assessment related to factors that may have precipitated the admission, education related to disease, treatment, expected course of illness, medications, dietary restrictions, further testing requirements, communication with post-discharge care team including follow-up appointments, and identification and referral to community services that may be needed [44].

The stress-filled, noisy, fast-paced, hectic environment of most EDs may have a negative impact the patient and their caregiver's ability to absorb new information [42, 44, 45]. Simplified printed and/or computerized instructions improve the patients and/or caregiver's knowledge and adherence. These instructions should be further individualized by being disease specific and adapted for patients over the age of 60. Utilization of prepared discharge materials on medications, lifestyle modifications, and symptom assessment can facilitate comprehensive discharge instructions with less time [46]. Verbal reiteration of the printed materials and opportunities for the patient and/or caregiver to ask questions should take place often. Repetition and reinforcement of the information improve patient's understanding [8]. Using the teach-back method will assist in assessing the patients and/or the caregiver's understanding [42, 47]. Any areas of confusion should be readdressed until the patient and/or caregiver is able to demonstrate understanding [44]. Checklists can be used to simplify responsibilities and help the patient and family feel prepared to assume responsibility of their care after discharge [48].

The excellent observation skills of nurses in the emergency department coupled with their frequent interactions with the patient and their caregivers enhance the discharge planning process [46]. Discharge teaching is often left to the nursing staff only, but all members of the health-care team should look for and capture these teachable moments. Incorporation of the discharge planning process into the acute assessment tools, standardized order sets, checklist, and ongoing documentation will help all members of the busy health-care team remain engaged in the discharge process [46]. Frequent collaboration provides opportunities for the development of the discharge and post-discharge plan [43, 46, 49–51].

Care coordination utilizing ancillary staff such as case managers (CM) can unburden the clinical staff [3]. Case managers are often specially trained nurses or social workers who provide extra support for patients identified to be at increased risk and have been successful in improving outcomes [25, 44]. The CM can develop the individualized discharge plans, facilitate the transfer of information to the next care setting, schedule follow-up appointments, reinforce information to the patient and caregivers, as well as assist in meeting the needs of the home environment such as durable medical equipment and home care [3]. Patients treated in the ED have a myriad of psychosocial issues such as homelessness, abuse, lack of insurance, and substance abuse which often exceed the capabilities of the bedside nursing and medical staff [3]. Case managers can be extremely helpful in managing these complex situations.

Although there is little research on prescription assistance and/or transportation assistance alone and its impact on outcomes, if available they should be utilized. In theory these services would address some of the known barriers to self-care often experienced by patients with heart failure [44].

Conclusion

Discharge planning is a complex process that begins with the first encounter in the emergency department and continues throughout the entire stay. All members of the health-care team both in the ED and the post-admission care team as well as the patient and his or her caregivers need to be involved. The plan should address the needs of the patient from his or her perspective as well as that of the

health-care team. It must be practical, individualized, and aimed at improving outcomes. It should be provided in written and verbal form at a level that the patient and their caregivers can understand as well as be shared with all members of the health-care team ideally through an electronic health-care record. The preponderance of published data on discharge planning continues to be focused on discharge from an inpatient setting; however, data is beginning to emerge related to discharge from the ED. Patient needs are not dissimilar from either locus of care. However, the need for additional research remains if we are to identify which specific aspects of discharge planning and post-discharge care result in better outcomes.

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Outpatient Medication Titration in Acute Heart Failure

19

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Background

Characterizing Heart Failure

Managing heart failure requires addressing both the American College of Cardiology/American Heart Association (ACC/AHA) stages and the New York Heart Association (NYHA) class at each visit. The staging of heart failure is independent of the ejection fraction. Patients with clinical heart failure may have either preserved or reduced ejection fraction. Specific recommendations and considerations for the management of patients with heart failure and preserved ejection are discussed at the end of the chapter. As a review, the ACC/AHA Task Force described heart failure as occurring in the following stages: stage A, high risk for heart failure but without structural heart disease or symptoms of heart failure; stage B, structural heart disease but without signs or symptoms of heart failure; stage C, structural heart disease with prior or current symptoms of heart failure; and stage D, refractory heart failure requiring specialized interventions [1]. The stage A patient may have hypertension, atherosclerotic disease, diabetes, obesity, and metabolic syndrome, be taking cardiotoxic medications, or have a strong family history of cardiovascular disease. Examples of stage B patients include those with a previous myocardial infarction, left ventricular remodeling with left ventricular hypertrophy, a reduction in left ventricular ejection fraction (LVEF), or asymptomatic valvular disease. Stage C patients have known structural heart disease and shortness of

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breath, fatigue, or reduced exercise tolerance. Stage D patients usually have marked symptoms at rest despite maximal medical therapy and require recurrent hospitalizations. Assessment of clinical history and review of prior testing, echocardiograms, electrocardiograms, and heart catheterizations, help establish appropriate staging.

The NYHA functional class is based solely on subjective information from patients who have known cardiac disease. Class I patients have no limitation of ordinary physical activity. Class II suffer slight limitation with ordinary physical activity. Class III have marked limitation with ordinary physical activity, and once in class IV, patients are unable to do any physical activity without limitations. Unlike classes I–III, class IV patients may have symptoms of heart failure or anginal syndrome at rest and are worsened by physical activity [2]. NYHA functional class is used in the design of most heart failure trials. Subsequently, most guideline recommendations are based on NYHA class which makes its determination in individual patients key to successful management.

Managing Heart Failure in the Outpatient Setting

We now have multiple drugs (angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor blockers, beta-blockers, and aldosterone antagonists) which are cornerstone therapies that improve outcomes for patients with heart failure and reduced ejection fraction [3–15]. Unfortunately, similar advances have not been made for patients with heart failure and preserved ejection fraction. Careful dosing of digitalis has been demonstrated to reduce hospitalizations for heart failure [16]. On the contrary, while digitalis has no impact on mortality, patients who have been taking digoxin chronically may experience worsening symptoms after its discontinuation [17]. Secondary analyses have shown additional survival benefit in African-Americans from the use of hydralazine and nitrates, potentially related to genetically reduced renin–angiotensin system activity [1, 18]. Because these medications have many overlapping side effects, including the potential for hypokalemia and hypotension, it may be challenging to achieve evidence-based doses within a single hospitalization or outpatient visit. A stepwise approach to initiation of heart failure medication and titration to therapeutic doses is recommended and can be guided by considering both ACC/AHA class and NYHA functional class of the patient.

Stage A Management: ACE Inhibitor or Angiotensin Receptor Blocker

The benefit of ACE inhibitors and ARBs in patients with heart failure is greater in stage C and D patients. However, given the additional cardioprotection for patients with risk factors for heart disease, an ACE inhibitor or ARB is also recommended for stage A or B patients with these cardiovascular risk factors [7]. Multiple clinical

Table 19.1 Titration of ACE inhibitors and ARBs

Medication	Initial dosage	Titration	Target dosage
Angiotensin-converting enzyme inhibitor			
Lisinopril [3]	5 mg daily	Double every 4 weeks	20–40 mg daily
Enalapril [4, 19]	2.5–5 mg BID	Double every 1–2 weeks	10–20 mg BID
Ramipril [22]	1.25 mg daily	Double every 2 weeks	1.25–10 mg daily
Captopril [5, 6]	12.5 mg BID or TID	Double every 4 weeks	25 mg BID–50 mg TID
Quinapril [5]	10 mg daily	Double after 4 weeks	20 mg daily
Angiotensin receptor blocker			
Valsartan [8]	40 mg BID	Double every 2 weeks	160 mg BID
Candesartan [9]	4–8 mg daily	Double every 2 weeks	32 mg daily

trials have shown morbidity and mortality reduction with various ACE inhibitors, leaving the physician with many options [7]. Finesse is required to reach therapeutic levels of ACE inhibitors or ARBs without causing undue side effects. Adjustment of medications at intervals of 1–4 weeks has been successful in clinical trials and can be done in the clinic or over the phone if appropriate follow-up is obtained to monitor for symptomatic hypotension, hyperkalemia, and worsening creatinine clearance (Table 19.1) [19]. Cough is a common side effect of treatment with ACE inhibitors, occurring in up to 35 % of patients and more frequently in women, nonsmokers, and people of Chinese descent [20]. For patients who develop a cough on ACE inhibitor treatment, an ARB is a suitable replacement. Cough with an ARB occurs at similar frequency to placebo, 2–3 %. Angioedema is an absolute contraindication to use of both ACE inhibitors and ARBs. The direct renin inhibitors are still under evaluation for their effect on clinical endpoints, but they appear to promote reduction in left ventricular mass that is similar to ARBs [21].

In the case of persistent hypertension (systolic blood pressure ≥140 or diastolic blood pressure ≥90) after up-titrating ACE inhibitors or ARBs, additional antihypertensive medications should be considered to achieve reduction in blood pressure, with the exception of nonvasoselective calcium channel blockers which should be avoided [23]. In the setting of advancing heart failure class, care must be made to exchange medications that were used for blood pressure control with ones that reduce morbidity and mortality in this population.

Stage B Management: Angiotensin-Converting Enzyme Inhibitor or Angiotensin Receptor Blocker, Beta-Blocker, and Implantable Cardiac Defibrillator

The main goal of drug therapy in stage B patients is attenuation and/or reversal of adverse cardiac remodeling by aggressive inhibition of neurohormonal axes, specifically the sympathetic and renin–angiotensin and aldosterone systems. This is accomplished by initiation and titration of an ACE inhibitor or angiotensin

Table 19.2 Titration of beta-blockers

Medication	Initial dosage	Titration	Target dosage	Special considerations
Beta-blocker				
Carvedilol [10]	3.125 mg BID	Double every 2 weeks	25 mg BID	Increased vasodilation and BP control, improved insulin sensitivity
Metoprolol succinate [13]	12.5–25 mg daily	Double every 2 weeks	200 mg daily	Less bronchospasm, less hypotension, dosed once daily
Bisoprolol [11, 12]	1.25 mg daily	Increase by 1.25 mg weekly until the dose of 5 mg is reached. Then increase by 2.5 mg every 4 weeks	5–10 mg daily	

receptor blocker followed by one of the three different beta-blocker options, carvedilol, bisoprolol, or metoprolol succinate, all of which have demonstrated incremental survival benefit when added to an ACE inhibitor or ARB [10–13]. The target dose of ACE inhibitor or ARB that should be reached prior to addition of a beta-blocker is debatable. However, dose-dependent incremental survival benefit has been more clearly demonstrated with beta-blockers than with ACE inhibitors, the latter of which impact survival significantly even when used at minimal doses [24, 25] In light of this, a commonly recommended strategy is to start an ACE inhibitor or ARB at a low to moderate dose, after which the focus shifts to initiation and titration of a heart failure-specific beta-blocker to either target or maximum tolerated dose. Titration of these medications should generally be made at 2-week intervals, holding dose titration in the setting of symptomatic hypotension or bradycardia (heart rate <60 beats/min, untreated second- or third-degree atrioventricular block) [10]. During titration of beta-blockade, systolic blood pressures in the 90–100 mmHg range may occur and should not cause alarm in the absence of near syncope or syncope (see Table 19.2).

Informing patients that beta-blockers can cause initial fatigue, but that it should improve with continued use, may help with compliance. In addition, consideration of switching between agents, or administration at bedtime, may reduce symptoms of fatigue. Specific aspects of an individual patient may impact the choice of beta-blocker used (Table 19.2). Metoprolol succinate is more beta-1 selective than carvedilol, has less vasodilatory effects, and is dosed once daily and therefore may be preferred in patients prone to bronchospasm, those with marginal blood pressure, or those whose compliance is a concern. Carvedilol may be considered as the initial agent in patients with coexisting hypertension or diabetes, since it exhibits peripheral alpha-receptor blocking effects that cause vasodilation and has also been shown to improve insulin sensitivity compared to metoprolol [26]. Patients should be taught how to monitor their blood pressure and heart rate at home on a regular basis, recognize abnormal blood pressure and heart rate, and have direct telecommunication

of these data to their providers. Telecommunication systems with close provider follow-up have helped improve patient outcomes, quality of life, and compliance while reducing hospitalizations [27–29]. This becomes especially important as patients advance in heart failure stage.

Stage C Management: Angiotensin-Converting Enzyme Inhibitor or Angiotensin Receptor Blocker, Beta-Blocker, Aldosterone Antagonist, Hydralazine and Nitrates, Loop Diuretic, and Biventricular Implantable Cardiac Defibrillator

The stage C population is more precarious. Having close contact with the stage C patient to detect changes in NYHA class will assist in improving patient satisfaction with care and quality of life and reduce hospitalizations [27, 28]. Patients in this stage should be advised about the "rule of 2s": (1) consume no more than 2 g of sodium daily, (2) weigh daily in the morning and double the dose of diuretic for that day if there is a weight gain of >2 lbs in 1 day, and (3) call health provider to share new information. Finally, hyponatremic patients should also institute a daily 2-L fluid restriction [1, 29–31]. Robust trials are still lacking to provide evidence to support these recommendations for sodium and fluid restriction, but they are intuitively supported guidelines that may change over time with new data from pending trials [1, 32]. A visit with a nutritionist or provider who can spend time educating heart failure patients about food labels and what products are high in sodium will also be helpful. These patients should contact their provider for complaints of new or recurrent heart failure symptoms (dyspnea, lower extremity swelling, inability to sleep lying flat) and new or recurrent angina symptoms. Structuring a clinic system to address patient complaints urgently can improve results [33].

Clinic visits should be tailored toward reaching target doses of medications, starting with ACE inhibitors or ARBs and then beta-blockers and dosing as previously described. Baseline hypotension may create reluctance to initiate or titrate these agents, all of which have antihypertensive effects. It is important to remember, however, that as long as patients do not have *symptomatic* hypotension and blood pressure is not profoundly reduced (i.e., systolic blood pressure <90 mmHg), those with the lowest baseline blood pressure may in fact derive the greatest benefits from therapy [34]. For the patients with NYHA functional class II–IV heart failure despite maximum tolerated doses of ACE inhibitor or ARB and beta-blocker, an aldosterone antagonist should also be initiated. Limitations to the use of aldosterone antagonists should be carefully considered, including rises in serum creatinine or potassium levels. In general, aldosterone antagonists may be initiated after the patient is on a stable dose of an ACE inhibitor, which can also affect creatinine level and cause retention of potassium. During initiation of an aldosterone antagonist, monitoring for an increase in creatinine to >2.5 mg/dL or potassium to >5 meq/L is important [1].

African-American patients may also be treated with hydralazine and isosorbide dinitrate for its morbidity and mortality benefit [18]. In non-African-American patients with persistent heart failure symptoms who do not have symptomatic

Table 19.3 Titration of aldosterone antagonists, digitalis, and hydralazine/nitrates

Medication	Initial dosage	Titration	Target dosage
Aldosterone antagonist			
Spironolactone [14]	25 mg daily	Double after 8 weeks	25–50 mg daily
Eplerenone [15]	25 mg daily	Double after 4 weeks	50 mg daily
Digitalis			
Digoxin [16, 17]		Based on CrCl, age, sex, and weight	0.625–0.250 mg daily (usually 0.125 mg sufficient)
Hydralazine/nitrates			
Hydralazine [18]	37.5 mg TID	Double after 2 weeks[a]	75 mg TID
Isosorbide dinitrate [18]	20 mg TID	Double after 2 weeks[a]	40 mg TID

[a]Titration time is not explicit in reported trials

hypotension, hydralazine and isosorbide dinitrate may prevent hospitalizations [35]. Patients with contraindications to ACE inhibitor or ARB should also be considered to be hydralazine and isosorbide dinitrate candidates for additional symptom control [1]. Headache and gastrointestinal intolerance occasionally prevent titration and should be monitored for when assessing compliance [1].

As the number of medications and complexity of dosing intervals increase, medical adherence can decline. Medication reconciliation at each clinic visit is helpful to confirm what medications a patient is actually taking and to explore any side effects that may adversely affect compliance. Having the patient describe how they take each medication, providing pillboxes, and addressing concerns with clinic pharmacy visits and social service consultation can also improve care [1, 36, 37].

Digoxin can be considered for patients with persistent symptoms after appropriate titration of ACE inhibitor, beta-blocker, aldosterone inhibitor, hydralazine, and nitrates. There is no mortality benefit from the use of digoxin, but it has been demonstrated to reduce hospitalizations for heart failure [16]. For patients already taking digoxin, cessation of treatment has been associated with a worsening of heart failure symptoms and clinical parameters [17]. We favor a digoxin dose no higher than 0.125 mcg daily, given that equal benefits have been observed regardless of the measured serum drug level, yet toxicities are more common at higher doses [38]. It may be preferential to use digoxin for rate control if effective rate control is not achieved with beta-blockade, rather than adding an alternate rate control medication, like verapamil or diltiazem, which could potentially worsen heart function [1] (see Table 19.3). Similarly antiarrhythmics other than amiodarone or dofetilide should be avoided in this population, given their cardiodepressant and proarrhythmic effects [1].

Table 19.4 Loop diuretic correlation table

Diuretic	Bioavailability (%)	IV-to-oral conversion	Relative potency (mg)
Bumetanide	75	1:1	1
Furosemide	50	1:2	40
Torsemide	80	1:1	20

Adapted from Young and Mills [41]

Diuresis

Diuresis provides symptomatic care that is usually needed to assist patients in maintaining a euvolemic state. Appropriate titration of the previously discussed medications can sometimes reduce the need for diuretics. Generally, diuretics cannot be avoided in NYHA class III–IV patients and those advancing to stage D. Loop diuretics are most effective for diuresis but have not been demonstrated to have clinical outcome benefits in and of themselves [39, 40]. Initial dosing of the loop diuretic should be determined based upon creatinine clearance and response to a trial with the patient. For lack of efficacy at one dose, the dose can be doubled until urine output is satisfactory. Initiation of furosemide may be considered as first line unless the patient has significant bowel edema or ascites that might suggest better absorption with torsemide or bumetanide [40] (see Table 19.4). However, if a patient has substantial bowel edema, IV diuretic administration may become necessary.

A rise in serum creatinine can be expected while titrating diuretic therapy, but for a rise in serum creatinine of 40 % or more, diuresis should be stopped or decreased, if possible [42]. The patient should keep a record of daily morning weights to assist in regulating diuretic dosing. When the patient has signs of hypervolemia, including pulmonary edema, elevated jugular venous pressure, S3 gallop, lower extremity edema, or ascites, the provider can target diuresis toward achieving dry weight. For example, a patient who usually takes furosemide 40 mg daily could, if still urinating well on furosemide 40 mg, change regimen to furosemide 40 mg BID or TID. If they were not responding to furosemide 40 mg daily, then an increase to furosemide 80 mg daily or higher would be appropriate. While adjusting diuresis, follow-up should be obtained within a few days after each dosing change to assess for appropriateness of diuresis and electrolyte alterations. Often potassium supplementation is required if the patient is not on an aldosterone antagonist. Hypo- and hyperkalemia are associated with higher morbidity in this population. Therefore, an objective is to keep the potassium close to 4 meq/L [1]. Occasionally, additional diuretic assistance is required and can be achieved by adding the thiazide diuretic, metolazone. This should generally be reserved for inpatient use given abrupt fluctuations in circulatory response, electrolytes, and creatinine clearance that can result from the use of metolazone. Progressively worsening creatinine clearance is associated with long-term morbidity in heart failure patients. Avoidance of nephrotoxic medications should be paramount, especially NSAIDs that effectively reduce renal blood flow.

Routine chest radiography and B-type natriuretic peptide levels are not indicated in the management of congestive heart failure. Repeat structural evaluation with echocardiogram is only needed when major clinical changes have occurred that result in a change in ACC/AHA stages or NYHA functional class [1].

Implantable Cardiac Defibrillator and Biventricular Implantable Cardiac Defibrillator Therapy

There is mortality benefit from implantable cardioverter defibrillator (ICD) devices in patients with ACC/AHA stage C heart failure and persistent structural disease who are on appropriate medical therapy. It is important for the provider to monitor medication titration goals and advocate for ICD or resynchronization therapy when indicated. For primary prevention of sudden cardiac death, a mortality reduction has been demonstrated for ACC/AHA stage C patients who have persistent LVEF $\leq$35 % at least 40 days postmyocardial infarction, NYHA functional classes II–III, and predicted survival >1 year [1, 43, 44]. Secondary prevention ICD therapy should be provided in ACC/AHA stage C patients with a history of cardiac arrest, ventricular fibrillation, or hemodynamically unstable ventricular tachycardia [1, 45].

Resynchronization is indicated for ACC/AHA stage C patients with LVEF $\leq$35 %, atrial fibrillation, dyssynchrony as evidenced by QRS $\geq$120 ms, NYHA functional classes III–IV, and on optimal medical therapy. ACC/AHA stage C patients with LVEF $\leq$35 %, NYHA functional classes III–IV, on optimal medical therapy who are dependent on frequent ventricular pacing may also benefit from biventricular synchronized pacing [1, 46–48].

Stage D Management: Angiotensin-Converting Enzyme Inhibitor or Angiotensin Receptor Blocker, Beta-Blocker, Aldosterone Antagonist, Hydralazine and Nitrates, Loop Diuretic, Biventricular Pacemaker, Heart Transplant, and Hospice

Evaluation of ACC/AHA stage D patients is geared toward palliation, unless heart transplant is an option. Life expectancy at this stage is greatly reduced. ICD therapy no longer provides benefit, as death is usually impending [1]. Beta-blockers can cause more harm than benefit and may need to be discontinued in the presence of symptomatic bradycardia, symptomatic hypotension, worsening fatigue, worsening dyspnea, or other signs of decompensated heart failure. ACE inhibitors, aldosterone antagonists, hydralazine and nitrates, and digoxin may still be useful if hypotension and renal function are not limiting, and effective diuresis becomes a mainstay of providing comfort. Given the high mortality among stage D patients, readdressing patient goals of care becomes very important. Options may include hospice, palliation with or without ICD deactivation, chronic inotropes, mechanical support with

"bridge" or "destination therapy," and heart transplant. Referrals to end-stage heart failure specialists can assist the provider in communicating the best care options to the patient.

Failure of Outpatient Management

Many reasons for heart failure readmission can be addressed and prevented in the outpatient setting with a good care plan. Common reasons for readmission include noncompliance with medical regimen and/or sodium and fluid restrictions, acute myocardial infarction, uncorrected high blood pressure, atrial fibrillation and other arrhythmias, addition of negative inotropic medications, pulmonary embolus, NSAID use, excessive alcohol or illicit drug use, endocrine abnormalities (diabetes mellitus, hyperthyroidism, hypothyroidism), and concurrent infections [1]. As above, a good telecommunication system and contact with providers (nurses, nurse practitioners or physician's assistants, or physicians) can help to identify issues before outpatient management fails [27–29].

Management of Heart Failure with Preserved Ejection Fraction

Up to 50 % of patients today who suffer from a heart failure syndrome have normal or only mildly reduced left ventricular systolic function, thereby labeled with the diagnosis of heart failure with preserved ejection fraction (HFpEF) [49]. Despite the wealth of evidence demonstrating reduction cardiovascular morbidity and mortality with the aforementioned drug therapies in patients with heart failure and reduced ejection fraction (HFrEF), the same benefits have not been observed in HFpEF. Furthermore, the relative inability of these drugs to impact cardiovascular outcomes in HFpEF in the same way as HFrEF patients has led to consideration of different pathophysiologic mechanisms, including coronary microvascular dysfunction, as possible contributors to this poorly understood entity, in addition to neurohormonal overactivation [50]. It is extremely common, however, to use drug therapies in HFpEF similar to those used in HFrEF, mainly due to the high prevalence of coexisting comorbidities, particularly hypertension, coronary artery disease, atrial fibrillation, diabetes, and chronic renal insufficiency, which frequently create additional independent indications for their use. Consequently, most patients with HFpEF are managed with some combination of ACE inhibitor, ARB, beta-blocker, aldosterone antagonist, and diuretic therapy.

ACE inhibitors should be first-line considerations for HFpEF patients with hypertension, stable chronic renal insufficiency, or diabetes. While they have never been clearly shown to reduce risk of hospitalization or mortality in HFpEF, they can improve symptoms and measures of functional capacity, as well as attenuate or even reverse concentric remodeling that contributes significantly to the pathophysiology of these patients [51, 52]. ACE-intolerant patients due to cough can be offered alternative treatment with ARBs, although evidence for any clear reduction in mortality or hospitalization rate is equally lacking with ARBs as well [53, 54].

Beta-blockers are commonly prescribed for HFpEF patients who have a history of coronary disease, prior myocardial infarction, or atrial fibrillation. One of the principal hemodynamic features of HFpEF is a marked increase in left ventricular filling pressure with any degree of tachycardia [55]. This creates a strong physiologic rationale for beta-blocker use since any heart rate reduction consequently increases the diastolic filling interval. Moreover, beta-blocker use in HFpEF improves certain indices of diastolic function and is certainly useful for controlling heart rate in atrial fibrillation, but their use has never demonstrated clear mortality or hospitalization rate reduction in this patient population [56].

In one major clinical trial, aldosterone antagonism with spironolactone did show reduction in hospitalizations for HFpEF patients, although mortality was not changed [57]. In the absence of any other truly effective pharmacologic agents available to reduce cardiac morbidity and mortality in these patients, initiation of spironolactone is generally recommended. However, as in all other patients being initiated on aldosterone antagonists or potassium-sparing diuretics, close follow-up of serum creatinine and electrolyte levels, particularly potassium, is necessary to allow for long-term safe use of this drug.

Novel Drug Therapies in 2016: Ivabradine and Sacubitril/Valsartan

In the last 5 years, two additional pharmacologic agents have demonstrated benefit in the management of patients of chronic heart failure with reduced ejection fraction and received FDA approval for their use, although not yet incorporated into treatment guidelines.

Ivabradine

Ivabradine, sometimes called a "funny" channel blocker, is a novel medication in its own drug class that acts specifically on the I_f channel of cardiomyocytes, which are highly expressed in the sinoatrial node. It initially emerged as a medication for ischemic heart disease that appeared to reduce in coronary events in patients who had persistently elevated resting heart rates [58]. It has since been shown to reduce heart failure hospitalizations in patients with chronic heart failure and reduced ejection fraction with persistently elevated resting heart rates (>70 BPM) despite maximum tolerated doses of beta-blockers [59]. The pharmacological advantage of ivabradine over beta-blockers is its ability to provide selective sinus node inhibition without the negative inotropic effects that are likely the cause of the majority of beta-blocker intolerance. It lowers heart rate purely as negative chronotropic agent without a transient depressant effect on contractile function. The latter is an undesired early effect of beta-blockers that must be endured prior to the improvement that is eventually observed as a result of increased cardiomyocyte beta-adrenoreceptor density. While the definition of beta-blocker intolerance is subjective and likely varies among each provider, ivabradine can be used as an additional agent for targeting heart

rate, a powerful predictor of many clinical outcomes in chronic heart failure. Symptomatic bradycardia and hypotension can still be observed with this drug, albeit likely less so than with beta-blockers. Visual disturbances known as phosphenes are also a described, many times self-limited side effect.

Sacubitril/Valsartan

The combination drug sacubitril/valsartan, tested in the multicenter trial PARADIGM-HF as the study drug, LCZ696, represents perhaps the largest advance in chronic heart failure therapy in the last 10 years [60]. It is a combination drug composed of two agents, one of which is valsartan, an angiotensin receptor blocker with proven efficacy in heart failure, and the other is sacubitril, a neprilysin inhibitor. Neprilysin is an endogenous endopeptidase that cleaves the biologically active natriuretic and vasodilatory peptides that are felt to be physiologically beneficial in chronic heart failure syndrome. Prior studies investigated this enzyme as a target for therapeutic inhibition but were unsuccessful due to adverse effects or lack of efficacy. The combination drug sacubitril/valsartan was investigated in HFrEF patients in the multicenter, double-blind, randomized clinical trial PARADIGM-HF in a head-to-head comparison against one of the first-line ACE inhibitor agents, enalapril. Sacubitril/valsartan demonstrated significantly greater reductions than enalapril in multiple clinical outcomes, including all-cause mortality, heart failure-related mortality, and heart failure hospitalizations [60]. The demonstrated benefits were strong enough to lead to early study termination and have subsequently led to the question whether therapy with sacubitril/valsartan should replace the initiation of an ACE inhibitor as first-line treatment for all chronic heart failure patients. While the seemingly unequivocal results of this single trial suggest this is not an unreasonable approach, it is important to note, however, that in subgroup analysis the advantage of sacubitril/valsartan was not observed in patients who were ACE inhibitor naïve prior to enrolling in the trial. Therefore, due to cost, an incompletely explored risk of dementia, and limited real-world experience with this medication, ACE inhibitors are still recognized as first-line treatment agents for patients at all stages of heart failure with reduced ejection fraction.

Summary

Comprehensive outpatient management of heart failure care has a substantial influence on short- and long-term morbidity, mortality, and quality of life in heart failure patients. Understanding the results of major clinical trials of heart failure therapies and applying proven therapies at tested doses are of prime importance in successful outpatient management of heart failure. Key goals include:

- Determine ACC/AHA heart failure stage and NYHA functional class at each visit.
- Titrate medications to goal doses that were tested in clinical outcome trials with close monitoring for adverse effects.

- Address patient concerns early and provide means for easy communication in order to improve medical adherence.
- Teach patients the "rule of 2s."
- Stage A patients should take an ACE inhibitor or ARB.
- Stage B patients should take an ACE inhibitor or ARB and a beta-blocker that has been shown to be efficacious in clinical outcomes trials.
- Stage C patents should take an ACE inhibitor or ARB, beta-blocker, and aldosterone antagonist. Hydralazine and nitrates should be added for African-Americans and used in patients who cannot tolerate ACE inhibitor or ARB. Consider adding digoxin. Determine diuretic dose needed. Consider indications for ICD and/or CRT-ICD therapy.
- Stage D patients should take an ACE inhibitor or ARB, aldosterone antagonist, hydralazine and nitrates, and possibly digoxin. Consider discontinuation of beta-blocker if decompensated heart failure occurs. Refer to an appropriate specialist for assistance with end-stage heart failure goals of care.
- Major roles of newer agents, including ivabradine and sacubitril/valsartan, are rapidly being defined in the management of chronic heart failure and prove this is a field ongoing constant evolution.

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Part V

Complications and Future Research

Drugs to Avoid in Acute Decompensated Heart Failure (ADHF): Contraindicated Medications and Interactions

20

Lindsey Aurora and James McCord

Vasodilators

Following diuretics, vasodilators are the most commonly used intravenous (IV) therapy for acute decompensated heart failure (ADHF), but strong evidence is lacking for the use of nitrates, nitroprusside, and nesiritide on clinical outcomes and therefore these drugs are most commonly used for symptomatic improvement [1]. The long-term use of angiotensin converting enzyme (ACE) inhibitors is associated with improved symptoms and lower mortality in patients with systolic heart failure. However, the benefits of early IV ACE inhibitors in ADHF have not been established and may actually be harmful. In the CONSENSUS 2 trial, early IV enalapril was studied in patients with acute myocardial infarction (AMI). In patients with AMI and ADHF, IV enalapril was associated with decreased survival 180 days after AMI [2]. The American College of Emergency Physicians supports the early use of IV ACE inhibitors [3], while the European Society of Cardiology does not [4]. Until studied further, IV ACE inhibitors should be avoided in the setting of ADHF.

The Heart Failure Society of America recommends the use of IV vasodilators as part of treatment for ADHF. Research has shown that only 18 % patients receive these medications and less than 1 % receive sodium nitroprusside [5]. Nitroprusside is considered an *older* agent which acts as an arterial and venous vasodilator, reduces systemic vascular resistance and left ventricular filling pressures, and increases cardiac output. Despite increasing studies evaluating beneficial effects of vasodilators in ADHF, there has been limited data on nitroprusside and long-term effects in ADHF. This agent has been associated with worse outcomes in patients with AMI

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and ADHF [6]. In a study of 812 men with presumed AMI, there was no difference in mortality rates between nitroprusside and placebo group. However, the efficacy of nitroprusside was related to the time of treatment such that the drug led to increased mortality with early administration from the onset of pain related to AMI (mortality at 13 weeks, 24.2 % vs. 12.7 %; $p = 0.025$) and decreased mortality with later treatment. Administration requires close hemodynamic monitoring due to the risk of hypotension, especially with a depressed cardiac output and unstable blood pressure [5]. Therefore, this drug should likely be avoided unless the clinical picture is one of hypertensive crisis, and prompt blood pressure control is clinically indicated.

Nesiritide was approved by the FDA in 2001, but retrospective data raised the issue of worsening renal function and increased mortality which led to a dramatic decrease in the use of this medication [7, 8]. The ASCEND-HF (Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure) trial was a randomized trial that studied 7,141 patients with ADHF. ASCEND-HF demonstrated that nesiritide improved heart failure symptoms but showed that older patients (>55 years) experienced a higher mortality rate [9]. Natriuretic peptides (NPs) cause vasodilation and decrease in renal perfusion pressures which can result in systemic hypotension and worsening of renal function [10]. This is important to keep in mind as studies have shown that glomerular filtration rate is the strongest predictor of mortality in ADHF. The Acute Decompensated Heart Failure National (ADHERE) registry showed that 63 % of patients with heart failure with renal dysfunction (GFR <60 mL/min) was strongly correlated with in-hospital mortality [11].

In 2015, the US Food and Drug Administration approved the use of sacubitril/valsartan (Entresto) for treatment of chronic and stable but symptomatic heart failure. Mechanism of blocking renin-angiotensin-aldosterone system along with inhibition of neprilysin, an enzyme that degrades natriuretic peptides, is one of the current leading strategies for symptomatic heart failure and for left ventricular ejection fraction less than 40 %. However, it is contraindicated in patients with a history of ACE inhibitor- or ARB-induced angioedema [10]. Entresto has not been specifically studied in ADHF in the emergency department and at this point should be avoided in this setting until further research.

Calcium Channel Blockers

Calcium channel blockers have negative inotropic properties and therefore should be avoided in ADHF as they have been associated with worse outcomes. In one study, post AMI patients with an ejection fraction <40 % who received diltiazem were more likely to develop clinical heart failure as compared to placebo [12]. Verapamil use has been associated with hemodynamic deterioration due to its negative inotropic effects and concern for worsening heart failure [13]. In addition, the dihydropyridines, such as nifedipine, have also been associated with clinical deterioration in patients with systolic heart failure [14].

Conversely, patients with diastolic heart failure in the setting of hypertension may benefit from diltiazem or verapamil by controlling blood pressure and slowing heart

rate, which can improve diastolic filling in this group of patients. Diltiazem can also be considered in patients with ADHF and atrial fibrillation with rapid ventricular response when there is not an adequate clinical response to digoxin or amiodarone.

New potential therapies include IV clevidipine, a short-acting dihydropyridine L-type calcium channel blocker that is arterial selective and has no effect on myocardial contractility or central venous pressure, making it a favorable therapy for patients with ADHF with elevated blood pressure [1]. However, safety profile needs to be elucidated because of reports of reflex tachycardia and resulting atrial fibrillation and further study is warranted [1].

Beta-Blockers

Beta-blockers have generally been avoided in patients with ADHF. Concern due to the negative inotropic effects and hemodynamic compromise leads physicians to stop beta-blockers even though evidence is lacking [15]. Furthermore, in clinical trials of beta-blockers for AMI, patients with significant heart failure have been excluded.

Many patients presenting with ADHF are on a regimen including beta-blockers and in most cases the drug can be continued. In a systematic review and meta-analysis evaluating effects of beta-blocker withdrawal in ADHF, discontinuation of beta-blockers was associated with increased mortality and rehospitalization [15]. Looking at the effects of beta-blocker withdrawal in patients being treated with inotropes, the improved outcomes are hypothesized to be secondary to the antiarrhythmic effects of beta-blockers as inotropes are pro-arrhythmic. Moreover, the IMPACT-HF study reported the rate of beta-blocker use at 60 days after discharge when initiated before discharge was 91 % compared to 73 % when initiated post-discharge. Therefore, this data suggests that discontinuation of beta-blockers during hospitalization results in decrease use after discharge, leading to poor long-term outcomes.

It is important to keep in mind that in patients presenting with hypotension or end-organ hypoperfusion where inotropic therapy is being considered, beta-blocker therapy may need to be discontinued. However, there is overwhelming data to support the long-term benefits of beta-blockers in patients with systolic heart failure. After patients have been compensated, an attempt should be made to reinstitute the beta-blocker. Short-acting beta-blocker therapy, such as esmolol, can be considered but should be used with caution in ADHF when uncontrolled cardiac ischemia is present or for control of tachyarrhythmia as necessary.

Antiarrhythmics

Class I antiarrhythmic drugs in the Vaughn-Williams classification system produce a greater negative inotropic and more frequent pro-arrhythmic effects in patients with systolic heart failure and thus should not be used in such patients [16]. The most common side effects seen in heart failure patients with this class are ventricular arrhythmias and sudden death [17]. The Cardiac Arrhythmia Suppression Trial

(CAST) demonstrated that the Class Ic agents (flecainide and moricizine) were associated with pro-arrhythmia and increased mortality in patients that suffered an AMI and had decreased systolic function [18, 19]. Another Class Ic agent, propafenone, should also be avoided because of a significant increase in mortality during heart failure episodes [17]. Class Ia drugs (procainamide, quinidine, disopyramide) have also been associated with increased mortality in patients with decreased left ventricular systolic function [17]. Class III antiarrhythmics include sotalol which is known to be a racemic mixture of D- and L-isomers, acquiring different effects on potassium channels and β-receptors. The Survival with Oral D-Sotalol (SWORD) trial revealed that the *d*-isomer of sotalol (pure potassium channel blocker) was associated with a higher relative risk of mortality in patients with an ejection fraction of 40 % or less. Even though there no studies directly evaluating ibutilide in ADHF, pro-arrhythmic effects are a concern in patients with ADHF [17]. Nonetheless, amiodarone has proven to be safe in patients with systolic heart failure and is recommended in heart failure accompanied by atrial fibrillation when clinically indicated [20].

Glycosides

Despite being one of the oldest cardiovascular agents, digoxin's mechanism of action and utility in medicine has been controversial due to concerns regarding clinical efficacy and safety profile [21]. Digitalis can be used as a rate control drug in atrial fibrillation and leads to improved symptoms in chronic systolic heart failure. Favorable hemodynamic effects include increase in ejection fraction and cardiac index along with reduction in the pulmonary capillary wedge pressure. The Digitalis Investigation Group study was a randomized, double-blind placebo controlled trial that included 6,800 chronic heart failure patients with NYHA classes II–III, EF ≤45 % which showed decreased mortality due to worsening heart failure with digoxin but concurrent increase in mortality due to other cardiac causes such as arrhythmias [21].

Caution is warranted in the setting of ADHF as it has been associated with adverse effects in AMI accompanied by heart failure [22]. In another study in patients with AMI and ADHF, the use of digoxin was a predictor of life-threatening pro-arrhythmic events [23]. However, utility of this agent may be considered in ADHF associated with atrial fibrillation with rapid ventricular response [24]. Patients who derive less benefit from digoxin therapy include female gender, those with hypertension, or a relatively preserved ejection fraction [21]. Cardiac glycosides still play an important role in patients with severe heart failure who cannot tolerate other disease-modifying agents.

Inotropes

Inotropes should be avoided in ADHF and only considered when there is significant systemic hypotension or end-organ hypoperfusion. In clinical trials such as OPTIME-CHF (Outcomes of a Prospective Trial of Intravenous Milrinone, a phosphodiesterase

inhibitor, for Exacerbation of Chronic Heart Failure) which randomized patients with ADHF to 48 h of milrinone infusion, use of inotropes was associated with more adverse events including high incidence of atrial fibrillation or flutter and hypotension [25]. Inotropes increase oxygen demand and may worsen arrhythmias or myocardial ischemia [26, 27]. Another randomized trial studying the short-term use of milrinone across 78 community and tertiary care hospitals in the United States did not improve signs or symptoms of ADHF, and thus there is no support for the routine use of IV milrinone as an adjunct to standard therapy in the treatment of ADHF [28]. Other trials have also demonstrated that the beta-agonist dobutamine is associated with adverse cardiac events when used in ADHF [29, 30]. Milrinone and dobutamine have similar hemodynamic effects including increase in cardiac output and decrease in cardiac filling pressures. Milrinone lowers filling pressures to a greater degree and leads to a greater decrease in systemic vascular resistance compared with dobutamine that greatly increases myocardial oxygen demand comparatively [25].

When either atrial or ventricular arrhythmias are of clinical concern, milrinone is preferred over dobutamine which more commonly worsens tachyarrhythmias [31, 32]. Since the site of action of milrinone is distal to the beta-adrenergic receptors, milrinone is preferred over dobutamine during concomitant beta-blocker therapy [33–35]. However, there is particular concern over safety of milrinone in the setting of ischemic heart failure and should be avoided in this situation [28, 36, 37].

Miscellaneous

There are numerous medications that can exacerbate heart failure and should be avoided or discontinued if clinically possible. Nonsteroidal anti-inflammatory drugs (NSAIDs) act by inhibiting prostaglandin synthesis by blocking cyclooxygenase II (COX-2). Lower renal prostaglandin levels may reduce glomerular filtration rate leading to sodium and water retention [38]. In addition, NSAIDs also inhibit cyclooxygenase I (COX-1) which results in decreased levels of thromboxanes. Increase in cardiovascular risk with use of NSAIDs is speculated to be due to variation in inhibition of these pathways as agents in this class acquire different affinities for the inhibition of COX-1 and COX-2 [39]. The cyclooxygenase II inhibitors, which block cyclooxygenase II, can also lead to fluid retention and do not appear to offer any advantage over standard NSAIDS. In fact, a more cardiotoxic effect is seen with COX-2 inhibition. Similarly, corticosteroids lead to fluid retention and elevated blood pressure secondary to mineralocorticoid-associated plasma volume expansion [17, 40].

Other drugs that should be avoided in patients with a history of heart failure include the thiazolidinediones (rosiglitazone and pioglitazone) which are used to treat type II diabetes. These agents may increase intravascular volume by 7 % and may lead to ADHF [41, 42]. Clinical trials have shown that administration of a thiazolidinedione, as monotherapy or in combination with a sulfonylurea or metformin, was associated with increased frequency of edema. In addition, combination with insulin further increased the frequency of edema to 13–16 % compared to 5–7 % with insulin alone [43].

Another agent, cilostazol, inhibits type 3 phosphodiesterase and is used for the treatment of intermittent claudication. The use of cilostazol is contraindicated in patients with ADHF as the drug may lead to increased heart rate and ventricular tachycardia [44]. Similarly, anagrelide is a phosphodiesterase 4 inhibitor which increases cyclic adenosine monophosphate (cAMP) levels resulting in increased calcium in the myocardium, producing positive inotropy and vasodilation. This may lead to potential worsening of left ventricular dysfunction and increased risk of supraventricular arrhythmias [17].

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Implications of Atrial Fibrillation in Heart Failure Management

21

Chad E. Darling and David D. McManus

Background

In part owing to the strong relationship between atrial fibrillation (AF) and heart failure (HF) with advancing age, both conditions commonly coexist with other chronic and acute medical conditions, such as chronic kidney disease or hyperthyroidism. The number of individuals who present to the emergency department (ED) with clinical symptoms based on AF and HF is likely to remain high as demographics of the population of the United States (USA) trend to an older age [1]. Both AF and HF can play a causative role in the development of each other. The fast, irregular heart rates often seen with AF may lead to the development of acute HF or, in patients with a history of HF, may result in clinical instability. In this chapter, we will focus on patients that present with both HF and AF with regard to epidemiology, ED evaluation, treatment, and implications for potential short-stay management.

Epidemiology

There are over 5.5 million people with HF [2] in the USA. Moreover, acute HF episodes are the leading cause of hospital admissions in the elderly [3], and over three quarters of all these admissions are initially cared for in the ED [4]. AF is also

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highly prevalent with over 2.2 million cases in the USA [5]. The incidence of AF has steadily increased in the past decade as the average age of the population has increased [6], and it often coexists with HF [7, 8]. Data from the Framingham Heart Study have found the cumulative incidence of AF in patients with HF approximates 25 % [8]. Unpublished data from the ongoing Worcester Heart Failure Study [7] have demonstrated that roughly a third of 4,536 patients hospitalized with acute HF had a medical history of AF and 25 % had electrocardiograms documenting AF on admission. It is generally felt that the combination of AF and HF portends a worse prognosis than having either disease alone although there is conflicting evidence in the literature. For instance, many studies have suggested that the survival of HF patients is decreased in patients with concomitant AF [8–11], while other studies have found no difference in the survival of HF patients with or without AF [12, 13]. There is significant heterogeneity in these studies which may, in part, explain these results. What is clear is that over time a range of clinical complications can develop in these patients (Table 20.1).

Etiologies

There are several conditions associated with both AF [14] and HF [15] such as essential hypertension, diabetes mellitus, coronary heart disease, valvular heart disease, dilated and hypertrophic cardiomyopathies, and bronchopulmonary disease. Most importantly, both AF and HF are risk factors for the development of each other (Table 20.2).

Table 20.1 Potential complications of AF and HF

Acute
Thromboembolic events, including stroke
Myocardial infarction Cardiogenic shock Acute renal failure Ventricular tachycardia/fibrillation Syncope
Subacute
Cognitive dysfunction
Diminished quality of life
Chronic renal failure
Peripheral edema Tachycardia-mediated cardiomyopathy
Chronic
Stasis ulcers
Shortened life span Diminished exercise capacity Depression Anxiety

Table 20.2 Common and overlapping conditions associated with AF and HF

Toxins (alcohol, cocaine) Anemia
Coronary heart disease Chronic kidney disease
Valvular heart disease
Cardiomyopathies (dilated, hypertrophic, tachycardia mediated)
Pericardial disease Constrictive/restrictive myocardial processes Diabetes mellitus
Essential hypertension
Bronchopulmonary disease
Thyroid abnormalities
Obesity
Stress/elevated catecholamines
Metabolic disturbances
Cardiac and non-cardiac surgeries Congenital heart disease Sleep apnea Smoking Sepsis/systemic infection

Patient Evaluation

History and Presentation

The presenting symptoms for AF and HF are relatively similar and nonspecific. Typical symptoms of AF include chest pain, light-headedness, fatigue, palpitations, nausea, and dyspnea [16]. The most common symptoms and signs of HF include dyspnea, peripheral edema, cough, orthopnea, chest pain, weakness, nausea/vomiting, and fatigue [17]. The characteristic electrocardiogram (ECG) findings of AF, along with an irregular pulse, are likely to be recognized early on in patients presenting with AF and HF. Once AF is recognized and assuming the patient is not unstable, there are several useful pieces of historical information to obtain. First, it is helpful to ascertain the history of the patient's current symptoms with a focus on whether or not the AF is a long-standing condition or new in the onset (e.g., <48 h), and whether or not the onset can be accurately identified. In patients with prior episodes of AF, a quick investigation of past ED treatment approaches may also be useful. If HF is suspected clinically, then it is important to gather information regarding prior episodes, potential precipitating factors such as diet, medication omissions/errors, and echocardiogram results (e.g., does the patient have primarily systolic or diastolic dysfunction). Lastly, other comorbidities and current medications the patient is taking, including anticoagulant, antiplatelet, and other cardiovascular (e.g., beta-blockers, digoxin, calcium channel blockers) medications, will help inform subsequent decision-making.

Table 20.3 Types of AF

AF type	Definition
Asymptomatic	AF without symptoms or patient awareness
Paroxysmal	A self-limited AF episode lasting <7 days
Persistent	AF continuing >7 days
Permanent	AF lasting >1 year or with cardioversion that has failed or not been tried
Perioperative	AF developing within 48 h after cardiac surgery
Lone	AF not caused by underlying heart disease
Recurrent	Having a history of two or more independent episodes of AF

With or without concomitant HF, AF presentations have been categorized in numerous ways such as *asymptomatic*, *paroxysmal*, *persistent*, *permanent, perioperative, lone, and recurrent* (Table 20.3) [14]. All of these categories refer to the timing of onset and/or duration of AF. For patients not requiring urgent cardioversion due to instability, the duration of AF is the most important factor in determining whether chemical or electrical cardioversion can be safely attempted in the ED.

Exam

For any patient with AF and HF, acquiring vital signs on presentation, setting up critical care monitoring, obtaining IV access, and performing a rapid exam are central to the initial assessment. The focus for patients with AF and HF needs to first be directed at determining if there are signs of instability such as hypotension, respiratory failure, ischemic chest pain, severe HF, or altered mental status. If these, or other signs of instability, are present and the patient is experiencing a rapid heart rate due to AF, then urgent synchronized cardioversion based on advanced cardiac life support [18] (see below) is indicated. At the same time, if HF is felt to be playing a significant role in the patient's presentation, then respiratory and pharmacologic therapies directed at the HF should be started. If the patient is stable, a thorough exam focusing on mental acuity, neurologic status, heart and lung auscultation, the abdomen, peripheral perfusion, and edema should be undertaken. Paying particular attention to the heart exam may uncover significant valvular disease, which may be contributing to the present symptoms.

Diagnostic Testing

For many patients who meet the clinical criteria for AF and HF, more than one underlying disorder may be contributing to the patients presenting symptoms. Thorough appreciation of all the underlying causes for the patient's signs and symptoms requires a careful diagnostic workup to achieve the best possible outcomes. In

general, the diagnostic testing in patients with AF and HF does not differ significantly from that of patients with HF alone. All patients should receive an electrocardiogram (ECG), cardiopulmonary monitoring, and a chest X-ray on arrival. On the ECG, you would look for the abnormalities such as the characteristic findings of AF, evidence of ischemia, and signs of preexcitation. Laboratory tests may vary with suspicion of certain etiologies for AF and HF but often will include basic hematology tests, serum markers of myocardial injury, a natriuretic peptide, electrolytes, and kidney function. Thyroid function tests, which may often be considered, have been found to be abnormal in many patients with AF but are only rarely (<1 % in a large registry [16]) felt to be the cause of the AF itself. In patients where there are concerns based on history, exam, or ECG for ongoing myocardial ischemia, valvular disease, or pericardial effusion, it may be useful to obtain an urgent echocardiogram in the ED.

Treatment of Symptomatic Patients with Atrial Fibrillation and Heart Failure

Hemodynamically Unstable Patient

The hemodynamically unstable patient with AF and HF needs urgent cardioversion if the instability is felt to be due to AF-mediated tachycardia. Significant acute HF may be a sign of instability in the AF patient regardless of whether the AF caused the HF or vice versa. In either case, converting the AF to sinus rhythm, even transiently, may normalize vital signs and facilitate treatment of the HF.

The preparation for emergent cardioversion includes administering analgesics and sedatives when possible. However, if the patient is suffering a severe decompensation, this step may have to be omitted. In addition for patients whose AF has lasted ≥48 h, intravenous heparin should be administered at the time of cardioversion and continued after the procedure as a bridge to 4 weeks of total anticoagulation [14]. The placement of the defibrillator pads is somewhat controversial but the anterior–posterior position is likely to be the most efficacious in the majority of AF patients [19]. The amount of energy required to convert the patient to sinus rhythm from AF is generally higher than that for atrial flutter [14] and also varies depending on whether the defibrillator is monophasic or biphasic. For monophasic, 200 J is a reasonable starting point, whereas for biphasic, 100 J is likely to be effective [14, 20, 21]. For patients with implanted pacemakers, cardioversion can proceed as usual, but care should be taken to avoid placing the defibrillator pad over the generator [14]. Although therapy with antiarrhythmic agents prior to cardioversion has been shown to increase efficacy of elective cardioversion [22], in the unstable patient, this is generally not an option.

In the setting of concomitant decompensated HF, the rate of recurrence of AF after successful cardioversion is likely to be high [23], so therapies aimed at improving HF should be started immediately once the patient is more stable. The use of antiarrhythmic agents, such as amiodarone, after cardioversion may help to prevent

early recurrence, but in the acute setting, the decision to use these agents should be made on a patient-by-patient basis [14] in conjunction with a consultant.

After cardioversion, in addition to treating underlying HF, it is important to obtain another ECG to evaluate for the presence of an acute coronary syndrome (ACS). Furthermore, this reevaluation should maintain a broad differential diagnosis so as not to miss other contributing conditions such as adverse medication reactions, alcohol or drug toxicity (e.g., digoxin), electrolyte disturbances, valvular heart disease, pulmonary emboli, and sepsis/septic shock.

Hemodynamically Stable Patient with Atrial Fibrillation and Heart Failure

Although HF in the setting of AF can be considered a sign of instability, many cases will be of milder severity and not require urgent cardioversion. These patients may fall into various categories such as rapid AF with mild HF, HF with only a history of AF, or HF and AF without tachycardia. In cases where urgent cardioversion is not needed, strategies to control rate, initiate anticoagulation if indicated, potentially convert the rhythm (electrical or chemical), and treat the underlying HF, will all need to be considered and instituted where appropriate.

Rate Control

Due to the risk of thromboembolism, initial heart rate (HR) control, rather than acute rhythm conversion, is likely to be the preferred treatment in the majority of cases. There are several rate-control agents that may be considered and include digoxin, calcium channel blockers, beta-blockers, and amiodarone. In cases where the onset of the AF episode is not clearly within 48 h, then anticoagulation should be initiated early on unless there is a specific contraindication. A reasonable target for rate control is ≤120 beats/min over the first few hours of treatment [24].

Digoxin

When considering rate control for patients with rapid AF and HF, digoxin may be particularly useful agent as it already has an established role in treating HF [25]. In the AF and HF patient, it may be considered a first-line agent [14, 24] and may be most efficacious when used in conjunction with typical AF rate-control agents, such as beta-blockers and diltiazem [14, 26]. The mechanism by which digoxin slows the HR in AF appears to be due to its effect on increasing vagal activity on the AV node [27–29]. In patients who are not on digoxin, it is administered acutely in a series of loading doses over several hours to approximately 1–1.5 g total dose, depending on clinical response [14, 30].

Several trials have examined digoxin use acutely for rapid AF. In the Digitalis in Acute Atrial Fibrillation (DAAF) trial, 239 patients with rapid AF were randomized to receive either digoxin or placebo and then followed over 16 h to determine the effect on HR and conversion to sinus rhythm [31]. In this trial, digoxin was not found to facilitate conversion to sinus rhythm but had a significant effect on rate at 2 h compared to placebo (mean HR 105 vs. 117 bpm). A smaller randomized trial of digoxin versus placebo for rate control found that digoxin's ability to slow HR was not evident until over 5 h after the first dose was given [29]. Hou et al. compared the ability of digoxin versus amiodarone to slow HR in patients with AF (approximately half of which had NYHA class IV HF) and found that after 1 h, digoxin slowed HRs approximately 10–15 beats/min compared to 30 for amiodarone. There are a number of conditions that either warrant caution or represent contraindications to the use of digoxin. First, AV nodal blocking agents such as digoxin care contraindicated in situations where a preexcitation syndrome such as Wolff–Parkinson–White is known or suspected. Other situations where digoxin should be used cautiously are with renal impairment, with electrolyte disturbances, and with the risk of toxicity when loading patients already on digoxin [30]. Lastly, digoxin may not work as well in the setting of high sympathetic tone [24, 28].

Calcium Channel Blockers

The calcium channel blockers diltiazem and verapamil have both been studied as agents for rate control in rapid AF. Both agents act within 5–10 min to decrease heart rate [28, 32]. In patients with AF and HF (particularly with a low EF), diltiazem is a better choice than verapamil as it has less of a negative inotropic effect and is less likely to lead to worsening HF and hypotension [15, 27, 28, 33]. Goldenberg et al. examined the effectiveness of diltiazem versus placebo to reduce heart rate in the patient with NYHA grade III or IV HF. In this study, 36/37 patients responded to the diltiazem with reduced rates within a median of 15 min compared to 0/15 placebo patients. Furthermore, there were only three adverse events (hypotension) suggesting that in many patients diltiazem may be safe [34]. Theoretically, the negative inotropic effects of calcium channel antagonists may be offset when these agents are used in combination with digoxin [27], but in patients with acute AF and HF, this has not been established. When compared to digoxin, diltiazem is significantly more efficacious in controlling heart rate over the first few hours of acute treatment [35, 36].

Beta-Blockers

Beta-blockers have a well-established role in the treatment of chronic HF [37]. However, in the presence of acute HF and AF, beta-blockers should be used carefully, if at all, with small incremental dosing [24] and close monitoring of the

patient's vital signs. Demerican et al. compared intravenous metoprolol and diltiazem with regard to slowing HR in patients with rapid AF and found that at 20 min, 80 % of the metoprolol patients had significant HR control versus 90 % in the diltiazem group (defined as either HR<100 or a 20 % decrease from the baseline). Furthermore, at all time points, diltiazem resulted in more HR slowing than metoprolol. However, in this trial, patients with class IV HF were excluded, and it is unclear how much HF was present overall. Where there is concern regarding the negative inotropic effects of beta-blockers in patients with HF, the ultrashort-acting beta-blocker esmolol may be a good choice [38]. Esmolol has a 9-min half-life, and therefore, if it needs to be stopped due to worsening HF or hypotension, its effects will rapidly diminish. It has been used in the setting of rapid AF after coronary artery bypass, where some degree of myocardial dysfunction is likely to be present and appears to be more effective than diltiazem and as safe [39, 40]. Esmolol has also been shown to be safe and effective when used in conjunction with digoxin for rapid AF [26].

Amiodarone

Amiodarone may also be considered for rate control in the AF and HF patient unless they are on other antiarrhythmics that should not be combined with amiodarone [24, 41, 42]. The 2006 AHA/ACC guidelines recommend that amiodarone or digoxin be used to acutely control rate in patients with AF and HF (class I recommendation) [14]. However, as it may facilitate conversion to sinus rhythm, it would ideally be used in cases where the patient either meets anticoagulation guidelines for cardioversion or will be given anticoagulants [24]. Amiodarone is also a common choice of agent to be used to maintain sinus rhythm in the AF and HF patient after cardioversion [14]. Dronedarone is a newer antiarrhythmic drug similar in structure to amiodarone. It has been studied in a number of trials looking at its ability to affect rhythm control for AF over the long term [43–45]. It currently has no role for acute rate or rhythm control. In addition, one clinical trial found excess cardiovascular mortality in a dronedarone-treated group of AF patients with poor left ventricular function (EF ≤35 %) [44].

Summary

In summary, HR control for patients with AF and HF can be approached with the usual medications used in patients without HF provided vital signs are monitored closely [14]. The use of digoxin with other rate-control agents may be beneficial, and amiodarone also has a heightened role in these patients [14]. Diltiazem rather than verapamil would be the best choice if calcium channel blockers are used, and incremental beta-blocker dosing or the use of esmolol may help avoid complications with these agents.

Rhythm Control/Conversion

A recent editorial examining rate versus rhythm-control strategies for AF in the ED [46] concluded that there was not enough evidence to support a rhythm-control strategy as opposed to the standard HR control for new-onset AF in the ED. However, Stiell and others have published on the safety and efficacy of acute cardioversion in the ED for patients with rapid AF, but these studies have excluded patients with more significant HF [47, 48]. Their results suggest that cardioversion of AF alone appears to be safe, and it is likely that at least a small percentage of the patients that have undergone cardioversion have had some degree of HF. It is worth noting, however, that in these studies, an antiarrhythmic agent such as procainamide is often given as a first attempt at cardioversion, which may not be feasible in patients with concomitant acute HF or low blood pressure [49]. This "preloading" with an antiarrhythmic may also be influencing their high success rates of electrical cardioversion.

Vernakalant is an investigational, relatively atrial selective, antiarrhythmic agent (approved in Europe but not by the FDA) that appears to be successful in converting AF to sinus rhythm. However, one published ED-based study had only a small minority (≤5 %) of patients with HF [50]. It is worth noting that if pharmacologic agents are given, the risk of thromboembolism and stroke appears to be the same as in patients who receive electrical cardioversion [14].

The main concern with acute rhythm conversion is the risk of thromboembolism, which appears to be the same in patients who receive electrical or chemical cardioversion [14]. However, in carefully selected AF patients (e.g., acute onset <48 h of AF), the risk is very low. 357 patients in one study who were admitted with AF ≤48 h who underwent electrical, chemical, or spontaneous cardioversion were found to have a risk of thromboembolism of less than 1 % [51]. This study did not include any patients with reduced EF where the risk of complications may be higher. As one potential treatment option, it seems reasonable to consider acute rhythm conversion in AF patients who have either a history of HF or milder acute HF. This decision will need to be made on a case-by-case basis taking into account each patient's presentation, history, anticoagulation status, and personal preferences.

Disposition Decisions

Disposition of the AF and HF patient may include any of the following: hospital admission, short-stay unit (SSU) admission, or discharge to home, rehabilitation hospital, or other extended care facilities including hospice. Despite the fact that acute coronary syndromes rarely present as AF alone [52], most patients with AF and HF are likely to require an admission to the hospital as the presence of both entities complicates their evaluation and treatment (see Fig. 20.1). However, the SSU may have a role in these patients as opportunities to reduce cost and improve the quality of care among Medicare recipients are sought as part of current health reform efforts. Among many others, there is likely to be a focus on strategies that

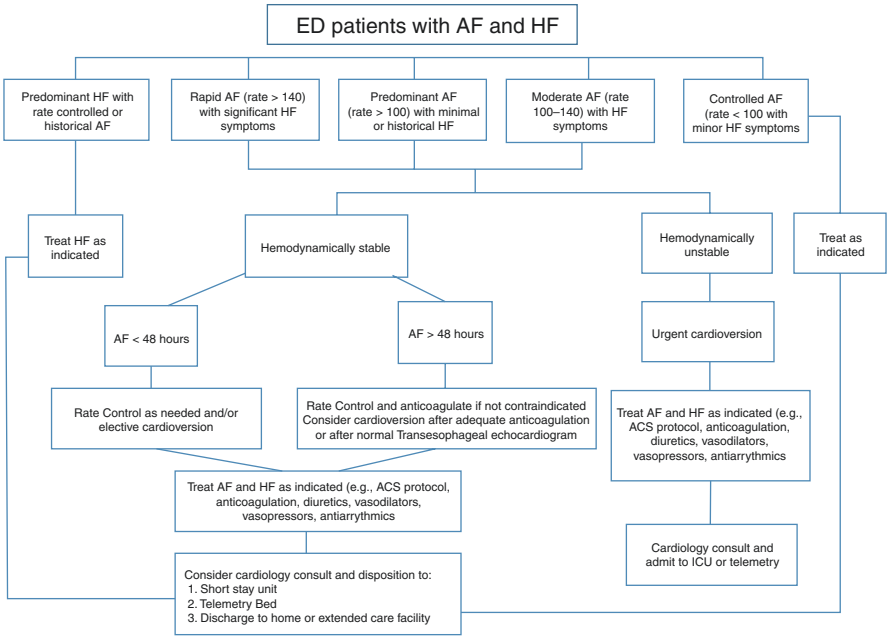

Fig. 20.1 Clinical management of patients with AF and HF

can identify patients who can be managed in a SSU and also prevent repeat ED visits and subsequent readmissions.

Transfer of Symptomatic Atrial Fibrillation and Heart Failure Patients to Short-Stay Unit

The most likely candidates for admission to the SSU are those that have rate-controlled AF with either historical or mild HF amenable to a short course (≤24 h) of observation care and treatment. Due to the presence of AF and HF and other associated comorbidities, the treatment plan will need to be individualized for each patient. Key data for risk stratification of these patients include their response to treatment in the ED, prior medical history (e.g., AF, HF, and ejection fraction), results of ED tests [e.g., troponin (associated with increased mortality in patients with HF [53])], electrolytes, renal function, overall patient appearance, and mental status. In the future, there is also likely to be an increasing number of patients with advanced HF and AF who are using left ventricular assist devices [54–56]. Although the information on the care of patients with these devices is lacking, their presence is likely to rule out observation admissions for the foreseeable future. While in the SSU, many issues will need to be addressed, and (Table 20.4) consultations with appropriate specialists should be arranged as indicated to help with pharmacotherapy options for AF and HF and to evaluate for potential invasive treatment (e.g.,

Table 20.4 General management for patients with AF and HF in the SSU

Continue critical care monitoring and establish treatment objectives for AF and HF
Evaluate response to emergency department treatment and adjust therapy as needed
Rule out and identify precipitating etiologies (e.g., renal failure, electrolyte disturbances, anemia, ischemia)
Consult with primary care physician and cardiologist as appropriate
Consider provocative cardiac testing
Consider echocardiography
Arrange for patient and family education (e.g., disease-specific education, medications, diet, self-care)
Arrange follow-up care (e.g., specialists, primary care physician)

pacemaker insertion, radiofrequency ablation, cardiac surgery evaluation). Primary care providers should also be contacted and kept abreast of the treatment and follow-up plans. As with admitted patients, the SSU should also provide patients with disease-specific education, review medication lists and address errors and issues of compliance, discuss dietary habits, and provide advice on self-management strategies. In addition, referral to HF management programs may cut costs and reduce readmissions [57–59].

Long-Term Management Considerations for Patients with Atrial Fibrillation and Heart Failure

There are a multitude of options for the long-term management of the patient with AF and HF. One of the first questions that may be addressed is whether a rate-control or rhythm-control strategy should be used for those with persistent or recurrent AF. For rhythm control, there are several long-term antiarrhythmic options to choose from based on the results of clinical trials and FDA approval such as β-blockers, flecainide, sotalol, amiodarone, and dronedarone, with amiodarone being the agent of choice in patients with advanced HF [14]. Long-term rhythm control may improve myocardial function, avoid anticoagulation, and prevent complications related to thromboembolism [60]. The advantages of a rate-control strategy are that antiarrhythmic drugs and cardioversion procedures can be avoided [60]. Several studies have compared these two strategies and found no significant differences in outcomes over time [61–63]. Specifically, in AF patients, the AFFIRM and RACE trials found a trend toward a decrease in mortality and/or in combined adverse outcomes associated with rate-control rather than a rhythm-control strategy [62, 63]. In an analogous fashion, Roy et al. studied rate versus rhythm control in 1,376 patients with EF < 35 %, HF symptoms, and a history of AF. Follow-up found no difference in the rates of death or other secondary outcomes between either strategy [61]. Current guidelines suggest that, in patients with AF and HF, decisions regarding rate versus rhythm control will need to be individualized and it is reasonable to use either approach [25].

Another potential long-term treatment is catheter ablation of AF foci. Hsu et al. studied the efficacy and safety of catheter ablation in patients with both AF and HF (reduced EF <45 %) as compared to patients with AF alone. They found that maintenance of sinus rhythm was achieved in >75 % of ablated patients with AF and HF. Those receiving catheter ablation had improved left ventricular function on follow-up testing [64]. Biventricular pacing (often with AV node ablation) has also been shown to be beneficial for patients with AF and HF [65, 66] and may be offered to carefully selected patients. Lastly, some patients may be referred for surgical treatment (maze procedure) for their AF [67]. Due to the number of treatment options, consultations with specialists are a key component of treatment.

The Use of Anticoagulant and Antiplatelet Therapies

Another key long-term therapy question to address in the SSU is the need for oral anticoagulation therapy. Concomitant HF increases the risk of stroke, and therefore, the need for consideration of pharmacologic prophylaxis is even more important in the patient with AF and HF. The decision to use long-term anticoagulants such as warfarin (or newer, novel anticoagulants) is based on an evaluation of various risk factors (e.g., age, hypertension, the presence of HF, and valvular heart disease) for stroke along with other factors (e.g., fall risk) and patient preferences. Several studies have described the features associated with stroke in patients with AF [68–71], and there are scoring systems such as $CHADS_2$ [69, 72] which can help with stroke risk stratification. Some patients will be deemed low risk, and only aspirin may be recommended, whereas higher-risk individuals may be prescribed long-term anticoagulation.

A newer anticoagulant option to consider is dabigatran which is an oral direct thrombin inhibitor. One prior study randomized anticoagulation treatment of dabigatran at two different fixed doses (110 and 150 mg) and compared it to adjusted dose warfarin with respect to rates of subsequent stroke, systemic embolism, or bleeding complications. Dabigatran use was found to result in similar or decreased rates of stroke and systemic embolism and similar rates of major bleeding events. The incidence of HF in this group was approximately 1/3 in each treatment arm [73]. Lastly, in patients who are not candidates for anticoagulation, antiplatelet medications may provide some protection against stroke. Aspirin plus clopidogrel has been found to result in lower rates of stroke/year in AF patients compared with aspirin alone but at the trade-off of an increased risk of bleeding (2.0 % vs. 1.3 % per year). These decisions must be made in consultation with a cardiologist or responsible primary care physician who will be following the patient after discharge from the SSU.

Summary/Conclusions

As the US population ages, the number of patients presenting with AF and HF will increase. Because of the number of etiologies and frequency of comorbidity, patients with concurrent AF and HF comprise a heterogeneous group that requires

customized treatment strategies. Despite their complexity, management of a small percentage of patients presenting with AF and HF in an observation/SSU setting may be feasible provided that there is access to necessary consultants and that patients are provided with detailed education and discharge planning. Determining selection criteria for entry into the SSU treatment pathway and evaluating outcomes of treatment will be key to determining the safety of this form of outpatient management for this growing population of patients.

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Cardiac Implantable Electronic Devices

22

Brian Hiestand

Introduction

Heart failure hospitalizations continue to increase, with the majority of these encounters beginning in the emergency department (ED) [1, 2]. A rapid, accurate diagnosis and early initiation of appropriate therapy are required for optimal outcomes [3]. Unfortunately, the typical presenting complaint for acute heart failure, dyspnea, is common to many disease states. It is frequently a challenge for the physician caring for the patient in the acute setting to determine the etiology of the presenting symptoms. Lab, radiology, and clinical findings are frequently insufficiently specific to definitively establish the diagnosis [4].

An overlooked potential source of additional information in heart failure patients is the cardiac implantable electronic device (CIED). In addition to their therapeutic indications, these devices record data that may assist in diagnostic and therapeutic decision-making. There are several potential indications for cardiac devices in patients with heart failure; therefore, these devices are frequently encountered in the acute care setting. Other patients with heart failure may have an indication for an implantable cardiac device but have not been recognized or referred for consideration of implantation.

Therapeutic Functions

The active functions of implantable devices can be broadly divided into two categories—arrhythmia termination and primary pacing. Defibrillation is the primary mode for termination of malignant ventricular tachydysrhythmias, although overdrive

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pacing may be attempted based on the functionality and programming capabilities of the device. Patients with heart failure are at substantial risk for both atrial and ventricular tachydysrhythmias, with subsequent clinical deterioration. The annual incidence of sudden cardiac death (SCD) in the United States is estimated at 0.2 % [5]. In patients with inducible dysrhythmias and chronic heart failure due to ischemia (the highest-risk subgroup), that incidence climbs to more than 30 %. Other high-risk groups include those with a history of cardiac arrest, ventricular tachycardia/ventricular fibrillation (VT/VF) survivors, those with an LV ejection fraction less than 35 %, and heart failure patients [6]. In the latter group, SCD comprises about 50 % of all deaths [7].

Patients with chronic heart failure who have survived VT/VF or SCD are at high risk for recurrence. Regardless of the degree of underlying structural disease (preserved vs. decreased systolic function) or etiology (ischemic vs. nonischemic cardiomyopathy), a CIED is recommended when quality of life and prognosis are such that sudden cardiac death prevention is a desirable goal [8]. It should be noted that such secondary prevention is not indicated in all survivors, i.e., patients with poor short- to intermediate-term prognoses will likely not benefit from CIED implantation as death is likely regardless of dysrhythmia protection.

Primary prevention, in contrast, refers to fatal dysrhythmia prophylaxis when a sustained VT/VF/SCD event has not yet occurred in a patient who is deemed to be at substantial risk. Multiple trials have demonstrated the superiority of CIED over medical therapy for primary prevention of sudden cardiac death in the heart failure population.

This benefit in patients with reduced EF (LVEF<35 %) has been demonstrated in both ischemic cardiomyopathy (MADIT, MADIT II) [9, 10] and nonischemic cardiomyopathy (SCD-HeFT) [11] in patients with symptomatic heart failure (New York Heart Association (NYHA) classes II–III). Therefore, patients with reduced ejection fraction and symptomatic heart failure should be considered for referral, after stabilization and treatment, for consideration of primary CIED placement.

In addition to arrhythmia management, CIED may be programmed to manage the beat-to-beat conduction of the failing heart. Slowed ventricular contraction can exacerbate preexisting cardiomyopathy, resulting in worsening contractile function as well as leading to unfavorable remodeling. The utilization of cardiac resynchronization therapy (CRT) with biventricular pacing is designed to overcome mechanical dyssynchrony by way of controlled synchronous depolarization of both ventricles. This technology has been demonstrated to enhance quality of life, decrease symptoms, and reverse remodeling [12]. The Multicenter InSync Randomized Clinical Evaluation (MIRACLE) trial enrolled 453 subjects with symptomatic heart failure (NYHA III or IV) with ventricular dyssynchrony (QRS ≥130 ms) and impaired systolic function (LVEF ≤35 %) [13]. All subjects received an implantable cardiac device with CRT capacity and were randomized to either 6 months of CRT or no pacing. At 6 months, the CRT group had demonstrated significant improvement in NYHA class, 6-min walk test, and quality of life metrics. In addition, fewer hospitalizations for heart failure were required in the CRT group (83 hospital patient-days vs. 363 hospital patient-days), although mortality was similar between groups.

The Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial randomized 1,520 patients with NYHA III or IV heart failure, reduced EF (≤35 %), and dysfunctional electrical conduction (QRS ≥120 ms and PR interval ≥150 ms) to either CRT with defibrillator (CRT-D), CRT alone, or optimal medical therapy [14]. Although the trial was complicated by a higher than the anticipated withdrawal rate from the medical therapy arm, CRT and CRT-D therapies were associated with a significantly decreased rate of the primary composite end point of death or hospitalization. Additionally, the CRT-D group had a significant reduction in all-cause mortality when compared to the optimal medical therapy group.

The benefits of CRT are clearer in patients with milder heart failure (NYHA III) than in patient with severe baseline disease [15]. In addition, CRT has shown little benefit in patients with a narrow QRS complex [16]. It had been suggested that patients with echocardiographic evidence of mechanical dyssynchrony but a narrow QRS complex might benefit from CRT. This hypothesis was tested in the EchoCRT study, which randomized 809 patients with reduced EF, NYHA III or IV heart failure, QRS ≤130 ms, and echocardiographic evidence of mechanical dyssynchrony to sham device or CRT therapy [17]. The trial was stopped early due to an increased rate of death in the CRT group, suggesting that CRT is not helpful and may be harmful in patients with a narrow QRS complex. However, in appropriate patients, multiple clinical trials have consistently demonstrated an improvement in quality of life measures as well as survival [13, 14, 18–22].

It is not our purpose to suggest that the recognition of implantable device indications and specialist referral for such is the standard of care in the ED or short-stay setting. However, the appropriate use of these devices in the evidence-based, guideline-recommended population (i.e., those with a class IA indication) is only about 40–50 % [23]. Even in academic, tertiary centers, standard referral patterns result in missed opportunities to get device-based therapies to at-risk patients; [24] physicians managing heart failure patients in the short-stay setting should be mindful of opportunities and resources that may decrease hospital admission recidivism and improvement in quality of life. Especially in underserved populations, the medical safety net provided by the ED and the subsequent short-stay setting may represent the best opportunity for appropriate referral for postdischarge device therapies.

Diagnostic Functions

In order for implantable devices to perform the active functions of defibrillation, cardioversion, or pacing, they must record and interpret the patient's intrinsic cardiac rhythm data. Different devices store modestly different parameters, although there are some consistent metrics between devices and manufacturers. In addition to devices that record rate, rhythm, and response data, there are an increasing number of devices that collect advanced telemetry data, including physiological information

such as heart rate variability, intrathoracic impedance, and patient activity level. Data from both basic and advanced monitoring parameters may be useful during the initial evaluation of the patient as well as to the physician caring for the patient in the short-stay unit.

Rhythm Data

Atrial fibrillation is the most common dysrhythmia in patients with chronic heart failure; even patients thought to be maintained in sinus rhythm may experience clinically silent paroxysmal atrial fibrillation episodes [25]. New-onset atrial fibrillation may be a worse marker for long-term survival, and many heart failure patients experience worsening symptoms with atrial fibrillation [26]. Conversely, there is an evidence that prolonged volume overload can result in atrial tachydysrhythmias, perhaps as a result of electrical instability due to atrial distension [27]. Discovery of atrial fibrillation as a precipitating event could lead to the consideration of several different medical management options that would not have been immediately apparent choices in the absence of such knowledge, such as initiating rate or rhythm controlling pharmacologic agents, starting long-term anticoagulation for stroke prophylaxis, or changing pacemaker programming parameters.

Heart Rate Variability

There is an intrinsic variability in the heart rate of healthy individuals due to both changes in physiologic demand and other diurnal patterns. As physiologic stress increases, this variance decreases due to an increase in sympathetic tone and an attenuation of the parasympathetic nervous system [28]. Implantable cardiac devices that monitor atrial depolarization can record atrial rates and calculate the variability in the intrinsic sinoatrial node function. The association between heart rate variability and heart failure exacerbation was established in a secondary analysis of MIRACLE [13]. Those patients randomized to active CRT functionality experienced a substantial improvement in heart rate variability, regardless of the use of beta-blocker therapy, which was associated with the improvement in multiple echocardiographic indices of cardiac function [29].

Heart rate variability has also been linked as an independent predictor of outcomes, as opposed to a marker of response to therapy. In a prospective observational cohort study of 288 patients receiving a CRT device for NYHA III or IV heart failure coupled with systolic dysfunction (LVEF $\leq$35 %), heart rate variability was significantly lower in patients experiencing hospitalization or death [30]. The decrease in heart rate variability was notable at a median 16 days prior to hospitalization.

Unfortunately, a decrease in heart rate variability is not specific to acute heart failure. Other illnesses and comorbidities that manifest with a ramping up of sympathetic tone also present with a decrease in heart rate variability, such as

seen in exacerbation of chronic obstructive pulmonary disease or various infectious states [31, 32].

Patient Activity

Accelerometers within the implanted device can provide a measurement of hours per day that the patient is moving and presumably physically active, although the actual degree of exertion is not captured with this measurement. As patients become more and more symptomatic with heart failure, exercise intolerance worsens and physical activity decreases [30]. Conversely, a study of patients receiving CRT pacing demonstrated that an increase in daily activity levels corresponded to improvements in NYHA class and exercise tolerance [33]. Patient activity levels have been shown to be less sensitive than decreased heart rate variability in predicting decompensation in the outpatient setting [30], although decreased physical activity levels have been shown to be predictive of subsequent heart failure decompensation within 30 days, when monitored in concert with other CIED monitoring parameters [34].

Intrathoracic Impedance

The measurement of intrathoracic impedance utilizes changes in electrical conduction within the cardiopulmonary structures of the chest to gauge fluid overload. As the total amount of tissue fluid increases, resistance (also known as impedance) to conduction of an electrical impulse between a pulse generator (pacemaker lead) and a sensor (generally the device canister) decreases. Therefore, a low impedance reading is a marker of pulmonic fluid congestion, correlates with wedge pressures and negative fluid balance during hospitalization, and begins to drop several days prior to the overt need for hospitalization [35]. Intrathoracic impedance has been evaluated as a predictor of heart failure decompensation in the outpatient arena in a number of studies [34, 36–39]. For example, in the FAST study [36], intrathoracic impedance monitoring was substantially more sensitive for heart failure decompensation than daily weight monitoring (76 % vs. 23 %) and had fewer false positives (1.9 vs. 4.3 events per patient-year). Unfortunately to date, no prospective studies have been able to successfully use impedance monitoring in the outpatient setting to avoid hospitalizations for acute heart failure.

Of potentially more impact within the acute care setting, Small et al. have demonstrated, in a retrospective analysis of registry data derived from patients with CRT-based intrathoracic impedance monitoring, a low likelihood of hospitalization due to acute heart failure in subjects whose fluid index did not cross the set threshold (0.14 hospitalizations/patient-years vs. 0.76 hospitalizations/patient-years in those patients with multiple threshold crossing events) [40]. It may be that in the absence of decreased impedance, a dyspneic patient being evaluated in the acute setting has an etiology other than acute heart failure due to volume overload for their presenting symptoms.

Pressure Monitoring

At the time of this writing, several implantable cardiac devices that directly monitor hemodynamic status are undergoing investigation. The CardioMEMS Heart Failure Sensor (CardioMEMS, Atlanta, Georgia) utilizes a pressure transducer implanted in the pulmonary artery to transmit data wirelessly to a handheld recorder [41]. In the CHAMPION study, a 550-subject prospective randomized trial of protocol-driven modulation of therapy based on daily pulmonary artery pressure readings, heart failure hospitalizations were reduced by 37 % compared to the standard care control group [42]. This was achieved by significantly more frequent dose escalations of both diuretics and vasodilators without an increase in renal failure when compared to the control group [43].

The HeartPOD system (St. Jude Medical, Minneapolis, MN) utilized a wired pressure transducer in the left atrium to record cardiac data [44]. The Hemodynamically Guided Home Self-Therapy in Severe Heart Failure Patients (HOMEOSTASIS) trial evaluated the feasibility of providing this data directly to the patient with recommended changes in medication therapy (diuretics or vasodilators) based on algorithms preprogrammed by the physician [45]. The lack of a control group limited the conclusions that can be drawn from this small study; however, this study led to a controlled trial of patient-facilitated management with the HeartPOD. That study, the Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy (LAPTOP-HF) trial (ClinicalTrials.gov Identifier NCT01121107) [46], was stopped early by the DSMB due to statistical futility of proving the primary end point when compared against the patient risk with device implantation.

Similarly, the RemonCHF device (Boston Scientific, Natick, MA) measures pulmonary artery pressures by way of a pressure transducer located in the pulmonary artery that provides on-demand interrogation powered by way of ultrasound transmission to and from a handheld unit that can be operated by the patient [47]. Although full success has not been realized with these investigational technologies, there is still substantial potential for future discovery in this innovative field.

The Acute Care/Short-Stay Setting

To date, clinical trials of implantable device data have been directed at utilizing these parameters to keep patients from decompensating to the point of requiring emergency department or hospital-based care in the first place. As a result, there is very little data examining the use of CIED data in the diagnosis and management of suspected acute heart failure in the ED and early hospital stay. Once the patient with a CIED presents with symptoms that may be due to acute heart failure, several challenges exist for treating physician. First, the doctor must determine if the patient's symptoms are truly due to acute heart failure. Given that the patient has severe enough heart failure to warrant placement of an implantable device, the a priori probability of decompensation is substantial. However, the use of CIED data may either serve as valuable confirmation of the presence of acute heart failure or

suggest another pathologic process is the etiology of the patient's symptoms. We have previously established in a prospective convenience sample that ED personnel can safely interrogate implantable cardiac devices and that such data can frequently confirm or rule out suspected diagnoses in the ED [48]. However, at this time, no studies have evaluated the diagnostic performance of implantable cardiac device data in differentiating acute heart failure from other disease entities that may present in similar fashion.

Once the physician has determined that acute heart failure is present, the next step should be to determine how best to treat the patient. The modalities chosen (diuresis, afterload reduction, inotropic support, and airway intervention) will depend greatly on the perfusion status and the volume status of the patient as well as the clinical severity of the presentation. Although respiratory compromise and systemic perfusion will be fairly obvious with routine exam, volume status may at times be difficult to discern—especially in the obese. Devices that measure volumetric data, such as intrathoracic impedance or hemodynamic monitors, may provide insight into the degree of appropriate diuresis required. This may allow the physician to adequately remove volume while avoiding the complications of overdiuresis and subsequent renal stress.

Finally, in the patient undergoing short-stay management of acute heart failure, it becomes critical to understand why the patient decompensated in the first place. Examination of the longitudinal data contained within the implantable device may provide key insights as to the underlying mechanisms that brought the patient to this state. Rhythm data may indicate increasing frequency of atrial fibrillation, which could require pacemaker reprogramming, pharmacologic management, or even AV nodal ablation to improve hemodynamic function. Rathman has reported the use of device data to uncover monthly cycles of subacute decompensation in a heart failure patient who was running out of medications each month and not resuming them until he had to, due to financial constraints [49]. Given that abnormalities in heart rate variability, patient activity levels, and fluid accumulation precede clinical decompensation by several days [30, 35, 39, 50], going over temporal data with the patient to evaluate medication, diet, and other lifestyle events such as exacerbations of comorbid illnesses may establish a causative link to behaviors or illnesses that led to acute heart failure.

Unfortunately, these possibilities, although grounded in a solid conceptual framework, have yet to be validated beyond anecdotal experience. As stated previously, the research effort to date has been directed at keeping the patient from requiring acute and short-stay care in the first place. While this is definitely a worthy goal and would benefit the patient, the truth of the matter remains that over one million hospitalizations for heart failure will occur annually [51]. There definitely remains a need for research to establish the additive value of basic and advanced CIED data for the evaluation and management of the patient with suspected acute heart failure. Until such research is established, however, it is certainly reasonable for those of us caring for patients who have this data readily available to evaluate and consider the recorded information in the context of the patient's presentation.

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Heart Failure and Kidney Disease: Management in the Short-Stay Unit

23

Shahriar Dadkhah and Korosh Sharain

Epidemiology

Heart failure (HF) is one of the fastest-growing diagnoses in North America. Approximately 5.8 million Americans have heart failure, and over 600,000 new cases are diagnosed each year [1]. Kidney disease is another rapidly growing diagnosis in North America, with approximately 26 million people in the United States diagnosed with chronic kidney disease (CKD) and 20 million more Americans at risk for developing CKD [2].

The prevalence of cardiovascular disease (CVD) is almost 70 % in patients with CKD compared to 35 % in patients without CKD [3]. Additionally, in patients with CKD, death from CVD is more common that progression to end-stage renal disease (ESRD) [3]. The most common cardiovascular complication in those with CKD is in fact heart failure [4]. Kottgen et al. demonstrated that the incidence of HF was threefold higher for individuals with CKD (defined as an estimated glomerular filtration rate (eGFR) of <60 ml/min per 1.73 m^2) compared to the reference group with an eGFR ≥90 ml/min per 1.73 m^2 [5].

Nomenclature

Like heart failure, kidney disease is classified into different stages. Renal function is estimated based on elevated serum creatinine levels or reduced glomerular filtration rate (GFR). The most common calculation is the modification of diet in renal

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Table 23.1 Stages of kidney disease

Stage	Description	GFR (mL/min/1.73 m^2)
1	Kidney damage with normal or ↑ GFR	≥90
2	Kidney damage with mild ↓ GFR	60–89
3	Moderate ↓ GFR	30–59
4	Severe ↓ GFR	15–29
5	End-stage renal disease (kidney failure)	<15 or dialysis

National Kidney Foundation [7]
GFR glomerular filtration rate

disease (MDRD) formula. Chronic kidney disease is defined as a GFR <60 mL/min/1.73 m^2 and has been associated with increased mortality, adverse cardiovascular events, and hospitalizations [6]. Table 23.1 provides the staging classification of kidney function.

Cystatin-C, which is less influenced by muscle mass than creatinine, has been shown to be superior in estimating GFR and predicting mortality and cardiovascular outcome than serum creatinine [8]. An elevated cystatin-C (>1 mg/L) in those with a GFR >60 mL/min/1.73 m^2 classifies preclinical kidney disease, which signifies an increased risk of cardiovascular disease (CVD) and CKD incidence and death [9]. Since it is a relatively newer marker, guidelines and cutoff values have not yet been defined for kidney disease, and its widespread use has been stunted. In one analysis of 3,418 individuals with CKD, serum cystatin-C levels alone estimated GFR as accurately as serum creatinine when adjusted for age, sex, and race [10]. The study concluded that an equation combining both serum creatinine and cystatin-C for calculating GFR would be the most accurate method for evaluating kidney function.

Interrelationship Between Heart Failure and Kidney Disease

The heart and the kidney are in constant communication with each other through released peptides and other neurohormonal mechanisms. This delicate relationship is responsible for regulating blood volume, vascular tone, and ultimately organ perfusion. The leading causes of kidney disease are diabetes, hypertension, and CVD; similarly, the leading causes of HF are diabetes, hypertension, coronary artery disease, and kidney disease. The so-called "traditional" CV risk factors are advanced age, diabetes, hypertension, and dyslipidemia with "nontraditional" CKD-specific risk factors being volume overload, anemia, and inflammation. However, the connection between these two pathologies extends beyond risk factors. In fact, kidney disease and heart failure are interrelated such that derangement of one organ consequently promotes derangement of the other. If dysfunction occurs in the intimate relationship between the heart and the kidneys, it is known as the cardiorenal syndrome. Figure 23.1 depicts this relationship.

The overwhelming prevalence of kidney disease in the heart failure population was demonstrated by Smith et al. [11]. In a meta-analysis of 16 studies including

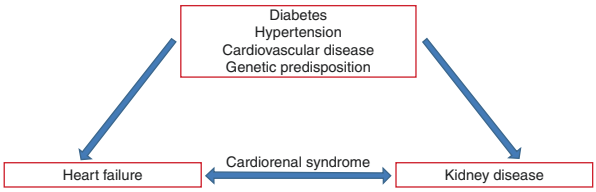

Fig. 23.1 Interrelationship between heart failure and kidney disease

80,098 patients with heart failure, Smith et al. discovered that 63 % of the patients with heart failure had concomitant renal impairment (defined as creatinine >1.0 mg/dL, creatinine clearance or estimated GFR <90 mL/min, or cystatin-C >1.03 mg/dL), while 29 % had moderate to severe renal impairment (defined as creatinine ≥1.5 mg/dL, creatinine clearance or estimated GFR <53 mL/min, or cystatin-C ≥1.56 mg/dL) [11]. Additionally, Smith et al. demonstrated that mortality increased as renal function decreased [11]. Specifically, there was a 15 % increased risk of mortality for every 0.5 mg/dL increase in creatinine and a 7 % increased risk of mortality for every 10 mL/min decrease in estimated GFR [11]. With continued advancements in medicine, patients with CVD are surviving longer and thus developing heart failure, similarly, CKD patients are surviving longer, and therefore, it is estimated that patients with combined heart and kidney disease will become even more prevalent.

The pathophysiological mechanisms which hasten LV failure in CKD are numerous. At least three mechanisms have been implicated including pressure overload from long-standing hypertension and vascular stiffness, volume overload from CKD, and non-hemodynamic factors such as inappropriate renin-angiotensin-aldosterone system (RAAS) activation which alters the myocardium [12]. Other than systolic dysfunction, diastolic dysfunction is common in CKD even in early stages and increases the risk of CHF and mortality [12, 13].

Several studies have demonstrated that renal impairment is strongly associated with poor outcomes in heart failure patients with systolic and diastolic dysfunction [14]; therefore, it is imperative to treat underlying kidney disease when managing heart failure. In fact, the reversal of renal dysfunction has been shown to improve cardiac function. Wali et al. demonstrated that hemodialysis patients with heart failure and a left ventricular ejection fraction (LVEF) of ≤40 % undergoing renal transplantation had a mean LVEF increase of 20 % 1 year post-renal transplantation, increasing from a mean LVEF of 32 % to a mean LVEF of 52 % [15]. Additionally, 70 % of the transplanted patients achieved normalization of cardiac function, defined as an LVEF ≥50 % [15]. This data demonstrates that renal insufficiency has a contributory role in heart failure progression.

Additionally, a study of 1,906 patients with heart failure concluded that impaired renal function was a better predictor of mortality than either heart failure class or LVEF [16]. It is important to note that the heart is not a victim in this relationship; in fact, the most common cause of mortality in CKD is CVD [17]. Therefore, the treatment of one organ system can dramatically improve the other. Figure 23.2 demonstrates how cardiac dysfunction or renal dysfunction can produce dysfunction in

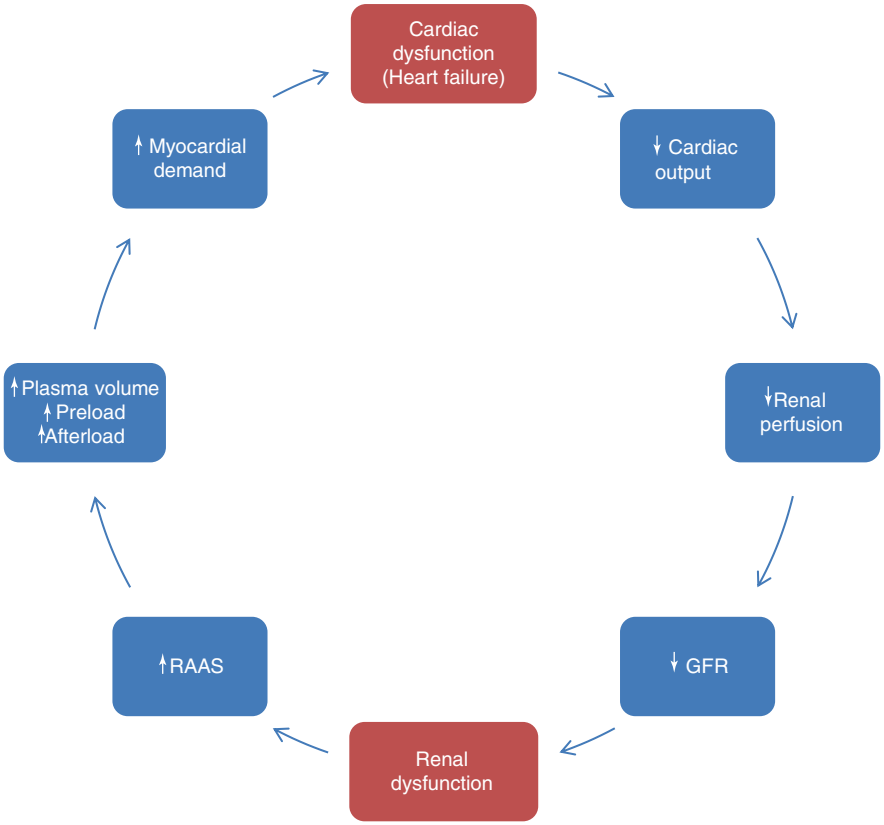

Fig. 23.2 Cardiorenal dysfunction cycle. *RAAS* renin-angiotensin-aldosterone system

the other organ. Attenuating or even halting the vicious cardiorenal cycle requires therapies that can interrupt the cycle at any point depicted. Table 23.2 lists the types of cardiorenal syndrome.

Evaluation and Management of Heart Failure with Concomitant Kidney Disease: Overview

Although there are well-established guidelines for managing heart failure alone and kidney disease alone, the management of their copresentation in the emergency department remains largely empirical due to the lack of significant randomized clinical trials. Most trials which evaluated heart failure management excluded patients with renal dysfunction out of concern that investigational treatments would potentially cause worsening renal function [18]. Therefore, there is a paucity of recommendations and guidelines for the management of HF patients with CKD, which represents a very high-risk patient population that is often overlooked and

Table 23.2 Cardiorenal syndrome classification

Type	Description	Example
1	Acute cardiac dysfunction leads to acute kidney injury	Acute heart failure
2	Chronic cardiac dysfunction leads to a progressive chronic kidney disease	Chronic heart failure
3	Acute kidney dysfunction leads to acute cardiac dysfunction	Acute kidney injury or glomerulonephritis
4	Chronic kidney disease leads to chronic cardiac dysfunction	Chronic kidney disease
5	An acute or chronic systemic disorder causes both cardiac and renal dysfunctions	Sepsis, diabetes, vasculitis, sarcoidosis

undertreated. However, medical therapy in HF patients with CKD is similar to those without CKD but with several important differences. Thus, most of the following are suggested management options without significant evidence-based guidelines accompanying them.

Managing heart failure in the emergency department is challenging but is made even more complex in the setting of kidney disease. It is important to understand the subtle differences when managing this specific patient population compared to heart failure patients alone. The management of cardiorenal syndrome in the emergency department requires individualized therapy. This involves a multifaceted approach in order to optimally manage both heart failure and kidney disease. Earlier chapters have indicated the proper management of heart failure in the ED and short-stay unit; therefore, this chapter will focus on the additional therapies recommended for patients with heart failure complicated by underlying kidney disease. Additionally, this chapter will focus on New York Heart Association (NYHA) heart failure classes 1–3 with CKD. Those with NYHA heart failure class 4 and those with CKD stage 5 or ESRD are considered high risk and are usually not appropriate for admission to a short-stay observation unit and thus will not be discussed in this presentation.

Biomarkers in Heart Failure with Renal Dysfunction: B-Type Natriuretic Peptide and N-Terminal Pro-B-Type Natriuretic Peptide

The plasma levels of B-type natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) are useful markers for the diagnosis and prognosis of heart failure. Since volume overload causing LV wall distention causes release of these peptides, their levels can be used to aid in the diagnosis and prognosis of acute exacerbation of heart failure. Many studies have demonstrated the diagnostic and prognostic value of BNP and NT-proBNP in heart failure (discussed in prior chapters). However, the utility of these markers is not as well established in the CKD population with HF. BNP and NT-proBNP have been shown to be useful diagnostic and prognostic markers in HF patients with CKD, but higher cutoff values may be

required [19, 20]. Several mechanisms have been proposed for the elevated BNP and NT-proBNP in patients with CKD and HF, including reduced renal clearance of the peptides due to CKD or increased peptide release by the myocytes due to advanced cardiac damage in renal dysfunction [19]. However, current studies suggest that BNP and NT-proBNP are increased mainly due to advanced cardiac pathology rather than impaired renal clearance [19]. Additionally, one study suggested that LV structural and functional changes in CKD are the primary cause of increased BNP levels in dialysis patients rather than a reduced plasma clearance [1, 21]. This is supported by another study where NT-proBNP and BNP were significantly higher, while LVEF was lower in patients with renal dysfunction [22]. It can be argued that higher levels of these peptides in this population signify a worse cardiac substrate. Furthermore, BNP and NT-proBNP were independent predictors of 1-year mortality in renal disease patients [22].

Biomarkers in Heart Failure with Renal Dysfunction: Myoglobin, CK-MB, and Troponin

The role of myoglobin in predicting myocardial ischemia is not appropriate in renal impairment. Several studies have demonstrated that myoglobin is falsely elevated in renal dysfunction, although CK-MB and troponin are not, due to different clearance mechanisms [23]. This is true for populations in which AMI was ruled in or ruled out [23]. In a study by McCullough et al., myoglobin was falsely elevated 100 % of the time in patients with advanced renal function (GFR <47 mL/min) [23]. The recommendation of the use of the multimarker approach still achieves the best negative predictive value for the presence of underlying ACS [24]. Cardiac troponins (cTn) can accumulate in CKD patients with CHF making elevated cTn in this population difficult to interpret; however, it remains a good predictor of mortality [25]. Evaluating a trend via serial sampling or comparing levels to a prior baseline is more informative.

Medical Therapy

The lack of evidence-based guidelines explains why management is variable in this population. In general, the management of heart failure in patients with concomitant kidney disease in the short-stay unit requires, first and foremost, the optimal treatment of the acute exacerbation of heart failure. Medical management of HF with CKD requires monitoring of fluid status. This requires physician awareness of the consequences of each drug used on both HF and kidney disease. Overly aggressive fluid reduction may damage renal function due to reduced perfusion. Yet increasing plasma volume to improve renal perfusion is detrimental to heart failure. Therefore, any changes in hemodynamics of this patient population must be closely observed. Fortunately, upon administration in the ED, many of the therapies initiated can be continued and monitored in the short-stay unit.

Diuretics

Diuretics are a mainstay therapy in HF management. Often, higher doses of diuretics are required to achieve appropriate diuresis in those with CKD [12]. In those with lower GFR, loop diuretics should be the first-line treatment as thiazide diuretics are less efficacious [26]. Intravenous administration is most effective due to the reduced bioavailability of oral agents in a hypoperfused edematous small bowel that may be present in heart failure. Diuretic resistance is a common therapeutic roadblock encountered in HF patients with CKD, in which the diuretic response is reduced even with "therapeutic" doses. Diuretic resistance can be due to reduced renal perfusion and delivery of drug to the kidney, tachyphylaxis and tubular resistance from chronic diuretic use, secondary hyperaldosteronism, or inadequate dosing [26, 27]. To overcome diuretic resistance, higher doses of diuretic are often required. Additionally, coadministration of loop diuretics with a thiazide diuretic such as metolazone can improve diuresis in this setting. However, volume and electrolyte derangements (hyponatremia and hypokalemia) are common and should be closely monitored. Unfortunately, the aggressive use of diuretics can result in worsening renal function via activation of neurohormonal systems.

Beta-Blockers

There is limited evidence about beta-blocker use in CKD and HF. It is thought that overactive sympathetic drive plays a role in LV hypertrophy and underlying cardiac substrate derangement in CKD. In a large systematic review, beta-blocker therapy was found to improve all-cause mortality by 28 % and cardiovascular mortality by 34 % in patients with CKD and chronic systolic heart failure although there was an increased risk of bradycardia and hypotension [28]. Multiple other studies have demonstrated that in patients with CKD and systolic heart failure, beta-blockers reduce mortality and hospitalizations [29]. In the short-stay unit, however, initiation of beta-blocker in acute heart failure should be used with extreme caution as explained in prior chapters.

Angiotensin-Converting Enzyme Inhibitor/Angiotensin-Receptor Blocker

The role of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs) in HF has been well established [30]. Unfortunately, their role in patients with HF and CKD is not well established. This is due to the relatively low number of randomized trials dealing with this patient population and the fear physicians have in exacerbating renal failure and hyperkalemia. Several studies, including that by McAlister et al., demonstrated that patients with renal insufficiency were less likely to receive ACEI, β-blockers, or spironolactone [14]. However, several studies have demonstrated the benefits of ACEI and ARB in this

patient population. One analysis of the Minnesota Heart Survey demonstrated a statistically significant reduction in 30-day and 1-year mortality in CHF patients with renal dysfunction not on dialysis who were given ACEI or ARB during their hospital stay [31].

In a review of 12 randomized clinical trials looking at ACEI use in patients with renal insufficiency, the authors demonstrated a 55–75 % risk reduction in the progression of renal disease among those on ACEI compared to those not on ACEI [32]. They also concluded that although serum creatinine levels increased by up to 30 %, they stabilized within the first 2 months of ACEI administration, and there was long-term preservation of renal function [32]. A worsening of renal function at initiation of an ACEI should be expected. However, the withdrawal of an ACEI should occur when creatinine rises 30 % above baseline or hyperkalemia (>5.5 mmol/L) develops within the first 2 months of ACEI treatment [32]. Another study demonstrated reduced 1-year mortality associated with ACEI and β-blocker use in heart failure patients, even after adjustment for serum creatinine, age, gender, NYHA class, hemoglobin, and other medications [14]. This was true for creatinine clearances <60 and ≥60 mL/min [14]. Khan et al. demonstrated that in HF patients with CKD, ACEIs were associated with reduced mortality and did not have adverse effects on renal function [33].

Although the use of ACEI and ARBs among patients with renal insufficiency is not established, their role in preserving kidney and heart function has been demonstrated. The use of these medications at low doses along with monitoring of electrolytes in heart failure patients with renal dysfunction should be considered in the short-stay unit and as a discharge medication with the follow-up of electrolytes and kidney function within a couple weeks of initiation. However, ACEI should be avoided in acute renal failure.

Nesiritide and Concerns with Renal Function

Nesiritide (synthetic BNP) is an effective vasodilator, diuretic, and RAAS inhibitor, performing these functions without significant reflex tachycardia. Nesiritide's main actions are at the renal level, dilating the afferent arterioles and constricting the efferent arterioles in order to increase intraglomerular pressure and increase GFR [34]. The indirect effects of nesiritide can improve the exacerbation of heart failure as they reduce preload, afterload, and myocardial oxygen consumption through vasodilation and diuresis. Unfortunately, these indirect effects can also lower systemic blood pressure and reduce renal blood flow and GFR [34].

The use of nesiritide for heart failure in renal disease has been constantly debated. Early studies indicated either no difference in kidney dysfunction with nesiritide use in acute decompensated heart failure versus placebo [35]. A meta-analysis which analyzed heart failure trials using varying doses of nesiritide suggested an increased risk of worsening renal function [36]. The worsening in renal function was linked to nesiritide's hypotensive effects. However, given limited controls, lack of covariable adjustments, and the use of non-FDA approved nesiritide doses have led many to criticize the study results [36].

On the other hand, other studies have demonstrated renal protective effects of nesiritide [37, 38]. Riter et al. demonstrated that low-dose nesiritide in HF and renal dysfunction did not have a significant reduction in systolic blood pressure which was seen with the standard dose [37]. His group showed that nesiritide was actually renal protective in which the low-dose group (2 mcg/kg bolus followed by 0.005 mcg/kg/min and 0.0025 mcg/kg/min without bolus) showed improvement in renal function demonstrated by a decrease in creatinine compared to standard nesiritide doses (2 mcg/kg bolus with an infusion of 0.01 mcg/kg/min). The low-dose group also received less furosemide compared to standard-dose nesiritide or no nesiritide group while achieving similar diuresis [37]. Although Riter et al. used a small sample size, the results were promising.

One of the earlier studies to demonstrate the renal protective effects of nesiritide was the NAPA study which evaluated the use of 0.01 mcg/kg of nesiritide without bolus against placebo in postcoronary artery bypass patients [38]. The authors concluded that nesiritide improved renal function postoperatively (measured by a smaller maximal increase in peak creatinine, better preservation of GFR, and greater urine output), reduced hospital length of stay, and decreased mortality at 180 days which they attributed to the improvement of renal function from nesiritide [38]. The VMAC trial demonstrated that compared to placebo, nesiritide resulted in significantly improved hemodynamics in patients with acutely decompensated heart failure [39]. Other results from VMAC included rapid and sustained decreases in cardiac filling pressures and a consistently reduced mean pulmonary capillary wedge pressure with nesiritide use. Nesiritide also significantly reduced patient-reported symptoms and dyspnea at 3 h compared with placebo and the standard of care, nitroglycerin [39].

More recently, several studies performed by Peacock et al. have demonstrated that the use of nesiritide in the observation unit was safe, reduced hospital admissions, reduced hospital readmission 30 days after discharge, and reduced overall length of stay [40, 41]. Since nesiritide is a synthetic form of the naturally occurring BNP released by the heart, it is self-limiting, and only blood pressure and heart rate need to be monitored [41]. Most recently, the ASCEND-HF trial, which included 7,141 patients, concluded that nesiritide slightly improved shortness of breath, relieved dyspnea, and did not increase the risk of kidney disease compared to placebo in the treatment of heart failure [42].

It is thought that patients with acute heart failure who have normal or increased blood pressures are the ideal candidates for nesiritide use [43]. This may actually represent a large proportion of patients as up to 50 % of patients with acute heart failure have systolic blood pressures greater than 140 mmHg [43].

Anemia Correction

Anemia in CKD has been extensively evaluated. In a study of over 5,000 patients with CKD, 48 % had anemia, defined as a hemoglobin ≤12 g/dL [44], and the prevalence of anemia increased from 27 to 76 % as GFR decreased from ≥60 to <15 mL/

min/kg^2 [44]. This is thought to result from a deficiency in erythropoietin due to renal dysfunction. Additionally, there is a high prevalence of anemia in the HF population. In the OPTIMIZE-HF registry, over half of the 48,000 patients admitted with HF had a hemoglobin <12 g/dL, and 25 % had moderate to severe anemia with hemoglobin levels between 5 and 10.7 g/dL [45]. Several studies have demonstrated a regression of LVH in CKD patients once their anemia was corrected [46]; however, studies have shown an increased risk of death and CV events with normalization of anemia with erythropoietin agents [47–49]. Cardiorenal anemia syndrome is a term used to emphasize the close interaction between these three entities.

Anemia in CHF is associated with increases in mortality, hospitalization, and morbidity rates irrespective of other factors [50]. Additionally, the more severe the anemia in CHF, the worse the associated mortality, hospitalization, and morbidity [50]. Correction of anemia with erythropoietin-stimulating agents such as erythropoietin or darbepoetin has been associated with an improvement in renal function, NYHA class, left systolic and diastolic function, quality of life, and reduction in BNP, morbidity, and hospitalization [50]. Yet, anemia is often unrecognized or untreated in CHF. One possible reason is the lack of a universally accepted definition for anemia in the HF population. Additionally, there is uncertainty regarding the most beneficial hemoglobin concentrations that should be achieved with erythropoietin-stimulating-agent treatment for HF. Recent data suggests that the lowest dose of erythropoietic agents that will maintain the hemoglobin level in the 10–12 g/dL range should be used [50, 51].

Rehospitalization and Patient Education

Almost one half of HF patients are rehospitalized within 6 months due to acute decompensation of their heart failure [52], many of which have underlying renal dysfunction. Patients with heart failure and kidney disease must be educated about how their behaviors and diet influence their underlying medical comorbidities. Salt restriction is especially vital for patients with HF and CKD [12].

Readmission rates are higher when there are psychosocioeconomic factors which hinder medication compliance, self-monitoring, and follow-up [53]. Dietitian counseling and outpatient case manager coordination should be promoted in this patient population specifically. Along with patient education and discharge instructions, institutions are providing patients with a mini booklet available through the American Society of Health-System Pharmacists (ASHP). This booklet provides an easy to view and read list of the medications the patient is taking, their dosing schedule, what the medication physically looks like, the start date and end date, the reason for the medication (in layman's terms), and the prescribing physician. Patients are instructed to keep this booklet with them as often as possible and bring it with themselves when presenting to the emergency department. Expanding this mini booklet to include additional information such as admission and discharge BNP levels, blood pressure, GFR, creatinine, and ECG can prove to be beneficial for this patient population that has such a high readmission rate. The information on the mini booklet will allow the

evaluating emergency physician to compare the current state of the decompensation to previous episodes. This approach can potentially improve door-to-treatment time, reduce length of stay, and improve overall patient care.

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