EMCREG International
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AUGUST 2007 VOLUME 3
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Diagnosis and Risk Stratification of Acute Heart Failure Syndromes

Dear Colleagues,

When considering the general topic of heart failure, we have come a long way from digitalis, mercurial diuretics, and rotating tourniquets. In this EMCREG-International newsletter, Dr. Alan Storrow, Associate Professor and Research Director of the Department of Emergency Medicine at Vanderbilt University discusses key issues in the diagnosis and risk stratification of patients with acute heart failure syndromes. Patients with heart failure and the physicians who treat them have benefited from an abundance of new research in the area. Specific review topics in this newsletter include:

- Background describing the massive scope of heart failure morbidity
- New nomenclature and clarification of old definitions
- Review of diagnostic needs and challenges
- Discussion of the natriuretic peptides for diagnosis
- New technologies for diagnosing heart failure
- Introduction to risk stratification models and observation units

As you all well know, emergency physicians man the front line when patients present with any acute illness. Heart failure is no exception. With an expected ten million individuals with heart failure by the end of this year, we must be able to accurately and efficiently diagnose and treat this high morbidity condition. Just as important, it is our responsibility to be cognizant of the new research, new language, and treatment progress in the subject. For instance, the catch-all words of "heart failure" can no longer be used to refer to any patient. Terms such as "diastolic heart failure" and "acute heart failure syndrome" have specific definitions and are replacing some of the older, less specific nomenclature. Perhaps the most significant contribution to AHFS diagnosis is the testing of natriuretic peptides. (NT)-proBNP and BNP both can be measured in the blood, but each has unique characteristics and differences. Knowledge of these attributes is critical to the diagnosis of AHFS. The interpretation of specific values in varied clinical settings hinges on your knowledge of the platform and its strengths and limitations. Future directions for heart failure diagnosis include the detection of sub-clinically apparent heart sounds, measurement of cardiothoracic width, new models for risk stratification, and heart failure observation units.

We hope that you enjoy and learn from this publication as we seek to provide emergency care givers with the most comprehensive and up-to-date information regarding new issues in the acute care field. Through EMCREG-International we strive to continue to provide concise and practical approaches for you to give outstanding care for your patients.

Sincerely,

W. Brian Gibler, MD
President,
EMCREG-International

Andra L. Blomkalns, MD
Director of CME,
EMCREG-International

Alan B. Storrow, MD, Associate Professor and Research Director, Department of Emergency Medicine, Vanderbilt University, Nashville, Tennessee

Learning Objectives:

1. Describe trends in heart failure epidemiology
2. Define the terms "heart failure," "acute heart failure syndrome (AHFS)," and "diastolic heart failure"
3. Describe the utility and limitations of natriuretic peptide testing
4. Describe novel methods for heart failure diagnosis
5. Describe the known risk model tools for AHFS

Introduction

The evaluation and management of emergency department (ED) patients with potential acute heart failure syndrome (AHFS) have remained a significant challenge for decades. Dramatically, unlike advances for the assessment and treatment of patients with acute coronary syndrome (ACS) (Table 1), the emergency physician's diagnostic tools for heart failure have remained limited. The complexity and morbidity of this syndrome alone has led to risk aversion and extremely high admission rates.

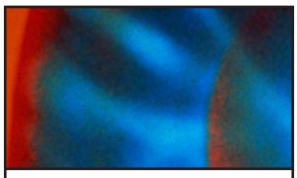
These difficulties, as well as the increasing prevalence and incidence of heart failure due to improved treatment of ACS and our aging population, has placed an enormous burden on healthcare resources worldwide. Recently, new diagnostic markers and maneuvers have become useful for diagnosis and risk assessment of AHFS. Familiarity with these approaches is essential to improving heart failure care and resource utilization.

Background

Heart failure is a worldwide problem of epidemic proportions and represents a tremendous burden to overall healthcare costs. More than five million Americans have heart failure and about 550,000 new cases are diagnosed each year in the United States alone.[1] The incidence is expected to increase dramatically due to our aging population, improved

Peer Reviewer for Industry Bias: Sean P. Collins, MD, Assistant Professor, Department of Emergency Medicine, University of Cincinnati, Cincinnati, OH

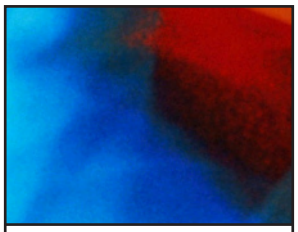
survival from ACS, and other management advances in cardiovascular diseases. Consequently, ten million people are expected to have heart failure by the end of the year 2007. Hospitalizations for heart failure exacerbations account for the largest expenditure in the care of these patients. It is estimated to be about $29.6 billion per year or, for Medicare patients, $5912 per discharge, more than double any cancer diagnosis.[1] This represents about 3% of the total national health care budget. If innovative approaches are not developed to reduce these staggering costs without compromising care, the economic burden may become unmanageable.



Based on ACC/AHA or AHRQ guidelines, it has been suggested up to 50% of admitted patients are low-risk and may be candidates for outpatient therapy, a potential savings of $2.5 billion.

One-third of known AHFS patients receive inpatient care each year, and at least 80% of ED presentations for AHFS are admitted to the hospital.[1,2] Emergency department patients seen, admitted, and treated in an inpatient bed for AHFS account for the majority of expenditures.[3] Up to 80% of patients discharged from the hospital with a primary diagnosis of heart failure come from the ED.[2,4] Based on American College of Cardiology/American Heart Association (ACC/AHA) and Agency for Healthcare Research and Quality (AHRQ) guidelines, it has been suggested that up to 50% of admitted patients are low-risk and may be candidates for outpatient therapy. This represents a potential savings of $2.5 billion dollars.[2,5]

Poor ED risk stratification, particularly overestimation of disease severity, is the fundamental cause of over-utilization of limited in-hospital resources for this rapidly growing patient population. Improving the ability of the emergency physician to decide on the most appropriate disposition for patients with AHFS is critical to maximizing the allocation of in-hospital resources.[6-8]



Heart failure can be most simply defined as a clinical syndrome resulting from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood.

Defining Heart Failure for the ED – A New Paradigm

Heart failure can be most simply defined as a clinical syndrome resulting from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood.[8] The cardinal manifestations are dyspnea and fatigue (exercise intolerance) as well as fluid retention (pulmonary congestion and peripheral edema). A recently coined and more appropriate ED or acute care term is "acute heart failure syndrome," defined as a gradual or rapid change in heart failure signs and symptoms resulting in a need for urgent therapy.[9] These signs and symptoms are primarily due to pulmonary congestion from elevated left ventricular (LV) filling pressures and can occur in patients with preserved or reduced ejection fraction (EF). The term "diastolic dysfunction" refers to an abnormality of LV filling or relaxation. Patients with diastolic dysfunction may present with similar symptoms of dyspnea and fatigue. These cases are referred to as "diastolic heart failure" or "acute heart failure with preserved EF."[10]

Admissions for AHFS are about 50% female, approximately 75% will have known heart failure, and nearly 50% will have a preserved EF.[11] In the western world, the usual causes are coronary artery disease, hypertension, and dilated cardiomyopathy.

Table 1. Comparison of acute myocardial infarctions and acute heart failure syndromes resulting in hospitalization in the United States

	AMI	AHFS
Incidence	1 million / year	1 million / year
Mortality		
Prehosp	High	Unknown
In-Hospital	3-4%	3-4%
60-90 days	2%	10%
Targets	Clearly defined thrombosis/ruptured plaque	Uncertain
Interventions in clinical trials	Beneficial	Minimum to no benefit or harmful
AHA/ACC recommendations	Level A	No Level A recommendations

ACC = American College of Cardiology; AHA = American Heart Association; AMI = acute myocardial infarction; AHFS = acute heart failure syndrome. Adapted with permission from Gheorghiades M., et al. Circulation 2005;112(5):3958-68.

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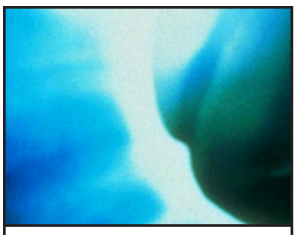
Current Diagnostic Challenges

Heart failure is a complex clinical syndrome characterized by impaired myocardial performance, neuroendocrine system activation, and intravascular volume overload. A well-defined method of diagnosis is of primary importance for management. A definitive diagnosis is often based on right heart catheterization or indirect measurement of EF via radionuclide scanning or echocardiography. These studies are often prohibitive as initial tests in the ED due to lack of immediate availability and cost. As a result, the ED diagnosis of AHFS has been based on history and physical exam findings along with ancillary tests such as chest radiography and electrocardiography (ECG).



Approximately one of every five patients admitted from the ED with AHFS have no signs of congestion on chest radiography.

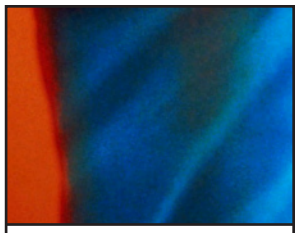
These traditional diagnostic tools have significant shortcomings for the diagnosis of AHFS.[12] Jugular venous distention and a third heart sound have been reported to have sensitivities of only 30% and 24% respectively.[13] Other signs and symptoms of fluid overload such as lower extremity edema and dyspnea also raise the suspicion of heart failure, but their lack of sensitivity makes them poor screening tools.

In addition, chest radiography and ECG have significant shortcomings. Twenty percent of cardiomegaly seen on echocardiogram is missed on chest radiograph.[14] Pulmonary congestion can be minimal or absent in patients with significantly elevated pulmonary artery wedge pressures.[15] Approximately one of every five patients admitted from the ED with AHFS has no signs of congestion on chest radiography.[16] Standard ECG results lack the sensitivity to act as a major screening tool.

Pulmonary artery catheterization is a widely used hemodynamic monitoring device for AHFS in critical care units. Recent and significant concerns that these catheters do not improve outcomes and may have unacceptable complication rates represent a compelling argument to develop noninvasive tools applicable to both the ED and critical care unit.[17, 18]

Natriuretic Peptides for Diagnosis and Risk Stratification

Natriuretic peptides are released under conditions of increased myocardial stretching and possess potent vasodilatory and natriuretic properties. This stimulus for release in the ventricles results in secretion of a prohormone (Pre-ProBNP) from the cardiac myocyte which is enzymatically cleaved into the biologically active B-natriuretic peptide (BNP) and the biologically inactive N-terminal (NT)-proBNP (Figure 1).



Natriuretic peptides are released under conditions of increased myocardial stretching and possess potent vasodilatory and natriuretic properties.

Both of the peptides can be measured and are commonly used for the diagnosis of AHFS. Recognizing the variability of both tests and the presence of an intermediate "grey zone", national organizations have recommended (NT)-proBNP levels (pg/dl) <300 and >1000, and BNP, <100 and >500 for "unlikely" and "likely" AHFS, respectively.[19, 20] Elevated levels in varying degrees can be found in other conditions not related to AHFS. These include pulmonary embolism, ACS, female sex,

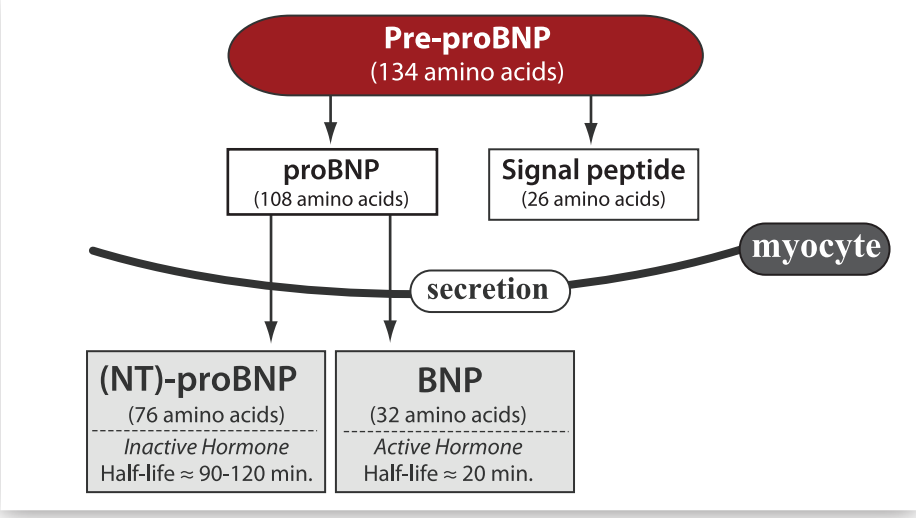


Figure 1: Secretion of N-terminal BNP and BNP from the cardiac myocyte.

renal insufficiency, and increased age. Obesity and AHFS pharmacologic treatment such as ACE inhibitors (ACEI) and angiotensin-renin blockers (ARB) can lower levels. Recommended "optimal" cut points for (NT)-proBNP have been suggested in the United States as 125pg/dl for those <75 years of age and 450 pg/dl for those ≥75 years of age. Natriuretic peptide levels are affected by renal function[21, 22] and this should be taken into account when they are used. Natriuretic peptide assays also possess variations that make it difficult to compare across platforms,[23] although this is unlikely to be clinically significant at the levels seen and acted upon in the ED.

Patient selection and the varied incidence of AHFS in the trials investigating these markers have made it difficult to extrapolate their exact findings to the general ED population. Sensitivities and specificities at different marker levels reflect physician estimates of the probability of an AHFS diagnosis. These assessments might be different under study circumstances than in a regular undifferentiated ED setting.[24] Variability can occur when comparing clinical trials to the general population due to patient selection and the prevalence or incidence of the outcome. Physician's estimates of the clinical probability for heart failure for subjects in the Breathing Not Properly Multinational Study (47% Low, 28% Uncertain, and 25% High), may not reflect a typical undifferentiated ED population.[24] This may explain some of the diagnostic test characteristic differences between the reported cohort and other populations.

Despite these limitations, BNP and (NT)-proBNP correlate quite well in predicting decreased EF and symptomatic AHFS. There are more similarities than differences between BNP and (NT)-proBNP (Table 2), thereby making assay selection more an issue of local preference and platform availability.

Despite these limitations, BNP and (NT)-proBNP correlate quite well in predicting decreased EF and symptomatic AHFS.

Several investigations have evaluated the prognostic ability of both natriuretic peptides. BNP may have the ability to predict future cardiac events[25] and may be better than a physician's ability to decide disposition strategy based on level of severity.[26] Similar findings have been reported for (NT)-proBNP.[27-29]

New Technologies for Detecting Heart Failure

Digitally Analyzed Heart Tones

Technology has been developed which may assist the clinician to better detect an S3 heart sounds at the bedside by measuring energy using an electronic stethoscope. Using a sophisticated software algorithm, information on the presence and intensity of an S3 can be made available in the ED. With continued development of such technology, our ability to detect extra heart sounds should improve significantly and potentially lead to improved diagnostic and prognostic strategies. Early results have shown promising specificity, an improvement in ED physician diagnostic confidence, and additive independent prognostic information.[30]

Vascular Pedicle Width and Cardiothoracic Ratio Measurements

A low-cost opportunity to enhance the non-invasive assessment of intravascular volume status entails the improved utilization of information already available on frequently obtained chest radiographs.[31] Vascular pedicle width (VPW) and cardiothoracic ratio (CTR) have been

Table 2. Comparison of N-terminal pro B-type natriuretic peptide (NT-proBNP) and B-type natriuretic peptide (BNP)

Property	NT-proBNP	BNP
Diagnostic cutpoints	300 pg/ml to exclude AHFS 1000 pg/ml to diagnose AHFS	100 pg/ml to exclude 500 pg/ml to diagnose
Half-life	• 60-120 minutes • Improved stability • May better differentiate mild AHFS because of better accumulation over time	• 20 minutes • Able to measure response to therapy at more frequent intervals
Renal insufficiency influences on diagnostic cutpoints	• Not extensively reported • Likely to have an influence on diagnostic cutpoints	Suggested cutpoint increased to 200 pg/ml
Age influences on diagnostic cutpoints	"Rule in" cutpoint should be adjusted based on age	• "Rule out" cutpoint left at 100 pg/ml to maximize sensitivity • "Rule in" cutpoint remains at 500 pg/ml
Prospectively validated in ED population	Yes	Yes

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reported to add to the differentiation of intravascular volume status using objective cutoffs.[31-33] Milne and colleagues initially described the borders and significance of the mediastinal vascular structures to distinguish the various causes of pulmonary edema and coined the term "vascular pedicle".[34] The radio-anatomic outline of the vascular pedicle is comprised of the azygous vein, superior vena cava, subclavian artery, and aorta (Figure 2).

Various factors associated with widening of the vascular pedicle demonstrate a correlation with blood volume.[34, 35] In one study, VPW and total blood volume were highly correlated (r=.80, p<.001) in upright, non-mechanically ventilated patients undergoing cardiac catheterization.[35] These investigators surmised that the observed widening of the vascular pedicle results from enlargement of the distensible right-sided venous structures of the mediastinal silhouette, namely the azygous vein and superior vena cava. Consequently, the width of the vascular pedicle may increase with intravascular volume administration and resultant venous distention, or with application of intrathoracic pressure leading to vascular compression. Of utmost importance, measurements reveal a high degree of reproducibility with high intra-reader and inter-reader correlation coefficients.[32, 36]

Vascular pedicle width measurements have been noted to vary with the manner in which the chest radiograph is performed. The VPW becomes wider with an anteroposterior view. Body position may also alter this measurement, such that an increase in the VPW occurs when moving from upright to supine positions as well as torso rotation to the right.

Like VPW, CTR has been reported to aid in the differentiation of intravascular volume status using objective cutoffs. Cardiothoracic ratio is calculated by dividing the maximum cardiac width by the maximum thoracic width.[37] Patients with a VPW > 70mm coupled with a CTR of > 0.55 are more than three times as likely to have a pulmonary artery wedge pressure > 18 mm Hg than are patients without these radiographic findings.[31, 32]

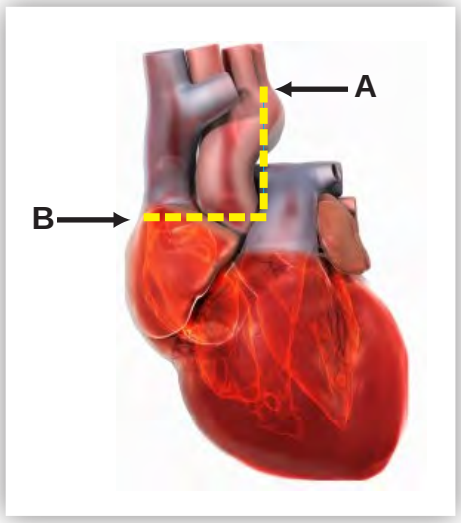

Figure 2: The radio-anatomic outline of the vascular pedicle is comprised of the azygous vein, superior vena cava, subclavian artery, and aorta. It is measured by: a) dropping a perpendicular line from the point at which the left subclavian artery exits the aortic arch (A) and b) measuring across the point at which the superior vena cava crosses the right main stem bronchus (B). Adapted with permission from Ely EW, Haponik EF. Chest 2002;121(3):942-50.

QRS Duration

QRS duration is an inexpensive measurement available on a standard ECG. A prolonged QRS ≥ ~120-150 ms has been used clinically as a marker of left ventricular dyssynchrony, poor prognosis in heart failure, selection criteria for cardiac resynchronization, remodeling, and reduced LVEF.[38, 39] Prolonged QRS has also been associated with increased mortality and sudden death in heart failure, as well as an independent predictor of cardiac death in a general medical population.[41-43]

These observations have been made in stable patients with chronic heart failure, known coronary artery disease, systolic dysfunction, or in the general population.[39-43] They have not been studied in the acutely decompensated patient with an unknown diagnosis.

Risk Stratification Models

Over the last fifteen years, several studies have considered ED-based risk models for heart failure patients.[7] Selker et al. developed a model to predict acute hospital mortality from data available to the ED physician within the first ten minutes of presentation - patients' age, systolic blood pressure and findings on ECG.[42] The model was prospectively validated for mortality, but its validity for morbidity and other acute sequelae is unknown. Additionally, the ability of the model to differentiate a low-risk patient that can be safely discharged home has not been assessed. The model was developed to identify the high-risk patient. Chin and Goldman developed a risk model using a larger number of variables including vital signs, comorbidities, ECG findings and laboratory data.[43] The model was successful in predicting morbidity as well as mortality, but it cannot accurately distinguish the low-risk patient. Katz et al. developed a model that could predict 81% of complications.[44] This model was based on ED information but included a 4-hour diuresis measure, making it unsuitable for use as a decision making tool in an emergency setting. Additionally, the results suggested a 19% missed complication rate making it unsuitable for safe implementation.

A recent study analyzed data from a registry of 65,275 patients with AHFS who were admitted to the hospital.[45] Using classification and regression tree methodology with recursive partitioning techniques, a model to predict in-hospital mortality was developed from 45 variables. The model is capable of predicting a risk for mortality as low as 2.1% and demonstrates that ED data can be used to identify low-, moderate-, and high-risk patient groups. Blood urea nitrogen, systolic blood pressure, and serum creatinine were the strongest predictors in this large report of in-hospital mortality in patients admitted with AHFS (Figure 3). While the author feels this model is perhaps the most compelling to date, it remains limited because 1) only the subset of admitted patients who required intravenous vasodilators were included, 2) only 39 of more than 100 variables available to the ED physician were considered, and 3) the model was designed only to predict mortality. An additional issue that has yet to be addressed in risk models using ED data is the relationship between the modeled events and the acute presentation for AHFS. It is not possible to show that the adverse outcomes were related to the acute event without intensive, prospective evaluation of outcomes.

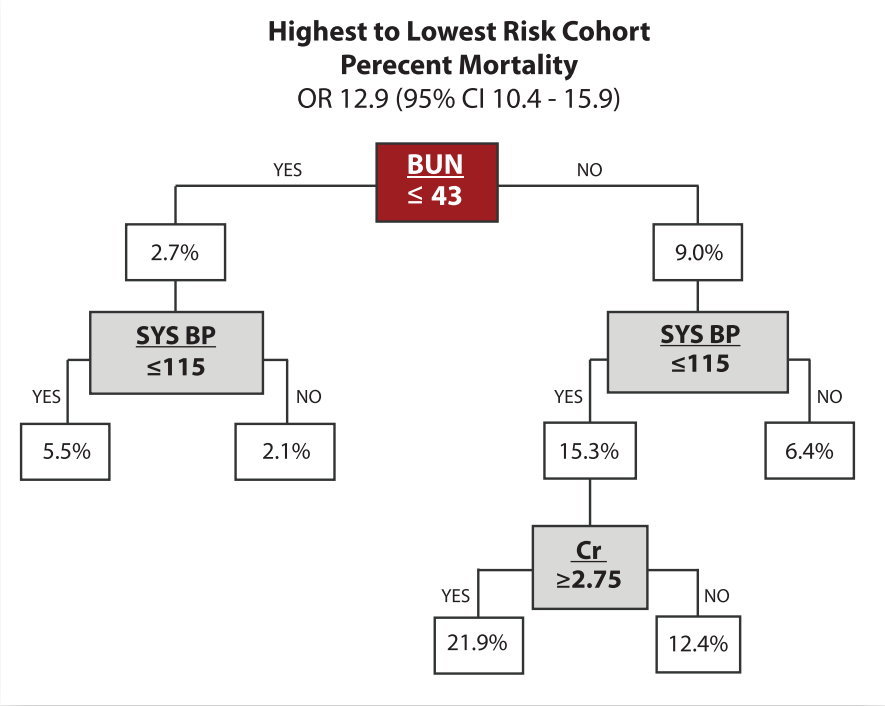

Figure 3: In-hospital crude mortality and risk stratification from the Acute Decompensated Heart Failure National Registry (ADHERE). An admission blood urea nitrogen (BUN) of 43 mg/dl or higher was the best predictor of in-hospital mortality, followed by a SBP < 115 mmHg. A serum creatinine level of 2.75 mg/dl or higher provided additional prognostic value. Adapted and reprinted with permission from Fonarow GC, et al. Risk stratification for in-hospital mortality in acutely decompensated heart failure: classification and regression tree analysis. Adapted with permission from Fonarow et al. JAMA 2005;293(5):572-80.

Other existing risk models for heart failure suggest this area of research will prove successful, but are limited for ED use (Table 3). They tend to be developed from retrospective review of inpatient charts using convenience samples and outcomes remote from the ED visit. While these models include data not generally available to the emergency physician, they provide some information which can provide a useful starting point for clinicians to base initial risk stratification decisions.

With the lack of validated risk-stratification tools, the observation unit (OU) provides a reasonable alternative to ED discharge or in-patient admission. An OU is an area where ED patients can receive extended evaluation and treatment for up to 24 hours in an attempt to further delineate their need for hospital admission. Preliminary research suggests the OU is a safe and resource efficient alternative to admission for AHFS patients.[46-53] Inappropriate candidates for the OU are those that have an expectation of 1) hospital stays greater than 48 hours, 2) diagnoses traditionally requiring hospitalization, 3) procedures or therapies requiring specialized hospital care, and 4) mortality.[54] Dispositions from OUs are usually made within 24 hours; however, because management for patients with AHFS is typically accelerated in the ED, OU stays of up to 48 hours can be considered.[55-58] Preliminary retrospective research has identified criteria that characterize AHFS patients suitable for safe OU admission and discharge. However, prospective validation is necessary to definitively characterize features of patients suitable for OU management so emergency physicians and cardiologists can increase OU utilization, decrease hospital admissions, and optimize care protocols.

A decision tool based on a validated ED risk model could improve assessment and initial disposition decisions. Similar approaches with other disease processes such as ACS and community acquired pneumonia have proven

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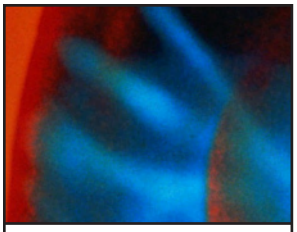
effective at safely decreasing admissions for low-risk patients. The ED OU could thus be a viable opportunity for disposition of low risk patients presenting with AHFS. A prospectively derived, multicenter, ED risk stratification model for patients with signs and symptoms of heart failure is needed and provides the focus of an ongoing National Heart, Lung, and Blood Institute R01 grant being directed by emergency medicine investigators.[59]

Summary

A change in the conservative decision paradigm for AHFS patients will require a novel approach. Even with the development of new diagnostic and prognostic tools, suboptimal ED risk stratification and the high rate of critical care admissions for AHFS patients have not changed in decades. Natriuretic peptides are most helpful to clinicians when there is an intermediate pre-test likelihood of disease, and the test is either very low or very high. Intermediate natriuretic peptide values are problematic and require further clinical correlation and investigation.[31, 32] Age, gender and to some extent, renal dysfunction, have an impact on natriuretic peptide levels and need to be considered when interpreting test results. Novel methods and markers are now being developed, many with very promising preliminary results, which could improve diagnosis and prognosis in the emergency setting. Optimally, a decision tool will be designed which can identify the low risk patient for continued care in an ED OU while allowing rapid disposition of the critically-ill AHFS patient to the intensive care unit or other inpatient setting.



A change in the conservative decision paradigm for AHFS patients will require a novel approach.

Table 3. Past modeling studies with reported outcomes and variables found to be significant indicators of risk.

Author / Year	N	Subject Type[a]	Study Type[b]	Outcome[c]	Significant Variables
Diercks / 2006	499	E	P	LOS <24h, 30 day events	SBP, troponin I
Burkhardt / 2005	385	I	R	Observation Unit discharge	BUN
Felker / 2004	949	I	R	60-day mortality/readmission	Age, SBP, BUN, Na, Hgb, # Past admits, Class IV symptoms
Lee / 2003	4031	I	R	30-day and 1 year mortality	Age, SBP, RR, BUN, Sodium
Harjai / 2001	434	I	R	30-day readmission	Sex, COPD, Prior admits
Rame / 2001	112	E	R	3-month readmission and mortality	RR
Cowie / 2000	220	I	R	16-month mort	SBP, Creatinine, Rales
Butler / 1998	120	I	R	Inpatient complications	O^2 sat, Creatinine, Pulmonary edema
Villacorta/1998	57	I	R	Inpatient and 6-month mortality	Sodium, Sex
Chin / 1997	257	I	R, S	60-day readmission and mortality	Marital status, Comorbidity Index Admit SBP, No ST-T changes
Chin / 1996	435		R	Inpatient complications	Initial SBP, RR, Sodium, ST-T changes
Selker / 1994	401	I	PA, R	Inpatient mortality	Age, SBP, T-wave flattening, HR
Brophy / 1994	153	E	P	44-month mortality	Prior HF admission, Sodium, IVCD, Amount furosemide given
Brophy / 1993	153	E	P	LOS and 6-month mortality	Left atrial size, Cardiac ischemia, Slow response to diuresis
Esdaile / 1992	191	I	PA, R	Inpatient mortality	Age, Chest pain, Cardiac ischemia, Valvular dz, Arrhythmia, New onset, Poor clinical response
Katz / 1988	216		R	2-day complications	4-hour diuresis, History of pulmonary edema, T-wave abnormalities, JVD
Plotnick / 1982	55		PA, R	Inpatient and 1-year mortality	Admit SBP, Dyspnea, Peak CPK

[a] I = In-patients, E = emergency department patients

[b] R = retrospective chart review, PA = patient assessment, S = survey, P = prospective

[c] Complications include mortality, LOS = length of stay

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CME Post Test

After you have read the monograph carefully, record your answers by circling the appropriate letter answer for each question.

1. **Both the incidence and prevalence of heart failure is decreasing in developed countries.**
   a. True
   b. False

2. **Acute Heart Failure Syndrome has been defined as a gradual or rapid change in heart failure signs and symptoms resulting in a need for urgent therapy.**
   a. True
   b. False

3. **The following describe natriuretic peptide testing for heart failure:**
   a. National organizations have recognized a "grey zone" for interpreting values
   b. Levels can be affected by renal function
   c. Elevated levels can be found after pulmonary embolism
   d. a and c
   e. a, b, and c

4. **Unlike acute myocardial infarction, acute heart failure syndrome has clearly defined therapeutic targets that lower 60-day mortality.**
   a. True
   b. False

5. **Preliminary AHFS risk models have identified factors such as BUN, serum creatinine, and systolic blood pressure as predictors of mortality in hospitalized patients with heart failure.**
   a. True
   b. False

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