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Rapid Clinical Assessment of Hemodynamic Profiles and Targeted Treatment of Patients with Acutely Decompensated Heart Failure

GREGG C. FONAROW, M.D. AND JIM EDWARD WEBER, D.O.*

The Ahmanson-UCLA Cardiomyopathy Center, UCLA Division of Cardiology, David Geffen School of Medicine at UCLA, Los Angeles, California; *Department of Emergency Medicine, University of Michigan, Ann Arbor, Michigan, USA

Summary: Acutely decompensated heart failure (ADHF) is characterized by hemodynamic abnormalities and neurohormonal activation that contribute to heart failure (HF) symptoms, end-organ dysfunction, arrhythmias, and progressive cardiac failure. The management of ADHF in the emergency department (ED) can be simplified and improved by a 2-min bedside assessment that identifies any of four possible hemodynamic profiles on the basis of clinical signs and symptoms. The profiles are based on whether congestion is present or absent (wet or dry) and perfusion is adequate or limited (warm or cold). A wet-warm profile is seen more frequently in the ED than any of the other three profiles (wet-cold, dry-warm, and dry-cold). The four clinically determined profiles have been shown to predict clinical outcomes and may be used to guide initial HF therapy. The goals of treating ADHF are to stabilize the patient, reverse acute hemodynamic abnormalities, rapidly reverse dyspnea and/or hypoxemia caused by pulmonary congestion, and initiate treatments that will decrease disease progression and improve survival. An ideal agent for the wet-warm profile would rapidly reduce pulmonary congestion, produce balanced arterial and venous dilation, promote natriuresis, lack direct positive inotropic effects, and not cause reflex neuroendocrine activation. Intravenous nesiritide in conjunction with loop diuretics has been found safe and effective as initial treatment for patients with the wet-warm profile. For the wet-cold profile, more intensive therapy and invasive hemodynamic monitoring may prove useful. This review will discuss the rapid clinical determination of hemodynamic profiles in patients presenting to the ED with ADHF and the options for their initial medical management. Case studies representing the wet-warm, wet-cold, dry-warm, and dry-cold profiles will be presented and discussed.

Key words: acutely decompensated heart failure, bedside assessment, emergency department, hemodynamic profile, natriuretic peptide, vasodilators

Acronyms

ADHERE®	Acute Decompensated Heart Failure National Registry
ADHF	acutely decompensated heart failure
ANP	A-type natriuretic peptide
BNP	B-type natriuretic peptide
BUN	blood urea nitrogen
CAD	coronary artery disease
CCU	coronary care unit
CI	cardiac index
DCM	dilated cardiomyopathy
ECG	electrocardiogram
HTN	hypertension
JVP	jugular venous pressure
LV	left ventricular
LVEF	left ventricular ejection fraction
OPTIME-CHF	Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure
PCWP	pulmonary capillary wedge pressure
PE	pericardial effusion

Drs. Fonarow and Weber are consultants and are involved in research for Scios and are members of its Scientific Advisory Board and Speakers' Bureau.

Addresses for reprints:

Gregg C. Fonarow, M.D.
The Eliot Corday Chair in Cardiovascular Medicine and Science
Professor of Medicine, UCLA Division of Cardiology
Director, Ahmanson-UCLA Cardiomyopathy Center
Director, UCLA Cardiology Fellowship Training Program
10833 Le Conte Avenue
CHS 47-123, Div. of Cardiology
Los Angeles, CA 90095, USA
e-mail: gfonarow@mednet.ucla.edu

Jim Edward Weber, D.O.
Assistant Professor of Emergency Medicine
University of Michigan, Ann Arbor, MI and
Director of Research, Hurley Medical Center, Flint, MI
One Hurley Plaza
Department of Emergency Medicine
Hurley Medical Center
Flint, MI 48503, USA
e-mail: jwmd@umich.edu

RF	renal failure
RHC	right heart catheterization
SVR	systemic vascular resistance
VMAC	Vasodilation in the Management of Acute Congestive Heart Failure

Introduction

Patients presenting to the emergency department (ED) with acutely decompensated heart failure (ADHF) pose a major health care problem.[1] They often are hemodynamically unstable and have disabling symptoms of dyspnea secondary to pulmonary congestion. Rapid assessment and treatment are frequently required to achieve clinical stability and obviate mechanical ventilation. After evaluation and stabilization in the ED, most patients will require hospital admission, although a low-risk subset may merit discharge following a period of observation. The in-hospital mortality for ADHF is 5–8%, the median duration of hospitalization is 5 days, and the rate of rehospitalization over the next 6 months is as high as 50%.[1, 2] From the years 1979 to 2000, the combined number of ED visits and subsequent rehospitalizations for ADHF increased from 377,000 to 999,000.[2] The estimated annual expenditure for inpatient management of ADHF is $12.7 billion.[2]

The goals in managing ADHF are to reverse acute hemodynamic abnormalities, rapidly relieve symptoms, and initiate treatments that will decrease disease progression and improve survival (Table I). In the past, ADHF was often viewed as merely a disorder of volume overload and low cardiac output. Early treatment strategies that focused on efforts to maximize cardiac output led to increased mortality.[3] Monotherapy with intravenous (IV) diuretics led to further increases in systemic vascular resistance (SVR) and additional deleterious neurohormonal activation.[4] It is now recognized that ADHF encompasses a range of hemodynamic profiles that can be clinically characterized to guide therapy. In most cases, ADHF is characterized by elevated left ventricular (LV) filling pressures (congestion) that reflect a combination of increased SVR and insufficient systolic and diastolic myocardial functional reserve.[3, 5, 6] This realization has shifted the treatment emphasis from diuretic monotherapy and/or IV inotropic agents to IV natriuretic peptides and vasodilators in combination with diuretics.[5] This more physiologic approach has been shown to relieve symptoms more rapidly and reduce morbidity more effectively. Thus, it has the potential to curb rising health care costs by reducing admissions, length of stay (LOS), and rehospitalization.

TABLE I Therapeutic goals in acutely decompensated heart failure

Goals	Endpoints or methods
Rapidly reverse acute hemodynamic abnormalities	Lower pulmonary capillary wedge pressure
Rapidly relieve symptoms and improve respiratory status	Relief of dyspnea and/or hypoxemia
Initiate treatment that will slow disease progression and improve long-term survival	Use of ACE inhibitors, beta blockers, and aldosterone antagonists prior to hospital discharge
Apply treatments cost effectively	Shortened EMC and hospital LOS, minimal use of ICU/CCU

Abbreviations: ACE = angiotensin-converting enzyme, CCU = coronary care unit, EMC = emergency medical care, LOS = length of stay, ICU = intensive care unit.

Hemodynamic Mechanisms in Acutely Decompensated Heart Failure

Until recently, the pathogenesis of ADHF was attributed to impaired contractility (systolic failure) and fluid accumulation in the lungs secondary to systemic volume overload.[6] It is now recognized that (1) no change in LV ejection fraction (LVEF) occurs with acute decompensation of chronic heart failure (HF) or after its reversal;[5, 6] (2) LV function is entirely normal in up to half of patients hospitalized for ADHF;[6] and (3) while decompensation of HF and pulmonary edema are almost always accompanied by elevated LV filling pressures and SVR, cardiac index (CI) may be low, normal, or increased.[5] Decompensation of HF and pulmonary edema may develop rapidly, within minutes or even over a few hours. Therefore, net fluid accumulation cannot be the sole mechanism of pulmonary edema. Recent data instead implicate a process in which a portion of the intravascular volume is redistributed to the lungs.[5, 6] Increases in SVR contribute to this rapid redistribution of fluid. Gandhi *et al.* found that echocardiographic LVEF was almost within normal range (LVEF = 0.50 ± 0.15) in patients presenting to the ED with pulmonary edema.[6] The most significant finding during acute pulmonary edema was diastolic dysfunction and elevated SVR.[6] Thus, peripheral vasoconstriction plays a major role in the process of decompensation in systolic and isolated diastolic dysfunction. In ADHF, an inappropriate increase in SVR is met with insufficient systolic and diastolic myocardial functional reserve.[5] This afterload mismatch causes a vicious cycle of events that sequentially includes atrioventricular valvular regurgitation, a decrease in forward stroke volume, and an increase in LV diastolic pressure. The increased LV diastolic pressure is transferred backward to the pulmonary veins, leading to pulmonary edema. Thus, the primary pathophysiologic mechanism of ADHF is elevation of LV filling pressure and fluid redistribution to the lungs as a result of afterload mismatch (excess vasoconstriction) rather than decrease in contractility. These hemodynamic alterations contribute to the symptoms, functional limitations, and clinical decompensation that result in ED visits and hospitalizations.[3, 5]

The hemodynamic parameter most closely related to symptoms of decompensation of HF and adverse clinical outcomes is elevation in LV filling pressures. Persistent elevation in LV filling pressures has been associated with an increased risk of progressive HF, sudden death, and overall mortality in patients hospitalized with decompensated HF. In a study of 1,156 patients hospitalized with ADHF due to systolic

dysfunction (mean LVEF = 0.20 ± 0.07) and treated with IV vasodilators and diuretics, the achievement of near-normal LV filling pressures (pulmonary capillary wedge pressure [PCWP] < 16 mmHg) resulted in a 1-year survival of 82% compared with only 65% (p = 0.00001) in patients with persistently elevated LV filling pressures (PCWP > 18 mmHg) (Fig. 1).[7] Hemodynamic measures at baseline such as right atrial pressure, pulmonary arterial pressure, systemic arterial pressure, CI, and heart rate were not predictive of mortality.[7] Multivariate analysis showed that independent predictors of total mortality at 1 year were a high PCWP (p = 0.001), low serum sodium (p = 0.002), increased LV end-diastolic dimension (p = 0.01), and low peak oxygen consumption on cardiopulmonary exercise testing (p = 0.001).[7] Contrary to conventional expectations, changes in CI have not been found predictive of outcome (Fig. 2).[7, 8] It has also been shown that even at levels below symptom threshold, elevated PCWP predicts worse outcome in patients with HF.[8] B-type natriuretic peptide (BNP), which is released from the cardiac ventricles in response to pressure or volume stimulus,[9] is elevated in patients with HF and closely correlates with elevated LV filling pressures. Levels of BNP have also been shown to predict independently rehospitalization or death in patients hospitalized with HF.[10] Elevations of LV filling pressure (whether determined by biologic assay or direct hemodynamic measurement, or inferred by symptoms of orthopnea) are associated with increased symptoms, more frequent hospitalizations, and increased mortality.[5]

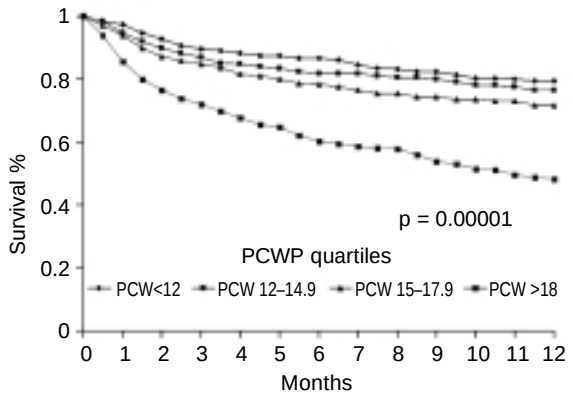

FIG. 1 Kaplan-Meier survival for 1,156 patients with acutely decompensated heart failure who are subgrouped for response to treatment, as defined by quartiles of pulmonary capillary wedge pressure (PCWP). On multivariate analysis, PCWP was an independent predictor of mortality, but resting cardiac index was not.[7]

Clinical Assessment of Hemodynamic Profiles

The rapid clinical assessment of patients with ADHF has been simplified by the introduction of a 2-min bedside examination that relies on physical signs and symptoms to determine which of the four possible hemodynamic profiles is present. This assessment, based on findings by Forrester *et al.* in patients with acute myocardial infarction,[11] has been described by Nohria *et al.*[12] The earlier work established correlations between clinical findings and hemodynamic measurements (PCWP and CI) that were obtained by Swan-Ganz catheterization. In addition, Forrester *et al.* showed that, in patients with acute myocardial infarction, physical findings could be used to identify four hemodynamic profiles that were predictive of short-term survival.[11] It has recently been shown that the classification of patients with advanced HF by these same four hemodynamic profiles can be used to predict early and late mortality.[12]

The assessment of patients with HF is based on whether clinical symptoms indicate that filling pressure is or is not elevated (wet or dry) and perfusion is or is not adequate (warm or cold), with combinations of these parameters yielding four possible hemodynamic profiles (Fig. 3). It relies on symptoms that have been shown to predict pulmonary artery catheter measurements that define congestion (wet) and hypoperfusion (cold); a PCWP ≥ 18 mmHg and a CI ≤ 2.2 l/min/m^2, respectively.[12] More than 80% of patients presenting to the

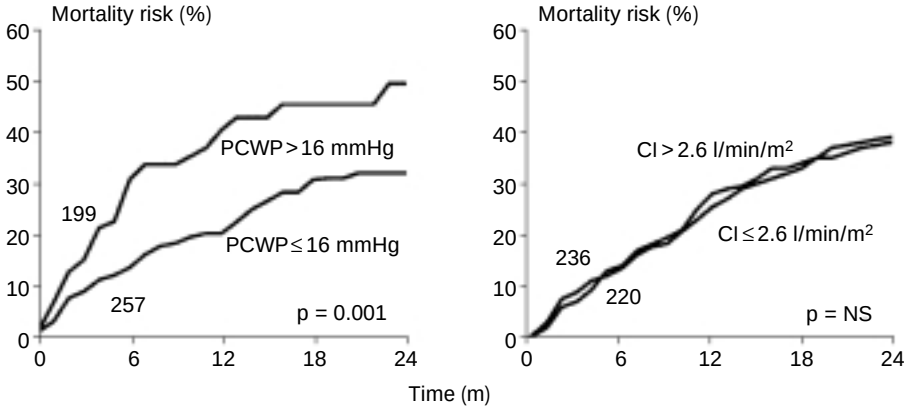

FIG. 2 Hemodynamic assessment in 456 heart failure patients after tailored therapy. In-hospital pulmonary capillary wedge pressure was predictive of subsequent mortality (p = 0.001), whereas cardiac index was not.

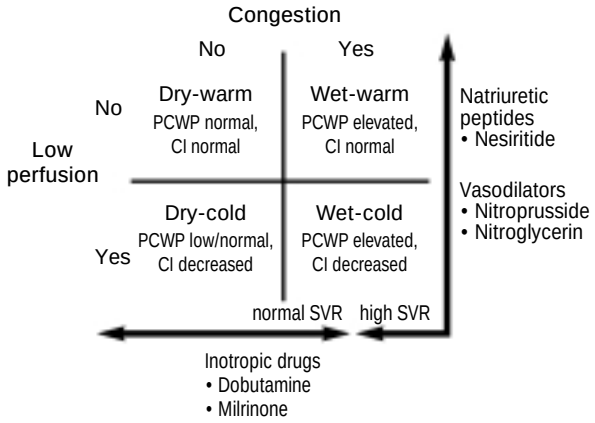

FIG. 3 Rapid clinical assessment of hemodynamic profiles. Bedside physical findings can be used to classify patients into four hemodynamic profiles based on whether the findings indicate a pulmonary capillary wedge pressure (PCWP) that is normal or elevated (congestion) and a cardiac index (CI) that is normal or decreased (low perfusion). Patients hospitalized with acutely decompensated heart failure usually have evidence of congestion (wet-warm or wet-cold). Patients with a wet-warm profile are ideally treated with intravenous nesiritide or another vasodilator in conjunction with an intravenous loop diuretic. SVR = systemic vascular resistance.

ED with ADHF have clinical congestion (i.e., are classified as being wet) and, if right heart catheterization were performed, would show elevated PCWP.[3] These patients may have adequate (wet-warm) or reduced (wet-cold) perfusion, with the majority showing elevation in SVR. Clinical indicators of congestion in the assessment of patients with HF include a recent history of orthopnea and/or evidence on physical exam of jugular venous distention, hepatojugular reflux, ascites, periperal edema, leftward radiation of the pulmonic heart sound, or a square wave blood pressure response to the Valsalva maneuver.[12] These indicators vary in utility. Rales are entirely absent in more than 80% of patients with chronically elevated filling pressures due to compensation of the pulmonary lymphatics.[3] Peripheral edema is a relatively insensitive indicator of elevated filling pressures in patients with HF and may have a noncardiac cause. A third heart sound may or may not be detected.[3] A patient with ADHF without congestion (dry) may have adequate (dry-warm) or compromised (dry-cold) perfusion. Compromised perfusion (cold) is indicated by a narrow proportional pulse pressure ([systolic – diastolic blood pressure]/systolic blood pressure < 25%), pulsus alternans, symptomatic hypotension in the absence of orthostasis, cool extremities, and/or impaired mental status.[12] The most assessable indicators of perfusion are blood pressure and pulse pressure.[3] In the assessment described by Nohria *et al.*, physicians synthesize findings on the presence or absence of the clinical indicators to make a subjective determination of the hemodynamic profile.[12]

The prognostic utility of the clinical profiling method was prospectively evaluated in 452 consecutively hospitalized patients with HF, 49% of whom had an admitting diagnosis of decompensated HF.[12] At baseline, 123 (27%) were classified as dry and warm, 222 (49%) as wet and warm, 91 (20%) as wet and cold, and 16 (4%) as cold and dry.[12] The profiles were predictive of outcome. Patients with the dry and warm profile had a low 6-month mortality relative to the three other profile groups (Table II).[12] Profiles wet and warm and wet and cold were independently associated with increased risk of death or cardiac transplant by univariate analysis (p = 0.02 and 0.003, respectively), and these two profiles were also independent predictors of the same endpoint (hazard ratio [HR] 1.83, p = 0.02; HR 2.48, p = 0.002, respectively).[12]

Modification of Clinical Profiles to Include the Cardio-Renal Syndrome

Increasingly, a significant number of patients with the wet and warm profile or wet and cold profile present with renal dysfunction. Elevated serum creatinine is an independent negative prognostic indicator in patients admitted with decompensated HF.[13, 14] Furthermore, preexisting renal dysfunction is a key predictor for developing worsening renal function during the treatment of decompensated HF.[15] A deterioration in renal function as a consequence of HF therapy has been associated with increased LOS and increased mortality.[15, 16] Therefore, special attention must be given to patients with renal dysfunction.

Treatment Strategies

The hemodynamic classification system may prove useful as a guide to initial therapy in patients with ADHF. An ideal agent for a patient with ADHF and congestion (wet and warm or wet and cold profile) would be one that rapidly reduces PCWP and consequently relieves symptoms of congestion and hypoxia, produces balanced arterial and venous dilation, promotes natriuresis, lacks direct positive inotropic effects, and does not cause reflex neurohormonal activation (Table III).[5] The initial treatment options for decompensated HF include IV loop diuretics, inotropic agents, vasodilators, and the natriuretic peptides.

Intravenous Loop Diuretics

Despite having been used as front-line therapy in patients with ADHF for many decades, IV loop diuretics have been

TABLE II Six-month mortality by clinically determined hemodynamic profiles[12]

Patient profile	N (%)	Six-month mortality (%)
Dry-warm	123 (27)	11
Wet-warm	222 (49)	22
Wet-cold	91 (20)	40
Dry-cold	16 (4)	17

TABLE III Characteristics of an ideal agent for patients with acutely decompensated heart failure and congestion (wet-warm or wet-cold profile)

- Produces vasodilation (venous and arterial)
- Rapidly decreases ventricular filling pressures
- Rapidly decreases symptoms of congestion
- Does not increase heart rate or directly increase contractility (decreases myocardial oxygen demand)
- Is not proarrhythmic
- Does not cause tachyphylaxis
- Provides neurohormonal suppression
- Promotes diuresis and natriuresis
- Is conveniently dosed (can be used with or without invasive hemodynamic monitoring)

sparsely studied in this role.[4] Acute use of IV furosemide causes a significant decrease in PCWP and right atrial pressure, an effect attributable to both venodilation and diuresis.[4] Concomitant effects, however, include a decrease in stroke volume, an increase in SVR, and pronounced neurohormonal activation.[17] Increases in activation of the renin-angiotensin-aldosterone system and the sympathetic nervous system (as reflected by plasma norepinephrine levels) occur shortly after a single IV dose of furosemide.[17] In a comparative trial, patients on high-dose IV loop diuretics did significantly worse than did patients on a combination of a low-dose counterpart and an IV vasodilator in all primary and secondary outcome measures, including need for mechanical ventilation (40 vs. 13%, $p = 0.004$).[18] By causing further neurohormonal activation and systemic arterial constriction, IV loop diuretics prevent normalization of ventricular filling pressures and limit relief of HF symptoms, setting the stage for early rehospitalization.

The deleterious effects of diuretic therapy on neurohormonal activation can also lead to renal vasoconstriction and decreased renal perfusion. While diuretics increase urinary volume, they often do so at the expense of decreased renal clearance.[19] This decline in the glomerular filtration rate not only results in decreased delivery of sodium and water, but also decreased delivery of diuretic medications. These effects can translate into diuretic refractoriness and progressive renal dysfunction. The development of renal dysfunction often leads to withdrawal of angiotensin-converting enzyme (ACE) inhibitors and diuretics until the creatinine normalizes, and frequently the patient is discharged with persistent volume overload and symptoms. A retrospective analysis of 48 patients hospitalized with decompensated heart failure demonstrated that 21% develop worsening renal dysfunction (mean creatinine 1.6 ± 0.3 to 2.6 mg/dl) as a consequence of diuretic therapy for decompensated heart failure.[15] This rise in creatinine was associated with an increased LOS (9 to 17 days) and increased mortality (relative risk [RR] 5.3).[15] Thus, IV loop diuretics may be required to reduce congestion in patients who are of the wet and warm profile and wet and cold profile, but may be more effective when combined with IV natriuretic peptides or vasodilators.

Inotropic Agents

The main effect of IV inotropic therapy in HF is to improve CI. Moreover, the use of IV inotropes in HF has been linked to an increased frequency of adverse events and, in some trials, increased mortality.[20] The Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF) study randomized 949 patients hospitalized with ADHF to treatment with placebo or a 48-h infusion of milrinone (0.5 mcg/kg/min) and found that the inotropic agent did not reduce LOS and was associated with a significantly greater frequency of adverse events (13 vs. 2%, $p < 0.001$) and a trend toward increased mortality (4 vs. 2%).[21] Compared with milrinone, the inotropic agent dobutamine is less likely to cause hypotension and is much less expensive, but it also increases heart rate and the risk of developing arrhythmias. Dopamine is frequently infused at low doses to attempt to improve renal blood flow and diuresis, but clinical trials have failed to demonstrate increases in urine output.

Positive inotropic agents pose risks of aggravating ischemia and arrhythmias. Weaning from inotropic support is often necessarily slow, potentially prolonging hospitalization, and may necessitate complex adjustment of concomitant oral regimens. Prolonged physiologic effects of inotropic infusions during hospitalization may mask inadequacy of a diuretic regimen and intolerance to vasodilator doses, setting the stage for readmission.[3] There is concern that the use of inotropes upon admission for decompensated HF may create inotrope dependence. Trials of outpatient use of dobutamine, milrinone, vesnarinone, enoximone, and xamoterol have shown increased mortality compared with placebo.[20]

Although the risk–benefit ratio of inotropic infusion is unfavorable for the majority of patients presenting with decompensated HF, this therapy can be life saving in patients with cardiogenic shock. Moreover, brief inotropic therapy may be appropriate for patients with acute decompensation and the dry and cold or wet and cold profile.[3]

Intravenous Vasodilators

There is a relatively sound physiologic rationale for using IV vasodilators to reverse acute HF decompensation, since such therapy primarily targets elevations of ventricular filling pressures and SVR.[5] Intravenous vasodilator therapy has not been associated with a worsening of myocardial ischemia (and actually reduces myocardial oxygen consumption) or the precipitation of ventricular arrhythmias,[3] and can ease and speed the transition to an oral regimen of an ACE inhibitor and diuretic.[22] A significant reduction (and near normalization) in ventricular filling pressures can be achieved with IV vasodilators and diuretics within 3 to 24 h in decompensated patients with HF with the wet and warm profile and the wet and cold profile with elevated SVR. These improved hemodynamics can be maintained over the following 8 months with an oral regimen of an ACE inhibitor and a diuretic.[23] Thus, IV vasodilators promote the rapid reversal of decompensation with complete or near normalization of resting hemodynamics that can then be maintained long term with an oral HF medical reg-

imen.[24] The vasodilator strategy can also facilitate the more rapid initiation and titration of other survival-enhancing HF medications, such as beta blockers, by promoting the rapid resolution of volume overload.

Sodium nitroprusside, a potent direct vasodilator, rapidly lowers filling pressures through venous and arterial vasodilation, with increases in cardiac output and consequent improvement in response to IV diuretics.[3] However, the administration of nitroprusside requires invasive monitoring with a pulmonary artery catheter in a cardiac care unit with suitably trained nurses and a staff capable of frequent dose titration. Monitored nitroprusside infusion rarely causes symptomatic hypotension, but is occasionally complicated by cyanide toxicity, the risk of which increases with dose, duration, and hepatic and renal dysfunction. In addition, nitroprusside has been shown to reduce renal perfusion in patients with preexisting renal dysfunction.[25]

Intravenous nitroglycerin, which causes arterial and venous dilation in patients with ADHF, has not undergone extensive clinical evaluation in this role. The Vasodilation in the Management of Acute Congestive Heart Failure (VMAC) trial showed a reduction in filling pressures with IV nitroglycerin comparable with placebo when added to standard care.[26] Headache as a side effect can limit the use of this agent. Dosing can be guided with or without invasive hemodynamic monitoring. Frequent up-titration in dose is required to achieve adequate symptomatic response. With higher doses of IV nitroglycerin, early tachyphylaxis has been seen.[27] The effect of nitroglycerin on neurohormonal activation has not been well studied.

Natriuretic Peptides

Endogenously generated natriuretic peptides, such as A-type natriuretic peptide (ANP) and B-type natriuretic peptide (BNP), are activated in response to atrial and ventricular pressure or expansion. The natriuretic peptide system counterregulates the sympathetic nervous system and has been shown to decrease plasma levels of epinephrine, aldosterone, and endothelin.[28] When stimulated, natriuretic peptide receptors activate guanylyl cyclase, causing an increase of intracellular cyclic guanosine monophosphate (cGMP) at the target organ, which mediates some of their effects. Studies have shown that BNP produces balanced vasodilation as well as some degree of natriuresis and lusitropy.[28] A rare property of natriuretic peptides is the ability to reduce LV filling pressures without an increase in heart rate or myocardial oxygen demand.[29]

Nesiritide is a recombinant form of human BNP approved for treatment of ADHF.[26, 30] It possesses many of the characteristics of an ideal agent for treating patients with ADHF, particularly those of the wet and warm profile (Table III). The IV administration of nesiritide has been shown to produce favorable hemodynamic effects, including balanced vasodilation associated with a rapid improvement in HF clinical symptoms. Administration of nesiritide produces a dose-related reduction in ventricular filling pressures and augmentation of LV stroke volume due to afterload reduction.[26] These effects appear to be sustained during continuous administration over 48 h and, compared with nitroglycerin, nesiritide produces more rapid reduction in PCWP and fewer adverse effects. The VMAC trial demonstrated that a 2 mcg/kg IV bolus given over 1 min followed by a fixed infusion of 0.01 mcg/kg/min reduces PCWP rapidly, significantly, and safely while improving self-reported scores on dyspnea index scales in patients who do or do not undergo monitoring of central hemodynamics by pulmonary artery catheter.[26] In this study, nesiritide was added to standard therapy (including dobutamine, dopamine, and parenteral diuretics) in patients hospitalized with ADHF due to a wide variety of causes. Compared with placebo plus standard care, nesiritide plus standard care produced greater hemodynamic and clinical benefits with fewer adverse effects.

Nesiritide may be started simultaneously with, or just prior to, IV diuretic therapy during the initial presentation of patients with ADHF and a wet and warm profile. It can be administered to wet and cold profile patients in conjunction with dopamine or inotropic agents such as dobutamine if these other agents are indicated. Nesiritide can be safely administered in the ED, observation unit, inpatient-telemetry or step-down unit, or other settings that generally cannot provide intensive monitoring.[26] Proarrhythmia has not been observed, and ventricular arrhythmias,[31] ventricular tachycardia events per 24 h,[32] repetitive ventricular beats/h,[32] and premature ventricular beats/h[32] occur much less commonly with nesiritide than with inotropic agents such as dobutamine. This is important because a history of ventricular arrhythmia is common among patients with acute HF. Whereas inotropic agents have been associated with increases in the incidence of myocardial infarction and in mortality in patients with coronary artery disease, nesiritide has not.[26] In the VMAC trial, symptomatic hypotension occurred in 4 and 5% of patients treated with nesiritide and nitroglycerin, respectively.[26] Nesiritide-induced hypotension caused no adverse sequelae and was easily reversed (fluid administration and/or patient repositioning). With a half-life of 15 to 20 min, nesiritide should not be titrated at frequent intervals as is done with other IV agents that have a shorter half-life.

Guiding of Initial Treatment by Clinical Profiles

Recent data suggest that both the timing and choice of initial therapy in the ED can have a significant impact on a patient's hospital course and clinical outcome, as well as intensity of care required. Early initiation of IV vasoactive medications appears to decrease inpatient LOS. From the Acute Decompensated Heart Failure National Registry (ADHERE®), patients who received vasoactive therapy in the ED had an overall LOS of 3.0 days, compared with 7.0 days if treatment was delayed until inpatient unit arrival ($p < 0.0001$).[33] A similar pattern was seen in the intensive/coronary care unit (ICU/CCU), where those patients treated with vasoactives in the ED showed a significantly shorter LOS than did those receiving in-hospital treatment (2.1 vs. 4.5 days, $p < 0.0001$).[33] Because a majority of patients with HF are seen initially in the ED, methods must be developed for the rapid identification of patients likely to benefit from early vasoactive therapy.[33]

For patients in the most common hemodynamic profile (wet and warm), the immediate goal of therapy is symptom relief and lowering of ventricular filling pressures (Table I). These patients are ideal candidates for nesiritide in conjunction with IV loop diuretics. Patients with the wet and cold profile may require more intensive therapy to achieve adequate diuresis, perhaps even with guidance by invasive hemodynamic measurements. These patients may have low cardiac output in the setting of elevated SVR and still respond well to natriuretic peptides or vasodilators in conjunction with diuretics (Fig. 3). Wet and cold profile patients with decreased or normal SVR may be good candidates for short-term inotropic therapy. The dry and warm profile patients have a good prognosis, do not require IV therapy, may not require hospitalization, and merit investigation of whether symptoms are due to non-ADHF causes (Fig. 4). Patients with the very uncommon dry and cold profile may benefit from a decrease or withdrawal of recently initiated beta blockers until better compensation is achieved. Bedside clinical profiling can also be used as a prognostic tool that guides triage decisions.

Optimization of Oral Heart Failure Therapies

After reversal of acute decompensation, comprehensive neurohormonal blockade with ACE inhibitors, beta blockers, and aldosterone antagonists can be initiated or dose adjusted

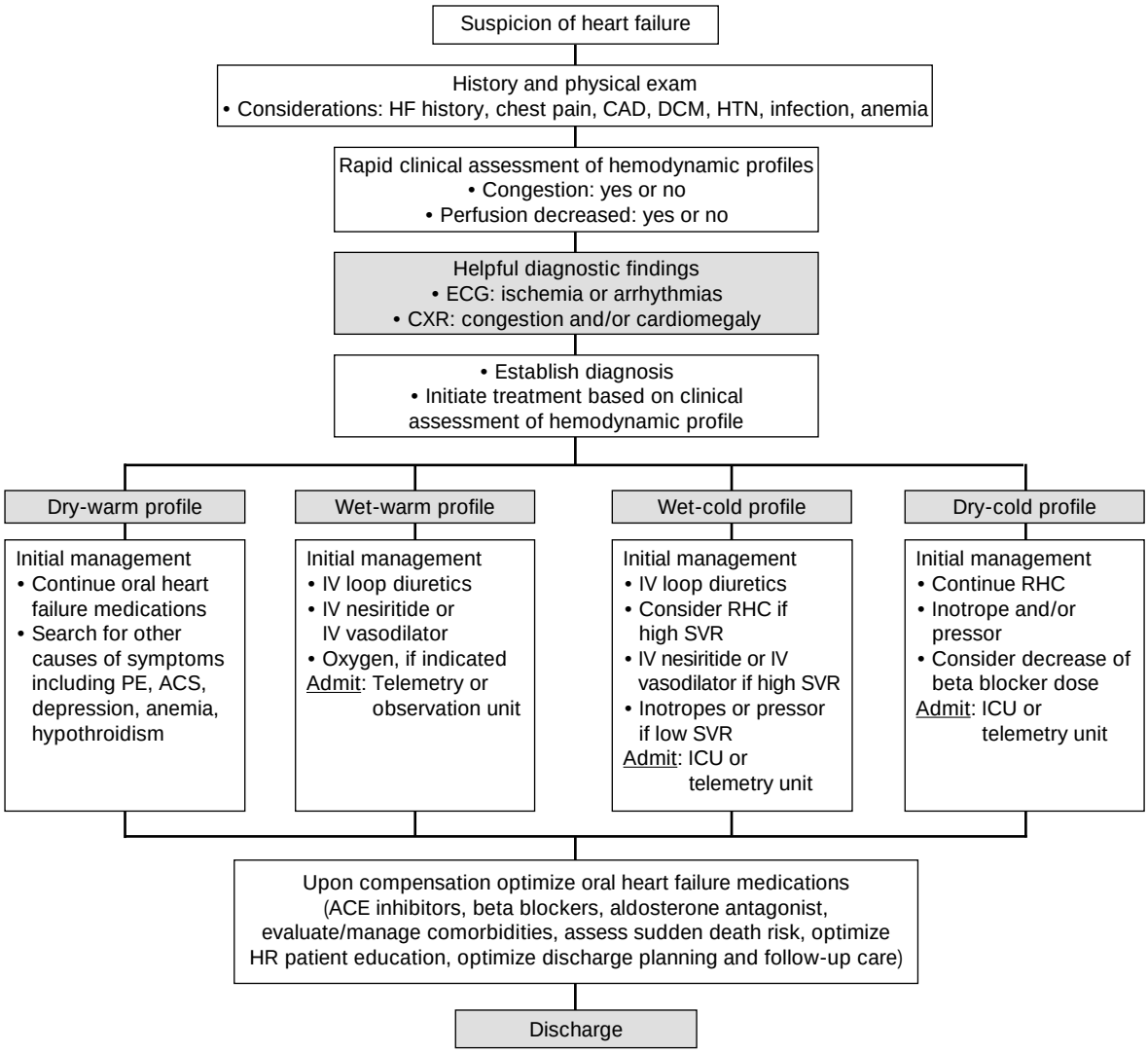

FIG. 4 Assessment and treatment algorithm for acutely decompensated heart failure. Initial heart failure treatment can be guided on the basis of the clinically assessed hemodynamic profiles. ACE = angiotensin-converting enzyme, ACS = acute coronary syndrome, CAD = coronary artery disease, BNP = B-type natriuretic peptide, CXR = chest x-ray, DCM = dilated cardiomyopathy, ECG = electrocardiogram, HF = heart failure, HTN = hypertension, ICU = intensive care unit, IV = intravenous, PE = pericardial effusion, RHC = right heart catheterization, minimal use of ICU/CCU, SVR = systemic vascular resistance.

to reduce disability or risk of hospitalization and death further.[1] Patients should be assessed for significant comorbidities, potential need for revascularization, and risk of sudden death. Nonpharmacologic therapy should be optimized and patient education provided prior to discharge.[1, 24] When combined with a comprehensive HF management program, the use of IV vasodilators to normalize ventricular filling pressure and oral HF medications to maintain this effect has been associated with an 85% reduction in hospitalization and improved functional capacity compared with conventional HF management.[24] The ED use of IV nesiritide as initial treatment to reverse decompensation rapidly may allow for earlier administration of beta blockers and other HF therapies that are contraindicated during decompensation. Thus, emergency physicians can contribute critically to the optimal management of ADHF by providing rapid diagnosis and initial therapy that will rapidly reverse decompensation and, in consequence, facilitate the initiation of evidence-based, guideline-recommended therapy for chronic HF (Table I).

Conclusions

In patients presenting with ADHF, elevated LV filling pressure and SVR directly contribute to fluid redistribution, pulmonary edema, and respiratory compromise. The rapid clinical assessment of patients with ADHF can be simplified by considering four possible hemodynamic profiles. Of these, the wet and warm profile is seen most commonly in the ED. While LV filling pressure is highly predictive of HF symptoms and clinical outcomes, resting CI is not. The traditional focus on acute maximization of cardiac output led to therapies that increased mortality. Hemodynamic optimization with rapid reduction in LV filling pressures and SVR appears to be the most important therapeutic goal for achieving clinical stability and reducing the long-term risk of fatal decompensation and sudden death in HF.

Nesiritide possesses many characteristics of an ideal agent for treating patients with ADHF. There is now compelling evidence supporting the initial use of nesiritide as opposed to inotropic agents or high-dose IV loop diuretic monotherapy for ADHF if cardiogenic shock is absent. After rapid reversal of decompensation, comprehensive neurohormonal blockade can be initiated to reduce disability and the risk of hospitalization and death further. The ED use of optimal pharmacologic treatment for HF can have a significant impact upon patient outcomes and resource utilization.

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