Congestion Is an Important Diagnostic and Therapeutic Target in Heart Failure

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Most hospitalizations for acute heart failure syndrome (AHFS) are related to clinical congestion as a result of high left ventricular diastolic pressure (LVDP) rather than to low cardiac output. Patients frequently develop "hemodynamic congestion" (high LVDP) several days to weeks before the onset of symptoms and signs of clinical congestion. By the time symptoms and signs are evident, patients generally require hospitalization. High LVDP increases left ventricular (LV) wall stress and possibly contributes to neurohormonal activation and LV remodeling, thereby contributing to progression of heart failure (HF). Congestion is a major predictor of both morbidity and mortality in HF. Some methods may aid in the evaluation of silent hemodynamic congestion, but these assessment tools are generally underused. Identification of hemodynamic congestion, before the clinical manifestations appear, may potentially prevent hospitalization and slow the progression of HF by allowing life-saving interventions to be implemented sooner.
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Acute heart failure syndrome (AHFS) is a major public health problem. It is characterized by a rapid or gradual onset of worsening symptoms of heart failure (HF), which often results in an unplanned hospitalization and a need for urgent therapy.[1] Many evidence-based pharmacologic, device, and surgical treatments for HF are available or under development.[2] As a result, HF

patients are living longer today compared with 10 years ago. Despite the improvement in survival, hospitalizations for HF have steadily increased over the last 20 to 30 years.

AHFS has traditionally been considered a problem of volume overload as a result of increased ventricular filling pressure and/or low cardiac output. Recent data from the Acute Decompensated Heart Failure Registry® (ADHERE), the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF), and the Euro Heart Failure Survey (EHFS), involving more than 200,000 patients with AHFS, have shown that low blood pressure (a manifestation of low cardiac output) accounts for a very small proportion of AHFS admissions (Table 1). In these registries, clinical evidence of volume overload (eg, dyspnea, edema, rales) was predominant.[1,3-5] These data suggest that the majority of AHFS hospitalizations are primarily due to systemic and pulmonary congestion, also referred to in this article as clinical congestion or simply congestion (dyspnea, edema, rales, jugular venous distention [JVD], radiographic findings of congestion, etc), as opposed to low cardiac output.

The purpose of this article is to describe the importance of and the approaches to clinical congestion and "hemodynamic congestion," defined as high right and/or left ventricular (LV) filling pressures/pulmonary capillary wedge pressure (PCWP), with or without clinical congestion.

A majority of hospitalizations for acute heart failure syndrome are primarily due to congestion rather than low cardiac output.

Epidemiology of AHFS

Hospitalizations for AHFS are increasing in the United States and in Europe. The most recent United States data indicate that 1,093,000 hospitalizations in 2003 were attributed to HF.[6] This figure represents an increase of 174% since 1979. The number of annual hospitalizations approaches 3 million if both primary and secondary discharge diagnoses are considered.[6,7]

Post-discharge mortality and recurrent hospitalization rates are high in this population. In-hospital mortality has ranged from 4% to 7% in large AHFS registries.[1,3,4,8] Post-discharge mortality is approximately 10% over the next 1 to 2 months according to registry and clinical trial data.[1,4,8,9] Hospital readmission is common, with 25% to 30% of patients being readmitted within the first 3 months after discharge.[1,4,8,9] It is estimated that $15.4 billion will be spent on HF hospitalizations in 2006. This figure accounts for almost 60% of the total direct costs for HF treatment.[6]

Table 1
Symptoms and Signs in Patients Presenting With Acute Heart Failure Syndrome

	ADHERE (n = 150,000)	EHFS (n = 11,327)	OPTIMIZE-HF (n = 50,000)
Any dyspnea (%)	89	70	90
Dyspnea at rest (%)	34	40	45
Fatigue (%)	32	35	23
Rales (%)	68	N/A	65
Peripheral edema (%)	66	23	65
Systolic blood pressure (mm Hg)			
< 90 (%)	2	< 1	< 8
90–140 (%)	48	70	44
> 140 (%)	50	29	48

Values are percentages. ADHERE, Acute Decompensated Heart Failure Registry; EHFS, Euro Heart Failure Survey; OPTIMIZE-HF, Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure. Data from Adams KF et al,[3] Cleland JG et al,[4] and Fonarow GC.[5]

Evidence of Congestion in Patients Hospitalized for AHFS

The clinical characteristics of patients hospitalized for AHFS were not well studied before large acute HF registries, such as ADHERE, EHFS, and OPTIMIZE-HF, were conducted.[3,8,10] These registries demonstrated that a higher proportion of patients were admitted with evidence of clinical congestion than with a low cardiac output state. Dyspnea, rales, and peripheral edema were present in the majority of patients. Most patients were normotensive or hypertensive on admission, and very few patients required inotropic agents for low cardiac output. These observations suggest that low cardiac output state is uncommon among patients hospitalized for HF (Table 1).

Data from the Vasodilation in the Management of Acute Congestive Heart Failure (VMAC) trial also

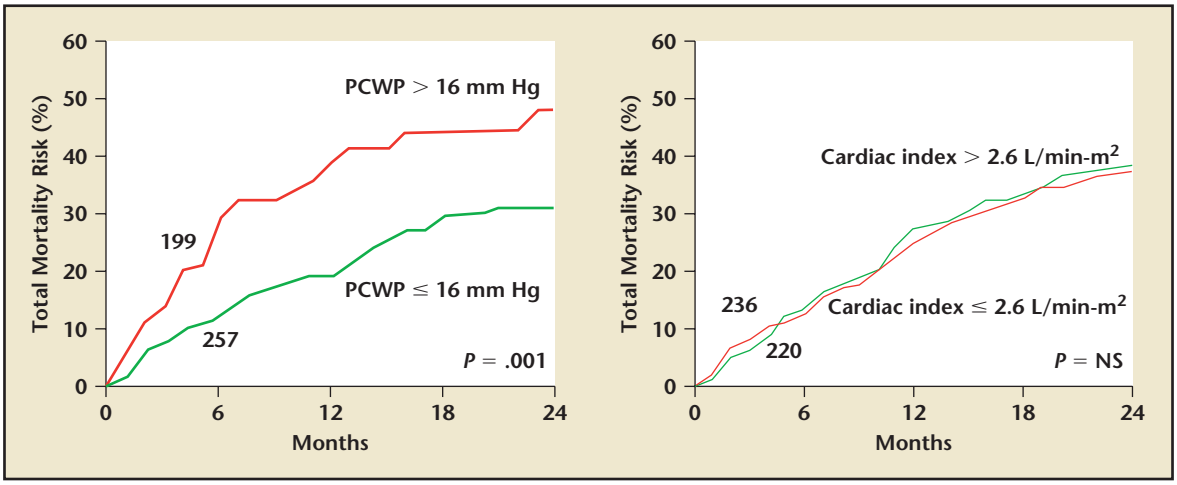


Figure 1. *Relationship between hemodynamic response and mortality.* ***Left:*** *Kaplan-Meier survival curves for 257 patients with near-normal left ventricular filling pressure (pulmonary capillary wedge pressure [PCWP] ≤ 16 mm Hg) and 199 patients with persistently elevated filling pressure (PCWP > 16 mm Hg) after administration of intravenous vasodilators.* ***Right:*** *Kaplan-Meier survival curves for 220 patients with a cardiac index ≤ 2.6 L/min/m² and 236 patients with a cardiac index > 2.6 L/min/m² after intravenous vasodilators. Reprinted with permission from Fonarow GC.*[13]

support the premise that the majority of AHFS patients have congestion rather than low cardiac output. Mean PCWP was high (28 mm Hg), whereas the mean cardiac index was preserved (2.2 L/min/m²).[11]

Congestion and Prognosis

In a retrospective analysis of the Acute and Chronic Therapeutic Impact of a Vasopressin 2 Antagonist in Congestive Heart Failure (ACTIV in CHF) trial, patients with dyspnea, edema, and JVD on admission had a 2- to 3-fold increase in their 60-day mortality.[12]

Other studies have demonstrated the prognostic importance of alleviating congestion before hospital discharge. In a study of 456 patients, 1-year survival was 81% among those patients with a PCWP of 16 mm Hg or less, as compared with 64% among those patients with a PCWP greater than 16 mm Hg after treatment with intravenous vasodilators and diuretics (Figure 1).[13] In contrast, mortality was not different for patients with a cardiac index of 2.6 L/min/m² or less, as compared with those with a cardiac index greater than 2.6 L/min/m².[13] The only factors associated with increased 1-year mortality in this analysis, in addition to a high PCWP, were low serum sodium, increased LV end diastolic dimension, and low peak oxygen consumption on cardiopulmonary exercise testing.

The Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) study also demonstrated that PCWP was one of the most important predictors of 6-month postdischarge survival. Cardiac output was not predictive of outcomes in this analysis. Other independent predictors of increased 6-month mortality were low systolic blood pressure, high blood urea nitrogen, and shorter distance walked on the 6-minute walk test.[14]

Freedom from congestion after hospital discharge has also been associated with improved survival at 2 years. Lucas and colleagues[15] studied 146 patients discharged from the hospital after an admission for decompensated HF. Symptoms were reassessed at 4 to 6 weeks after discharge. Patients were categorized according to whether they had no, mild, or moderate symptoms of congestion. Survival at 2 years was 87%, 67%, and 41% for the no, mild, and moderate congestion groups, respectively.

A retrospective analysis of the Studies of Left Ventricular Dysfunction (SOLVD) treatment trial demonstrated that physical examination findings indicative of congestion are associated with higher mortality.[16] The presence of elevated jugular venous pressure (JVP), third heart sound, or both was associated with a 17% increased risk of all-cause death, a 43% increased risk of hospitalization for HF, a 28% increased risk of death or hospitalization for HF, and a 47% increased risk of pump-failure death. Thus, evidence of congestion on physical examination has important prognostic implications.

The severity of symptoms has also been associated with a patient's willingness to trade length of life for better quality of life.[17] In a study of 99 patients with predominantly New York Heart Association Class III HF, higher degrees of JVP elevation were associated with lower time trade-off scores, indicating that patients were willing to give up some length of life for better quality of life. Similar findings were observed with the visual analogue scale for breathing. Patients with more severe dyspnea were willing to trade length of life for improved health.[17]

Although congestion is the main reason for hospitalization, it is often inadequately treated during hospitalization. In effect, in the ADHERE registry approximately 50% of patients did not have a clinically relevant decrease in body weight. As a result, patients often remain symptomatic at the time of discharge. The Initiation Management Predischarge: Assessment for Carvedilol Therapy in Heart Failure (IMPACT-HF) study reported that patients had fatigue (57%), dyspnea on exertion (57%-60%), and orthopnea (10%-14%) at the time of discharge.[18] In these patients, clinical events including worsening symptoms requiring a change in therapy (31%-32%), rehospitalization (22%-25%), unscheduled HF visits (3%-4%), and death (3%-5%) were common. These data generated the hypothesis that persistent hemodynamic congestion that is not recognized and adequately treated before discharge is an important cause for high rates of postdischarge morbidity and mortality in HF patients.[18]

Although some patients experience a significant symptomatic improvement during hospitalization, they often continue to have a high PCWP (hemodynamic congestion).

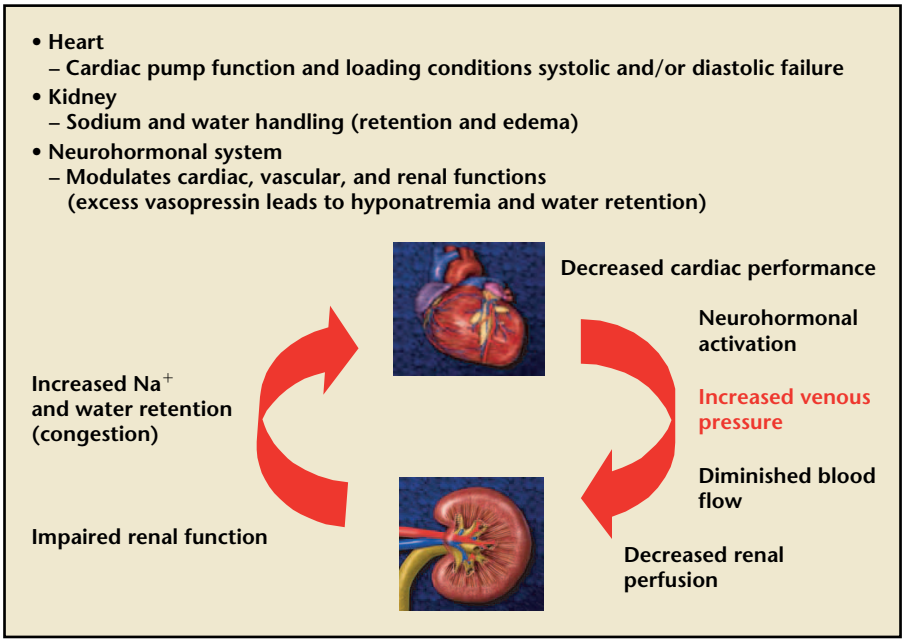


Figure 2. *Pathophysiology of congestion in heart failure. Figure adaptation courtesy of William T. Abraham, MD.*

In the VMAC trial, although more than 60% of patients in the placebo group and more than 70% in the treatment groups reported improved dyspnea at 3 hours, the PCWP continued to be at 22 and 26 mm Hg, respectively.[11] The presence of congestion with persistently high PCWP, despite improvement in dyspnea, likely contributes to the high postdischarge readmission rates.

Pathophysiology of Congestion

Cardiac dysfunction, renal impairment, and neurohormonal activation play a significant role in the development of congestion (Figure 2).

Abnormalities of systolic or diastolic function lead to increased left ventricular diastolic pressure (LVDP) and impaired volume regulation. The increased LVDP and increased blood volume translate into backward failure, which results in increased PCWP. Analogous to fluid mechanics, if the pulmonary vascular bed is considered as a confined system, congestion can be expressed as an increased weight of the fluid column. In a uniform fluid such as blood, the weight of the fluid column equals the total pressure or force of that column. Thus, as force is transmitted through a fluid as a pressure wave, the pressure across pulmonary capillaries (ie, PCWP) is a good estimate of the pressure across that fluid column.[19] The increased PCWP might further lead to increased pulmonary artery pressure, increased right ventricular and atrial pressures, tricuspid regurgitation, and ultimately development of the symptoms and signs of systemic congestion (Figure 3). Increased PCWP can lead to redistribution of excess fluid within the lungs, resulting in interstitial and alveolar edema. However, this redistribution depends not only on hydrostatic pressure but also on several other factors, including the plasma oncotic pressure, integrity and permeability of the alveolar-capillary membrane, and lymphatic

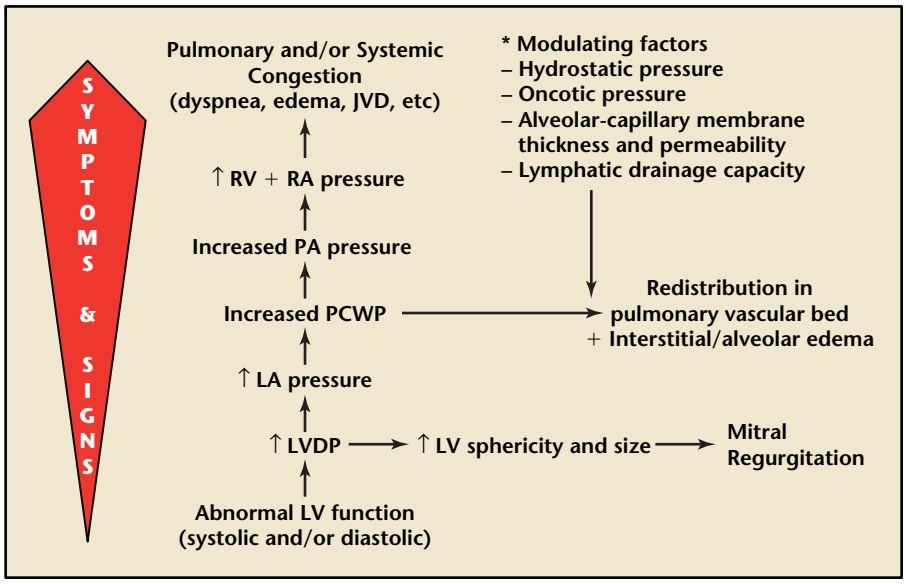


Figure 3. *Relationship between signs and symptoms of congestion and hemodynamic abnormalities. JVD, jugular venous distention; RV, right ventricular; RA, right atrial; PA, pulmonary artery; PCWP, pulmonary capillary wedge pressure; LA, left atrial; LV, left ventricular; LVDP, left ventricular diastolic pressure.*

drainage. In chronic HF, there is a decrease in alveolar-capillary membrane permeability and an increase in lymphatic drainage. Therefore, even very high PCWPs may not necessarily lead to interstitial and/or alveolar edema.

Accordingly, symptoms and signs of congestion may not be apparent or detectable until several days or weeks after the onset of PCWP elevation. Moreover, even when present, these symptoms can be nonspecific.

Progressive activation of neurohormonal systems may also contribute to congestion.[20] The sympathetic nervous system, renin-angiotensin-aldosterone system, and elevated vasopressin levels can contribute to increases in systemic vascular resistance and sodium/water retention.

Renal dysfunction contributes to the development of congestion through impaired sodium and water handling. This has been attributed to decreased cardiac output and systemic vasodilation.[21] However, most patients with AHFS do not have a decreased cardiac output nor vasodilation. In AHFS, renal dysfunction may also be the result of neurohormonal activation, in particular vasopressin and/or high venous pressure (Figure 2). Data from an experimental dog model demonstrated an inverse relationship between glomerular filtration rate and central venous pressure suggesting that congestion may contribute to renal abnormalities (Figure 4).[22]

Consequences of Congestion

Clinical and experimental data suggest that congestion might have an important role in the pathophysiology of HF, and it might promote the deterioration of LV function and progression of the disease (Table 2). Increased LV filling pressures augment LV wall stress, contributing to chamber dilatation and spherical remodeling of the ventricle. This cardiac remodeling may cause secondary mitral insufficiency.[23] Elevated filling pressures may lead to subendocardial ischemia. Subendocardial ischemia increases the risk of ventricular arrhythmia and contributes to the progression of LV dysfunction and remodeling by myocyte loss through necrosis and apoptosis. A significant number of patients with AHFS have increased serum troponin levels that correlate with poor short- and long-term prognoses.[24,25] This increase in troponin may be the result of subendocardial necrosis secondary to a high LV

Figure 4. *Relationship between increasing central venous pressure (CVP) and glomerular filtration rate (GFR) in dogs. Reprinted with permission from Firth JD et al.[22]*

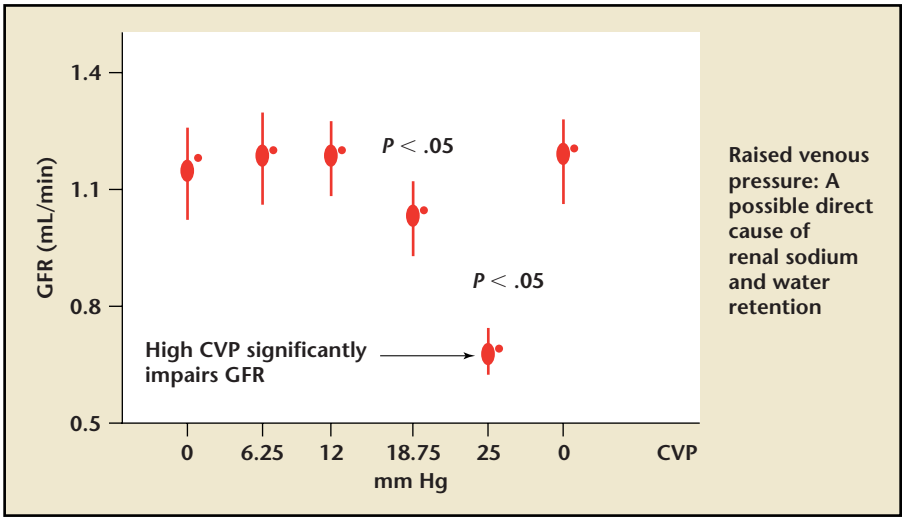


Table 2
Potential Deleterious Effects of a High Left Ventricular Diastolic Pressure in Heart Failure

- Subendocardial ischemia and cell death by necrosis or apoptosis
- Changes in extracellular matrix structure and function
- Changes in left ventricular shape (sphericity) and size
  - Increased afterload
  - Secondary mitral regurgitation
- Impaired cardiac venous drainage (diastolic dysfunction)
- Lowered threshold for arrhythmias
- Progression of left ventricular dysfunction and remodeling

Table 3
Factors That May Predispose to Myocardial Injury in Acute Heart Failure Syndrome

- Decreased coronary perfusion due to high left and right ventricular pressures and/or low systemic blood pressures
- Further activation of neurohormones with endothelial dysfunction (ischemia)
- Inotropic stimulation of viable but non-contractile (eg, hibernating) myocardium

filling pressure when associated with a decreased blood pressure in patients with myocardium at risk (eg, hibernating myocardium).[26]

Small increases in myocardial water content, induced by hypoalbumic perfusion, have been shown to impair contractility, passive filling, and coronary flow rates.[27] It is likely that increased right atrial pressure that interferes with cardiac venous and lymphatic drainage may result in cardiac edema that could impair both systolic and diastolic cardiac function.

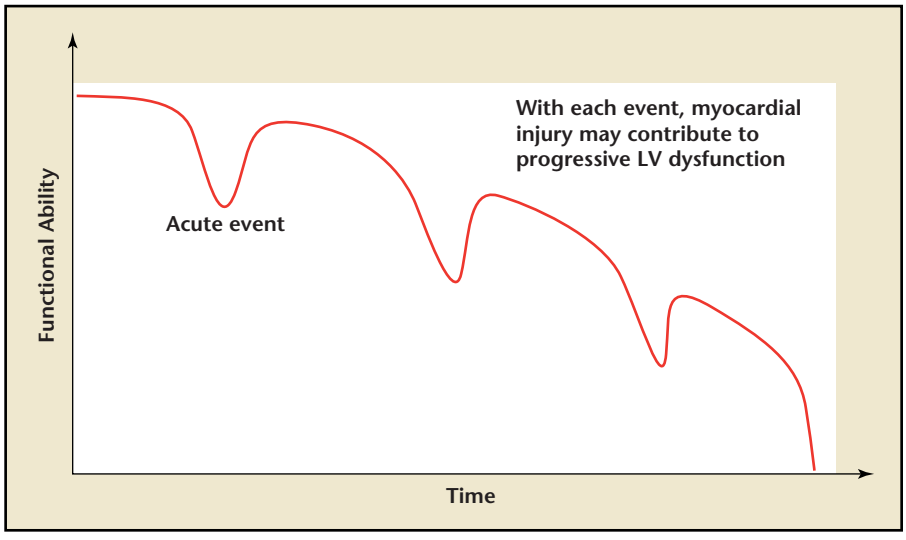
As a result of these factors, each episode of worsening congestion resulting in hospitalization for AHFS might contribute to the progression of LV dysfunction, which in turn would increase the risk for future cardiac events. This progression is characterized by short periods of stability, with more frequent hospitalizations as the clinical syndrome progresses (Table 3, Figure 5).[28]

Clinical Presentation of AHFS

The majority of patients presenting with AHFS have evidence of congestion at the time of admission.[3] Based on blood pressure on presentation, AHFS patients can be subcategorized into the following groups (Table 1):

1. Hypertensive group (systolic blood pressure [SBP] > 140 mm Hg): Patients have pulmonary (dyspnea, rales, radiographic congestion, flush pulmonary edema) but not systemic congestion (peripheral edema).[29] The acute development of pulmonary congestion is related to an abrupt increase in systemic pressure often unexplained in patients with abnormal diastolic function, and it results in an acute increase in PCWP. A greater proportion of patients are women, and they are more likely to have relatively preserved ejection fraction, a previous history of hypertension, and less coronary artery disease. Symptoms usually develop abruptly in these patients. This group represents approximately 40% of all AHFS patients.
2. Normotensive group (SBP between 90 and 140 mm Hg): Patients admitted with pulmonary and systemic congestion (dyspnea, peripheral edema, etc). The signs and symptoms develop gradually over days or weeks. These patients have significant edema, weight gain, JVD, S3, and positive hepatojugular reflux. This group represents 50% of all AHFS patients.

Figure 5. *Episodes of an acute exacerbation of heart failure contribute to the progression of heart failure. LV, left ventricular. Adapted with permission from Gheorghiade M et al.[28]*



3. Hypotensive group: (SBP < 90 mm Hg): Patients usually have a low cardiac output with symptoms and signs of organ hypoperfusion (eg, increases in BUN). Most of these patients have advanced, or end-stage HF, and respond poorly to therapy.[30] This group represents less than 10% of all AHFS patients.

Hemodynamic Congestion Versus Clinical Congestion

Table 4 lists the characteristics of hemodynamic congestion (high LVDP that is usually measured by the PCWP). Hemodynamic congestion may or may not be associated with clinical congestion. In fact, the majority of patients with a high LV filling pressure do not have clinical congestion, defined as dyspnea, orthopnea, pulmonary rales, JVD, or peripheral edema.

In almost all patients with AHFS the LV filling pressure is mildly elevated. Among these patients a significant number develop hemodynamic congestion several days to weeks before symptoms and signs of congestion are evident. Thus, increased LV filling pressure, even when severe, is often clinically silent. The presence of hemodynamic congestion may not be recognized until patients are decompensated and require hospital admission.[31,32] Friedman[33] reported that dyspnea was noted only 3 days before admission in patients hospitalized for AHFS. On the other hand, increases in intrathoracic fluid as early as 18 days before a hospitalization have been detected by intrathoracic impedance monitoring.[34] The Chronicle® Implantable Hemodynamic Monitor (Medtronic, Inc., Minneapolis, MN) detected increases in pressure parameters days to weeks before hospitalization for HF exacerbation (Figure 6).[35] In addition, patients may not ever develop clinical manifestations of congestion leading to AHFS, even though their LV filling pressures may persist at high levels for long periods of time.

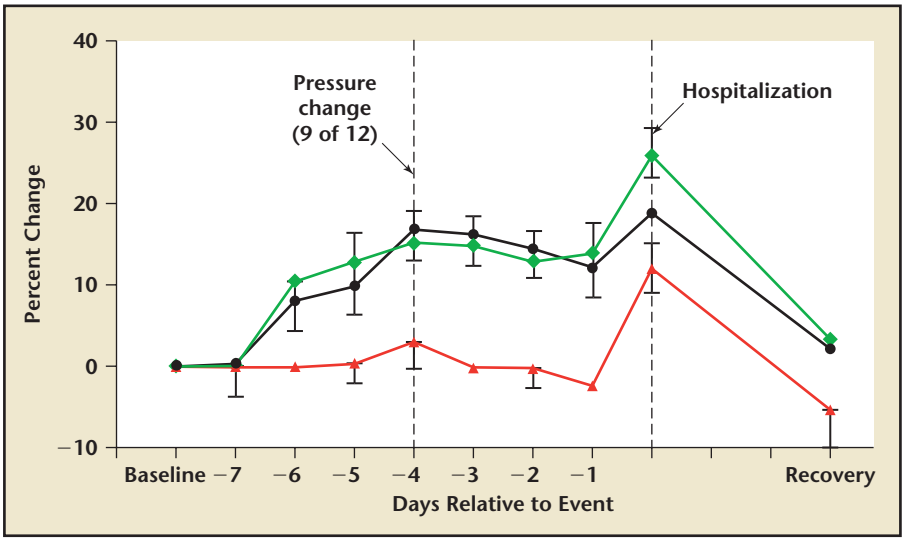


Figure 6. *Pressure changes occurred in 9 of 12 events 4 ± 2 days before hospitalization (major). Percent changes in right ventricular systolic pressure (black circles), estimated pulmonary artery diastolic pressure (green diamonds), and heart rate (red triangles). Reprinted with permission from Adamson PB et al.*[35]

It must also be recognized that even when present, HF signs and symptoms are not specific or properly assessed. Dyspnea is a nonspecific symptom associated with many diseases. In general, clinical manifestations of HF are nonspecific and relatively insensitive.[32,36] In a prospective assessment of 50 patients with known chronic HF, it was found that rales, edema, and elevated JVP were absent in 18 of 43 patients with PCWP of 22 mm Hg or greater. The combination of these signs had a sensitivity of 58% and a specificity of 100%.[32] Phonocardiographic assessment of third (S3) and fourth (S4) heart sounds are also insensitive markers of HF. In a study of 90 patients, the sensitivity of an S3 to detect an elevated LV end-diastolic pressure, reduced LV ejection fraction, or elevated B-type natriuretic peptide level was 41%, 52%, and 32%, respectively. The values were similar for S4: 46%, 43%, and 40%, respectively. The specificity values were higher (S3: 92%, 87%, and 92%; S4: 80%, 72%, and 78%).[37] Importantly, the negative predictive values of those

Table 4
Characteristics of "Hemodynamic Congestion" (High LVDP)

- Hemodynamic congestion precedes (days or weeks) signs and/or symptoms of clinical congestion (dyspnea, edema, rales, JVD, etc) that often require hospitalization
- Hemodynamic congestion may be present in the absence of (or after improvement of) signs or symptoms of clinical congestion
- Improved methods of monitoring hemodynamic congestion might improve clinical management and outcomes

LVDP, left ventricular diastolic pressure; JVD, jugular venous distention.

Table 5
Predictive Ability of Signs and Symptoms to Detect PCWP > 18 mm Hg

Parameter	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Dyspnea on exertion	66	52	45	27
Orthopnea	66	47	61	37
Edema	46	73	79	46
JVD	70	79	85	62
S3	73	42	66	44
CXR				
Cardiomegaly	97	10	61	
Redistribution	60	68	75	52
Interstitial edema	60	73	78	53
Pleural effusion	43	79	76	47

Values are percentages. PCWP, pulmonary capillary wedge pressure; JVD, jugular venous distention; CXR, chest X-ray. Data from Chakko S et al[40] and Butman SM et al.[41]

parameters for detecting a high PCWP are very low (Table 5).

These data emphasize the point that methods to detect hemodynamic congestion before it is clinically evident would allow patients to be identified before they become fully decompensated and require hospitalization. This early identification might allow for implementation of life-saving interventions, such that AHFS hospitalizations could be prevented and disease progression could be slowed. Studies are needed to determine whether early patient identification could significantly impact the morbidity and mortality of AHFS. These studies should evaluate the effect of early detection and treatment of hemodynamic congestion on the hospitalization rate, optimization of existing therapy, and cardiovascular mortality.

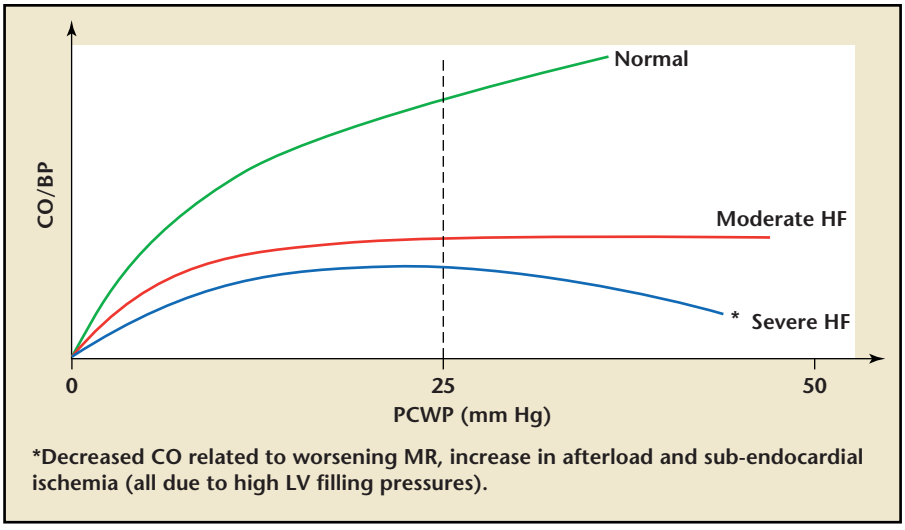
Evaluation of Congestion

Physical Examination

Physical examination can provide useful information about hemodynamic congestion in an HF patient. In the absence of PCWP measurement, assessment of (1) orthostatic blood pressure changes, (2) blood pressure changes with the Valsalva maneuver, (3) heart rate and/or blood pressure response to sublingual nitroglycerin administration, or (4) dyspnea in a supine position may be helpful in identifying patients with high LV filling pressures, even in the absence of clinical congestion.[38] The absence of dyspnea when a patient is moved abruptly from a sitting to a supine position tends to exclude a very high LVDP.

Patients with normal LV filling pressures tend to have lower cardiac output (CO)/SBP in response to measures that result in a decrease in preload (Figure 7). In patients with high LV filling pressures, however, reducing preload by moving them from a supine to an upright position, performing the Valsalva maneuver, or administering sublingual nitroglycerin will not decrease CO/SBP.[38] These measures may even result in increased CO/SBP, which indicates a more severe degree of congestion. This is related to the fact that in patients with systolic dysfunction a very high LVDP may cause increased afterload (increased wall tension) and secondary mitral insufficiency.

Figure 7. *Relationship between left ventricular (LV) filling pressures and cardiac output (CO) in normal individual and patients with moderate or severe heart failure (HF) with systolic dysfunction. BP, blood pressure; PCWP, pulmonary capillary wedge pressure; MR, mitral regurgitation.*



The Valsalva maneuver is defined as a sustained forced expiratory effort or strain, against a closed glottis. In normal subjects, arterial blood pressure response to the Valsalva maneuver is an initial rise associated with the onset of straining (phase 1), followed by a sharp fall to below baseline levels as the straining is maintained (phase 2). Short decrease of arterial blood pressure at the release of the straining (phase 3) is followed by a distinct overshoot of the arterial pressure (phase 4), creating a typical sinusoidal response. Typically, only phases 2 and 4 are detected, because phases 1 and 3 are generally too short to be noticed. The examiner should listen for the Korotkoff sound during phases 2 and 4.

Three types of responses to the Valsalva maneuver can be observed: a sinusoidal response is the normal pattern, the absence of overshoot indicates congestion, and a square wave indicates severe congestion. In a square wave response, arterial blood pressure increases initially (phase 1), it continues to remain raised during the entire duration of strain (phase 2), and it falls to resting levels at release (phase 3). The intermediate response of absent overshoot is observed in patients with less severe HF. It manifests as normal phases 1 through 3 with an absence of arterial pressure overshoot after release of the strain (Figure 8).[38,39]

The patient should be sitting or in the supine position to assess the blood pressure and heart rate response to sublingual nitroglycerin. Baseline blood pressure and heart rate should be measured. The patient should be given nitroglycerin 0.4 mg sublingually. Blood pressure and heart rate should be measured after 3 to 5 minutes. Repeat measurement after 15 minutes is optional. A decrease in blood pressure suggests a normal or low PCWP, no change in blood pressure suggests a high PCWP, and an increase in blood pressure suggests a very high PCWP.

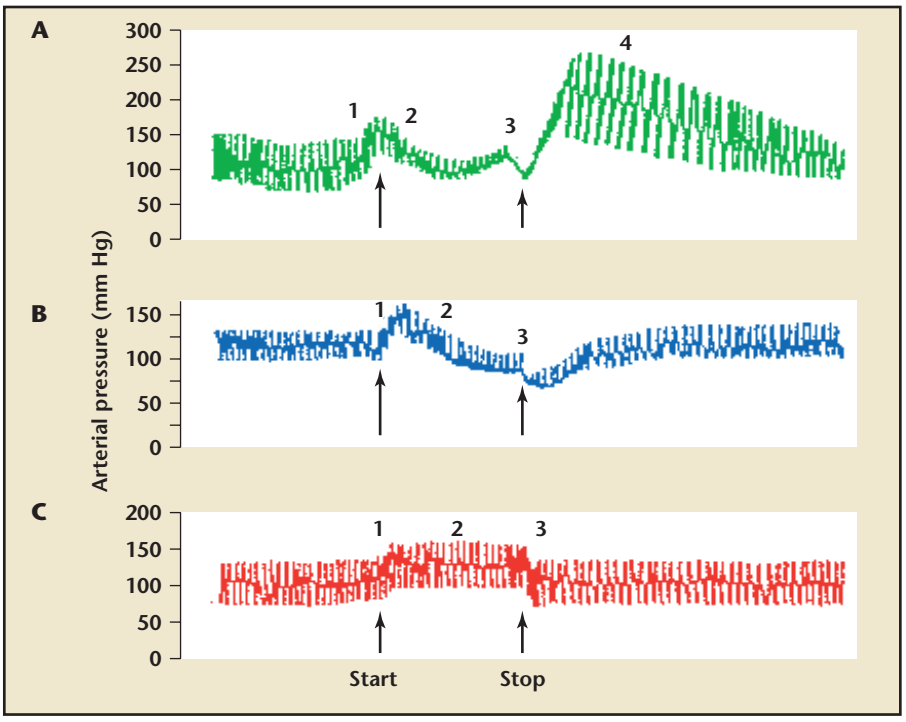


Figure 8. *Blood pressure response to Valsalva maneuver in various clinical situations.* **(A)** *Sinusoidal arterial pressure response (normal).* **(B)** *"Absent overshoot" arterial pressure response (mild heart failure).* **(C)** *"Square wave" response (severe heart failure). Adapted with permission from Felker GM et al[38] and Zema MJ et al.[39]*

Chest X-Ray

Congestion may be manifested on chest x-ray (CXR) as cardiomegaly, redistribution of pulmonary vessels, increased density and enlarged hilar vessels, perihilar haze, perivascular and peribronchial cuffs, Kerley lines, and sometimes as alveolar edema. Although these radiological manifestations of congestion are often present in HF patients, they are relatively slow to respond to either increases or decreases in PCWP.

Several studies have investigated the ability of symptoms, signs, and CXR findings to predict a PCWP greater than 18 to 20 mm Hg. Physical findings (orthopnea, edema, rales, S3, and elevated JVP) or radiographic signs (cardiomegaly, vascular redistribution, and interstitial and/or alveolar edema) had poor predictive value for identifying patients with PCWP values of 30 mm Hg or greater. Radiographic pulmonary congestion was absent in 53% of patients with PCWP of 16 to 29 mm Hg and in 39% of patients with PCWP of 30 mm Hg or greater.[40] Although CXR can be a useful tool in the evaluation of HF patients, the absence of CXR findings does not exclude the presence of a high PCWP (hemodynamic congestion) (Table 5).[40,41]

Echocardiography and Ultrasonography

Echocardiography is considered useful for the diagnosis of HF and evaluation of systolic and diastolic function. Echocardiography can also provide useful information about LV end diastolic diameter, left atrium

diameter, and pulmonary artery pressure. However, echocardiography does not routinely assess hemodynamic congestion and does not reflect systemic congestion.

Potentially, pulmonary congestion can be evaluated by obtaining an ultrasound scan of the lung. The lung has traditionally been considered poorly accessible to ultrasound techniques, but in patients with pulmonary congestion, images defined as "ultrasound lung comets" (ULC) can be depicted by scanning with cardiac probes along the intercostal spaces.[42] This technique is a reliable, regional, quantitative, and easy method to assess the presence of extravascular lung water (EVLW). A significant correlation exists between the number of ULC and pulmonary congestion by radiographic signs, interstitial edema documented by computed tomography, measurement of EVLW by the indicator dilution technique, and PCWP.[43-45]

The absence of chest x-ray findings does not exclude the presence of a high PCWP.

Body Weight

Measurement of body weight is another method for monitoring fluid overload. However, daily weights monitored over time are of limited usefulness because they are not reliable predictors of HF status. Weight gain may reflect normal fluctuations, variation in time or conditions of weight, or improved appetite. In addition, decreased weight can be observed in patients with advanced HF due to the loss of muscle mass and fat stores associated with cachexia. This weight loss can mask fluid retention. Although congestion is the main reason for HF hospitalizations, the ADHERE Registry data showed that nearly 50% of patients have minimal or no weight loss during their hospital stay.[5]

Cardiac Natriuretic Hormones

Before the development of the B-type natriuretic peptide (BNP) assay, no laboratory tests were available for the diagnosis, risk stratification, or follow-up of HF patients.[46] Cardiac natriuretic hormones play an important role in the regulation of cardiovascular homeostasis and fluid volume. Elevations in LVDP and impaired volume regulation lead to an increased release of BNP from the cardiac ventricle.[47] Blood concentrations of BNP and the amino-terminal fragment of its precursor hormone (NT-proBNP) have been shown to be diagnostically useful as biochemical markers of congestive HF. In the Breathing Not Properly (BNP) Study, BNP levels correlated with the severity of HF.[48]

Blood concentrations of BNP and NT-proBNP have also been shown to decrease as hemodynamics are normalized in patients receiving intravenous therapy for AHFS. In addition to this established role in LV HF, there is evidence that plasma BNP and NT-proBNP concentrations also have a diagnostic role in right ventricular systolic dysfunction and pulmonary arterial hypertension.[49] A high predischarge BNP level is a strong, independent marker of death or readmission in patients with AHFS.[50] Thus, BNP and NT-proBNP levels are useful in the diagnostic and prognostic evaluation of AHFS patients.

BNP and NT-proBNP levels, however, are not likely to be used to follow dynamic changes in hemodynamic congestion because their pattern of production and release is too slow to reliably mirror hemodynamic variations. The optimum interval between blood collection for BNP and NT-proBNP is 7 days. Significant changes in BNP might not occur until 1 week or more after an initial test sample, and even then, changes occur only approximately 50% of the time.[51] Moreover, a change in BNP of 130% or NT-proBNP of 90% is necessary before results of serially collected data can be considered statistically different.[52]

Clinicians must recognize that elevated cardiac natriuretic hormone levels might also be found in other physiological and pathological conditions. Diseases that are associated with increased BNP levels include pulmonary disease, renal disease, or hepatic cirrhosis. Patients with these conditions often exhibit symptoms similar to those of HF, increasing the difficulty of making a correct diagnosis.[53]

Intrathoracic Impedance Monitoring

Another potential method for assessing the development of pulmonary congestion is to measure intrathoracic impedance. Intrathoracic impedance is inversely correlated to PCWP and fluid balance. It decreases before the onset of symptoms and before hospitalization for fluid overload. An intrathoracic impedance monitor provides an early warning of congestion that might allow physicians to intervene by adding or titrating medications, possibly preventing the need for hospitalization.[34]

Pulmonary Capillary Wedge Pressure

PCWP is the best estimate of pressure across the pulmonary vascular bed. It defines the degree of pulmonary congestion, but its usefulness in clinical practice is limited because of the invasive nature of its assessment.

Treatment of Congestion

Non–potassium-sparing diuretics are the mainstay of therapy for AHFS with volume overload. They quickly and effectively relieve symptoms of congestion. However, their long-term effects on morbidity and mortality have never been assessed in randomized, controlled clinical trials. Diuretics produce numerous effects that could adversely influence clinical outcomes, including hypotension, electrolyte abnormalities, worsening renal function, and neurohormonal activation. As a result, the use of diuretics, especially in high doses, has been associated with increased morbidity and mortality.[54-57] Given the limitations of diuretic therapy, alternatives to treat congestion are under investigation and consist of vasopressin antagonists and/or ultrafiltration.[58]

The ACTIV in CHF trial demonstrated that the vasopressin antagonist tolvaptan relieves congestion by inducing aquaresis with a significant decrease in body weight and normalization of hyponatremia in those patients with hyponatremia.[12,59,60] These results have been obtained without worsening renal function or inducing changes in heart rate and/or blood pressure.[12,59,60] The role of these agents in the management of AHFS is being tested in a large, global mortality trial.[61]

Conclusions

In summary, the vast majority of AHFS hospitalizations are related to clinical congestion, rather than to a low cardiac output state. Patients develop hemodynamic congestion (high LVDP) several days to weeks before the onset of symptoms and signs of clinical congestion. By the time symptoms and signs are evident, patients generally require hospitalization, where congestion is often inadequately treated.

Congestion may contribute to HF. Although some methods (eg, orthostatic blood pressure changes, etc) may aid in the evaluation of silent hemodynamic congestion, these are generally underused. It is plausible that early identification of hemodynamic congestion, before the clinical manifestations arise, could prevent hospitalizations for AHFS and slow the progression of HF by allowing life-saving interventions to be implemented sooner. Studies are needed to evaluate the effect of early identification of congestion on outcomes in HF patients. ■

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Main Points

- Hospitalizations for acute HF syndrome (more than 1 million annually in the United States) are primarily due to congestion rather than low cardiac output. A large number of the patients still have congestive symptoms at hospital discharge.
- In the development of congestive symptoms, hemodynamic congestion (elevated left ventricular filling pressures) precedes clinical congestion (dyspnea, edema, rales, etc) by days to weeks.
- Persistent hemodynamic congestion that is not adequately recognized and treated before discharge is associated with adverse clinical outcomes in HF patients; on the other hand, post-discharge freedom of pulmonary congestion is associated with a better prognosis.
- Detection and treatment of hemodynamic congestion before it is clinically evident may prevent hospitalization and progression of HF.
- Without the use of invasive pulmonary artery catheter, measurements of heart rate and/or blood pressure changes in response to orthostatic change, the Valsalva maneuver, and sublingual nitroglycerin administration may aid in identifying patients with high LV filling pressures even in the absence of clinical congestion.

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