Congestion in Acute Heart Failure Syndromes: Importance of Early Recognition and Treatment

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The vast majority of acute heart failure syndrome (AHFS) hospitalizations are related to clinical congestion, rather than to a low cardiac output state. Patients develop hemodynamic congestion (high left ventricular filling pressure) several days to weeks before the onset of clinical symptoms and signs. Congestion is an important predictor of both mortality and morbidity in patients with AHFS. As a result, congestion is an essential evaluative and therapeutic target in AHFS patients. It is plausible that early identification of hemodynamic congestion, before the clinical manifestations are present, could reduce the need for hospital admission and readmission.
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Acute heart failure syndromes (AHFS) are the direct cause of approximately 1 million hospitalizations and a contributing factor in an additional 2.4 million hospitalizations each year in the United States,[1,2] accounting for nearly 60% of the annual total direct costs of heart failure (HF).[1,3] Although in-hospital mortality rates are only in the range of 3% to 4%, the 60- to 90-day mortality rate increases to approximately 10%, and the readmission rates during this period approach 25%.[1,4-7] 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 involving over 200,000 patients have shown that most AHFS hospitalizations are primarily caused by volume overload or congestion.[8-9] Nevertheless, systemic and/or pulmonary congestion often are not appropriately treated during hospitalization for AHFS, which results in patients being discharged with improved symptoms yet with persistently elevated left ventricular (LV) filling pressures (hemodynamic congestion). This ultimately may lead to early readmission when symptoms of congestion recur. The IMPACT-HF study reported that although the majority of patients are admitted with signs and symptoms of congestion, approximately 60% are being discharged with continuing symptoms of dyspnea or fatigue. In this study, 45% of these patients experienced worsening HF, and 25% required re-hospitalization within 60 days post-discharge.[10]

Failure to recognize and adequately address congestion seems also to increase morbidity and mortality risk. Lucas and colleagues[11] studied 146 New York Heart Association class IV HF patients 4 to 6 weeks following hospital discharge. Patients were divided into 3 groups according to their residual symptoms and signs of congestion (orthopnea, jugular venous distention [JVD], peripheral edema, and weight gain) and need for increased diuretic dose. Two-year survival was 87% in patients with no residual symptoms of congestion, 67% in patients with 1 or 2 residual symptoms of congestion, and 41% in patients with 3 or more residual symptoms of congestion. Freedom from congestion, pulmonary capillary wedge pressure (PCWP) on therapy, LV dimension, and use of an angiotensin-converting enzyme inhibitor were identified as significant univariate predictors of improved survival.[11] Similarly, in a post hoc evaluation of the data from the Acute and Chronic Therapeutic Impact of a Vasopressin Antagonist in Congestive Heart Failure (ACTIV) trial, severe congestion (defined as the presence of dyspnea, JVD, and peripheral edema) at baseline was associated with an increase in 60-day mortality risk of 8.1%, versus 4.9% in patients without severe congestion.[7] The Studies of Left Ventricular Dysfunction (SOLVD) reported that congestion (determined by JVD and/or S3 gallop) was associated with a 15% relative increase in the risk of death and a 40% relative increase in HF hospitalizations during a 5-year follow-up period.[12]

Failure to recognize and adequately address congestion seems to increase morbidity and mortality risk.

Additional studies of patients hospitalized for AHFS reported that a PCWP of ≤ 16 mm Hg prior to hospital discharge was an independent predictor of improved 1-year survival (80.8%, vs 64.1% in patients with persistently elevated LV filling pressure [$P = .001$]); in contrast, no survival benefit was reported with improvements in cardiac index.[13] The Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) study also demonstrated that PCWP, and not cardiac output, was one of the most important predictors of 6-month post-discharge survival. Other independent predictors of 6-month mortality were low systolic blood pressure, high blood urea nitrogen, and shorter distance walked on the 6-minute walk test.[14]

Clinical Congestion Versus Hemodynamic Congestion

The progressive volume retention can occur gradually and often precedes by several days the development of symptoms and subsequent hospitalization. Adamson and colleagues[15] evaluated the efficacy of using an implantable monitor to continuously assess right ventricular hemodynamics in 32 patients with HF. Twelve of these patients ultimately required admission for AHFS, and 9 of these 12 sustained > 20% increases in right-sided pressures, consistent with volume retention. This hemodynamic change occurred 4 ± 2 days prior to the development of symptoms and subsequent hospitalization, with a further increase detected in the 24 hours immediately prior to hospitalization.[15]

In a study by Mahdyoon and colleagues,[16] only 7 of 22 patients (32%) with elevated PCWP (≥ 25 mm Hg) had moderate-to-severe pulmonary congestion detected by chest radiography; 6 patients (27%) had no radiographic evidence of pulmonary congestion. Similarly, rales, edema, and elevated mean jugular venous pressure were absent in 18 of 43 patients with elevated PCWP (≥ 22 mm Hg) in another evaluation.[17] Overall, the combination of clinical signs had only a 58% sensitivity in detecting patients with elevated PCWP.[17]

Therefore, although elevated LV filling pressures are present in a majority of patients hospitalized with AHFS,[18] congestion is often clinically silent for days or weeks and is often not recognized until admission.[15,16] Given this phenomenon, the elevation of the LV filling pressures that occurs early can be termed "hemodynamic congestion," as opposed to

Table 1
Pathophysiologic Processes Induced by Hemodynamic Congestion

- Increase of left ventricular wall stress; change in the shape of the ventricle with repositioning of papillary muscles and secondary mitral insufficiency
- Increase of angiotensin II release and endogenous protease activity, leading to changes in the extracellular matrix structure and function and increasing collagen synthesis (fibrosis)
- Myocyte loss may result from subendocardial ischemia due to high left ventricular filling pressure (especially in acute heart failure syndrome patients with hypotension and/or coronary artery disease and hibernating myocardium)
- High right atrial pressure results in impaired venous drainage and contributes to the impairment of diastolic function

"clinical congestion," which occurs later and is evidenced by dyspnea and orthopnea, pulmonary rales, peripheral edema, and JVD.[19] The discussion of hemodynamic versus clinical congestion describes 2 points on a continuum in the development of volume overload, but may serve to raise awareness among clinicians that hemodynamic derangements precede clinical manifestation in patients with HF.

Congestion: Importance of Early Recognition and Treatment

Congestion may induce several deleterious pathophysiological processes, as well as contribute to hospitalization for AHFS[20] (Table 1).

AHFS represent a perfect storm for myocardial injury that in itself can contribute to the progression of HF (Figure 1). This is related not only to further activation of neurohormonal abnormalities, sub-endocardial ischemia related to high LV filling pressure, and worsening renal function, but also to medications currently given to correct severe hemodynamic abnormalities leading to hospitalization. In addition, because of severe hemodynamic abnormalities and renal dysfunction, it is more difficult to implement life-saving therapy that includes β-blockers, angiotensin-converting enzyme inhibitors, and aldosterone blocking agents (Table 2). Since hospitalization often is a result of severe congestion that started days or weeks before, the hypothesis that has been generated is that early detection of congestion (hemodynamic congestion) may result in implementation of life-saving therapies and, more likely, may lead to the use of lower doses of detrimental medications, eg, high-dose diuretics and inotropic agents, that are commonly given in this patient population (Table 3).

For instance, non–potassium-sparing diuretics are the mainstay of therapy for congestion in patients with AHFS.[21,22] However, loop diuretics can produce numerous undesired effects that could adversely influence clinical outcomes, including hypotension, electrolyte disturbances, worsening renal function, and excessive neurohormonal activation.[23-27] As a result, the use of diuretics, especially at high doses, has been associated with increased morbidity and mortality.[28-34]

Furthermore, use of non–potassium-sparing diuretics often does not sufficiently relieve volume overload in patients with AHFS.[11] In the ADHERE registry, 89% of patients presented with symptoms of volume overload, and 88% of patients received intravenous diuretic therapy.[8] Despite this, only 50% of patients were asymptomatic at the time of discharge, and 51% had little or no weight loss (< 5 pounds) during their hospitalization.[8]

Current Methods for Evaluating Congestion

The ability to identify hemodynamic congestion before symptoms arise may possibly avoid hospitalizations and reduce disease progression in patients with HF.[35,36] Physical examination can provide useful information about hemodynamic congestion in AHFS patients. In the absence of PCWP measurement, assessments of orthostatic blood pressure changes, the Valsalva maneuver, and/or the response of heart rate or blood pressure to sublingual nitroglycerin may

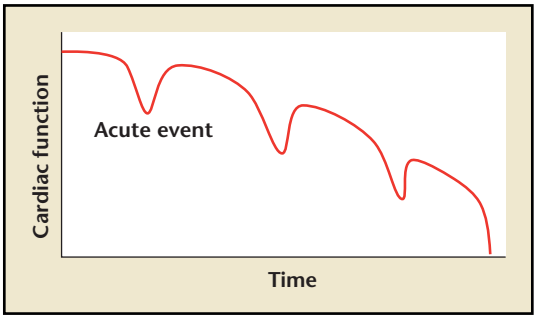

Figure 1. *With each admission for heart failure syndrome, there is a short-term improvement, but the patient leaves the hospital with a further decrease in cardiac function.*

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Table 2
Possible Deleterious Effects of Unrecognized and Untreated Hemodynamic Congestion

- Contributes to the progression of acute heart failure syndromes (myocardial injury and renal dysfunction)
- Main cause of admission and readmission for acute heart failure syndromes
- Associated with increased mortality rates

Table 3
Importance of Early Recognition of Hemodynamic Congestion

- Allows for adjustments in therapy that can prevent hospitalizations
- May prevent progression of heart failure
- May reduce likelihood of employing high-dose diuretics and inotropic agents during hospitalization
- Makes it more practicable to start life-prolonging therapies for heart failure
- May reduce cost of heart failure care

be helpful in identifying patients with high LV filling pressures, even in the absence of clinical congestion.[37]

Although chest x-rays can be a useful tool in the evaluation of HF patients, the absence of findings does not exclude the presence of high PCWP.[38] Physical findings (orthopnea, edema, rales, third heart sound, and elevated jugular venous pressure) or radiographic signs (cardiomegaly, vascular redistribution, and interstitial and/or alveolar edema) have poor predictive value for identifying patients with PCWP values ≥ 30 mm Hg.[38]

Surrogate markers such as monitoring for signs and symptoms of congestion and daily weight measurements are used routinely in the outpatient setting to detect the warning signs of AHFS. However, monitoring daily weight over time is of limited usefulness because it is not a reliable predictor of HF status. Echocardiography, another important tool in the diagnosis of HF, can be used to evaluate both systolic and diastolic function. However, ≤ 50% of HF patients exhibit normal pumping function by echocardiography, and this tool can therefore be limited in these patients.[39]

Other noninvasive inpatient diagnostic tools are also typically used to evaluate congestion. Serum measurements of natriuretic peptide levels of brain-type natriuretic peptide (BNP) or N-terminal (NT) proBNP can be used as a surrogate marker of elevated PCWP.[40-44] Nevertheless, they are not likely to be used to follow dynamic changes in congestion, as their pattern of production and release is too slow to reliably mirror hemodynamic variations. Significant changes in BNP may not occur until ≥ 1 week after an initial test sample, and, even then, changes occur only approximately 50% of the time.[43] Moreover, a change in BNP of 130% or in NT-proBNP of 90% is necessary before results of serially collected data can be considered statistically different.[44]

The gold standard for evaluating congestion in hospitalized patients is the measurement of PCWP, which can closely approximate LV filling pressure, detecting "hemodynamic congestion" even in its early, preclinical state. However, conventional PCWP measurement involves invasive catheterization, limiting its clinical use, especially in the outpatient setting. Implantable hemodynamic monitors allow for ambulatory monitoring of estimated PCWP and adjustments in HF medications based on these readings.[15] Preliminary studies suggest a reduced risk of HF events with access to ambulatory hemodynamic readings in a cohort of patients being followed in centers that provide HF disease management.

Another potential method to assess the development of pulmonary congestion is to measure intrathoracic impedance. Intrathoracic impedance has been inversely correlated to PCWP and fluid balance. This device provides an early warning of congestion that may allow physicians to intervene by adding or titrating medications, possibly preventing the need for hospitalization.[45]

Conclusions

The vast majority of AHFS hospitalizations are related to clinical congestion, rather than to a low cardiac output state. Patients develop hemodynamic congestion several days to weeks before the onset of clinical symptoms and signs. By the time symptoms and signs are evident, patients generally require hospitalization.

Pulmonary congestion is of major prognostic importance in patients with AHFS and is an important predictor of both mortality and morbidity. As a result, congestion is an essential evaluative and therapeutic target in AHFS patients. It is plausible that early identification of hemodynamic congestion, before

the clinical manifestations are present, could reduce the need for hospital admission and readmission, may decrease the likelihood of employing injurious medications that are commonly given during hospitalization, and may allow implementation of the use of life-saving therapies for HF. ■

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Main Points

- The ability to identify hemodynamic congestion before symptoms arise may possibly avoid hospitalizations and reduce disease progression in patients with heart failure (HF).
- Since hospitalization often is a result of severe congestion that started days or weeks before, the hypothesis that has been generated is that early detection of congestion (hemodynamic congestion) may result in implementation of life-saving therapies and, more likely, may lead to the use of lower doses of detrimental medications that are commonly given in this patient population.
- The gold standard for evaluating congestion in hospitalized patients is the measurement of pulmonary capillary wedge pressure (PCWP), which can closely approximate left ventricular filling pressure, detecting "hemodynamic congestion" even in its early, preclinical state. However, conventional PCWP measurement involves invasive catheterization, limiting its clinical use, especially in the outpatient setting. Serum measurements of natriuretic peptide levels of brain-type natriuretic peptide (BNP) or N-terminal proBNP can be used as a surrogate marker of elevated PCWP.
- In the absence of PCWP measurement, assessments of orthostatic blood pressure changes, the Valsalva maneuver, and/or the response of heart rate or blood pressure to sublingual nitroglycerin may be helpful in identifying patients with high LV filling pressures, even in the absence of clinical congestion.
- Although echocardiography is a very important tool in the diagnosis of heart failure, rarely, if ever, can it be used to assess the degree of hemodynamic and/or systemic congestion.

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