Are Hemodynamic Parameters Predictors of Mortality?

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• Hemodynamics • Heart failure pathophysiology • Mortality

The heart failure (HF) syndrome is a common and complex condition associated with significant mortality. Over the past 2 decades, despite important advances in pharmacotherapy and devices, hospital admissions for HF have risen more than 150% and represent the most common reason for hospitalization in persons over 65 years of age.[1,2] Clinical decompensation is a critical event for the patient who has HF and has major prognostic implications including significant mortality. A seeming paradox is that although most patients do not die during the index hospitalization (mortality averages 5%–8%), there is a 10% risk of death in the ensuing 60 to 90 days, and the 1-year mortality following an acute HF exacerbation approaches 35%.[2–5] Ahmed and colleagues,[6] reviewing data from the Digitalis Investigation Group trial, found that incident hospitalization is associated with significant subsequent mortality compared with those with no prior hospitalization for HF (hazards ratio [HR] 2.49, 95% confidence interval [CI], 1.97–3.13; $P < .0001$). A recent post hoc analysis of the Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity (CHARM) database demonstrated similar findings: HF hospitalization was independently associated with increased mortality (HR, 3.15; 95% CI, 2.83–3.50; $P = .0001$).[7] The reason for this dramatic impact of hospitalization on the natural history of HF has not been elucidated but is the focus of ongoing clinical investigation. One hypothesis, related to the current topic, is that congestion (and consequently abnormal hemodynamics) persists in some patients despite clinical improvement during the hospitalization.[8]

Because HF represents a progressive condition that is a manifestation of the interplay of multiple pathobiologic perturbations, the identification of specific factors associated with a poor prognosis that may represent viable therapeutic targets has been challenging. The list of predictors of increased mortality has grown exponentially in recent years in concert with the improved understanding of the HF syndrome and its various clinical manifestations during disease progression.[9] Several predictive algorithms have been created to assist the clinician in risk assessment for the individual patient, particularly when considering referral for advanced therapies such as cardiac transplantation or mechanical support.[10–16] Unfortunately, with the exception of those few patients who go on to receive a cardiac transplant or a left ventricular assist device (LVAD), knowledge of the specific mortality risk for the individual does not necessarily alter therapy or translate to improved outcomes. The question therefore may be asked whether mortality prediction really is helpful in the majority of patients who are not yet candidates for transplantation, given the current recommendation, that certain therapies (angiotensin-converting enzyme inhibitors, beta-blockers, aldosterone antagonists) always must be used.

To address this issue, one must consider that although a relatively strong evidence base exists for patients who have chronic, stable HF, the same does not apply to those at greatest risk for

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death, specifically patients who have recent or ongoing decompensation.[2,17–19] In this HF cohort therapeutic approaches beyond the current evidence base often are necessary for symptom relief with the expectation for improved outcomes. Although, given the current relevance of neurohormonal antagonism, many clinicians may consider the focus on the hemodynamic paradigm obsolete, the authors of this article believe that in the high-risk subgroup of patients who have decompensated HF, hemodynamic derangement is a consistent finding, is prognostically important, and is linked closely to symptoms, disease progression, and survival. Although yet to be proven in randomized trials, tailoring therapy to hemodynamic targets may be even more valid in the current era of HF management, when novel direct and indirect methods for monitoring hemodynamics are available clinically or are being investigated.[20,21] Furthermore, it is clear that merely ensuring the introduction of evidence-based therapies at the time of hospital discharge does not guarantee freedom from early rehospitalization or death.[22]

This article addresses a question that the authors consider to be somewhat rhetorical: ''Are hemodynamic parameters predictors of mortality?'' The specific hemodynamic abnormalities and pathophysiologic consequences distinctive to the patient who has decompensation are reviewed. The data that implicate abnormal hemodynamics as a treatment target associated with increased mortality are addressed. The focus is on patients who have decompensated HF, defined as left ventricular systolic dysfunction and an acute, subacute, or gradual worsening of symptoms while receiving optimal medical therapy.[2,4] This subgroup of patients who have HF represents those who have disease progression despite therapies designed to prevent or delay HF evolution. This subgroup is representative of the HF population in which the association between hemodynamic derangement and mortality is most evident and in whom ''tailored therapy'' to a specific hemodynamic target may be most pertinent.[20,23–25]

THE HEMODYNAMICS OF DECOMPENSATION

HF decompensation in a patient who has previously stable, chronic HF represents approximately 75% to 80% of all hospitalizations for HF according to large international registries.[26–29] These patients, despite optimal medical therapy in the outpatient setting, often have reduced functional capacity on a chronic basis and may have some degree of volume overload, even when perceived to be clinically compensated. Left ventricular wall stress, because of left ventricular dilatation, usually is elevated, and ''compensatory'' neurohormonal mechanisms are heavily involved.[2] When decompensation occurs, leading to hospitalization, clinical findings of congestion usually are readily apparent. The most common congestive findings and frequency of occurrence according to the Acute Decompensated Heart Failure National Registry (ADHERE) database are dyspnea and dyspnea at rest (90% and 34%, respectively), pulmonary rales (67%), and peripheral edema (66%).[26] The decompensation process, which may occur over days to weeks, is associated with progressive hemodynamic deterioration manifest primarily as an increase in left ventricular filling pressure (LVFP) and secondary pulmonary hypertension. In the Vasodilation in the Management of Congestive Heart Failure trial,[30] those admitted for decompensated HF in whom invasive hemodynamic monitoring was performed with pulmonary artery catheterization (PAC) had a pulmonary capillary wedge pressure (PCWP) of 25 to 30 mm Hg but preserved cardiac output. The PCWP, in the absence of mitral stenosis or pulmonary venous disease, generally correlates well with the LVFP. In HF there are several possible reasons for elevated LVFP, including sodium and medication noncompliance. High LVFPs, often a consequence of worsening left ventricular function regardless of cause, underlie most of the symptoms observed on presentation.

It is recognized that specific clinical conditions often associated with decompensated HF, such as atrial fibrillation, myocardial ischemia, and hypertension, result in elevated LVFP. As stated earlier, this process may occur gradually without an immediate change in symptomatology and in most cases results from volume or pressure overload with fluid redistribution to the pulmonary vasculature.[31] Unfortunately, the sensitivity of congestive symptoms as a predictor or warning of high LVFP is poor. In other words, the ''absence'' of symptoms or physical findings does not guarantee that LVFP is optimal. Several studies have evaluated the sensitivity of symptoms, physical findings, or chest radiographs to predict increased PCWP, concluding that signs and symptoms have a relatively poor predictive value for identifying patients who have a PCWP higher than 30 mm Hg. In a study by Mahdyoon and colleagues,[32] only 7 of 22 patients (32%) who had an elevated PCWP had chest radiographic findings consistent with pulmonary venous hypertension or congestion. In another study, clinical signs had only a 58% sensitivity in detecting patients who had a significant elevation