Can We Predict and Prevent the Onset of Acute Decompensated Heart Failure?

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Watch the disease in time: For when, within the dropsy rages, and extends the skin, in vain for helebore the patient cries, and sees the doctor, but too late is wise: Too late for cure, he proffers half his wealth; ten thousand doctors cannot give him health.

—Benjamin Franklin,
Poor Richard’s Almanack, 1749

This rather pessimistic representation of heart failure (dropsy) in the 18th century has some relevance to the presentation of acute decompensation in patients with chronic heart failure in our current century, despite the availability of various therapies that prolong survival and decrease the morbidity of this disorder. In 2006, >1 million hospitalizations for acute decompensated heart failure (ADHF) occurred, and the number of heart failure hospitalizations have increased 175% since 1979. The vast majority of these occurred, and the number of heart failure hospitalizations have increased 175% since 1979.1 The vast majority of these patients, 75.6%, had a history of heart failure,2 and the in-hospital mortality was 3.2%. Patients with preserved left ventricular (LV) systolic function have a slightly lower in-hospital mortality (2.9%) compared with those with an LV ejection fraction ≤40% (3.9%); however, the 3-month mortalities were similar at 9.5% to 9.8%.3 Rehospitalization rates remain high at 29% to 30% for patients with both preserved and decreased LV systolic function, and rehospitalization is an independent predictor of 1-year mortality, especially in elderly patients.4 In addition, patients with ADHF are at greater risk for death and morbidity than those with stable chronic heart failure.5 Thus, the natural history of heart failure may be altered by repeated episodes of decompensation requiring hospitalization. Finally, a tremendous financial burden is involved in the treatment of ADHF. Of the $30.2 billion spent on heart failure care in 2006, $17.8 billion (59%) was related to in-hospital care, an increase of $2.4 billion over the previous year.1

The development of ADHF is a complex process that involves various hemodynamic, neurohumoral, and vascular abnormalities that result in worsening heart failure symptoms, manifested primarily by congestion.6 The initial inciting event has not been determined, and there may be an interplay of a number of factors, including activation of neurohormones (angiotensin II, norepinephrine, vasopressin), renal sodium and water retention, elevation of ventricular diastolic pressures with worsening dilatation and remodeling, development of “functional” mitral regurgitation, decreased coronary perfusion, and the development of renal insufficiency. Ultimately, myocardial injury may occur that could lead to further deterioration in myocardial function and progression of chronic heart failure. In most cases, a progression of pathophysiological processes occurs over days to weeks and results in a fluid-overloaded state. A significant increase in extracellular fluid volume may occur initially without evidence of edema or pulmonary congestion.7 Yet, it is in the early stages of decompensation when effective therapy could prevent further deterioration and prevent the need for more aggressive therapy and hospitalization. Although the majority of patients with either preserved or decreased LV systolic function present with dyspnea (89%) or peripheral edema (66%),2 these symptoms and signs usually appear late in the development of ADHF, and often renal insufficiency, or cardiorenal syndrome, develops, which interferes with a successful response to outpatient oral therapy. An effective, early evaluation of fluid overload, elevated cardiac filling pressures, or cardiac neurohumoral activity could result in a change in therapy that would halt the downward progression of worsening heart failure and restore the cardiac and systemic circulation to its chronic, stable state. To be effective, a diagnostic paradigm would need to have a high predictive value for ADHF requiring hospitalization, and it must be detectable early enough to allow a favorable response to a change in heart failure management. The goals of early detection of ADHF would be to decrease morbidity and hospitalization, to improve symptoms and quality of life, and perhaps to prevent worsening of cardiac function. It is also possible that a decrease in mortality could occur.

An increase in body weight would be expected with an increase in fluid volume with the development of ADHF. Early changes in body weight may herald the development of ADHF and are a signal to change medical management. An increase in self-reported body weight has been shown to occur about 11 days before a hospital admission for ADHF, and the increase in weight preceded the onset of dyspnea by 3 days.8 Guidelines from both the American College of Cardiology/American Heart Association and the Heart Failure Society of America recommend that patients obtain a scale and follow their weights at home after a heart failure hospitalization.9,10 However, changes in body weight may not

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be reliable over time because there may be an increase in nonfluid weight and because fluid retention may occur without a significant increase in body weight as a result of the simultaneous loss of muscle mass owing to cardiac cachexia. Fluctuations in daily weights occur with reported poor correlations between weight gain and both dyspnea and edema in heart failure patients,11 and a small study comparing clinically stable with deteriorating heart failure patients demonstrated poor sensitivity (55%) of weight gain as a predictor of clinical deterioration.12 However, in this study of self-reported weights, an increase of 2.0 kg or 2% in body weight was highly specific (74%) for clinical deterioration. The measurement of brain natriuretic peptide levels also was not helpful in predicting deterioration.

In this edition of Circulation, Chaudhry and colleagues13 report the results of a case-control study of patients referred to a home monitoring program in which daily weights were recorded digitally and transmitted telephonically to a nurse at the monitoring center who tracked changes in weight and reported any increase of >5 lb over a 3-day period to the patients’ physician. Patients who had a prior hospitalization for ADHF were eligible for the study, and changes in weight were compared between those patients rehospitalized for recurrent ADHF and control patients who did not require rehospitalization. A separate analysis of changes in weight was performed in patients who were hospitalized for non-heart failure reasons compared with control patients. Patients were matched for age, similar baseline body weight, gender, and New York Heart Association functional class. The overwhelming majority (97.4%) of these patients had class III heart failure. Patients were referred to the home monitoring system by their managed care organizations, and the mean duration of monitoring was between 9 and 10 months. No differences existed in comorbid conditions between the cases and controls except for a slightly greater use of β-blockers in patients rehospitalized with recurrent ADHF. Unfortunately, diuretic use was not tracked, and no information was collected on LV systolic function. This was an older population of heart failure patients (mean age, 74 years), and 55% were female, suggesting that a large number of these patients may have had preserved systolic function. Patients rehospitalized with heart failure experienced a gradual increase in body weight beginning about 30 days before rehospitalization, and these changes in daily weight were statistically greater than in the control patients. No increase in body weight was present in patients rehospitalized for non–heart failure reasons compared with control patients. In addition, an accelerated increase in body weight began ~7 days before rehospitalization in the patients with recurrent ADHF. The amount of weight gain >2 lb over the week preceding hospitalization was proportionally related to the risk of hospitalization, with an odds ratio of 4.98 for patients who gained >10 lb. When body weight was treated as a continuous variable, the matched odds ratio for rehospitalization for ADHF was 1.07 for each additional pound of weight gain.

This study provides the best evidence to date that increases in body weight caused by fluid retention resulted in hospitalization for ADHF. Although physicians were notified about any significant increase in weight in this study, no information is provided to determine whether a change in medical therapy affected the ultimate outcome of hospitalization. In addition, the criteria for hospitalization were not defined, and information on hospitalization and other pertinent medical data were obtained by patient self-report through telephone interviews. Despite these concerns, the results of this study support using changes in body weight assessed by telephonic monitoring as a means to predict hospitalization for ADHF. More data on other clinical outcomes, the responses to changes in heart failure therapy based on the provided information of increased weight gain, and a cost analysis to determine the cost versus benefit of such a monitoring system are lacking. A prior study using the same commercial transtelephonic system, the Weight Monitoring in Heart Failure (WHARF) trial, evaluated the role of body weight monitoring in patients with LV systolic dysfunction.14 This multicenter, randomized, controlled trial compared the effect of transtelephonic monitoring with symptom monitoring on rehospitalization and mortality in patients with class III (75%) and class IV (25%) heart failure. All patients were referred and followed by cardiologists, and no significant differences in medical therapy existed between the 2 groups. In contrast to the present study by Chaudhry and colleagues,13 no differences were present in the rate of hospitalization for ADHF between the 2 groups. However, patients followed up with electronic monitoring had a 56.2% reduction in mortality over a 6-month follow-up period. No statistically significant differences existed in medication use between the 2 subject groups at 6 months to explain the lack of effect of the electronic monitoring on the hospitalization end point. The authors concluded that the mortality benefit reflected a favorable effect on the acuity and progression of heart failure despite the lack of effect on utilization (hospitalization). This lack of benefit may be related to a “ceiling effect” seen when patients with mild heart failure, class I and II, or patients with access to advanced heart failure specialty programs do not demonstrate a benefit from these advanced electronic monitoring systems.15 As in the study of Chaudhry et al, no cost analysis was included in the WHARF trial. The differences in the prediction of hospitalization between the 2 studies may be related to differences in the population of heart failure patients because those in the WHARF trial had significant LV systolic dysfunction, whereas the study by Chaudhry et al probably included a large number of patients with preserved ventricular function. In addition, patients in the WHARF trial were followed up in heart failure specialty clinics, and the type of cardiac care was not specified in the Chaudhry et al study. Because the therapeutic response to sudden weight gain was not specified in either study, treatment bias that could have affected the results in either study is possible. However, both studies indicate an improvement in cardiac outcomes with transtelephonic monitoring of body weight.

Another approach to the early evaluation of changes in physiological parameters that lead to ADHF has been device-based monitoring.16 These devices can be in addition to existing implantable devices such as implantable cardioverter-defibrillators or biventricular pacemakers, but stand-alone monitoring devices also are being investigated that primarily evaluate physiological parameters and have no
direct therapeutic function. To date, these devices have been used primarily in patients with advanced heart failure secondary to LV systolic dysfunction in whom implantable devices have been shown to have morbidity and mortality benefits. The advantage of these devices is that they often detect changes in fluid balance, cardiac autonomic function, or cardiac hemodynamic function earlier than significant changes in body weight or symptoms.

Impedance monitoring relies on the concept that increases in lung water secondary to fluid overload result in a decrease in electrical impedance. The Medtronic Impedance Diagnostics in Heart Failure Trial (MID-HeFT) evaluated whether decreases in intrathoracic impedance preceded the onset of worsening heart failure symptoms and hospitalization for ADHF. Measurements of intrathoracic impedance were obtained every 6 hours between a right ventricular lead and the pacemaker generator, and physicians were blinded to the impedance data. There was an inverse correlation between elevations in pulmonary capillary wedge pressure and reductions in intrathoracic impedance, confirming the validity of the impedance data. There was an inverse correlation between elevations in pulmonary capillary wedge pressure and reductions in intrathoracic impedance, confirming the validity of the measurement as a determination of volume overload. Importantly, reductions in impedance occurred approximately 15 days before the worsening of symptoms and need for hospitalization for ADHF. This technique was 77% sensitive for detecting hospitalization for volume overload, and an impedance reduction algorithm, the “fluid index,” was developed to detect early changes in volume overload that could initiate changes in therapy to normalize fluid balance. This technique has limited value during the first 30 days after implantation because of the effects of soft tissue edema around the pacemaker generator. Other factors besides volume overload can affect intrathoracic impedance. To date, information on the effect of such monitoring on the prevention of ADHF and other cardiac outcomes is limited. No cost analysis has been performed to determine the potential cost benefit of these devices.

Other devices have evaluated the role of heart rate variability and changes in right ventricular systolic and diastolic pressures and estimated pulmonary artery diastolic pressure in the diagnosis of worsening heart failure. Use of these implantable hemodynamic monitors allows earlier detection of the abnormalities that lead to ADHF compared with changes in body weight and symptoms (the Table). However, it remains to be determined whether this device-based monitoring of heart failure patients is cost effective and whether the use of devices will result in improved clinical outcomes and a reduction in the incidence of ADHF. It also is unclear whether this technology can be applied to the large number of patients with heart failure with preserved ventricular function in whom devices are not currently used for long-term management. In the meantime, the use of more limited monitoring strategies such as assessment of serial changes in body weight may be the first step to reducing the clinical and financial burden of ADHF.

Finally, it is important to note that once ADHF has occurred, aggressive therapy to alleviate volume overload during a hospital admission plays an important role in preventing recurrence and the need for rehospitalization. In the Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) trial in which patients with ADHF secondary to severe systolic LV dysfunction were treated with intravenous diuretics in addition to other intravenous therapies, the mean weight loss required to reduce both right atrial and pulmonary capillary wedge pressures to mildly elevated levels was 4.0 ± 5.4 kg. The establishment of a stable diuretic dose is an important predischarge imperative, and patients should be euvolemic at the time of discharge. This will allow the determination of a “dry weight” that can be used in the outpatient management of medical therapy for heart failure and can serve as a baseline for comparison.

Predicting the development of ADHF in chronic heart failure patients remains a challenge, and the search for the optimal diagnostic strategy that will improve the outcome of these patients continues. More studies are required to determine the efficacy of the various currently available monitoring techniques before a standard approach can be recommended. Ultimately, a system that favorably influences decision making on the part of the treating physician is required to reduce the incidence of ADHF and its adverse effects on the natural history of patients with chronic heart failure.

Disclosures
Dr Wolfel is a member of the speakers’ bureau for GlaxoSmithkline.

References


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