Current Approaches to Monitoring and Management of Heart Failure

Clyde W. Yancy, MD, FACC, FAHA, FACP

Division of Cardiology, Department of Internal Medicine, University of Texas Southwestern Medical Center at Dallas, Dallas, TX

Decompensation in patients with congestive heart failure remains a treatment problem. Earlier detection of decompensation may result in a lessened need for hospitalization and perhaps an interruption of the as-yet-undetermined processes during decompensation that lead to an adverse effect on the natural history of heart failure. B-type natriuretic peptide is produced by right and/or left ventricular tissue in response to an increase in ventricular wall stress and may be used as an indicator of decompensation. New directions in monitoring now include novel device-based algorithms that determine either intraventricular pressure or intrathoracic impedance. When combined with clinical assessment, weight monitoring, and symptom assessment, these newer monitoring platforms may yield improvements in the natural history of heart failure.
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Patients with heart failure who are treated with contemporary evidence-based medical therapy are currently able to enjoy significant improvements in both life expectancy and quality of life. Mortality risk due to heart failure is at least 50% better when compared to historical data, and many of the currently available treatment options, both drugs and devices, are able to positively affect exercise capacity, patient self-assessment of functional capacity,

and overall state of well-being.[1] What remains problematic is the tendency for decompensation, which is frequently of sufficient severity that hospitalization is warranted.[2]

Once the patient is hospitalized, the encouraging expectations in outcomes are dampened. The 1-year risk of death after an index hospitalization for heart failure is 33% and even the 30- to 90-day risk for death is as high as 10%—a value that rivals the 30-day mortality risk of an acute coronary syndrome.[3] Considering that the 6-month risk for re-hospitalization is approximately 50%, it is evident that hospitalization for heart failure and/or the events leading up to hospitalization change the natural history of the disease (Figure 1).[3] Clearly, hospitalization represents the extreme of decompensated heart failure. Thus, it is readily apparent that strategies geared toward identifying decompensation and/or those that anticipate severe episodes of decompensation would indeed be of value in the management of heart failure.

Whereas the improvement in the risk of death due to heart failure is largely due to diminution of the exaggerated adverse neurohormonal response to heart failure, reverse remodeling of the left ventricle, and/or amelioration of the sudden death risk, decompensation is largely due to hemodynamic alterations. This important distinction reflects the dichotomous nature of the management of this illness. It is imperative that all patients with heart failure and impaired systolic function receive appropriate evidence-based therapies, usually neurohormonal antagonists, to alter the natural history of heart failure. Yet to improve symptoms, drugs and/or devices that relieve congestion, reduce afterload, and improve cardiac output are important. Titrating or adjusting those drugs and devices that impact symptoms requires an assessment of symptoms or disease state, that is, *monitoring* of the patient with heart failure is necessary to optimize both therapy and clinical outcomes. See Table 1 for a list of treatments associated with improved outcomes and those that affect symptoms.

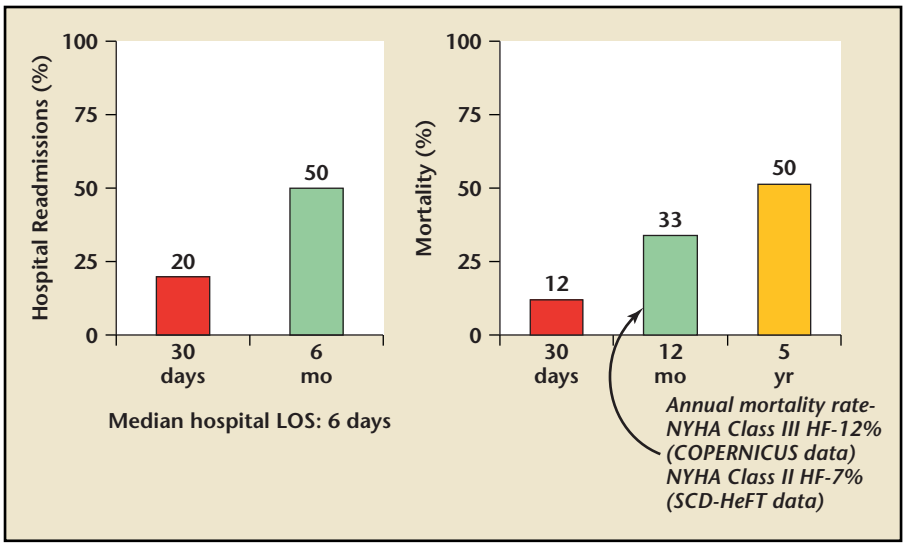


Figure 1. *Outcomes in hospitalized patients with heart failure. HF, heart failure; LOS, length of stay; NYHA, New York Heart Association. Data from Jong P et al.[3]*

Therefore an appropriate goal in the treatment of patients with heart failure is proactive monitoring for direct or indirect evidence of hemodynamic alterations consistent with decompensation. Surprisingly, there is no standard definition of decompensation and no agreed-upon surrogate that is the standard metric for decompensation. Moreover, frank decompensation may represent a far advanced scenario that is characterized not only by ventricular stress, but also perhaps ventricular injury. This would provide a physiologic rationale for the obvious change in

Table 1
Treatment Options for Heart Failure

Intervention	Morbidity/Mortality Benefit	Symptom Benefit
Diuretics	⇔	⇑
ACE inhibitors	⇑	⇑
Angiotensin receptor antagonists	⇑	⇑
Beta-blockers	⇑	⇑
Aldosterone antagonists	⇑	⇔
Isosorbide dinitrate/Hydralazine	⇑	⇑
Implantable defibrillator	⇑	⇔
Cardiac resynchronization therapy	⇑	⇑

⇑, increased; ⇔, neutral effect. ACE, angiotensin-converting enzyme.

the natural history of heart failure that is engendered by an episode of decompensation. Capturing these events early would appear to be of reasonable benefit. There has been much interest and investigation regarding weight change, biomarkers, noninvasive and invasive monitoring, and clinical risk scoring to aid in the determination of decompensation. However, this diagnosis remains a clinical assessment that is highly individualized for each patient with heart failure. Thus, there is no reference point that is the sine qua non for decompensated heart failure.

Several data sources that categorize decompensated heart failure with concomitant hemodynamic monitoring remarkably demonstrate that a low cardiac output (ie, hypoperfusion), is not the common cause of decompensation sufficient to warrant hospitalization. It is in fact evidence of congestion, measured as increased atrial filling pressures, that is the more common hemodynamic alteration.[4] Congestion would necessarily implicate either volume overload or at least volume redistribution. Intuitively, relief of decompensation would therefore correspond to weight loss in the acute care setting. Using this simple metric of weight loss during hospitalization for heart failure, it is evident, based on data from the Acute Decompensated Heart Failure Registry® (ADHERE), that nearly 50% of all patients hospitalized with heart failure experience little or no weight loss and a surprising number of patients are discharged *heavier* than the admission weight (Figure 2).[5,6] Clearly this is a quality initiative and is likely the reason the data from ADHERE reveal that only 44% of patients with decompensated heart failure are discharged free of symptoms. Nearly 40% are sufficiently symptomatic that discharge to home is not reasonable and alternative models of care are required including long-term acute care facilities, nursing homes, and hospice.[5] For those patients who have severe congestion at the time of hospitalization (measured as obvious jugular venous distension and overt edema), the risk of death 60 days after hospitalization is twofold that of those with the absence of severe congestion.[7] Long-term outcomes are also influenced by the absence or presence of congestion. When congestion is measured as a derived point score based on the presence of orthopnea, jugular venous distension, weight gain, diuretic adjustment, and/or leg edema, those patients with the highest risk score have a nearly 50% risk of death at 24 months but those patients with the lowest risk score have only a 10% risk of death at 2 years.[8] Data derived from nearly 1000 patients managed in a university heart failure clinic further support the risk of death or heart failure hospitalization in patients with demonstrable evidence of congestion. The presence of elevated jugular venous pressures was associated with a hazard ratio of 1.15 for all-cause mortality and 1.32 for heart failure–related hospitalization. When combined with the presence of an audible S-3 gallop, the risk of death over 5 years of follow-up was 17% higher and the risk of a heart failure–related hospitalization was 43% higher when compared to patients with neither finding.[9]

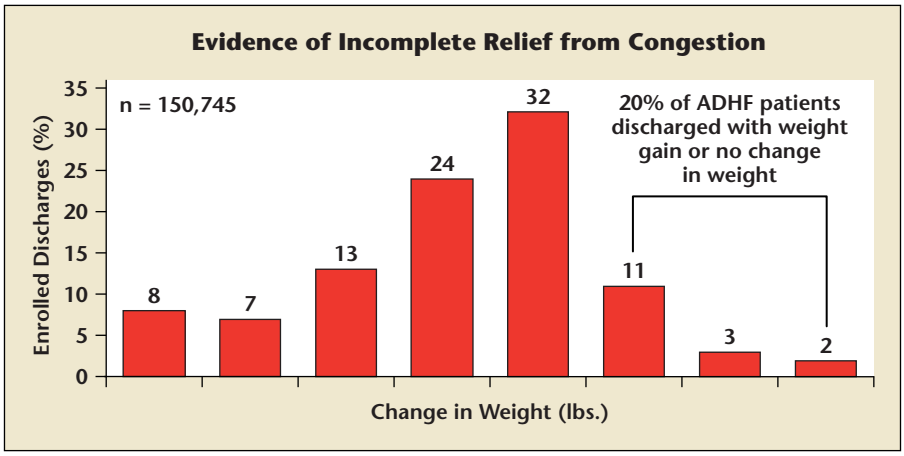


Figure 2. *Change in weight during hospitalizations. All enrolled discharges (n = 150,745), from October 2001 to December 2004. Note: For the chart, n represents the number of patients who have both baseline and discharge weight, and the percentage is calculated based on the total patients in the corresponding population. Patients without baseline or discharge weight are omitted from the histogram calculations. ADHF, acute decompensated heart failure. Adapted from ADHERE® Registry.*[6]

The foregoing discussion confirms the clear role of clinical assessment for the patient with heart failure both at the time of initial evaluation and serial follow-up. This is validated by the American College of Cardiology/American Heart Association 2005 Guidelines for the Management of Chronic Heart Failure.[1] The clinical assessment of heart failure, which includes a careful history and physical examination as well as routine laboratory work, received a class I recommendation at baseline or initial evaluation of heart failure. Especially at the time of serial evaluations, there is also a class I recommendation for the assessment of volume status and weight.[1] See the guideline statements regarding monitoring of patients with heart failure in Table 2. To mitigate the consequences of congestion, patients are advised to follow

Table 2
Guideline Statements Regarding Monitoring of Patients With Heart Failure (HF)

- Recommendations for the Initial Clinical Assessment of Patients Presenting With HF:
  - Class I: History & physical examination; routine laboratory studies including serum creatinine, blood urea nitrogen; 12-lead electrocardiography; chest radiograph; echocardiograph; left heart catheterization if angina is present
  - Class IIa: Catheterization; VO_2 max; B-type natriuretic peptide measurement
  - Class IIb: Noninvasive imaging
  - Class III: Biopsy, measurement of neurohormones
- Recommendations for Serial Clinical Assessment of Patients Presenting With HF:
  - Class I: Functional class; "volume status & weight"
  - Class IIa: Serial measurement of left ventricular ejection fraction and remodeling
  - Class IIb: Serial B-type natriuretic peptide measurement

Data from the American College of Cardiology/American Heart Association 2005 Guidelines.[1]

low sodium diets, monitor weights daily or frequently, and many are placed on flexible diuretic regimens. These intuitive measures represent clinical empiricism, as trials affirming the benefit of these patient-focused strategies have not been done. Because there is great variation in third space volumes from patient to patient, waiting for the presence of edema is too late to engage a change in management. Many patients are able to conceal up to 10 lb. or more of extracellular fluid before frank edema is present. The usual recommendation is for patients to notify a healthcare provider once there is a greater than 3-lb weight gain in 2 to 3 days. Whether more sophisticated weight monitoring with electronic scales and transtelephonic transmission of weights to a central station with reporting of weight changes to specialized management centers represents a better strategy than home monitoring alone has been studied but is not yet clear.[10]

The newest modality that purports to yield insight regarding the absence or presence of decompensated heart failure and/or congestion is the application of biomarkers. The biomarker of greatest interest is B-type natriuretic peptide (BNP).[11] BNP is a 32-amino acid peptide that is produced by right and/or left ventricular tissue in response to an increase in ventricular wall stress. The elaboration of BNP parallels the degree of neurohormonal activation and as such becomes a useful barometer in assessing disease severity. Among the several causes of an increase in ventricular wall stress is an increase in left ventricular filling pressures. Thus, an increase in BNP may in part represent evidence of congestion. Because several other causes of an increase in BNP are known (eg, ischemia, pulmonary embolism, etc) it cannot be assumed that any increase in BNP represents pathognomonic evidence of congestion. Nevertheless, BNP elevations do correspond with clinical evidence of decompensation, and the plasticity of BNP synthesis makes it an intriguing marker of congestion and thus decompensation. Published data comparing BNP to standard clinical signs and symptoms of heart failure remarkably demonstrate that the odds ratio, regarding the diagnosis of heart failure, for an elevated BNP compared to a number of standard clinical assessments is nearly 30 (Table 3).[12] The early data that substantiated the potential benefit of BNP demonstrated that in males presenting with acute dyspnea, an elevated BNP was not only predictive of the diagnosis of heart failure, but that the magnitude of BNP elevation corresponded to disease severity.[13] It is now accepted that the assay of BNP (as well as the assay of NT-BNP[14]) represents a useful adjunct in the *diagnosis* of heart failure—especially when there is clinical ambiguity (Figure 3).[15] A major advantage of BNP assay that has not been fully exploited is in prognostication after an episode of acute decompensated heart failure. At the time of admission, an elevated BNP and especially a concomitantly elevated troponin-I carries a significant risk for short-term mortality. As well, a persistently elevated BNP (ie, > 700 pg/m), at the time of discharge is clearly associated with an increased event rate over the 6 months after hospital discharge and perhaps should be regarded as a stimulus for more intensive disease management.[16,17]

There remains no mandate to make BNP a routine assessment of

Because there is great variation in third space volumes from patient to patient, waiting for the presence of edema is too late to engage a change in management.

Table 3
Predictors of Heart Failure (HF)

Predictor	*P*	Odds Ratio (95% CI)
Age	.04	1.02 (1.00–1.03)
JVD	.04	1.87 (1.04–3.36)
Rales	<.001	2.24 (1.41–3.58)
History of MI	<.001	2.72 (1.63–4.54)
Edema	<.001	2.88 (1.81–4.57)
Cephalization	<.001	10.69 (5.3–21.5)
History of HF	<.001	11.08 (6.6–18.8)
BNP ≥ 100 pg/mL	<.001	29.60 (17.8–49.4)

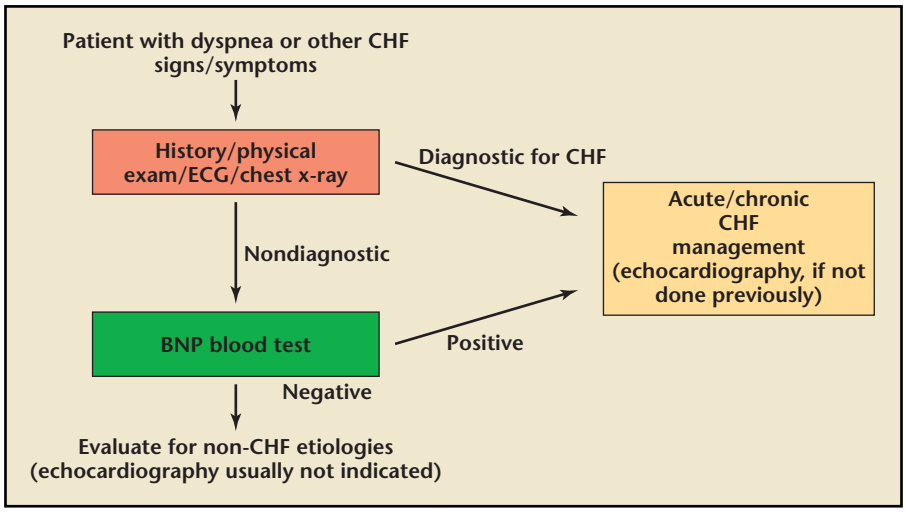
JVD, jugular venous distention; MI, myocardial infarction; BNP, B-type natriuretic peptide. Adapted with permission from Maisel AS et al.[12]

patients with heart failure and there is even less enthusiasm to use BNP as a serial management tool. There are some data regarding the potential role of NT-BNP as a serial management strategy but the available data are from small numbers of patients with short-term follow-up. A large multicenter trial designed to address this question has recently ended due to futility. Thus, the advantage of BNP assay in the diagnosis of heart failure has not yet been duplicated in the serial follow-up of patients with chronic heart failure and the serial assessment of BNP to manage patients with heart failure is not given a high recommendation in the current guidelines. Recent reimbursement guidelines from CMS also dissuade the overzealous measurement of BNP.

Yet another strategy to facilitate the monitoring and management of patients with chronic heart failure has been the use of thoracic bioimpedance. Bioimpedance is based on the fundamental principles of Ohm's law, that is, resistance is proportional to the voltage drop across a circuit and the current applied to that circuit. When a known low level current is applied across the thorax, the propagation of that current is attenuated or enhanced by the inherent resistance in the thorax. Fluid content is the only dynamic variable in the thorax, and given that fluid represents a better conductor of electricity, any increase in thoracic fluid would be associated with a decrease in resistance and an increase in the conductance of any applied current. As well, the change in resistance across the thorax from systole to diastole is proportional to stroke volume (Figure 4). Thus, bioimpedance offers the theoretical benefit of a noninvasive parameter that assesses both flow and congestion. Small, single-center studies have correlated various parameters derived from bioimpedance with measured invasive hemodynamics.[18] The recently reported results of the PREDICT trial now suggest that in patients recently discharged from the hospital, a point score derived from external thoracic impedance cardiography correctly anticipates imminent decompensation measured in weeks. Whether this strategy will prove beneficial in a chronic care model is awaiting further investigation in the PREVENT trial.[19]

The gold standard for hemodynamic assessment has long been the invasive assessment of intracardiac filling pressures and cardiac output. Because of its invasive nature and associated costs, right heart catheterization is not appropriate as a chronic management strategy for heart failure. However, in the hospitalized patient with advanced disease or

Figure 3. *Heart failure diagnostic algorithm. CHF, congestive heart failure; ECG, electrocardiogram; BNP, B-type natriuretic peptide. Adapted with permission from Maisel A.*[15]



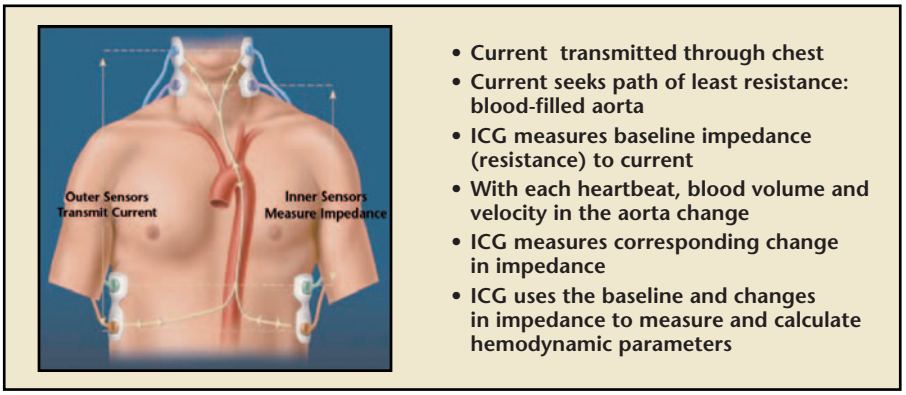
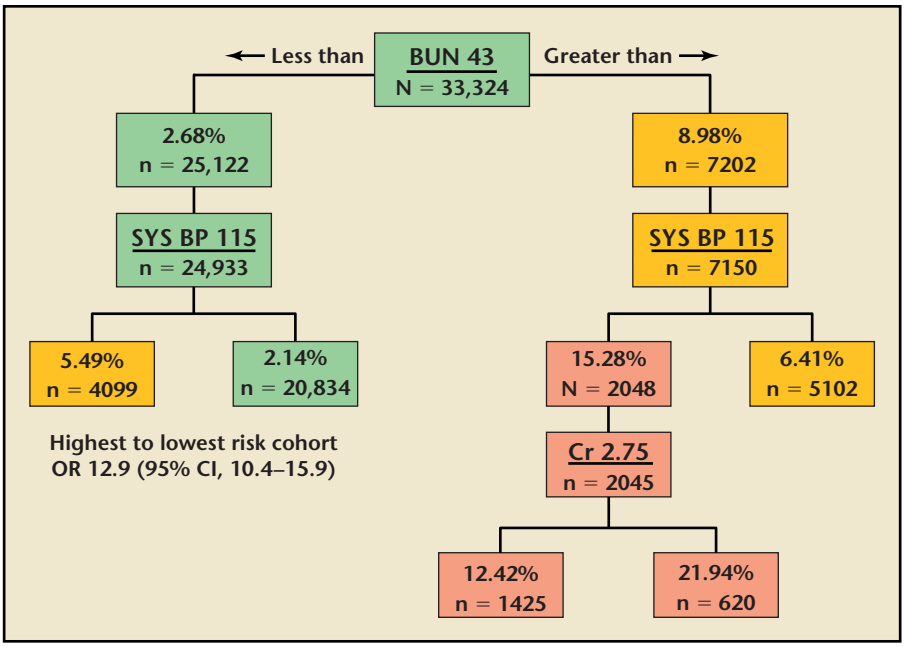


Figure 4. *Impedance cardiography (ICG) method.*

when clinical ambiguity exists, the application of right heart catheterization has been deemed a potentially useful adjunct to clinical assessment. The true benefit of right heart catheterization has only recently been tested in the ESCAPE trial.[20] This National Institutes of Health (NIH)-sponsored randomized trial tested a management strategy of decompensated heart failure in patients with advanced disease facilitated by data from right heart catheterization versus clinical judgment alone. It is apparent that those patients with severe heart failure enrolled in this trial clearly had evidence of congestion at the time of hospitalization with a mean pulmonary capillary wedge pressure of ~ 25 mm Hg. With therapy guided by hemodynamic assessment, filling pressures were substantially reduced and concomitantly cardiac output was increased. Despite these very favorable adjustments in the hemodynamic profile, a comparison of clinical outcomes between the hemodynamically guided group versus the group guided by clinical assessment failed to show a meaningful difference.[20] These data need to be interpreted carefully as the sites involved in this trial were all very experienced heart failure centers and the bedside clinical acumen of the investigators was considerable. It is likely that the outcomes in this trial were more influenced by the experience of the investigators. It is clear, however, that decongestion of the decompensated patient, whether determined by bedside evaluation or hemodynamic monitoring, resulted in better than expected outcomes in this very ill patient population. A role for invasive assessment of hemodynamics in heart failure still exists but its application should likely be reserved for those patients with an uncertain hemodynamic profile at the bedside or for those patients in whom the response to acute therapeutic interventions is not ideal.

Finally, patients with decompensated heart failure do not experience the same natural history even if the assessment of congestion is similar. A recently derived risk algorithm from ADHERE now clearly demonstrates that when decompensation is accompanied by an elevated BUN (> 43 mg/dL), systolic blood pressure lower than 115 mm Hg, or an elevated creatinine (> 2.75 mg/dL), the inpatient mortality risk is increased. For the patient who has none of these variables, the inpatient risk of death due to heart failure is lower than 3%, but for the patient in whom all three variables are present, that risk is increased to greater than 20% (Figure 5).[21] Thus, not only is it important to determine whether decompensation is present, it is also important to understand the context

Figure 5. *ADHERE® CART: predictors of mortality. Red indicates high risk; orange indicates medium risk; and green indicates low risk. BUN, blood urea nitrogen; SYS BP, systolic blood pressure; Cr, creatinine. Adapted with permission from Fonarow GC et al.[21]*



in which it occurs as both the treatment and the prognosis may vary considerably.

Summary

The foregoing discussion demonstrates that to date, the optimal monitoring strategy for patients with heart failure remains clinical assessment. The necessity for monitoring is clearly focused on anticipating decompensation and in turn reducing the need for hospitalization. The hope is that earlier detection of decompensation will result in a lessened need for hospitalization and perhaps an interruption of the as-yet-undetermined processes during decompensation that lead to an adverse impact on the natural history of heart failure. Clearly, there are clinical care niches where evidence does suggest a benefit of one or more monitoring technologies, mostly in the inpatient suite as opposed to outpatient care. Either the cost and/or the invasive nature of the available monitoring strategies precludes extrapolation of these methodologies into the outpatient arena. Yet, it is this patient population in whom the imperative to anticipate decompensation is highest—in part because of the dramatic change in the natural history of heart failure related to hospitalization.

Future strategies in the monitoring of heart failure should focus on the outpatient arena. Ease of acquisition, data reliability, and a demonstration of an ability to improve clinical outcomes are all reasonable goals for new monitoring strategies in heart failure. New directions in monitoring now include novel device-based algorithms that either determine intraventricular pressure[22] or intrathoracic impedance.[23] Emerging data from the COMPASS trial (unpublished) are yielding evidence that hemodynamic derangements *precede* symptoms and that practitioner awareness of these changes and subsequent intervention reduce adverse event rates. A smaller database also suggests that interventions based on knowledge of intracardiac bioimpedance mitigated clinical events.[22] Although these are preliminary data from small patient populations, they introduce the potential benefit of novel monitoring strategies to change the natural history of heart failure. When combined with clinical assessment and the simple strategies of weight monitoring and symptom assessment, it is hoped that these newer monitoring platforms will yield improvements in the morbidity and perhaps even the mortality of heart failure. ■

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Main Points

- Decompensation in patients with congestive heart failure is difficult to predict, detect, and treat.
- Monitoring the patient with heart failure is necessary to optimize both therapy and clinical outcomes.
- Biomarkers, such as B-type natriuretic peptide, may help define decompensation.
- Novel device-based algorithms that either determine intraventricular pressure or intrathoracic impedance, combined with clinical assessment, weight monitoring, and symptom assessment may improve the morbidity of heart failure.

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