Treating Hemodynamic Congestion Is the Key to Prevent Heart Failure Hospitalizations*

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“One once was lost, but now am found. Was blind, but now I see.”
—John Newton, “Amazing Grace” (1)

One of the greatest challenges in the management of patients with chronic heart failure is forecasting and preventing the development of acute worsening leading to hospitalizations. Despite current best practice guidelines, including management within a heart failure clinic, early follow-up after hospitalizations, measuring daily weights, and frequent patient contact, rehospitalization for heart failure occurs at a rate close to 50% over 6 months (2). The major reason for this unacceptably high event rate is our failure to understand and recognize the dissociation between clinical congestion and hemodynamic congestion.

When patients with chronic heart failure are in a compensated state, there is equilibrium between intravascular and extravascular hydrostatic pressure, oncotic pressure, and lymphatic capacity. However, when intravascular hydrostatic pressure exceeds extravascular hydrostatic pressure to an extent that the lymphatic system cannot compensate for this imbalance, patients develop acute hypervolemic decompensated heart failure. Clinical congestion occurs when the increase in the left atrial filling pressures is associated with signs and symptoms such as dyspnea, rales, edema, and weight gain. The elevation of left atrial filling pressures without overt clinical congestion has been termed hemodynamic congestion and it has been shown to precede clinical congestion by days or even weeks (3). The rate at which clinical congestion develops is related to the rapidity of the rise, duration, and magnitude of the left atrial pressure change. Thus, clinical congestion is only the tip of the iceberg of the hemodynamic derangements that herald the condition worsening.

The clinical methods available to detect the onset of hemodynamic congestion and the transition from compensated to decompensated state rely on patient symptoms, physical examination, daily weights, and serial biomarker measurements, such as B-type natriuretic peptide. Unfortunately, these methods have been shown to have insufficient sensitivity and specificity to reliably detect the development of acute decompensation (4).

The advent of implantable hemodynamic sensors has yielded tremendous insight in understanding the hemodynamic congestion and the gradual transition to a decompensated state, identifying time periods at risk and opportunities for intervention. The COMPASS-HF (Chronicle Offers Management to Patients With Advanced Signs and Symptoms of Heart Failure) study found that the length of time over which pulmonary artery diastolic pressure remained abnormally elevated was the hemodynamic factor most closely associated with the transition from chronically compensated to acute decompensated heart failure. In that study, a value over 60 mm Hg · days had a hazard ratio of ~26 in predicting a heart failure hospitalization within 6 months of enrollment (5), suggesting that high chronic ambulatory filling pressures

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may merit more intense intervention, even in patients who appear to be clinically stable or improved after recent hospitalization.

Whereas the COMPASS-HF trial results indicated that proactively treating high filling pressures may result in a lower heart failure hospitalization rate, the CHAMPION-HF (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in Class III Heart Failure) study was the first trial to prove that ambulatory monitoring of intracardiac pressures was clinically useful when translated into systematic pharmacological interventions (6). The study unequivocally showed that, compared with the standard of care, ambulatory hemodynamically guided management resulted in a 33% decrease in heart failure hospitalizations, which predicted a favorable impact on heart failure disease progression as evidenced by further reductions in hospitalizations and a trend towards a decrease in mortality during the long-term (18 months) follow-up (6).

Although a lot of clinicians still remain skeptical of the results of the CHAMPION-HF trial, not fully grasping how the simple knowledge of hemodynamics could have led to such marked decrease in heart failure hospitalizations, we have to understand that no monitoring tool improves patient outcomes without appropriate medical decision making. To that end, the study by Costanzo et al. (7) in this issue of JACC: Heart Failure elegantly describes in detail the pharmacological interventions that, tailored to the intracardiac hemodynamics, were responsible for these successful outcomes. The stepped-up pharmacological algorithm used in the CHAMPION-HF trial recommended use of sequential doses of diuretics and nitrates in order to bring down and maintain the pulmonary artery diastolic pressure below 20 mm Hg. Importantly, the algorithm also provided guidance of de-escalation of diuretics and nitrates if the filling pressures were low, to prevent hypovolemia and the ensuing hypotension and renal dysfunction.

In this setting, more than twice as many medication changes occurred in the active monitoring group compared with the blind therapy group. Diuretics were the most frequently adjusted medications in both groups, but the number of dose changes was almost 3-fold higher in the active monitoring than in the blind therapy group. The frequency of decreases in medication doses was also significantly greater in the active monitoring group, with diuretic dose reductions accounting for the higher frequency in medication decreases in the active monitoring group than in the blind therapy group. As expected, the overall diuretic dose and frequency of changes were higher in patients with higher baseline pulmonary artery diastolic pressure, although the difference in the magnitude of frequency of dose changes between the active monitoring and the blind therapy group widened with increasing values of the filling pressures. Patients at highest risk for hospital admissions (those needing diuretic adjustment during the study) had a 38% lower hospitalization rate if they were assigned to the active monitoring group compared to the blind treatment group. Based on clinical judgment, almost 40% of patients in the blind treatment group were deemed to not need diuretic changes compared with only 18% in the active monitoring group (in which the assessment was based on hemodynamics). Interestingly, these blind treatment group patients had 85% higher heart failure hospitalization rate compared with the active monitoring group, suggesting that risk stratification into a “low diuretic intervention group” was less accurate on the basis of clinical information alone. Remarkably, even though the average change in dose of loop diuretics from baseline to 6 months was significantly higher in the active monitoring group, the estimated glomerular filtration rate was similar in the 2 groups overall, including in the patients with impaired renal function at baseline (estimated glomerular filtration rate below 60 ml/min/1.73 m²). This is a very important finding, because in the CHAMPION-HF trial, the observed decrease in heart failure hospitalizations (related to hemodynamic management) was not achieved at the expense of worsening renal function, as seen in many other similar studies that used the plasma hemocentration as a surrogate for euvoolemia (8).

During the 6 months of the follow-up, 43% of patients in the active monitoring group had adjustments of their vasodilators (almost all occurring in patients who already had diuretic adjustments) compared with only 17% of patients in the blind therapy group. The active monitoring group experienced a significant increase in doses of nitrates and hydralazine from baseline to 6 months, whereas there were no significant increases in doses in the patients in the blind therapy group. The percentage of blind therapy patients given nitrates and hydralazine had a minimal and nonsignificant increase from baseline to 6 months, whereas the percentage of patients given vasodilator therapy nearly doubled in the active monitoring group by 6 months. Another extremely important finding reported by Costanzo et al. (7) is that the changes in vasodilator therapy had a divergent relationship in the 2 treatment groups with the degree of elevation in the baseline pulmonary artery diastolic pressure: there was no
difference in the number of changes of vasodilator therapy in the blind treatment group between patients with low/normal/high filling pressures (average 0.5 changes/patient), but there was a clear linear relationship in the active monitoring group in which the patients with the highest baseline filling pressures had 2 to 3 times more vasodilator changes compared with those in the low/normal range. Importantly, in both groups these changes occurred in patients who already had adjustments of their diuretic doses, highlighting the difficulty in identifying hemodynamic congestion by clinical signs and symptoms alone. The hemodynamic-guided stepped-up pharmacological approach resulted in the preservation of the baseline pulmonary artery diastolic pressures (\(\sim 19\) mm Hg in both groups) in the active monitoring group (median reduction of \(-3.0\) mm Hg \(\cdot\) days), whereas the filling pressures increased significantly over the 6 months follow-up in the blind therapy group (median increase of \(98\) mm Hg \(\cdot\) days).

The elegant analysis by Costanzo et al. (7) of the stepped-up pharmacological algorithm and ambulatory pulmonary artery pressures completes the circle, linking reduction of elevated pulmonary artery pressures (hemodynamic congestion) to reduced heart failure hospitalization rates through a more frequent adjustment of diuretics and vasodilators compared with changes triggered by clinical signs and symptoms alone (clinical congestion).

Lastly, the analysis underscores the vital importance of specifying both the targets of therapeutic interventions and the algorithm guiding such interventions to validate a new management strategy.

We have been lost for far too long in trying to figure out that heart failure is ultimately a hemodynamic disorder, and its management has to target hemodynamics. We have been blind for far too long, but now we can finally see.

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