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EDITORIAL

Inpatient Management of Heart Failure: Are We Shooting at the Right Target?

Inpatient management of patients with heart failure (HF) is under duress. For years, the focus has been on quickly treating patients and discharging them in order to reduce or control the cost of care. A target of reducing length of stay to 5 days was identified (1). More recently, as reimbursements started to penalize early readmissions, the focus of care of patients with HF turned from "early discharge" (rushing to get patients out of the hospital) to "effective discharge." This shift in focus highlights the need for a reliable target for providers to aim at that could signal that patients are stable for discharge. More traditional means of assessing discharge readiness, such as change in weight, physical examination, and symptoms, have proved to be insufficient, as exemplified by the persistently high rate of rehospitalization within 30 days of discharge in patients with HF (2).

McQuade and colleagues present the current evidence on natriuretic peptides (NPs) as markers of risk in patients with HF (3). Their systematic review of clinical trials and studies evaluated NP thresholds (either a specific level or a percentage reduction from admission) as a means to determine risk for future clinical events in patients with HF. From a group of 44 studies, patients with HF who either reduced NP to a target level (primarily a brain-type NP [BNP] level ≤250 pg/mL) or achieved a percentage reduction (primarily a reduction in amino-terminal pro–brain-type NP [NT-proBNP] level of ≥30%) had a reduced likelihood of all-cause mortality and the combined end point of cardiovascular mortality and rehospitalization.

What is clear from the data summarized by McQuade and colleagues is that patients who achieve a substantial decrease in NP levels during in-hospital treatment tend to have better outcomes than those who do not. This seems to be true regardless of the choice of biomarker (BNP or NT-proBNP) or whether the decrease is absolute (to a specific threshold value) or relative (a percentage decrease from an earlier value, typically at hospitalization). The results are not surprising given what we know about the ability of NPs to predict outcomes in various clinical settings. The fact that changes in NP levels reflect changes in outcomes seems to be well-established in patients with both acute and chronic HF (4). What remains uncertain is the extent to which a strategy of care targeting a specific decrease in NP level can actually improve outcomes. The authors frame their conclusions around "achieving" an NP threshold, but most of the studies included in the analysis were prospective cohort studies with no treatment protocol guided by NP levels or targeting an NP threshold. Such a question can be answered only by properly designed prospective randomized, controlled trials (RCTs). Although many such studies have been done in patients with chronic HF (5), the data on hospitalized patients with HF are much less robust.

Two completed phase 2 RCTs tested the hypothesis that treating to a target NP level (an absolute threshold in one and a percentage reduction in the other) would improve clinical outcomes (6, 7). Both studies randomly assigned participants before discharge but after they achieved clinical stability. Participants in the guided group who did not achieve the target had delayed discharge and intensification of therapy (8). The studies differed in important ways, including the timing of randomization, the specific NP goal, and the success of achieving the specified NP target. Neither study showed improved outcomes with an NP-guided strategy, although patients in either group who achieved the NP target had the best prognosis (thus confirming the findings of the observational studies).

McQuade and colleagues rightly identified the need for additional RCTs to properly address this question. They provide several recommendations with regard to study design, including use of a clear intervention algorithm, a large sample size to maintain a trial's validity, use of a hybrid BNP target that incorporates an absolute threshold of a level of 250 pg/mL or less or a decrease of at least 30% from admission levels, and multiple follow-up durations extending from 30 days to 1 year. In addition, trials that enroll and randomly assign patients at the time of admission may be more applicable to the real world than those that do so later in the hospitalization.

Although desirable, such a trial faces important barriers. For one, it is not clear whether patients who do not achieve target NP levels during hospitalization fail to do so due to inadequate treatment (in either intensity or duration) or because their underlying HF is too severe to respond adequately to standard interventions. The former suggests that a strategy focused on intensifying therapy with a "discharge goal" of achieving a specific NP target would likely be beneficial. In the latter case, such efforts are unlikely to be fruitful, other than simply identifying patients at the highest risk. It is unclear whether all admitted patients with HF would be risk-stratified in a similar manner by NP levels. Inclusion of admitted patients with de novo HF reduces the overall risk of the cohort (9). In addition, it is not clear what "intensified treatment" in the face of failure to achieve NP goals should entail—more diuretics? Higher doses of neurohormonal drugs or vasodilators? Longer length of stay or intensified postdischarge follow-up? At present, our limited options for treating hospitalized patients with HF significantly limit our ability to intensify therapy even in patients identified as being at higher risk.

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Natriuretic peptides may be the right target for a clinical trial, but we may not be ready to shoot. The failed phase 2 RCTs underscore the need for greater understanding of the relationship among specific interventions, NP levels, and outcomes when considering the design of future RCTs. Even without a clinical trial, providers should consider incorporating NPs into their clinical practice as a means to risk-stratify patients; guide expectations; and inform treatment decisions, such as the need to consider palliative care or mechanical support.

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