Outcomes in Patients With Heart Failure With Preserved Ejection Fraction
It Is More Than the Heart*
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In this issue of the Journal, Ather et al. (1) report on the impact of noncardiac comorbidities on outcomes in patients with heart failure (HF) with preserved ejection fraction (HFrEF). Their findings are credible, important, and timely. HFrEF is the most common form of HF in the population, is dominant among the elderly, and is increasing out of proportion to HF with reduced ejection fraction (HFrEF), and its prognosis is worsening, while that of HFrEF is improving. The pathophysiology of HFrEF is incompletely understood, and the few clinical trials to date have been negative, such that there are few evidence-based treatments to improve outcomes. It has become clear that there are some important missing pieces in the HFrEF puzzle, and the findings of Ather et al. provide potentially critical insight.

Ather et al. (1) used the U.S. Department of Veterans Affairs External Peer Review Program database, which had EF measurements in more than 17,000 ambulatory patients with HF. Among these, they found 9,442 patients who had EFs measured within 1 year before or 3 months after HF diagnosis. Those with preserved EFs had more noncardiac comorbidities (4 on average) than those with reduced EF. Patients with HFrEF were overrepresented among those with the greatest numbers of noncardiac comorbidities. During 2-year follow-up, patients with HFrEF had more noncardiovascular hospitalizations and fewer HF-related hospitalizations than those with HFrEF. However, in both groups, non-HF hospitalizations dominated and were 3 times greater in patients with HFrEF and 2 times greater in those with HFrEF than HF hospitalizations. Cause-specific mortality was not reported, but several noncardiac comorbidities were independent predictors of total mortality and were similar in both groups, except chronic pulmonary disease, which was a stronger predictor in patients with HFrEF.

Previous studies have established that elderly patients hospitalized with a primary diagnosis of HF often have multiple noncardiac comorbidities (5.5 on average) (2). These patients have frequent rehospitalizations, resulting in high health care costs and patient burden. Importantly, nearly two-thirds of their subsequent hospitalizations are non-HF-related, and approximately 50% are noncardiac (3,4). Furthermore, the majority of patients with HFrEF (55%) die from noncardiovascular causes (5).

The implications of these data for understanding HFrEF are profound. As Ather et al. (1) point out, they might help explain the neutral outcomes of the large HFrEF trials to date. In the I-PRESERVE (Irbesartan in Heart Failure With Preserved Ejection Fraction) trial, although many noncardiac comorbidities were exclusions from the trial, approximately 50% of events during follow-up were noncardiac (6). In the PEP-CHF (Perindopril in Elderly People With Chronic Heart Failure) trial, although many noncardiac comorbidities were exclusions from the trial, approximately 50% of events during follow-up were noncardiac (6). In the PEP-CHF (Perindopril in Elderly People With Chronic Heart Failure) trial, although many noncardiac comorbidities were exclusions from the trial, approximately 50% of events during follow-up were noncardiac (6). In the PEP-CHF (Perindopril in Elderly People With Chronic Heart Failure) trial, although many noncardiac comorbidities were exclusions from the trial, approximately 50% of events during follow-up were noncardiac (6).

Improving HF outcomes in elderly patients, regardless of EF, has proven difficult. Several recently reported trials of promising intervention strategies, including telemonitoring, novel strategies for dosing of loop diuretics, brain natriuretic peptide agonists, and long-term disease management, have had disappointing results. Importantly, these interventions were highly disease specific, as they were in the HFrEF trials, and assumed that outcomes would be predominantly cardiovascular and would be driven solely by cardiovascular-specific mechanisms. However, the data from Ather et al. (1) and many other sources uniformly do not support this assumption.

This important information suggests that a key to improving outcomes in elderly patients with HFrEF is embracing and addressing their multiple comorbidities. Some might retort that this is not the cardiologist’s job. However, if we want to improve outcomes in this disorder, which accounts for the majority of patients with HF, we must lead the effort and develop new strategies. Our specialty has a strong heritage of doing so. About 50 years ago, angiography was a skill primarily of radiologists. About 30 years ago, cardiologists entered the domain previously exclusive to hematologists and made major advances in thrombolysis. Others may reply that we already do a fine job of treating comorbidities. However, the published outcomes data do not support that contention.

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How might this knowledge regarding noncardiac comorbidities lead to the development of new, innovative strategies to improve outcomes in elderly patients with HFrEF? Recognition is a first step. Physicians who treat these patients will understand that HF in an elderly patient is a marker of reduced reserve capacity, not only in the cardiovascular system but also in multiple organ systems, and often globally. Such patients also have high rates of frailty, which can be measured quickly, objectively, and reproducibly and has strong independent prognostic power (7). Furthermore, disease-specific (HF) therapy alone may result in short-term improvement but may have only a modest impact on overall long-term outcomes. Therefore, a more comprehensive approach is needed.

Years ago, inpatient geriatric assessment units, staffed by multidisciplinary teams, were developed and shown in prospective trials to improve key outcomes in elderly patients with acute medical syndromes. This provides cardiologists a template for a comprehensive management approach in elderly patients with HF. Cardiologists could also partner with geriatricians to co-lead multidisciplinary teams. This model has been successful after orthopedic surgery in the very elderly. Both models would be facilitated by sequestration of HF patients to specific geographic units within the hospital.

After hospital discharge, elderly patients with HF remain frail and have prolonged skeletal muscle dysfunction that impairs mobility, which is a major risk factor for readmission, falls, pneumonia, and death (7). However, HF is not an approved indication for cardiac rehabilitation. Furthermore, nearly all exercise rehabilitation trials in HF were conducted in patients who had not had recent hospitalizations. Yet these are the patients at greatest risk. Innovative strategies to address frailty and promote early mobility and comprehensive rehabilitation are needed, along with the trials to systematically test them.

Finally, future trials should recruit patients and assess outcomes that faithfully reflect the disorder in the population (8). For HFrEF, patients in the community are overwhelmingly very elderly (mean age >75 years), predominantly women (about 70%), and have 4 or 5 noncardiac comorbidities. No trial to date has achieved these parameters. Patients with typical comorbidities and frailty should be included rather than excluded, as is usually done, unless clearly contraindicated. The outcomes used in these trials should reflect total events and not focus solely on disease-specific outcomes, which are a minority of events in this population. This will more accurately reflect the impact of treatment on patient burden and health care utilization. Finally, function and quality of life should be emphasized, because these outcomes are often as important as survival for elderly patients.

External pressures are mounting that may accelerate uptake of these data. Because of its high cost, the Centers for Medicare and Medicaid Services (CMS) has designated HF as 1 of only 3 specific diagnoses to receive hypercritical attention. HF outcomes are now publicly reported by CMS for every hospital. Multiple demonstration programs have been planned or implemented by CMS to reduce HF hospitalizations. Beginning in 2012, CMS will penalize hospitals with below-average total outcomes in their patients with HF, including subsequent non-HF rehospitalizations, by reducing their total payments for all diagnoses in all patients admitted to their hospitals. This will place several million dollars at risk annually for individual hospitals. Successful hospitals will appreciate that most rehospitalizations in patients with HF are non-HF-related and will use these data to develop new strategies. Others will continue to pursue the diminishing returns from strategies based solely on disease-specific management.

It seems paradoxical that in patients with “heart” failure, the majority of outcomes are not only non-HF, they are noncardiovascular. As we have in the past, cardiologists should take a leadership role in addressing this problem and use these data to develop new strategies to improve outcomes in the large and growing segment of the population with HFrEF.

**References**


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