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## Treat comorbidities to improve outcome of heart failure with preserved ejection fraction

According to observational studies, nearly half of all patients with chronic heart failure (HF) have a preserved ejection fraction (EF).<sup>1</sup> These patients have a high all-cause mortality after hospitalization: 3% to 6%, in-hospital mortality; 10% to 12%, 60- to 90-day mortality; 22% to 29%, 1-year mortality; and 65%, 5-year mortality.<sup>2,3</sup>

Unlike in patients with HF and reduced ejection fraction, few large randomized controlled trials have been specifically designed for patients with HF and preserved EF. These trials have shown minimal benefit, resulting in the belief that there are few evidence-based therapies for patients with HF with preserved EF, and thus that this kind of HF is "therapy-resistant".

In trials and registries, patients diagnosed with HF with preserved EF are typically elderly (mean age, 75 years), more often women (~65%), and frequently have multiple comorbidities, including hypertension (55% to 77%), coronary artery disease (CAD) (36% to 53%), atrial fibrillation (32% to 41%), diabetes mellitus (32% to 45%), chronic kidney disease (23% to 26%), and cerebrovascular disease (15%), as well as obesity and anemia.

Three large randomized clinical trials in patients with HF with preserved EF and hard end-point data have been completed to date: the Candesartan in Heart Failure—Preserved (CHARM-Preserved),<sup>4</sup> the Ancillary Digitalis Investigation Group (Ancillary DIG) trial,<sup>5</sup> and Perindopril in Elderly People with Chronic Heart Failure (PEP CHF) trial.<sup>6</sup> None showed improvement in survival; all showed fewer hospitalizations and better quality of life in HF with preserved EF patients. Mortality due to cardiovascular causes was responsible for 70% of deaths, and noncardiovascular causes for ~ 30% of deaths. Of the patients who died from a cardiovascular cause, about half died of progressive HF. During the follow-up period (about 2 years), the hospitalization rate due to HF worsening accounted for a minority of patients.

In the community-based, multicenter Management to Improve Survival in Congestive Heart Failure (MISCHF) study, 312 of

1291 patients (24%) had an EF greater than 50%, and during a 6-month follow-up, 44% of these patients were rehospitalized; only approximately 50% were rehospitalized for HF, with the rest of the rehospitalizations due to non-HF causes.<sup>7</sup> In a contemporary 5-year prospective population-based study from France, conducted from 2000 to 2006 in 368 patients who were hospitalized for HF with preserved EF, death was due to cardiovascular causes in 59% and noncardiovascular causes in 41%.<sup>8</sup>

Thus, both trials and Registries highlight the importance of non-HF cardiovascular and noncardiovascular causes of increased morbidity and mortality in patients with HF with preserved EF. Because such patients often have important comorbid conditions, and because these comorbidities strongly influence outcomes, clinicians should aggressively identify and treat conditions such as hypertension, CAD, atrial fibrillation, diabetes, chronic kidney disease, and cerebrovascular disease in these patients rather than waiting for new HF, with preserved HF-specific treatments to emerge.

Such recommendations have been extended to the elderly who comprise the majority of patients with HF with preserved EF. In the Hypertension in the Very Elderly Trial (HYVET),<sup>9</sup> aggressive treatment of hypertension in patients aged 80 years or older resulted in decreased cardiovascular events and improved survival, with the greatest benefit occurring for the HF end point.

**For practicing clinicians who provide care for patients with HF with preserved EF, the message is clear: treat now by treating comorbidities.<sup>10</sup>**

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