Systolic and Non-Systolic Heart Failure Equal Threats

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ROCHESTER, Minn. -- Mortality rates for heart failure patients with preserved left ventricular ejection fraction (non-systolic) are similar to those for patients with a reduced ejection fraction (systolic). However, a higher systolic pressure on admission was a marker of better prognosis.

ROCHESTER, Minn., Nov. 7 -- Mortality rates for heart failure patients with preserved left ventricular ejection fraction (non-systolic) are similar to those for patients with a reduced ejection fraction (systolic), according to separate studies.

In a Mayo Clinic study of ejection fraction and diastolic function in 556 community-living patients, 308 (55%) had preserved ejection fraction (≥50%), while more than 40% also had isolated diastolic dysfunction, Vronique Roger, M.D., and colleagues reported in the Nov. 8 issue of the Journal of the American Medical Association.

Yet at six months, mortality was 16% for patients with preserved ejection fraction as well as for those with a reduced ejection fraction (age- and sex-adjusted hazard ratio, 0.85; 95% CI, 0.61-1.19; P=.33), found the investigators.

The patients were Olmstead County residents with incident or prevalent heart failure (inpatients or outpatients) prospectively recruited from 2003 to 2005. Approximately 80% of the patients had diastolic dysfunction. However, patients with a reduced ejection fraction had more moderate or severe diastolic dysfunction than patients with preserved ejection fraction (odds ratio, 1.67; 95% confidence interval, 1.11-2.51; P=.01), the researchers reported.

Patients presenting with isolated diastolic dysfunction (preserved ejection fraction, often called non-systolic heart failure) made up 44% of the patients with heart failure in the community, the researchers said.

Finally, both low ejection fraction and diastolic dysfunction were independently related to higher levels of brain natriuretic peptide (BNP), the researchers reported.

Limitations of the study include some degree of participation bias, because the residents were identified through Mayo Clinic electronic medical records, the researchers wrote. Furthermore, they said, the racial and ethnic composition of the study might limit the extrapolation of the data to under-represented groups, though the suggested that the study may provide benchmarks for needed comparisons to other populations.

A strength of the study was its community-based approach, and the fact that its design allowed classification of diastolic function in the vast majority of cases.

In this large community-based study, most of the patients had preserved left ventricular ejection fraction and evidence of diastolic dysfunction, the Mayo researchers wrote.

The prevalence of moderate and severe diastolic dysfunction among heart failure patients with preserved ejection fraction was strikingly higher than that observed in elderly patients with cardiovascular disease but without heart failure. This, they said, supports the hypothesis that diastolic dysfunction is present in a large segment of heart failure patients with preserved ejection fraction.

The importance of characterizing the pathophysiology of heart failure with preserved ejection fraction is underscored by the high mortality rate of these patients, which is comparable, they said,
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to that of patients with reduced ejection fraction.

Similar observations regarding the frequency and poor prognosis of heart failure in patients with preserved left ventricular ejection fraction, were reported in the same JAMA issue by, Gregg Fonarow, M.D., of UCLA Medical Center in Los Angeles, and colleagues at a variety of other institutions.

The cohort study used data from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) registry for patients hospitalized with heart failure at 259 U.S. hospitals in 2003 and 2004.

The researchers reported that patients with higher systolic blood pressure on admission had a better prognosis than those with lower systolic blood pressure. In addition, the researchers found no significant difference for in-hospital and post-discharge mortality rates between patients with preserved versus reduced left ventricle systolic function.

Hospital and post-discharge outcomes were based on 48,612 patients 18 or older with heart failure. Of 41,267 patients assessed, 21,149 (51.2%) had preserved left ventricular function (preserved systolic function).

Post-discharge outcomes were based on a prespecified subgroup of 5,791 (10%) of patients with follow-up data. The mean age of the patients was 73; 52% were women, and 74% were white.

The findings were as follows:

- Patients with higher systolic blood pressure were more likely to be female and black and to have preserved systolic function.
- Fifty percent (51.2%) of the patients had systolic blood pressure higher than 140 mm Hg at admission.
- Patients with lower systolic blood pressure at hospital admission had higher hospital and post-discharge mortality rates.
- Higher systolic blood pressure at admission was associated with lower hospital mortality rates: 7.2% (< 120 mm Hg), 3.6% (120-139 mm Hg), 2.5% (140-161 mm Hg), and 1.7% (>161 mm Hg). (Post-discharge mortality rates in the follow-up cohort by systolic blood pressure at admission were 14.0%, 8.4%, 6.0%, and 5.4%, respectively. Prehospitalization rates during follow-up were similar regardless of systolic blood pressure at admission: 30.6% (< 120 mm Hg), 29.9% (120-139 mm Hg), 29.9% (120-139 mm Hg), 30.3% (140-161 mm Hg), and 27.6% (> 161 mm Hg) (P=.31).

Systolic hypertension, common in patients hospitalized for heart failure, is an independent predictor of morbidity and mortality in patients with heart failure with either reduced or relatively preserved systolic function, the researchers said.

This analysis focused on systolic blood pressure because previous studies found less of a relationship between diastolic blood pressure and outcomes in patients with acute heart failure, the researchers said. More important, they added, systolic blood pressure at admission was predictive of outcome independently of diastolic blood pressure.

However, the perception that patients with normal or elevated systolic blood pressure are less ill or at lower risk than those with hypotension and do not need to be treated aggressively is faulty. It should be noted, they cautioned, that the rate of rehospitalization was similar regardless of systolic blood pressure.

These results should be evaluated in the context of several limitations, the researchers pointed out. First, the trial was not a prospective randomized study and unmeasured variables may have been present. Furthermore, they said, systolic blood pressure was not collected prior to admission or after discharge so that chronic changes could not be followed over time.

Summing up, the researchers wrote that the OPTIMIZE-HF analysis indicates that systolic blood
pressure assessment at admission provides important, independent prognostic information. Heart failure patients with low systolic blood pressure (<120 mm Hg) at hospital admission are at the highest risk for mortality despite the use of pharmacological therapies, findings that support previous studies.

Prospective studies should be designed to test the hypothesis that systolic blood pressure at admission is useful for risk stratification, the investigators said, especially because elevated systolic blood pressure appears to signal specific pathophysiological processes that differ from those in patients with low systolic blood pressure.

Low systolic blood pressure at hospital admission identifies patients who have a poor prognosis despite medical therapy. These findings may have important therapeutic implications because characteristics and outcomes differ greatly among patients with heart failure with varying systolic blood pressure, Dr. Fonarow concluded.

In an editorial in the same JAMA issue, Per Hildebrandt, M.D., of Roskilde University Hospital in Roskilde, Denmark, wrote that the findings of these two studies have important clinical implications.

The Mayo study adds substantial new evidence about the prevalence and prognosis of heart failure with reduced and also preserved left ventricular ejection fraction and diastolic heart failure in the community.

Similar observations regarding the high frequency and poor prognosis of hospitalized heart failure in patients with preserved left ventricular ejection fraction were also reported with results from the OPTIMIZE-HF registry.

The findings in both studies that approximately half of patients with heart failure, whether observed in the community or in the hospital, have preserved systolic function and that mortality in these patients is similar to that for patients with heart failure and reduced systolic function have important implications.

Just as heart failure with reduced left ventricular ejection fraction has long been recognized as a common and serious disease and has been the subject of a number large-scale clinical trials, the entities of heart failure with preserved ejection fraction and diastolic dysfunction deserve equal attention, Dr. Hildebrandt said.

Deciphering the mechanisms and developing evidence-based treatments for these major public threats deserve the highest priority, he concluded.

Dr Hildebrandt reported receiving honoraria from Astra-Zeneca, Bristol-Myers Squibb, GlaxoSmithKline, Merck, Novartis, Pfizer, Sanofi-Aventis, Servier, and Takeda.

The researchers reported that GlaxoSmithKline funded the OPTIMIZE-HF registry under the guidance of the OPTIMIZE-HF Steering Committee. GlaxoSmithKline was involved in the design and conduct of the OPTIMIZE-HF registry and funded data collection and management through Outcome Inc, and data management and statistical analyses through the Duke Clinical Research Institute. The sponsor was not involved in the management, analysis, or interpretation of data or the preparation of the manuscript. GlaxoSmithKline reviewed the manuscript prior to submission for publication.

The list of firms or organizations with financial relationships to the researchers included Otsuka, Sigma Tau, Merck, Pfizer, Sanofi-Aventis, Novartis, Bristol-Myers Squibb, Scios Inc., Debbio Pharm, Errekappa Terapeutici, GlaxoSmithKline, Protein Design Labs, Medtronic, Guidant, Abbott, AstraZeneca, Amgen, Wyeth, Biotronik, CHF Solutions, Heart Failure Society of America, Myogen, Orlis Medical, Otsuka Maryland Research Institute, Paracor, Boehringer-Ingelheim, ResMed, Respironics, Scios Inc, CardioKine, CardioKinetix Inc, Inovise, Savacor Inc, RespMed, Respironics, St Jude Medical, Actelion, NitroMed, Novacardia, RenaMed, Sigma Tau, Cardiodynamics, Millennium, Titan, Biosite, Remon Medical Technologies, Artesion Therapeutics, Cotherix, Edwards Lifescience, Kos, Takeda, and Orlis Medical.
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