Strategies for management of heart failure with preserved ejection fraction

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Heart failure with preserved ejection fraction (HFpEF) contributes substantially to hospitalizations, morbidity, and mortality worldwide. Prevalence is estimated to be roughly 2% of the population and is increasing concurrently with diabetes, atrial fibrillation, obesity, and an aging population [1]. Echocardiography is usually adequate to distinguish HFpEF from heart failure with reduced or mid-range ejection fraction, which is important for treatment and prognostication [2]. Effective management strategies for HFpEF are lacking. To date, no randomized trials have shown a mortality benefit, and few have shown clear evidence of reduced hospitalizations.

A variety of indices can be measured to estimate myocardial performance during diastole. When abnormal, diastolic indices are supportive, but not necessary, for the diagnosis of HFpEF [3]. Abnormal diastolic indices are a risk factor, but it remains unclear if treatments can reduce progression to clinical HFpEF [4,5].

In this issue of the Journal, Sharifov et al. report data from a cohort of symptomatic patients undergoing coronary angiography for the evaluation of possible obstructive coronary artery disease. Study participants agreed to undergo cardiac magnetic resonance imaging to evaluate diastolic indices which were linked to drug treatments for coronary artery disease, hypertension, diabetes, and dyslipidemia. They conclude that subjects meeting the study definition for adequate treatment of these conditions had an association with superior diastolic indices. While not explicitly a study of HFpEF patients, 89% had chest pain, 66% had dyspnea, and improvement of diastolic parameters is primarily relevant to the management of HFpEF, more than other conditions.

The findings are aligned with current recommended strategy for the management of HFpEF, aggressive treatment of underlying conditions that may contribute to symptoms in HFpEF [6]. Application of the study findings, however, differs from clinical practice in a few important ways. Hypertension is not managed based on the presence or absence of a specific drug class within a patient’s pharmacological regimen. Adequate control of diabetes is defined by glycated hemoglobin levels, and the study design discounts diabetic patients who have controlled their blood glucose using diet alone. Moderate or high intensity statin therapy is a mainstay in the management of coronary artery disease, however angina treatments much be tailored to individual patients. In addition to frequently causing headaches, nitrates were shown in a randomized trial to be associated with less physical activity and no improvement in quality of life compared to placebo in HFpEF patients [7].

Some promising data are presented in supplementary table 8. Here the authors link diastolic indices, such as left ventricular end-diastolic pressure (LVEDP), to treatment with specific drug classes. They observed lower LVEDP with a nitrate/beta-blocker combination and with a calcium channel blocker in absence of nitrates. This may inform future study of a medication specific strategy, similar to the approach used for HFpEF. Future investigations would be strengthened by linking pharmaceutical treatments to presence and severity of symptoms, imaging-based diastolic indices, and natriuretic peptides, all of which should all change in concert if the study hypothesis is correct.

New strategies for HFpEF may involve use of specific medication classes as noted in this study, although other studies on available compounds, such as inorganic nitrates and inhaled nitrates, and new compounds, such as soluble guanylate cyclase stimulators, are also underway [1]. Angiotensin receptor neprilysin inhibitors hold promise as a strategy for HFpEF [8]. While we wait for those studies to be performed, we should not lose sight of the fact that there is ample room to improve the population’s cardiovascular risk profile. The American Heart Association’s Annual Heart Disease and Stroke Statistics Update for 2019 demonstrates how far we still have to go, with only 19.9% of the US population (≥ 50 years of age) at goal blood pressure and only 27.2% at goal cholesterol [9]. (Fig. 1) In European populations, statins are underutilized and failure to meet cholesterol goals is similar to the US [10].

Disclosures

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Conflict of interest statement

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Fig. 1. Prevalence of cardiovascular health metrics among US adult over age 49. This stacked bar graph shows the proportion of adults with poor (red), intermediate (yellow), and ideal (green) metrics of selected risk factors for cardiovascular health. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

References

[1] Zakeri R, Cowie MR. Heart failure with preserved ejection fraction: controversies, challenges and future directions. Heart. 03 2018; 104(5): 377–384.
[2] J. Webb, J. Draper, L. Fovargue, et al., Is heart failure with mid range ejection fraction (HFmrEF) a distinct clinical entity or an overlap group? Int J Cardiol Heart Vasc. Dec 21 (1–6) (2018).
[3] M.R. Zile, W.H. Gaasch, J.D. Carroll, et al., Heart failure with a normal ejection fraction: is measurement of diastolic function necessary to make the diagnosis of diastolic heart failure? Circulation. 104 (7) (Aug 2001) 779–782.
[4] S.H. Wan, M.W. Vogel, H.H. Chen, Pre-clinical diastolic dysfunction, J. Am. Coll. Cardiol. 63 (5) (Feb 2014) 407–416.
[5] M. Cameli, E. Incampo, S. Mondillo, Left atrial deformation: useful index for early detection of cardiac damage in chronic mitral regurgitation, Int J Cardiol Heart Vasc. 17 (Dec 2017) 17–22.
[6] Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. Oct 2013; 62 (16): e147–239.
[7] M.M. Redfield, K.J. Anstrom, J.A. Levine, et al., Isosorbide mononitrate in heart failure with preserved ejection fraction, N. Engl. J. Med. 373 (24) (Dec 2015) 2314–2324.
[8] T. Biering-Sorensen, A. Shah, B. Claggett, et al., The angiotensin receptor Neprilysin inhibitor (ARNI), Sacubitril/valsartan improves left ventricular myocardial deformation in heart failure with preserved ejection fraction, J. Am. Coll. Cardiol. 71 (11) (2018).
[9] Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics-2019 update: a report from the American Heart Association. Circulation. 03 2019; 139 (10): e56-e528.
[10] I. Dykun, D. Wiefhoff, M. Totzeck, et al., Disconcordance between ESC prevention guidelines and observed lipid profiles in patients with known coronary artery disease, Int J Cardiol Heart Vasc. Mar 22 (2019) 73–77.