Letter by Moody et al Regarding Article “Prevalence and Significance of Alterations in Cardiac Structure and Function in Patients With Heart Failure and a Preserved Ejection Fraction”

To the Editor:

Zile and colleagues should be commended for providing important new data that suggest that the measurement of left ventricular (LV) mass as a continuous variable informs the prognosis of patients with heart failure with preserved ejection fraction (HFPEF). They finish their article by suggesting that the correction of abnormal LV structure and function in HFPEF constitutes a reasonable therapeutic target to reduce morbidity and mortality in such patients. This is an important conclusion, although the authors do not provide any information on the underlying causes for the structural remodeling associated with HFPEF, which may in turn have guided potential treatments. One such target is aldosterone, which, in the presence of sodium overload, is a major cause of the development of increased LV mass, fibrosis, and stiffness in all forms of heart failure, as well as the frequently coexisting condition of chronic kidney disease (CKD). Abundant evidence shows that aldosterone is a potent stimulus to cardiac, vascular, and renal inflammation and fibrosis. Raised aldosterone concentrations are associated with an adverse prognosis in studies of patients with heart failure, cardiovascular disease, and CKD. Furthermore, despite the increasing use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, aldosterone levels frequently remain elevated as a result of the phenomena of aldosterone escape and aldosterone breakthrough. Although patients diagnosed with HFPEF are typically elderly (mean age, 72 years), a significant proportion have underlying CKD (31%), suggesting that the progression of HFPEF should not be considered merely an age-related process. Despite nearly one third of the study’s HFPEF cohort fulfilling criteria for stage 3 CKD (estimated glomerular filtration rate <60 mL·min⁻¹·1.73 m⁻²), the effects of a reduced estimated glomerular filtration rate on LV mass, diastolic dysfunction, and the primary cardiovascular outcome (death from any cause or hospitalization for a cardiovascular cause) were not examined.

We have shown that in patients with stage 2 and stage 3 CKD, even when blood pressure is within the normal range, both aortic and LV stiffness are increased, producing a pattern that resembles HFPEF closely. In the same population, we demonstrated subclinical LV systolic dysfunction with evidence of impaired longitudinal systolic deformation on echocardiography. Improvements in LV mass, arterial stiffness, and LV systolic and diastolic function were evident after treatment with the mineralocorticoid receptor blocker spironolactone.

We suggest that (1) CKD may contribute to the underlying pathophysiological substrate—probably myocardial fibrosis—from which LV hypertrophy and diastolic dysfunction emerges and (2) treatments such as mineralocorticoid receptor blockers or aldosterone synthase inhibitors, which block the deleterious action of aldosterone, are likely to prove to be highly effective treatments for HFPEF by correcting the associated adverse changes in LV structure and function.

Disclosures

None.

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References
