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CORRESPONDENCE

## Letters to the Editor

# Heart Failure With Normal Left Ventricular Ejection Fraction May Be Due to Systolic Dysfunction

Further to the review article on heart failure with a normal ejection fraction (HFNEF) (1), the authors note that HFNEF is associated with hypertension in up to 88% of individuals. Observational studies have shown that there is a significant increase in left ventricular mass but with a relatively normal end-diastolic volume compared with control patients (2). The authors also confirm that there are contractile abnormalities as assessed by strain, strain rate, and peak annular systolic velocities (1,3). Interestingly, systolic velocities correlate ($r = 0.81$) with the severity of the diastolic velocities in *both* heart failure with preserved ejection fraction and in heart failure with a reduced ejection fraction (4). An example of a nonhypertensive etiology of HFNEF is sarcomeric hypertrophic cardiomyopathy. This disorder is associated with myocardial disarray and is caused by a number of gene abnormalities, each of which encodes a contractile protein; both of these abnormalities would be expected to cause contractile dysfunction, and yet the ejection fraction is usually normal or increased.

This apparent contradiction of a normal ejection fraction with widespread (i.e., global) and significant contractile abnormalities in HFNEF is difficult to understand. However, it is plausible that an increase in left ventricular end-diastolic wall thickness would lead to greater thickening in systole given the same longitudinal and mid-wall circumferential shortening. Therefore, in the presence of contractile dysfunction and concentric left ventricular hypertrophy, radial wall thickening (end-systolic wall thickness minus end-diastolic wall thickness) could be within normal limits. The external volume of the heart alters little during the cardiac cycle; therefore, the inward endocardial displacement, endocardial fractional shortening, and ejection fraction would be normal. In summary, at least some examples of HFNEF may be explained by the combination of concentric left ventricular hypertrophy and contractile dysfunction despite the ejection fraction being preserved (5).

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## Reply

In an attempt to further reconcile the paradoxical finding of a normal left ventricular ejection fraction (LVEF) in patients with heart failure with normal ejection fraction (HFNEF), Dr. MacIver proposes that left ventricular (LV) hypertrophy per se augments wall thickening and thereby maintains LVEF in the presence of impaired contractility. While conceptually this may be plausible, the evidence for such a mechanism appears limited. Contrary to this proposition, previous studies have demonstrated that in the presence of lower longitudinal systolic myocardial velocity and variable changes in radial strain, patients with HFNEF or subclinical LV diastolic dysfunction have preserved LVEF in the absence of a significant rise in LV mass (1,2). The mechanism by which this apparent compensation occurs is not clear; however, it has been proposed that preserved circumferential strain and LV twist may contribute (2). These changes may be the result of the relative hypertrophy of mid-wall myocytes, realignment of myocytes, or alterations in the pattern of mechanical activation of fibers of varying spatial orientation resulting in changes in their afterload according to the time of contraction.

Whereas the presence of LV hypertrophy, for example in hypertrophic cardiomyopathy, may be associated with a normal or even high LVEF, studies suggest that wall thickening is reduced and that the preserved LVEF is a function of a smaller LV end diastolic volume (3).

Currently, the key clinical challenge in each patient with a diagnosis of HFNEF is to develop a comprehensive understanding of the pathophysiologic basis of their symptoms on an individual basis. In many cases, it may be difficult to resolve whether symptoms are due to intrinsic LV dysfunction, or whether additional factors such as impaired vasodilatory response, impaired chronotropic competence, fluid overload, ventriculo-vascular mismatch (4), or as suggested very recently, abnormal pulmonary vascular reactivity (5) might play a role. The adoption of other assessment modalities may also be required, including a formal evaluation of the hemodynamic response to exercise to shed light on the pathophysiology of this poorly understood and difficult to manage disease.

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