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Losing track by tracking speckles

Letter to the Editor

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Inclusion of patients whose symptoms are not due to left ventricular dysfunction has undoubtedly contributed to the neutral outcome of many trials of heart failure with preserved ejection fraction (HFpEF). Exertional breathlessness is common in older people. Many are empirically prescribed a loop diuretic in an attempt to relieve symptoms, often without further investigation. This may obscure a diagnosis of HFpEF (1). Obesity, or common problems in older age, such as chronic lung or joint disease, might provoke symptoms during exercise. Decreased activity levels will reduce skeletal muscle function, complicating the interpretation of symptoms and clinical investigations.

In landmark trials, natriuretic peptides have consistently been the strongest predictor of outcome and therefore, if HFpEF is considered a disease that has serious consequences, must be considered a key diagnostic test (2).

We congratulate Mordi and colleagues (3) on their study on patients, with either HFpEF (n=62) or hypertension (n=22), and 28 healthy controls. All subjects underwent cardiopulmonary exercise, very detailed echocardiography and cardiac magnetic resonance imaging (cMRI). Two major findings were reported: firstly, global longitudinal strain (GLS) by speckle tracking worsens as the disease progresses from healthy individuals, to overt HFpEF (4). By contrast, other echocardiographic measurements, such as E/E' (endorsed by guidelines and used in clinical practice to diagnose HFpEF (5)), did not. Secondly, myocardial extracellular volume (ECV) measured by cMRI best discriminates amongst the three populations, leading the authors to suggest a potential role for ECV as an inclusion criterion and surrogate endpoint in clinical trials of HFpEF.

We have several concerns about the populations studied. In a large proportion of those thought to have HFpEF, cardiac dysfunction was likely not to be the primary cause of their symptoms: their median BNP was only 52 ng/L, and more than a quarter had BNP levels below 35 ng/L, a cut-off recommended by European Society of Cardiology (5) to exclude serious cardiac dysfunction. Moreover, despite the inclusion of a group of people with severe exercise intolerance diagnosed as having heart failure, fewer than 50% were prescribed a loop diuretic. By comparison, a loop diuretic *was* prescribed to more than a third of the patients with hypertension despite a lack of recommendation from guidelines; perhaps loop diuretics were masking the presence of HFpEF. Finally, 25% of healthy controls supposed to have “normal” BNP, had a BNP > 35 ng/L, which would have qualified them for a diagnosis of HFpEF if they had reported breathlessness at any point. There was thus substantial overlap between the three groups of subject.

Baseline cardiac rhythm was also not reported: we suspect that all patients enrolled in that study were in sinus rhythm. Although sinus rhythm might be the norm for studies in hypertension, it is highly unusual for patients with HFpEF, amongst whom at least a third is expected to have permanent atrial fibrillation (4, 5). The authors stated that left atrial dilation was one of the key criteria used to diagnose HFpEF, but left atrial dimensions were not reported.

Future studies might confirm that GLS and ECV are useful diagnostic tools to track patient's journey from asymptomatic to overt HF, and may help unravel the complex pathophysiology of HFpEF. However, a common international diagnostic standard is required and this must include, in the current state of knowledge, natriuretic peptides.

References

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