

## Heart failure with mid-range ejection fraction: Two overlapping entities?

### *Insuficiencia cardíaca con fracción de eyección intermedia: ¿Dos entidades superpuestas?*

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#### To the Editor,

We have read with interest the article by Javaloyes *et al*<sup>1</sup> which reviews the new heart failure status (HF), depending on the left ventricular ejection fraction (LVEF): HF with mid-range ejection fraction (HFmrEF - LVEF 40-49%), where it is concluded that it is probably more of a transitional state than a nosological entity in itself.

At present, it is known that HF with reduced (HFrEF) and preserved (HFpEF) ejection fraction are well-differentiated nosological entities<sup>2,3</sup>. Heart failure with reduced ejection fraction is more common in younger men with ischemic heart disease; in contrast, HFpEF is more frequent in older women with high blood pressure and atrial fibrillation<sup>2</sup>. In fact, HFrEF biomarkers have been proven to be more related to cell growth and metabolism, and those present in HFpEF are associated with inflammation and extracellular matrix reorganization processes<sup>3</sup>. In addition, when the degree of myocardial fibrosis is studied by magnetic resonance imaging, it is known that it varies according to ischemic or non-ischemic etiology, and that the type of myocardial fibrosis constrains long-term prognosis<sup>4</sup>. Therefore, we may suppose that HFrEF is a frequent result of a disease that more or less strongly affects the pump-functioning of the heart (most frequent in ischemic heart disease), and HFpEF generally develops progressively over the years due to age-related conditions (arterial hypertension and atrial fibrillation), or senility itself<sup>5</sup>, which gradually lead to chronic in

flammation and myocardial or vascular fibrosis, or both.

Therefore, HFmrEF, more than a transient status, seems to be the presence of two concurrent nosological processes, such as, the existence of ischemic cardiomyopathy in a heart having already begun a senility process. In fact, the degree of comorbidity, fragility and disability, and even precipitating factors in case of decompensation, in subjects with HFmrEF are similar to those in patients with HFpEF<sup>6-9</sup>, although with an ischemic heart disease frequency comparable to that of HFrEF<sup>2</sup>, and it is probably these non-cardiological variables that are likely to prompt results in the short and long term<sup>10,12</sup>.

Considering the above, there is a need to ascertain HF phenotypically better, based on biomarkers and imaging techniques, in order to know which substrate is more meaningful to our patient, and thus be able to make a more personalized approach and develop future personalized treatments.

#### CONFLICTS OF INTERESTS

None.

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## Heart failure with mid-range ejection fraction: Two overlapping entities? Reply

### *Insuficiencia cardíaca con fracción de eyección intermedia: ¿Dos entidades superpuestas? Respuesta*

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#### To the Editor,

We would like to thank Martín-Sánchez *et al*<sup>1</sup> for their comments on our heart failure (HF) with mid-

range ejection fraction (HFmrEF) review<sup>2</sup>, and we would like to clarify some of the aspects reported. They relate that HFmrEF, more than a transitional state, seems to be the presence of two concurrent