

Letters

TO THE EDITOR

Diet-Induced Obesity HFpEF Murine Models



We read with great interest the state-of-the-art review from Valero-Muñoz et al. (1) in a recent issue of *JACC: Basic to Translational Science*. The authors described the more commonly used murine models of heart failure with preserved ejection fraction (HFpEF). They emphasize the importance of including the number of comorbidities typically seen in patients with HFpEF, in addition to the cardiac diastolic dysfunction, which, to date, represent a cardinal point of HFpEF diagnosis. In this comprehensive review, one model appears to be missing, which considering the high prevalence of obesity and metabolic abnormalities in patients with HFpEF, is of utmost importance.

Female and male mice fed with a diet rich in sugars and/or saturated fatty acids (i.e., Western diet) develop severe cardiac diastolic dysfunction, elevated filling pressures, exercise intolerance, as well as myocardial fibrosis, measured at both noninvasive and invasive assessments (2-4). Despite a mild reduction of systolic function reported in mice fed with the Western diet, left ventricular ejection fraction remains 50% or higher, as seen in patients with HFpEF.

The effects appear to be related to the specific nutrients in the diet: a diet rich in saturated fatty acids and/or sugars promotes HFpEF, and one rich in “healthy fats,” namely unsaturated fatty acids (UFAs), preserves cardiorespiratory fitness, body composition, and cardiac diastolic function in obese patients with HFpEF (5). Similarly, mice fed with a diet rich in UFA and low in saturated fatty acids and sugars showed a preserved cardiac diastolic dysfunction and did not gain excess body weight compared with mice fed with an isocaloric diet with similar content of total fat, proteins, and carbohydrates, but rich in sugars and saturated fatty acids.

Of note, a pilot study aimed at increasing UFA consumption in obese patients with HFpEF is currently ongoing (NCT03310099).

In conclusion, we congratulate the authors for their extremely comprehensive and well-written review, but suggest the addition of Western diet-induced obesity to the list of murine models of HFpEF, which presents not only with severe diastolic dysfunction, but also with the typical metabolic abnormalities reported in a large proportion of patients with HFpEF.

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All authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Basic to Translational Science* [author instructions](#) page.

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