

**REPLY: Navigating Nutritional Nuances
in the Research of Heart Failure With
Preserved Ejection Fraction**



We are delighted that Drs Dev and Ahmed found our study¹ of interest. Their comments highlight the importance of malnutrition in patients with heart failure with preserved ejection fraction (HFpEF) and its potential to influence therapeutic interventions. Our study's main focus was to explore the underlying biological mechanisms responsible for skeletal muscle pathology in HFpEF, which we harnessed to identify therapeutic targets via combined caloric restriction (CR) with exercise.¹ We found that CR with exercise rescued muscle pathology in a rat model of HFpEF, whereas pharmacologic cardiac therapies did not.¹ That similar mechanisms underlying muscle growth were affected in both animals and patients with HFpEF suggests a conserved response that, as we highlighted, warrants further investigation.¹

In complex pathologies such as HFpEF, any therapeutic approach requires the optimization of multiple variables, and we welcome the suggestion that nutritional status should form part of this. Indeed, future studies incorporating comprehensive nutritional status assessments before recommending CR in patients with HFpEF seem essential. Unfortunately, physicians often overlook nutritional status, focusing primarily on pharmacologic therapy. Therefore, introducing controlled CR in clinical practice may have the additional benefit of allowing malnutrition to be routinely screened in these patients. However, the lack of standardized definitions for malnutrition and varied assessment tools currently pose a limitation.² In our study,¹ we noted that CR with exercise requires further investigation to ensure efficacy in patients with HFpEF.

Drs Dev and Ahmed further highlight difficulties in translating CR and exercise to the clinic in HFpEF and how malnutrition may limit applicability. Randomized controlled trials have shown that CR and exercise in obese, older patients with HFpEF is safe and feasible and improves muscle performance and quality of life.^{3,4} Unfortunately, malnutrition was not evaluated in these studies,^{3,4} although one may consider that a significant number of patients included would have been malnourished, on the basis of the prevalence cited by Drs Dev and Ahmed. Despite this, no unfavorable responses were reported.^{3,4} Although exercise can counteract frailty in malnourished adults,⁵ more studies are needed on

the effects of CR. Nevertheless, as more than one-half of patients with HFpEF are not diagnosed as malnourished, CR with exercise offers a feasible treatment for a significant proportion of this patient population.^{3,4}

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The 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 [Author Center](#).

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