Reply to Letter to the Editor: “Sexual Dimorphism in the Heart Failure Population”

I read the letter from Çoner¹ with great interest, suggesting that sexual dimorphism may be related to mitochondrial gene expression in heart failure (HF), especially HF with preserved ejection fraction (HFPoEF). The author discussed several studies supporting this argument, starting with a recent study by Cao et al.¹⁰ that identifies the mitochondrial gene Acsl6 as a genetic determinant of diastolic dysfunction in mice.

Since our study demonstrating the diversity in presentation, management, and in-hospital outcomes of acute heart failure (AHF) between male and female patients was an observational recording study, we mainly shared our observations. Of the 1606 patients admitted to the Journey HF-TR study with AHF, 918 (57.2%) were male and 688 (42.8%) were female.¹² The female gender was well represented in the study. While the proportion of patients with HF with reduced ejection fraction (51.0% vs. 72.4%, \( P < .001 \)) was higher in men than in women, the proportion of patients with HF with mid-range ejection fraction (23.7% in women vs. 16.2% in men, \( P < .001 \)) and HFPoEF (25.3% in females vs. 11.4% in males, \( P < .001 \)) were higher in females than males.³ Although the mean left ventricle ejection fraction was higher in the female gender (35.9% vs. 30.3%, \( P < .001 \)), in-hospital mortality was higher than in the male gender (9.3% vs. 6.4%, \( P = .022 \)).³

Mitochondrial dysfunction is accountable for the development of most cardiovascular diseases (CVDs).⁴ Mitochondria-targeted therapy for CVDs have received increasing attention in recent years.⁴ It is now clear that HFPoEF is not an innocent pathology. It is one of the pathologies that has been extensively researched in terms of its underlying mechanism and treatment. As Çoner¹ points out, our observational study can only help speculate on the mechanisms of HF. Well-designed studies comparing mitochondrial mechanisms in HF with different EF levels between well-matched cohorts of 2 sexes may shed light on this issue. Omic technologies can be used for this purpose.

REFERENCES