Endothelin 1: A Potential Prognostic Biomarker for Heart Failure with Preserved Ejection Fraction and Pulmonary Hypertension?

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Dear Editor,

Heart failure (HF) is the major cause of mortality in patients with cardiovascular diseases. Patients with heart failure with preserved ejection fraction (HFpEF) who develop pulmonary hypertension (PH) were shown to have increased short- and long-term mortality [1]. Better understanding of the pathophysiology behind this phenomenon and identifying prognostic markers are imperative to identify high-risk patients and improve outcomes. Recently, we read with great interest the article by Chowdhury et al. [2] published in *Cardiology* showing that endothelin 1 (ET-1) is predictive of 1-year heart failure hospitalization in HFpEF patients, and elevated ET-1 levels were found to be associated with long-term mortality in HFpEF. This study highlights the role of ET-1 in developing PH in HFpEF patients and also explores the potential of ET-1 as a prognostic biomarker.

Other studies have been carried out on this topic. Meoli et al. [3] showed that ET-1 in patients with combined pre- and postcapillary PH (Cpc-PH) was higher, compared to those without PH or with isolated postcapillary PH. These findings implicate an elevated ET-1 as a marker of, and a potential contributor to, the development of Cpc-PH in this population. Moreover, ET-1 is a 21-amino acid peptide which is primarily produced in the pulmonary vascular endothelium and works on ET-A and ET-B receptors. On

the contrary, the contribution of ET-1 to abnormalities in endothelial function, vascular compliance, and PH, implicates ET-1 in the pathophysiology of HFpEF. Therefore, ET-1 inhibition could have therapeutic applications in HFpEF. In support of this, Valero-Munoz et al. [4] demonstrated that dual ET-A/ET-B receptor inhibition improved HFpEF by abrogating adverse cardiac remodeling via antihypertrophic mechanisms and by reducing stiffness.

Collectively, the available evidence suggests a potential prognostic biomarker for HFpEF. Interestingly, ET-1 may serve as a potential prognostic marker for developing PH in HFpEF. Thus, further studies with larger sample sizes are required to validate that ET-1 can potentially be used as a prognostic biomarker in the future. Early identification of HF patients with higher risk can lead to earlier intervention, which may potentially improve outcomes.

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There are no competing interests to declare. The authors have no conflicts of interest to disclose.

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