

HFpEF and BREATH2 score: From Prognostic Risk to Etiological Heterogeneity

To the Editor,

Risk stratification in heart failure with preserved ejection fraction (HFpEF) remains challenging because diagnostic probability and prognostic risk do not necessarily reflect the same clinical features. In this context, the study by Yalvaç et al¹ provides an interesting perspective by evaluating the BREATH2 score as a predictor of 1-year mortality in these patients. The authors found that BREATH2 was independently associated with mortality and showed greater prognostic discrimination than H₂FPEF, while its performance did not significantly differ from HFA-PEFF. These findings extend the potential utility of a score originally developed as an echocardiography-independent screening tool for HFpEF and raise the broader question of what clinical dimension BREATH2 actually captures.²

An interesting question arising from these results is what the prognostic performance of BREATH2 actually represents. The score incorporates age, atrial fibrillation, coronary artery disease, elevated natriuretic peptides, anemia, cardiomegaly, and electrocardiographic left ventricular high voltage.² Several of these variables are established markers of cardiovascular or systemic disease burden and are themselves associated with adverse outcomes. Thus, as appropriately suggested by Yalvaç et al¹, BREATH2 may perform well precisely because it captures multidimensional clinical vulnerability.

The present findings support this interpretation. Non-survivors had markedly higher NT-proBNP and creatinine and lower hemoglobin, while BREATH2 remained independently associated with mortality after adjustment for creatinine and NT-proBNP. Conversely, H₂FPEF, which was specifically developed to estimate the probability of HFpEF, showed limited discrimination for mortality.¹ This divergence between diagnostic probability and prognostic risk is conceptually relevant: the characteristics identifying a patient as likely to have HFpEF may not necessarily be those determining prognosis.

This observation also intersects with the broader challenges surrounding HFpEF classification. We previously suggested that contemporary HFpEF screening strategies may predominantly identify a phenotype characterized by exercise intolerance, cardiovascular comorbidity burden, and biomarker abnormalities rather than identifying patients prone to developing acute heart failure with overt fluid overload and congestion.^{3,4} The present study provides an interesting prognostic counterpart to this concept: BREATH2 may identify a particularly vulnerable phenotype because its components capture the burden of underlying cardiovascular and systemic abnormalities.

Importantly, Yalvaç et al¹ excluded significant primary valvular heart disease and hypertrophic or restrictive cardiomyopathy, but different underlying cardiac substrates may still be represented within the HFpEF label. This distinction may be clinically relevant because patients presenting with preserved or mildly reduced ejection fraction and objectively confirmed acute congestion frequently exhibit

LETTER TO THE EDITOR

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identifiable alternative cardiac pathologies rather than isolated diastolic dysfunction.⁵

Future studies evaluating BREATH2 according to etiological HFpEF phenotypes could therefore clarify whether its prognostic value primarily reflects HFpEF severity or, more broadly, the vulnerability of the heterogeneous population currently classified as HFpEF. Moving from diagnostic probability and risk prediction toward etiological characterization may ultimately provide information more directly relevant to individualized management.

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