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Revisiting Triglyceride-Glucose Index in HCM and HFpEF: Clarifying Confounders and Interpretative Limitations

LETTER TO THE EDITOR

To the Editor,

We read with great interest the study by Liu et al[1] investigating the association between the triglyceride-glucose (TyG) index and prognosis in patients with hypertrophic cardiomyopathy (HCM) and heart failure with preserved ejection fraction (HFpEF).[1] The finding that higher TyG levels were associated with lower all-cause and cardiovascular mortality is intriguing, as it challenges the well-established adverse role of insulin resistance in cardiovascular disease. Several methodological and clinical aspects warrant clarification before these findings can be integrated into clinical interpretation.

The study measured TyG values at "admission," but did not clarify whether patients were enrolled during acute decompensation, elective hospitalization, or outpatient evaluation. Since metabolic and hemodynamic profiles vary significantly across these contexts, the absence of this information restricts the interpretation of TyG's prognostic significance. Although all participants were symptomatic (NYHA class II-IV, NT-proBNP ≥300 pg/mL), these inclusion criteria alone do not confirm an acute heart failure state. Given that metabolic indices fluctuate under acute stress, distinguishing between acute and chronic presentations is crucial for accurate prognostic assessment.

A paradoxical observation was that the highest TyG quartile, which also had the highest prevalence of diabetes (21.3%), exhibited the most favorable survival outcomes.[1] The authors hypothesized that this reflects adaptive metabolic remodeling in HCM, where glucose oxidation becomes a compensatory energy pathway under chronic pressure overload.[1] However, subgroup analyses by diabetes status were not reported, limiting mechanistic inference.

Therapeutic management variables likely influenced outcomes. Despite an atrial fibrillation prevalence of 21.7%, only 13.3% of patients were anticoagulated.[1] Such underuse could have increased the incidence of cardiovascular events, confounding survival differences. Additionally, digoxin use, discouraged in obstructive HCM due to potential worsening of outflow obstruction, was significantly higher in the lowest TyG quartile (6.6% vs. 1.8%, $P = .049$). Furthermore, data on aldosterone antagonists, SGLT2 inhibitors, and device therapy (implantable cardioverter defibrillator or pacemaker) were not provided. Contemporary HCM and HFpEF management guidelines emphasize evidence-based therapies and comprehensive device consideration to improve survival outcomes.[2,3]

Echocardiographic data also appear incomplete. While the authors reported left atrial diameter, neither left atrial volume index nor left ventricular mass index was included, despite their established roles in HFpEF diagnosis and phenotyping.[4]

In summary, Liu et al[1] provide a thought-provoking contribution suggesting that higher TyG levels may represent adaptive metabolic remodeling rather than maladaptive insulin resistance in HCM-HFpEF. However, incomplete data on clinical recruitment, diabetes stratification, medical therapy, and structural characterization limit interpretability. Future prospective studies incorporating standardized

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heart failure management, advanced metabolic imaging, and explicit differentiation of acute versus chronic HF states are required to validate whether TyG reflects true metabolic adaptation or residual confounding.

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