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Reply to the Letter to the Editor: "Revisiting Triglyceride-Glucose Index in HCM and HFpEF: Clarifying Confounders and Interpretative Limitations"

LETTER TO THE EDITOR
REPLY

To the Editor,

We thank the readers for their thoughtful comments[1] and interest in our study 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). We appreciate the opportunity to clarify several key methodological and clinical aspects raised in the letter.

The readers emphasize the importance of the clinical context in which TyG was measured. Our study predominantly enrolled patients during stable clinical states, primarily from outpatient or elective hospital evaluations. We acknowledge that in a retrospective multicenter study, it is challenging to uniformly ascertain and document the acuteness of presentation for every patient. This is a recognized limitation of the study design. However, to mitigate the potential confounding effect of acute hemodynamic stress on our primary findings, our statistical models extensively adjusted for key markers of disease severity and potential instability, including New York Heart Association class, N-terminal pro-B-type natriuretic peptide levels, systolic blood pressure, and renal function.[2] This helps to control for the influence of clinical status on the observed associations. We agree with the readers that future prospective studies should explicitly stratify enrollment based on acute versus chronic status to validate and refine these findings.

The observation that the highest TyG quartile was associated with better survival is indeed intriguing. We agree that subgroup analyses by diabetes status would have been informative. In fact, as presented in Figure 4, a pre-specified subgroup analysis based on diabetes status was indeed performed.[2] The results demonstrated that the association between a higher TyG index and reduced risk of all-cause mortality (Figure 4A) and cardiovascular mortality (Figure 4B) was consistent in both non-diabetic and diabetic subgroups. Specifically, in non-diabetic patients, the TyG index was significantly associated with lower all-cause mortality (hazard ratio (HR): 0.63, 95% CI: 0.48-0.82, $P = .001$) and cardiovascular mortality (HR: 0.49, 95% CI: 0.35-0.68, $P < .001$). In diabetic patients, the point estimates for the TyG index also suggested a trend toward reduced risk for both all-cause mortality (HR: 0.92, 95% CI: 0.53-1.58, $P = .755$) and cardiovascular mortality (HR: 0.89, 95% CI: 0.45-1.78, $P = .750$), although these associations did not reach statistical significance, likely due to the small sample size of this subgroup (n = 137, 12.5% of the cohort). Critically, the P-values for interaction for diabetes status were non-significant ($P = .213$ for all-cause mortality and $P = .097$ for cardiovascular mortality). This indicates that the relationship between the TyG index and survival outcomes was not statistically different between diabetic and non-diabetic patients. The protective trend observed in the overall cohort was thus consistent across diabetes status, strengthening the notion that the TyG index may reflect a broader metabolic state relevant to HCM-HFpEF prognosis, rather than being merely a proxy for diabetic dysglycemia.

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We acknowledge the readers' concerns regarding the underuse of anticoagulation in atrial fibrillation and the uneven distribution of digoxin use across TyG quartiles. Our multivariable models adjusted for a wide range of clinical covariates. However, we recognize that unmeasured or residual confounding, such as differential use of sodium-dependent glucose transporters 2 inhibitors, aldosterone antagonists, or device therapy may persist. Future prospective studies should incorporate detailed treatment data to better account for these factors.

Although left atrial volume index and left ventricular mass index are valuable in HFpEF phenotyping, our diagnostic criteria for HFpEF incorporated multiple echocardiographic parameters. Echocardiographic parameters for the diagnosis of HFpEF in our study include septal early diastolic mitral annular velocity (e') <7 cm/s, lateral e' <10 cm/s, tricuspid regurgitation velocity >2.8 m/s, left atrial volume index >34 mL/m^2, left ventricular ejection fraction ≥50%, E/e' >8, and E/A ≤0.8, or defined according to reported diastolic dysfunction.[2] While left ventricular mass index was not routinely available in this multicenter retrospective cohort, we include other structural and functional indices to minimize bias.

In conclusion, we agree that the relationship between the TyG index and prognosis in patients with HCM and HFpEF is complex and may reflect both metabolic adaptation and residual confounding. This highlights the need for prospective studies incorporating standardized metabolic imaging, detailed phenotyping, and comprehensive treatment data.

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REFERENCES

1. Bektaş H, Akkaya F, Hoşoğlu Y. Revisiting triglyceride glucose index in HCM and HFpEF: clarifying confounders and interpretative limitations. *Anatol J Cardiol*. 2026;30(4):281-282.
2. Liu L, Zheng Y, Ma H, et al. Association between triglyceride-glucose index and prognosis of patients with hypertrophic cardiomyopathy and heart failure with preserved ejection fraction. *Anatol J Cardiol*. 2025;29(11):619-629. [CrossRef]