THE ANATOLIAN JOURNAL OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

Reply to the Letter to the Editor: "Commentary on the Prognostic Interpretation of the Triglyceride-Glucose Index in Patients with Hypertrophic Cardiomyopathy and Heart Failure with Preserved Ejection Fraction"

LETTER TO THE EDITOR REPLY

To the Editor,

We thank the reader[1] for their thoughtful commentary and for engaging with our study[2] on the triglyceride-glucose (TyG) index in patients with hypertrophic cardiomyopathy (HCM) and heart failure with preserved ejection fraction (HFpEF). We appreciate the opportunity to address the methodological and pathophysiological points raised.

The reader rightly notes that an elevated TyG index is conventionally associated with insulin resistance and adverse outcomes in the general population. However, we propose that the observed protective association in HCM-HFpEF may reflect a context-dependent metabolic phenotype unique to this population. In HCM, chronic pressure overload induces a shift in myocardial substrate utilization from fatty acid oxidation toward glucose oxidation, a well-documented adaptive response to maintain energetic efficiency.[3] This metabolic remodeling is supported by positron emission tomography studies showing increased glucose uptake in hypertrophied myocardium.[4] Thus, a higher TyG index in this specific setting may not solely reflect systemic insulin resistance but could also indicate enhanced myocardial glucose availability. While we acknowledge the observed protective effect requires further mechanistic validation, it is consistent with prior evidence in HCM populations.[5]

We agree that the unequal distribution of diabetes and related treatments across TyG quartiles is an important consideration. However, our multivariable models are adjusted for diabetes status and key comorbidities.[2] Furthermore, during the study period, the use of sodium-glucose cotransporter 2 inhibitors in this multicenter Chinese HCM-HFpEF cohort was not widespread, minimizing their potential confounding effect. Nevertheless, we recognize that unmeasured or residual confounding, including detailed antidiabetic therapy, cannot be entirely excluded in a retrospective design.

Regarding phenotypic heterogeneity, our cohort indeed included varied HCM subtypes. However, this reflects real-world clinical diversity, and our models adjusted for relevant echocardiographic parameters, including left ventricular diameter, left atrial diameter, right atrial diameter, maximum wall thickness, and left ventricular outflow tract gradient to mitigate confounding.[2] We agree that future studies with deeper phenotyping are needed to explore subtype-specific associations.

We also acknowledge the limitation regarding sudden cardiac death. With only 56 events, the analysis was underpowered to detect modest associations, a point explicitly stated in the Study Limitations part of our study.[2] This does not negate

Yi Zheng[1,#]
Lei Liu[2,#]
Xiaoping Li[3,*]
Tong Liu[1,*]

[1]*Tianjin Key Laboratory of Ionic-Molecular Function of Cardiovascular Disease, Department of Cardiology, Tianjin Institute of Cardiology, Second Hospital of Tianjin Medical University, Tianjin, China*
[2]*Department of Cardiology, Suining Central Hospital, Suining, China*
[3]*Institute of Cardiovascular Diseases & Department of Cardiology, Ultrasound in Cardiac Electrophysiology and Biomechanics Key Laboratory of Sichuan Province, Sichuan Provincial People's Hospital, School of Medicine, University of Electronic Science and Technology of China, Chengdu, China*

Corresponding author:
Tong Liu
✉ liutongdoc@126.com

Cite this article as: Zheng Y, Liu L, Li X, Liu T. Reply to the letter to the editor: "Commentary on the prognostic interpretation of the triglyceride-glucose index in patients with hypertrophic cardiomyopathy and heart failure with preserved ejection fraction." *Anatol J Cardiol.* 2025;XX(X):1-2.

#These authors contributed equally.
*joint senior authors.

DOI:10.14744/AnatolJCardiol.2025.6052

the robust associations observed for all-cause and cardiovascular mortality in a large, well-characterized cohort.

In conclusion, while the paradoxical association challenges conventional interpretations, it underscores the importance of contextualizing biomarkers within specific disease pathophysiology. We agree that prospective studies with detailed metabolic profiling, standardized therapies, and external validation are essential. Our findings highlight a potentially unique role of TyG in HCM-HFpEF that warrants further investigation.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declare that this study received no financial support.

REFERENCES

1. Yılmaz A. Commentary on the prognostic interpretation of the TyG index in patients with HCM and HFpEF. *Anatol J Cardiol*. 2025.
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]
3. Taegtmeyer H, Sen S, Vela D. Return to the fetal gene program: a suggested metabolic link to gene expression in the heart. *Ann N Y Acad Sci*. 2010;1188:191-198. [CrossRef]
4. Aoyama R, Takano H, Kobayashi Y, et al. Evaluation of myocardial glucose metabolism in hypertrophic cardiomyopathy using 18F-fluorodeoxyglucose positron emission tomography. *PLoS One*. 2017;12(11):e0188479. [CrossRef]
5. Meng X, Gao J, Zhang K, et al. The triglyceride-glucose index as a potential protective factor for hypertrophic obstructive cardiomyopathy without diabetes: evidence from a two-center study. *Diabetol Metab Syndr*. 2023;15(1):143. [CrossRef]