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Concerns Regarding the Interpretation of Triglyceride-Glucose Index as a Protective Factor in Hypertrophic Cardiomyopathy

LETTER TO THE EDITOR

To the Editor,

We read with interest the article by Liu et al[1] investigating the association between the triglyceride-glucose (TyG) index and outcomes in patients with hypertrophic cardiomyopathy (HCM) and heart failure with preserved ejection fraction (HFpEF). While the study is notable for its large sample size, we have significant reservations regarding the interpretation of the TyG index as a protective factor.

The central claim that a higher TyG index reflects beneficial metabolic remodeling is not supported by recent mechanistic evidence. On the contrary, studies indicate that increased myocardial glucose utilization in HCM is a marker of underlying mitochondrial dysfunction and an inadequate energy state, not an adaptive protection.[2,3] For example, research by Vaniya et al[2] demonstrates that this metabolic shift co-occurs with significant lipid peroxidation and cardiolipin damage, hallmarks of metabolic distress. Another study describes a self-perpetuating cycle of decline in HCM where such metabolic changes ultimately worsen diastolic function.[3] This directly contradicts the proposed framework of protective adaptation.

A critical flaw is the lack of genetic data, which severely limits the interpretability of the findings. Metabolic disturbances in HCM are highly genotype specific.[2] The observed protective association could be entirely confounded by the uneven distribution of genetic subtypes within the cohort, rather than representing a true biological effect.

Furthermore, the results starkly contradict the established literature in general HFpEF populations, where a high TyG index is a consistent marker of insulin resistance, inflammation, and worse prognosis.[4,5] The authors' explanation for this reversal in HCM patients is not substantiated by a plausible biological mechanism.

Methodologically, the study is underpowered to assess the relationship with sudden cardiac death, a paramount endpoint in HCM, due to the low event count. The diagnostic criteria for HFpEF, reliant on an N-terminal pro-B-type natriuretic peptide (NT-proBNP) cut-off not validated in HCM, also introduces potential bias.

In summary, the assertion of a protective TyG index is premature. The observed association must be interpreted with extreme caution, considering the conflicting mechanistic data, unaddressed genetic heterogeneity, and inconsistency with broader HFpEF research. Future studies integrating genetic data, myocardial metabolic phenotyping, and TyG trajectories are needed to clarify whether TyG reflects true protective metabolic flexibility or serves as a surrogate marker of unmeasured disease characteristics.

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REFERENCES

1. 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]
2. Vaniya A, Karlstaedt A, Gulkok D, et al. Allele-specific dysregulation of lipid and energy metabolism in early-stage hypertrophic cardiomyopathy. *J Mol Cell Cardiol Plus*. 2024;8:100073. [CrossRef]
3. Wijnker PJM, Sequeira V, Kuster DWD, Velden JV. Hypertrophic cardiomyopathy: a vicious cycle triggered by sarcomere mutations and secondary disease hits. *Antioxid Redox Signal*. 2019;31(4):318-358. [CrossRef]
4. Zhou Q, Yang J, Tang H, et al. High triglyceride-glucose (TyG) index is associated with poor prognosis of heart failure with preserved ejection fraction. *Cardiovasc Diabetol*. 2023;22(1):263. [CrossRef]
5. Wang T, Xu J, Zhang H, Tao L, Huang X. Triglyceride-glucose index for the detection of subclinical heart failure with preserved ejection fraction in patients with type 2 diabetes. *Front Cardiovasc Med*. 2023;10:1086978. [CrossRef]