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LETTER

Comment on "Association Between Triglyceride-Glucose Index and Malignant Risk in Thyroid Nodules: A Cross-Sectional Analysis" [Letter]

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Dear editor

We read with great interest the article by Qiu entitled "Association Between Triglyceride-Glucose Index and Malignant Risk in Thyroid Nodules: A Cross-Sectional Analysis".[1] This study explored the association between triacylglycerol-glucose index (TyG) and papillary thyroid cancer (PTC) through large-sample cross-sectional data, which provided valuable clues for an in-depth understanding of the relationship between metabolic abnormalities, thyroid function and tumor risk. While recognizing the authors' work, we would like to take this opportunity to share some constructive methodological suggestions with the authors.

First, we note that the authors adjusted for a variable highly correlated with TyG (glucose) as a confounder and included it in their multifactor logistic regression model. We believe that this practice may have affected the accuracy of the model. This is due to the fact that TyG itself is calculated from GLU, and controlling for GLU again as a covariate essentially constitutes a double adjustment of the independent variable components potentially masking the true effect of TyG.[2] This may also explain why TyG was significant in the unadjusted model (OR=1.67), but significance completely disappeared in the adjusted model (OR=0.94), and even became a protective factor. Therefore, it is crucial that these relevant covariates with strong covariances should be excluded from the modeling.

Second, although the authors performed subgroup analyses of factors such as TyG and autoimmune antibodies, there was no stratified modeling of sex with BMI. Indeed, from a clinical epidemiological point of view, the risk of thyroid cancer is approximately 2–4 times higher in women than in men, with differences stemming in part from metabolic status and hormones.[3] The TyG index, as a metabolic surrogate, has metabolic pathways that may be more coupled to a female-specific endocrine background.[4] Therefore, a stronger association may be found if the relationship between TyG and PTC risk could be reassessed in the context of gender and BMI subgroups.

From the authors' baseline data displayed in Table 1,[1] lipid indices (TC) were more significantly associated with PTC ($p<0.01$), while GLU (fasting glucose) was not significantly different between the benign and malignant groups ($p=0.06$). However, in the ROC analysis, the AUC for TyG was only 0.476. We were curious whether combining TG with GLU to calculate the TyG index would somehow make the glycemic component mask the lipid correlation. We suggest that the authors could further plot the individual ROC curves of TG and GLU for comparison and continue to observe the differences in the predictive ability of TG, GLU and TyG. This approach could provide initial clarity on whether TyG is indeed the best combined metric with TyG.

Overall, Qiu's study provides important clues for exploring the relationship between metabolism and risk of thyroid malignancy, but we believe that there are still shortcomings in variable construction, modeling, and consideration of key subgroups. These limitations may have led to a statistically "negative" result for TyG, rather than a lack of clinical value.

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Data Sharing Statement

Data sharing is not applicable as no data were created or analysed in this communication.

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Author Contributions

Zhiwei Hu and Hua Dong: Methodology, Formal analysis, Writing - Original Draft; Yuchang Fei: Conceptualization, Methodology, Supervision, Writing - Review & Editing. All authors agreed on the journal to which this communication will be submitted, reviewed and agreed on all versions of the communication before submission, during revision, the final version accepted for publication, and any significant changes introduced at the proofing stage and agreed to take responsibility and be accountable for the contents of this communication.

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Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this communication.

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