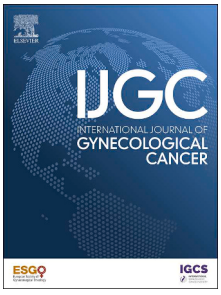
LETTER

Correspondence on "Clinical correlation between metabolic biomarkers and chemoresistance in gestational trophoblastic neoplasia" by Kong et al



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Highlights

- Metabolic markers exhibit non-linear, co-regulated patterns that defy logit-linearity.
- Parametric assumptions limit interpretability under shared metabolic variance.
- Odds-ratio attribution becomes unstable with correlated predictors.
- Unsupervised techniques reveal latent metabolic signal structures.
- Statistical methods enhance robustness and improve translational reliability.

Keywords:
Metabolic Biomarkers; Logistic Regression; Non-linear Associations; Parametric Assumptions; Multi-faceted Approach

Kong and colleagues[1] make an important contribution by developing a metabolic-lipid nomogram for predicting single-agent chemoresistance in low-risk gestational trophoblastic neoplasia. However, several methodologic considerations warrant further discussion. Because the authors relied on multi-variable logistic regression, the analytical framework inherently assumes logit-linearity and additivity, which may over-simplify the biological behavior of metabolically interrelated biomarkers.[2] Low-density lipoprotein cholesterol, total cholesterol, fasting glucose, and β-human chorionic gonadotropin are physiologically co-regulated and often exhibit non-linear thresholds and hierarchical dependencies. Under such conditions, logit-linearity is unlikely to hold, and odds ratios may conflate shared metabolic variance with putative independent effects, limiting interpretability. Moreover, interpreting odds ratios as indicators of relative contribution may obscure latent metabolic patterns underlying chemosensitivity.[3] Such structural complexity warrants analytic strategies capable of capturing non-linearity and redundancy.

To address these limitations, unsupervised feature-structuring approaches such as Feature Agglomeration and Highly Variable Gene Selection can reduce dimensionality and reveal coherent metabolic clusters prior to modeling.[4,5] Complementing logistic regression with non-parametric association measures (Spearman's ρ, Kenρdall's τ) would help determine whether the reported associations reflect stable biological patterns rather than model-driven artifacts. Incorporating these strategies would strengthen the robustness and translational reliability of metabolic predictors in studies of chemoresistance prediction.

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Declaration of Competing Interests None declared.

Data Availability No new data were created or analyzed in this study.

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