

# Letter to the Editor

## Methodological issues in multivariable logistic regression

Dear Editor,

Recently, Kose et al<sup>1</sup> investigated the predictive values of novel inflammatory indexes (neutrophil-to-lymphocyte ratio, NLR and lymphocyte-to-monocyte ratio, LMR) in patients with coronary artery disease (CAD). They reported that after adjusting for confounding factors, LMR, but not NLR, was associated with high SYNTAX score. This study is well designed; however, it has several limitations.

First, both NLR and LMR were included in the generalized linear model (logistic model) as continuous variables, based on the linear assumption. However, in clinical practice, both low and high neutrophil or lymphocyte counts were associated with various disorders. In addition, one retrospective study<sup>2</sup> of sepsis found that both low and high NLR were associated with increased mortality. Another study<sup>3</sup> also reported a "V" shape relationship between another similar CBC-derived ratio (platelet to lymphocyte ratio) and poor outcome in neurological disorder. Based on these findings, it may be not appropriate to directly include NLR/LMR as continuity variables in generalized linear regression models, and we suggest that polynomial or spline function regression may be a potential solution to this limitation.

Second, in the current study, only 17 patients had positive events (high SYNTAX score), while seven confounders were included in the multivariable logistic model. According to the current consensus, at least 5-10 positive events (in this case, high SYNTAX score) per confounder are required to reach a stable result in multivariable logistic regression<sup>4</sup>. This may be one reason why most confounders were non-significant in the current model.

Third, neutrophil, lymphocyte and monocyte accounted for almost all white blood cells.  $NLR = \text{neutrophil/lymphocyte}$ , and LMR can also be calculated by the neutrophil and lymphocyte counts:  $LMR = \text{lymphocyte}/(1 - \text{neutrophil} - \text{lymphocyte})$ . Therefore, evaluation of multicollinearity should be reported when included both NLR and LMR in the same logistic model.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

### References

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