Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios can only predict the severity of COVID-19 if the criteria for a biomarker are met

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We were interested to read the article by Wulandari et al. on a retrospective study on the value of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in predicting the severity of SARS-CoV-2 infection (SC2I) in critically ill patients.[1] In 221 patients diagnosed with severe SC2I infection between August 2021 and March 2022, severe SC2I patients were found to have high NLR and PLR values.[1] The highest NLR and PLR values were found in SC2I patients with renal failure.[1] It was concluded that elevated NLR and PLR levels could serve as potential prognostic markers for predicting disease severity in these patients, especially those with renal disease.[1] The study is encouraging, but some ambiguities should be clarified.

Firstly, the study design is unsuitable for assessing whether NLR and PLR can actually serve as prognostic factors in severely ill COVID-19 patients. The study was retrospective and had no control group.[1] Retrospective designs have several disadvantages: Some data may be missing, the accuracy of the data cannot be easily verified, desired missing or new data can no longer be generated, references to specific studies are often untraceable, and the design does not allow for follow-up studies. A control group is needed to provide a standard of comparison for the trial results. It makes it possible to study the effects of the independent variable alone without adding confounding conditions. During an experiment, a scientist must consider what their independent variable is and what is to be tested.

The second point is that NLR is a very non-specific parameter, as it can be elevated in numerous other diseases (e.g. cholangitis, post-surgery, ischemic stroke, thyroid cancer) and is considered a prognostic factor.[2] Therefore, NLR and PLR can only be considered as a prognostic factor for the severity of critically ill SC2I patients if all these other diseases have been excluded in each of the included patients.

The third point is that the severity of the infection depends not only on parameters reflecting the intensity of the infection, but also on other factors, such as the type and intensity of the immunological response, concomitant diseases and comedications, and genetic background. As far as the immunological response is concerned, the course of SC2I depends strongly on the type of antibodies produced in response to the SARS-CoV-2 virus. This variable immunological response may be responsible for the involvement of organs other than the lungs. These include the brain, heart, endocrine organs, kidneys and gastrointestinal tract. Therefore, we should know whether only patients with lung involvement or also patients with involvement of other organs were included. We should also know whether comorbidities were systematically recorded and to what extent they influenced the NLR and PLR figures.

In summary, it can be said that this interesting study has limitations that relativize the results and their interpretation. Removing these limitations could strengthen the conclusions and reinforce the message of the study. All unanswered questions need to be clarified before readers can uncritically accept the study's conclusions. Before NLR and PLR can be recommended as biomarkers of SC2I severity, their suitability as biomarkers needs to be confirmed by appropriately designed studies.

REFERENCES

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