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LETTER TO THE EDITOR

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Dear Editor,

I read the current review on neutrophil-to-lymphocyte ratio (NLR) by Dr. Zahorec with great interest (Zahorec, 2021). To the best of my knowledge this is one of the most comprehensive summaries on the topic that has been published. I would like to make some comments related to this article.

In general, using the NLR as a monitor for the host immune response is an intriguing idea and possibly the most attractive feature is that it is simple, available in every hospital and extremely cheap. Based on the robust literature the author provided in his review it has several potential indications. However, I would like to depict some limitations of this concept.

Definitions

The manuscript often refers to the term Systemic Inflammatory Response Syndrome (SIRS) defined by Bone and co-workers that had been used worldwide for decades after the first Consensus Conference on the topic in 1991 (Bone, 1992). This approach dealt with signals such as fever, leukocytosis, etc., as signs of "sepsis" or at least systemic inflammation. However, systemic inflammation is not "bad" per se. This is the results of an inevitable immune response that is required to concur any injury or illness, let it be damage or infection related – a topic that is discussed in detail in the current review in the context of pathogen and damage associated molecular patterns (PAMP and DAMP). Therefore, the problem in the critically ill is not the systemic response, but when it becomes "dysregulated". When the two components of the immune system - the innate and the adaptive – lose their physiological balance, and pro-inflammation (task of the innate) overwhelms anti-inflammation (duty of the adaptive), hyperinflammation can occur and immune response becomes the enemy of the host rather than a protective force. This is nicely depicted in the most current Sepsis-3 definitions, which has made the term SIRS obsolete in the critical care setting (Singer, 2017). Therefore, any research using the "old" terminology should be revisited and revised.

Cut off values

My second comment was inspired by the "NLR-meter" depicted in Figure 2 in the article (Zahorec, 2021). In general, the host immune response shows a huge scatter when it comes to inflammatory marker levels, let it be C-reactive protein (CRP), procalcitonin (PCT) or in fact NLR. If one looks at any article published on biomarkers in the context of sepsis, this scatter is obvious, meaning a huge overlap in the values between the groups of patients regardless of the severity or etiology. In other words, a patient in septic shock can have slightly elevated PCT levels in pneumogenic septic shock, as compared to a patient with peritonitis caused septic shock, although the clinical picture is identical (Trásy, 2016 - 3). Therefore, one has to be extremely cautious when making decision – i.e.: to start antibiotics for example -, solely based on one single biomarker level. In two recent studies we have shown that PCT kinetics are superior to absolute values and a have much better sensitivity to predict the presence of infection or antibiotic appropriateness (Trásy, 2016 – 3,4). Although, the scale recommended by Zahorec gives ranges potentially wide enough to capture individual responses, I personally found evaluating changes over time, i.e.: kinetics, more reassuring at the bedside.

Predicting outcome:

Finally, there are some comments in the review on the outcome predictive value of NLR. Although it was not discussed in detail, I feel that this topic deserves a sentence or two. In my view, biomarker-based survival prediction will never become our daily clinical practice and it shouldn't. Mainly for reasons discussed above, which is related to the individual response of the patients for a specific insult resulting in the huge variability of any biomarker levels. Nevertheless, predicting outcome would be of utmost importance and we have never felt it better than during these difficult times of the COVID-19 pandemic, when intensive care unit (ICU) resources became exhausted within days. But still, decisions on who should be admitted to ICU will never be done based on one single level of biomarker, regardless how well it performs.

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