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Opinion Paper

High neutrophil to lymphocyte ratio as a prognostic marker in COVID-19 patients

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Systemic inflammation has been reported as a new predictor for COVID-19 outcomes. Thus, we highlight in this viewpoint the importance of the neutrophil to lymphocyte ratio in COVID-19 pandemic-infected patients.

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COVID-19 pandemic is rapidly spreading across the world. During hospitalization, common clinical features include acute respiratory infection, fever, pneumonia, cough, fatigue, and inflammation [12]. In addition, increased plasma levels of inflammatory cytokine have been found in patients with COVID-19 [13]. The neutrophil-lymphocyte ratio (NLR) has been shown to serve as a reliable indicator of severe COVID-19 [1,4]. Additionally, critically ill COVID-19 patients show higher NLR when compared with non-ICU patients [5]. Xia et al., 2020 [2] found that approximately 80% of SARS-CoV-2 patients infected with bilateral pulmonary involvement have increased NLR.

A Chinese study aimed at assessing the NLR cut-off value for progression of disease reported that NLR >3.3 is independently associated with more severe COVID-19 (HR: 2.46, 95% CI 1.08–4.56). Furthermore, NLR >3.3 was associated with lower survival compared with NLR <3.3 (NLR >3.3: 6.3 days and NLR <3.3: 13.5 days) [6]. Another Chinese study performed in Hubei Provincial Hospital of Integrated Chinese and Western Medicine included 32 moderate and 31 severe cases and found an optimal cut-off of NLR >4.7 is an independent risk factor for severe COVID-19 [7]. Afterward, a European study conducted in Italy showed that severe patients are also older and had higher NLR compared with non-severe patients, suggesting that NLR may be a useful marker to early screening of COVID-19 patients [8]. Surprisingly, the risk of in-hospital mortality is 8% higher for each unit increase of NLR (OR: 1.08, 95%CI: 1.01–1.14), and patients from tertile 3 (NLR 4.85–88.09) have a 15-fold higher risk of death than patients from tertile 1 (NLR 0.54–2.21) [9].

In addition, several chronic diseases may influence the circulating leukocyte count, and thus NLR. Qin et al. reported in a cohort study that 44% of COVID-19-infected patients had at least one co-morbidity, mainly hypertension, diabetes, cardiovascular disease, or chronic obstructive pulmonary disease [10]. On the other hand, low NLR has already been associated with lower risk of hospitalization in patients with chronic diseases, such as renal disease and diabetes [11]. Likewise, in our previous study it was observed that a high NLR is associated with increased risk of sarcopenia in hospitalized cancer patients [12], as another group had found an inverse correlation between NLR and the Mini Nutrition Assessment, which was also an independent factor in predicting malnutrition in elderly subjects [13]. Given that patients with chronic diseases may progress from mild symptoms to severe disease, NLR should be monitored starting from hospitalization, because high NLR concentrations potentiate the symptoms’ severity and thus the mortality rate of COVID-19 (Fig. 1).

As strengths of this manuscript, we highlight that NLR is an easily measurable and non-costly marker of systemic inflammation for the hospital clinical routine. However, as a limitation, we emphasize that recently two COVID-19-specific and more accurate prognostic scores have been described. First, the COVID-GRAM [14] is able to predict a risk score based on outcomes of COVID-19-infected patients during
the hospital admission, which included ten variables, namely: chest radiographic abnormality; age; dyspnea; haemoptysis; unconsciousness; cancer history; number of comorbidities; lactate dehydrogenase; direct bilirubin; and NLR. Second, the C: co-morbidity, A: age, L: lymphocyte count, L: lactate dehydrogenase (CALL) score in-

Indeed, NLR is a low-cost marker compared to cytokines, since in the clinical routine it is common to use the blood count. Therefore, NLR is a useful systemic inflammation marker for screening COVID-19-infected patients and may be used as a useful indicator of a poor prognosis at the initial moment of hospitalization. In addition, we highlight the importance of further investigations to incorporate the assessment of the nutritional status of these patients.

Authorship

GDP, MCMDD, and AL wrote the article and approved the final version of this manuscript.

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Declaration of competing interest

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References

[1] Liu J, Li S, Liang B, Wang X, Wang H, Li W, et al. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. EBioMedicine 2020;55:102763.

[2] Xia XY, Wu J, Liu HL, Xia H, Jia B, Huang WX. Epidemiological and initial clinical characteristics of patients with family aggregation of COVID-19. J Clin Virol : Off Publ Pan Am Soc Clin Virol 2020;127:104360.

[3] Yang Y, Shen C, Li J, Yuan J, Wei J, Huang F, et al. Plasma IP-10 and MCP-3 levels are highly associated with disease severity and predict the progression of COVID-19. J Allergy Clin Immunol 2020;146(1):119–27, e114.

[4] Lagunas-Rangel FA. Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein ratio in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. J Med Virol 2020. https://doi.org/10.1002/jmv.25819, Online ahead of print.

[5] Sun S, Cai X, Wang H, He G, Liu Y, Lu B, et al. Abnormalities of peripheral blood system in patients with COVID-19 in Wenzhou, China. Clinica chimica acta. international journal of clinical chemistry 2020;507:174–80.

[6] Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. Int Immunopharm 2020;34:106594.

[7] Xia X, Wen M, Zhan S, He J, Chen W. An increased neutrophil/lymphocyte ratio is an early warning signal of severe COVID-19. Nan fang yi ke da xue xue bao — Journal of Southern Medical University 2020;40(3):333–6.

[8] Ciccolullo A, Borghetti A, Zileri Dal Verme L, Tosoni A, Lombardi F, Garovich M, et al. Neutrophil-to-lymphocyte ratio and clinical outcome in COVID-19: a report from the Italian front line. Int J Antimicrob Agents 2020;56(1):106017.

[9] Liu Y, Du X, Chen J, Jin Y, Peng L, Wang HHX, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. J Infect 2020;81(1):e6–12.

[10] Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. Clin Infect Dis : Off Publ Inf Dis Soci Am 2020;71(15):762–8. https://doi.org/10.1093/cid/ciaa248.

[11] Diaz-Martinez J, Campa A, Delgado-Enciso I, Hain D, George F, Huffman F, et al. The relationship of blood neutrophil-to-lymphocyte ratio with nutrition markers and health outcomes in hemodialysis patients. Int Urol Nephrol 2019;51(7):1239–47.

[12] Borges TC, Gomes TL, Pichard C, Laviano A, Pimentel GD. High neutrophil to lymphocytes ratio is associated with sarcopenia risk in hospitalized cancer patients. Clin Nutr 2020. https://doi.org/10.1016/j.clnu.2020.05.005, S0261-5614(20)30221-1.

[13] Kay T, Ackgoz SB, Yildirim M, Nalbant A, Altas AE, Cinemre H. Association between neutrophil-to-lymphocyte ratio and nutritional status in geriatric patients. J Clin Lab Anal 2019;33(1):e22836.

[14] Liang W, Liang H, Ou L, Chen B, Chen A, Li C, et al. Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitali-

[15] Grifoni E, Valoriani A, Cei F, Vannucchi V, Moroni F, Pelagatti L, et al. The CALL score for predicting outcomes in patients with COVID-19. Clin Infect Dis : 2020. https://doi.org/10.1093/cid/ciaa686. Online ahead of print.