Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Opinion Paper

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

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SUMMARY

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.

COVID-19 pandemic is rapidly spreading across the world. During hospitalization, common clinical features include acute respiratory infection, fever, pneumonia, cough, fatigue, and inflammation [1,2]. In addition, increased plasma levels of inflammatory cytokine have been found in patients with COVID-19 [1,3]. 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 1.98–4.56). 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 comorbidity, 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-10-infected patients during

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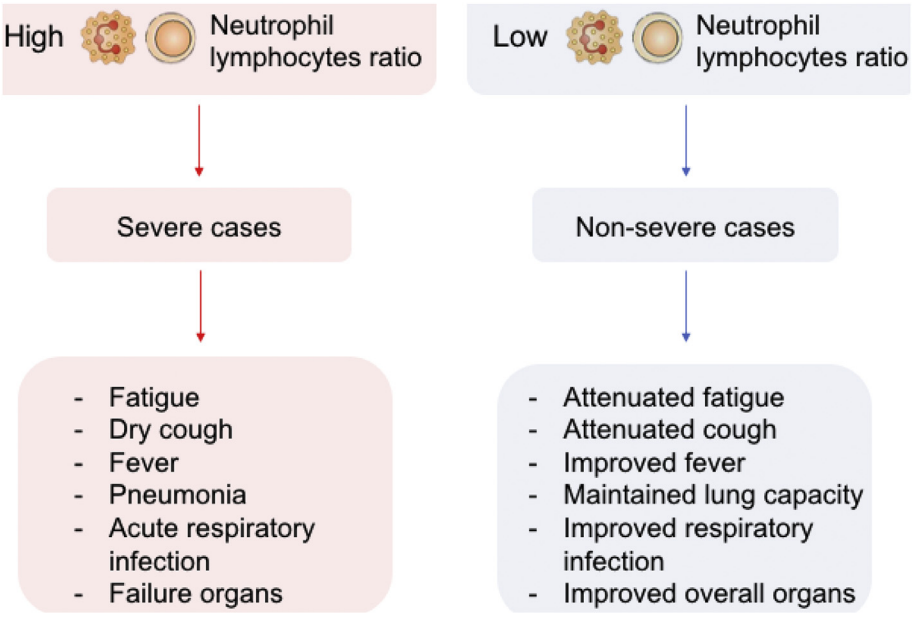

Fig. 1. Neutrophil-lymphocytes ratio during the COVID-19 pandemic. High neutrophil-lymphocytes ratio (NLR) leads to severe complications in the COVID-19-infected patients, such as fatigue, dry cough, fever, pneumonia, acute respiratory infection, failure organs and poor quality of life. On the other hand, maintenance of blood NLR concentrations may to ameliorate the impairment immune system response. Therefore, NLR is useful marker in clinical routine to screening the prognosis in the COVID-19-infected patients.

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 involves four items and was aimed at predicting the clinical worsening, but not the progression of severe cases [15].

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

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Declaration of competing interest

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