Letter to the Editor

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Value of neutrophil to lymphocyte ratio as a biomarker in colorectal adenocarcinoma

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We read with great interest the recently published article by Kilincalp *et al.* (2014) in which the authors aimed to elucidate the efficiency of the neutrophil/lymphocyte ratio (NLR), the platelet/lymphocyte ratio (PLR), and the mean platelet volume (MPV) as tools for the preoperative diagnosis of colorectal cancer (CRC) and their usefulness in the follow-up of CRC. They concluded that surgical tumor resection resulted in a significant decrease in NLR, PLR, and MPV. Their results suggest that NLR, PLR, and MPV may be used as easily available additional biomarkers for CRC in screening the general population as well as in postoperative follow-up (Kilincalp *et al.*, 2014). However, we would like to share our thoughts and experiences with Kilincalp *et al.* (2014).

First, as indicated in the original study, some clinical conditions that may affect the total and differential white blood cell (WBC) count were excluded to avoid possible confounders for NLR. As is known, diabetes mellitus (DM) and hypertension (HT) are the most common chronic diseases frequently observed in the current study population evaluated in the original study (CDC Diabetes Public Health Resource). There are several studies indicating that a high level of NLR may reflect ongoing vascular inflammation and play an important role in the pathophysiology of HT, DM, and even prediabetes. Similarly, NLR results can be affected by these metabolic confounders (Pusuroglu *et al.*, 2014; Sefil *et al.*, 2014; Shiny *et al.*, 2014). However, patients included in the original study were not evaluated in terms of DM and HT. In addition, in such studies aimed to determine predictive markers by using laboratory results, it would be better to identify a specific WBC count range within the exclusion criteria (Sertoglu *et al.*, 2014). It is well known that the WBC reference ranges may vary depending on many factors such as the population studied, the individual laboratory, and the instruments (e.g. types of collection tubes) or measurement methods used (e.g. waiting period before analysis) (Sertoglu and Uyanik, 2014). Determining the specific WBC count range as well as clinical conditions likely to affect the WBC count could avoid a possible bias in patient selection.

Second, NLR integrates the detrimental effects of neutrophilia (an indicator of inflammation) and lymphopenia (an indicator of physiological stress) and has emerged as a useful prognostic marker in many studies, which claim inflammation as the main cause of pathology (Kayadibi *et al.*, 2014). To assess the value of the NLR in this patient group, it is important to determine whether the increase in NLR is a result of a low count of lymphocytes or a high neutrophil count. However, neutrophil and lymphocyte counts were not provided in the original study. Therefore, it cannot be stated that inflammation alone is responsible for this increase in NLR. Moreover, the lack of data on other inflammatory markers has led to the lack of any evidence confirming the presence of inflammation in these patients. As is known, decreased lymphocyte count has been associated with malnutrition and lymphopenia and it is used as an indicator of malnutrition (Omran and Morley, 2000). As a result, a decrease in the lymphocyte count increases NLR. However, the nutritional status of participants was not evaluated and there is no effective laboratory indicator identifying malnutrition as the cause of lymphopenia in the original study (White *et al.*, 2012). As is known, serum proteins, particularly albumin, have often been used to assess malnutrition. Albumin has a relatively long half-life, ~14–20 days, and because of this, has been considered a marker of chronic nutritional status (Banh, 2006). Therefore, it would be better to assess at least albumin levels to evaluate the correlation between albumin levels and nutritional status in the current study.

In conclusion, NLR itself, alone without other inflammatory markers as well as neutrophil and lymphocyte counts, may not accurately provide information on the presence of inflammation in these patients, and excluding patients with metabolic confounders with an effect on NLR could avoid a possible bias in patient selection.

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Conflicts of interest

There are no conflicts of interest.

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