

Response to reviewer 1:

Question 1: In the introductory part, authors could mention another roles of neutrophil/lymphocyte ratio, like: Radulescu D, Baleanu VD, Padureanu V, Radulescu PM, Bordu S, Patrascu S, Socea B, Bacalbasa N, Surlin MV, Georgescu I, Georgescu EF. Neutrophil/Lymphocyte Ratio as Predictor of Anastomotic Leak after Gastric Cancer Surgery. *Diagnostics* (Basel). 2020 Oct 9;10(10):799. doi: 10.3390/diagnostics10100799.

Answer 1: The diagnostic role of NLR has been mentioned in the introduction part.

Question 2: The conclusions must be more specific and concise.

Answer 2: The conclusions have been modified to be more specific and concise.

Response to Reviewer 2:

Question 1: The authors assessed other blood markers also, such as platelet/lymphocyte and lymphocyte/monocyte ratios, in the present study. However, these blood markers were significantly correlated with prognosis. How do the authors discuss about these results?

Answer 1: In the discussion part, we discussed in detail our handling and views on these results. “In our study, the LMR was not statistically related with prognosis of osteosarcoma patients. However, among the six included studies, two of them reported significantly positive association of lower LMR with poorer OS [16,28]. Remarkably, Yang S et al. seemed to report conflicting results [27]. According to the Kaplan-Meier survival curve, patients with lower LMR had poorer OS than patients with higher LMR did; however, the univariate analysis indicated that higher LMR was a risk factor for worse OS [27]. After excluding this study, the pooled HR was 0.69 (95% CI: 0.55-0.87, P=0.002) by combining the remaining studies. Thus, we deem that LMR is also a valuable prognostic indicator in osteosarcoma patients, but more relevant studies are needed to further verify this.”

Question 2: In this study, NLR and GPS have the clinical utility for predicting prognosis in patients with osteosarcoma. The authors should indicate the future perspective of NLR and GPS in the clinical management of patients with osteosarcoma.

Answer 2: In the discussion part, we put forward some opinions and suggestions.

“Based on our findings, we suggested that the NLR and GPS should be considered for the assessment of disease status and formulation of therapy strategies and osteosarcoma patients with higher pretreatment NLR or GPS might receive more aggressive treatment and follow-up. Besides, it is worth exploring whether anti-inflammation treatment, reducing the NLR and GPS, is beneficial for osteosarcoma patients with high NLR or GPS.”

Response to *Science editor*:

Question 1: I have one issue for discuss: NLR is a biomarker which was studied in detail for hematological cancers and demonstrate value in survival, but in solid tumors results are inconsistent with each other, especially for platelet/lymphocyte ratio (PLR) and lymphocyte/monocyte ratio (LMR). What are your future perspectives for NLR and GPS in the clinical management for osteosarcoma?

Answer 1: In the discussion part, we put forward some opinions and suggestions.

“Based on our findings, we suggested that the NLR and GPS should be considered for the assessment of disease status and formulation of therapy strategies and osteosarcoma patients with higher pretreatment NLR or GPS might receive more aggressive treatment and follow-up. Besides, it is worth exploring whether anti-inflammation treatment, reducing the NLR and GPS, is beneficial for osteosarcoma patients with high NLR or GPS”.

Question 2: Second, what will be the value of NLR or GPS: demonstrate early recurrence? Just poor survival (not including neoadjuvant or adjuvant therapy)
Actually another specific biomarkers (as circulating cell tumors –CTC- or ctDNA) are

demonstrating early recurrence and poor survival. Is there data for this biomarkers for osteosarcoma?

Answer 2: As presented in our results, NLR and GPS were significantly associated with DFS, which meant NLR and GPS also play a role in predicting recurrence of osteosarcoma patients. Unfortunately, for the CTC or ctDNA, few studies explored their clinical role in osteosarcoma patients after careful literature reviewing.

Question 3: Third, most patients recruited in meta-analysis were from China, which limits the reproducibility of results. Did authors consider more studies different from China or which were the search criteria for including most patients from this population?

Answer 3: To be honest, as mentioned in the discussion part, this is one of the limitations of this study. Actually, most of included studies (11/13) are from the PubMed, EMBASE or Web of Science databases and our search strategy is very objective. Besides, all authors are well-educated in English and have no limitations in the language.

Question 1: The authors did not write their ORCID numbers. Please write it at the beginning of the main text.

Answer 1: The ORCID numbers of authors have been added at the beginning of the main text.