Author’s response to reviews

Title: The prognostic significance of the neutrophil-to-lymphocyte ratio and the platelet tolymphocyte ratio in giant cell tumor of the extremities

Authors:

Zhenhao Chen (chenzhenhao17@126.com)
Guanglei Zhao (gzhao@fudan.edu.cn)
Jun Xia (hudbt17089@gmail.com)
Feiyan Chen (chenfy73@163.com)
Li Jiang (charleyii@163.com)

Version: 1 Date: 11 Jan 2019

Author’s response to reviews:

Firstly, thank you very much for the review. We have made corrections according to your suggestion as follows,

Reviewer reports:

Fei Gao (Reviewer 1): This is an interesting study on NLR and PLR in GCTBs which revealed they are associated with postoperative recurrence and NLR was an independent risk factor for potential clinical predictive value.

I have a few comments:

1. There were serious problems on the design of this study. No control was found in the manuscript as the author described, the results of peripheral blood tests were not compared with those of normal population.

Response: we are not focus on the level of NLR and PLR among all people. We focused on the level of NLR and PLR in the patients with giant cell of bone. What we wanted to tell was patients with high NLR, relatively, may have worse outcome. It was not necessary to compare patients with normal population. The article in supplementary material, called “S1”, also did not compare with normal people.
2. It might not be so accuracy for optimal cutoff values of NLR and PLR because the sample size is too small, that might lead to controversial conclusion.

Response: This study only focused on patients treated in our hospital, and concluded that patients with high NLR had a higher risk of recurrence, and the cut-off value was only to classify the measurement data into classified data. If the indicator is to be used clinically, a large sample of studies is needed to determine a cut-off value. And we will follow up further to verify this result.

3. The Figures are not clear.

Response: Highest-quality images exported by SPSS software has been placed in the file "Figure".

4. The description of imaging and methods should be more detailed, special for figure legends.

Response: We have modified the figure legend at the end of the article (page 19), and the table legend has been added (file “Table”). The description of the image and method has been modified (Results section).

5. There are many, many English errors in the paper that must be corrected before the paper can be considered further, for example Page 11 Line 27. It would be helpful if have a native English speaker to review the paper with you.

Response: I’m sorry for the English errors I had made. The article has been carefully revised now.

6. It not focused on the clinical significance between NLR, PLR and the progression and prognosis of GCTBs in Discussion section.

Response: We modified the discussion section and added the pathogenesis of giant cell of bone. In discussion section, we first discuss the rationality of different results, then describe the meaning of the results.

Dedong Cao, M.D. (Reviewer 2): In this retrospective study, the authors tried to evaluate the connection between NLR and PLR and the prognosis of patients with giant cell tumor. They found that NLR (HR=4.18, 95% CI: 1.83~9.57) was an independent prognostic factor for giant
cell tumor of bone. The study sounds good and are well written. However, several concerns should be addressed.

1. Why the NLR and PLR before treatments were chosen as the factors but not other immune indicators, besides the reason mentioned in the introduction.

Response: Perhaps the description in the introduction was not very clear, there are several reasons for the NLR and PLR were chosen. First of all, the NLR and PLR can be used to assess the inflammatory and immune state of the body. If the NLR and PLR associate with the prognosis of giant cell tumor of bone, it may help us understand the pathogenesis of giant cell tumor of bone. Second, the prognostic value of the NLR and PLR have been evaluated in many tumors, which confirms that NLR and PLR can be used to predict tumor prognosis and response to treatment. Furthermore, NLR and PLR, as an extension of routine blood examinations, are easy to obtain and promote. (modified in background section)

2. In the abstract section, this sentence "The clinical parameters of 163 patients who were diagnosed with GCT of the extremities from July 2008 to July 2018 were retrospectively analyzed." told us some of the patients could be diagnosed and included in 2018. Did these patients reach the end of follow-up? When did these patients receive surgery or other anti-tumor treatments, and entered the follow-up stage?

Response: We reviewed that clinical data of patients diagnosed with giant cell tumor of bone from July 2008 to January 2018. The deadline for the follow-up was July 2018. I’m sorry for the mistake I had made, it has been changed in the article.

In order to collect as many samples as possible, recent patients were included. The data of these patients have been collected completely, but the follow-up time is not very long, which is a limitation in this study.

3. It is mentioned in the method section that all inflammatory markers were obtained before anti-tumor therapy, such as surgery. Please specific the timing of blood test, and the times of testing. Two weeks before surgery or other?

Response: All inflammatory markers were measured within 3 days prior to the surgery as part of the routine preoperative workup.
4. For the participants, did they have other chronic diseases, such as diabetes? These diseases history could have a huge impact on the results of blood test.

Response: On the one hand the age of patients with giant cell of bone are relatively young, most of them do not have chronic diseases such as diabetes, etc., on the other hand we do had an exclusion criterion, that is patients who had chronic diseases such as diabetes and chronic obstructive pulmonary disease would be excluded. Thus, all patients in the study have no chronic diseases. (line 24, page 4)

5. The definitions of high or low NLR and PLR are important to determine the predictive roles of NLR and PLR. The optimal cutoff value was used to divide the patients into two groups. Did the authors try other higher cutoff values, and what's the results. In addition, the prognostic roles of NLR and PLR should be compared with factors that have been well known in this tumor, or clinical imaging result, such as CR, PR or metastasis.

Response: We use the Youden index to determine the cut-off value, which has the best sensitivity and specificity, and our results proved that the cut-off value in the article can indeed be used as a prognostic indicator of giant cell tumor of bone. All patients underwent expanded curettage or extensive resection, the tumor was removed totally. Therefore, CR or PR is not considered, and the prognosis of giant cell tumor of bone is usually indicated by the recurrence rate.

Only three patients had local recurrence while got distant metastasis. Metastasis rate of all patients was only 1.8%. If metastases were defined as endpoint events, the number of metastatic endpoints in this study was small due to sample size limitations, and fewer patients would be subdivided into different groups, making it impossible to perform subsequent survival analysis.

6. How did the authors minimize the selection bias.

Response: We minimize the selection bias by the followings,

Firstly, the inclusion of patients in this study was stringently in accordance with the inclusion and exclusion criteria. The diagnosis and the recurrence of the disease are based on the same strict standards. Some patients who suffered other diseases that affect NLR or PLR, such as diabetes, are excluded directly. Besides, Huashan Hospital is a relatively large hospital, and the patients come from all over China, which guarantees the representativeness of patients. All patients had undergone standard surgical procedures.
7. Please state the reasons of lost to follow up.

Response: 15 patients were lost to follow up, because we failed to contract the patients or their families. (line 19, page 7)