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Inflammatory tumor microenvironment is closely related to cancer. In the manuscript “The predictive value of inflammatory markers for pathological response of ipsilateral supraclavicular lymph nodes and for prognosis in breast cancer after neoadjuvant chemotherapy”, authors explored the predictive value of inflammatory markers for pathological response of ipsilateral supraclavicular lymph nodes (ISLN) and for prognosis in breast cancer with ISLN metastasis after neoadjuvant chemotherapy (NAC).

Couple questions are required to be answered before accepted.

- (1) In the introduction, please supplement the introduction of tumor microenvironment in the breast cancer. Please enrich the progress of the diagnosis, prognosis and the treatment for breast cancer in the introduction.

Reply1: We have already supplemented the introduction according to your opinions.

Change in the text: we have modified our text as advised(see Page3, line 4-5, line 9-11, line 12-15).

- (2) In the paper, the case samples were too small. How to handle with the issue. It is the better to provide the representative IHC images with ER, PR and HER2.

Reply2: We cannot deny that the number of cases included in this study is relatively small. There are two reasons: first, the proportion of breast cancer patients with ipsilateral supraclavicular lymph node metastasis is about 1-4.3% lower in the whole breast cancer population, which results in very few cases that can be found clinically. Second, all patients included in this study are high-quality clinical cases. Because this study strictly screened the chemotherapy regimens of patients, the chemotherapy regimens of the patients were homogeneous, thus eliminating this important factor that can cause differences in prognosis and pCR. At the same time, the total number of 85 and 90 patients meets the effectiveness of all applied statistical methods. Therefore, we believe that although the sample size is small, it still has certain clinical value. In the future, we will continue to collect such patients for large-scale research.

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(3) The measure method of NLR and PLR should be described detailed and briefly.

Reply3: NLR and PLR were obtained by calculating peripheral blood cell count and were defined as absolute neutrophil count divided by absolute lymphocyte count and absolute platelet count divided by absolute lymphocyte count, respectively.

Change in the text: we have modified our text as advised(see Page4, line 5-8)

(4) How to identify the pathological response? Please supplement in the methods.

Reply4: pCR was defined as Miller-Payne grade 5 of tumor after NAC or only ductal carcinoma in situ.(Specimens of breast masses, axillary lymph nodes and supraclavicular lymph nodes were obtained by modified radical mastectomy and supraclavicular lymph node dissection, and their pathological response were determined according to this standard).

Change in the text: we have modified our text as advised(see Page4, line 20-23)

(5) Why not to analyze the correlation between peripheral blood inflammatory cytokine and pathological response and prognosis? Why to focus on platelet in the paper? Please supplement in the discussion.

Reply5: First of all, the correlation between peripheral blood inflammatory cytokine and pathological response and prognosis is an interesting question. This study aims to explore the correlation between peripheral blood inflammatory markers (neutrophil count, lymphocyte count, platelet, NLR, PLR) and pathological response and prognosis. Peripheral blood count is a routine examination item in clinical work. All peripheral blood counts in this study come from patients' routine treatment process. Therefore, the conclusion of this study has reference significance and economic value for other treatment centers. Peripheral blood inflammatory cytokine is not a routine clinical examination item. Compared with peripheral blood inflammatory markers, its application value to other treatment centers is lower because it needs to be retested. In the correlation analysis between multiple peripheral blood inflammatory markers and prognosis, only platelets show correlation with prognosis. Then through searching the literature, we found that platelets have a very big relationship with tumors, so platelets were the focus in the discussion.

Change in the text: we have modified our text as advised(see Page7, line15-17; Page8, line1-3)

(6) How to treat for breast cancer patients with ISLN after neoadjuvant chemotherapy?

Reply6: For breast cancer patients with supraclavicular lymph node metastasis, patients

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after neoadjuvant chemotherapy should continue to undergo modified radical mastectomy and supraclavicular lymph node dissection, and continue to undergo local radiotherapy after surgery.

Change in the text: we have modified our text as advised(see Page6, line 24-27)