

Peer Review File

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Reviewer Comments

1. First of all, my major concern for this study is the low sensitivity of SII for complete response (0.618), which suggest this is failed study of the predictive accuracy of SII. The authors need to combine other biomarkers and clinical factors to improve the predictive accuracy; otherwise, the clinical question appropriate for the current data is only the prognostic roles of SII for the complete response and recurrence or metastasis.

Reply 1: We have revised the title and conclusion accordingly. Page 1, line 3-5 and page 3, line 68-69.

2. Second, the title did not indicate the other outcome of this study, recurrence or metastasis, and the clinical research design, i.e., a retrospective cohort study.

Reply 2: We have revised the title accordingly. Page 1, line 3-5.

3. Third, the abstract is not standardized and needs further revisions. The background did not clearly indicate the clinical importance of predicting complete response and recurrence or metastasis and the limitations of known prognostic factors and biomarkers. The methods did not describe the inclusion of subjects, the assessment of baseline clinical factors and biomarkers, follow up procedures, outcome measurements of complete response and recurrence or metastasis, and main statistical methods for assessing the predictive accuracy. The results need to first report the clinical characteristics of the study sample and rates of complete response and recurrence or metastasis, as well as the sensitivity and specificity of SII for complete response and recurrence or metastasis. The conclusion needs to be tone down due to the poor predictive accuracy and I suggest the authors to have comments on the clinical implications of the findings.

Reply 3: We have revised the abstract accordingly. However, due to the limitations of the fund. We failed to add more words (no more than 350). See page 2-3, line 40-69.

4. Fourth, the introduction of the main text needs to indicate the clinical importance of predicting the treatment response and recurrence or metastasis of HER2 positive breast cancer patients, review all known prognostic biomarkers in BC, have comments on the limitations and the predictive accuracy of these known biomarkers, clearly indicate the clinical needs for new prognosis prediction biomarkers, explain why SII is potentially accurate for predicting the treatment response and recurrence or metastasis, and describe the clinical significance of this research focus.

Reply 4: We have revised the introduction. See page 4, line 101-118.

5. Fifth, the methodology of the main text needs to describe the clinical research design, sample size estimation, and outcome measurement of recurrence or metastasis. In statistics, please consider to combine other biomarkers to improve the predictive accuracy and please analyze the predictive value of SII for recurrence or metastasis. Please report the statistical methods for assessing the predictive accuracy and the threshold values for AUC, sensitivity and specificity for a good predictive biomarker.

Reply 5: We have added accordingly. See page 5, line 131-134, page 6, line 173-177 and

page 7, line 219-221.

6. Finally, please consider to cite the below related papers:

- Wang Q, Wang X, Yang Y. Advances in neoadjuvant therapy for HER2-positive breast cancers: a narrative review. *Gland Surg* 2022;11(8):1415-1423. doi: 10.21037/gs-22-439.

- Yuan JQ, Xiao Z, Wang SM, Guo L. The prognostic effect of HER2 heterogeneity and YAP1 expression in HER2 positive breast cancer patients: a retrospective study. *Gland Surg* 2022;11(2):451-465. doi: 10.21037/gs-22-52.

Reply 6: Added, see refs 9 and 10.