Peer Review File

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Reviewer A

While the normogram offers some predictive information regarding nodal status following NAC, your manuscript does not comment on its role in the light of other techniques of determining nodal status. For example, some authors have suggested the use of clipping the nodes at the point of initial biopsy for identification after NAC and before surgery. How does your approach compare with this?

Reply 1: We appreciate this kind suggestion very much. This model evaluated the possibility of positive axillary lymph nodes in breast cancer patients after NAC by using the limited preoperative data before and after NAC, and assessed the feasibility of SLNB after NAC in a less invasive manner, since preoperative biopsy after NAC will bring more pain to the patient. 2. Partial lymphatic occlusion after NAC and abnormal lymphatic flow were all considered at the beginning of this model, given that SLNB results in high false negative rate of biopsy. Thus, we hope to evaluate the axillary lymph node status after NAC more accurately through the mathematical model. 3. In the future, it is expected to further improve the accuracy of model prediction by combining the mathematical model with the method of post-operative biopsy of NAC. Changes in the text: we have modified our text as advised (see page 13,line 15-19)

As a minor point, on page 4, line 11, perhaps the authors may consider a different term, rather than 'destroy', to depict the impact of surgery on the nerves and lymphatic vessels in the axilla during a complete dissection.

Reply 2: Thank you very much for pointing out the problem. After careful consideration of your suggestion, we believe the word “injury” is more appropriate. Changes in the text: we have modified our text as advised (see page 6, line 1)

Reviewer B

I would like to recognize the effort for this interesting study to the authors.

Wang et al. have studied the clinical factors related to axillary lymph node metastasis after NAC in order to create a Nomogram. They concluded in 5 factors to create this Nomogram which can be applied in both cN1 and cN0 with AUC of 0.7926 (95% CI, 0.7187–0.8665) and 0.8165 (95% CI, 0.7381–0.8949), respectively.

1) Why do the authors include patients who received a mastectomy? What about conservative surgery, which is the most common surgery?

Reply 1: In order to meet the objectives of the study, patients undergoing axillary lymph node dissection should be included. In the process of case collection, it was found that almost all the patients undergoing axillary lymph node dissection after neoadjuvant chemotherapy chose total mastectomy, while breast conserving surgery was relatively rare, which may be related to the data collected earlier, and at that time breast conserving surgery had not been widely used. Due to the small number of breast-conserving patients, it is impossible to draw valuable conclusions through stratified analysis. Moreover, if integrated into the construction of the model, the accuracy of the model may be affected, and the significance in verifying the effect of the model is limited.

2) Do the authors protocol include a PAAF of the axillary suspicious lymph nodes prior to NAC? Or the decision about cN0 vs cN1 it is only based in ALN BI-RADS system?

Reply 2: The assessment of cN0 and cN1 was based on pathologic findings of ultrasound-guided biopsy of suspected lymph nodes before neoadjuvant chemotherapy. And I feel very sorry. May I ask what is the abbreviation of PAAF or what does it stand for? Although I have searched a lot of materials, I still can't find the specific meaning of PAAF.
Changes in the text: we have modified our text as advised (see page 3,line 5，6)

3) Why do the authors fixed in 14% the ki67? Do they have any ROC curve to fixed this limit? Furthermore, in table 1, the Ki-67 should be showed as categorical, not in mean.
Reply 3: We appreciate this kind suggestion very much. We searched a number of guidelines about this issue. According to guidelines of Chinese Society of Clinical Oncology (CSCO), Ki-67 is distinguished by a 14% threshold from high to low.

4) I encourage the authors to re-define the “tumor regression” variable. Maybe, the could categorize in “tumor regression” a patient with clinical or radiological downstaging (i.e clinical T2 to T1 after NAC) in order to make more reproducible this variable. Furthermore, the downstaging after NAC is one of the most factors which impact in the patient prognosis.

Reply 4: Thank you very much for pointing out the problem. The description here is inappropriate. It should be corrected in the text that tumor regression should be defined as an assessment of tumor size based on pre-NAC and post-NAC color doppler ultrasound. Although tumor size regression can be defined in a variety of ways, the original intention of the model design is to solve the most urgent problem in the

simplest way and improve the model's generalization performance. Therefore, the degree of tumor regression is defined as > 1 or ≤1.
Changes in the text: we have modified our text as advised (see page 10, line 3)

5) Do they know their rate of pathological complete response after NAC?

Reply 5: Since there are different definitions of pathological remission rate, in the present study, we choose to define it as both primary tumors and lymph nodes are considered to be free from any cancer cells. By reviewing the original data, 68 of the 320 included cases have achieved pathological complete response, PCR=21.25%.