Peer Review File

Article information: https://dx.doi.org/10.21037/gs-21-608

Reviewer Comments

This paper entitled “Prognostic Value of Residual Cancer Burden and Miller - Payne system after Neoadjuvant Chemotherapy for Breast Cancer” conducted at Peking University First Hospital, is very interesting at the first glance. The study explores a very important topic in breast oncology, which is the prognostic estimation of patients post neoadjuvant treatment based on pathological response.

My review was structured in topics related to the article structure, writing and content. The impressions are below as follows:

Abstract:
Structure – coherent, sumarizes main findings of the study and draws assertive conclusions.
Writing – good level of English
Content – reports accurately the data from the main article sections

Introduction:
Structure – well structured, nice flow of ideas progressions and defining the problem
Writing – good level of English
Content – reports accurately the data from the core articles on the topic currently available

Material and methods:
Structure – well structured, clear and precise
Comment 1: Line 97 and 98 – does any patients with pre-menopausal received GNRH analogue associated with hormonal therapy?
Reply 1: For premenopausal women, tamoxifen ± ovarian suppression or ablation was considered according to current guideline.
Changes in the text: Line 101-102

Comment 2: What is the indication of neoadjuvant treatment for this institution? There are 52 patients that received neoadjuvant treatment with a T1 tumour – are all of those triple negative?
Reply 2: This was indeed our negligence, we added indications for NAC in our center. Of 52 patients, there were 17 cases of TNBC, 19 cases of HER2+, and 32 cases of cN+
Changes in the text: Line 80-83.

Writing – good level of English
Content – missing what would be the criteria for not inclusding a patient due loss of follow-up.

Comment 3: What is the minimum expected?

Reply 3: We have added the definition of lost to follow-up. Usually, if a patient did not attend our hospital as an outpatient, we would collect information via telephone interviews or letter once a year. Lost to follow-up is defined as absence of any postoperative information from the patient. The minimum follow-up time is 6 months. In fact, the 5-year follow-up rate is over 95% in our certer.

Changes in the text: Line 135-136

Results:

Structure – well structured, clear and precise

Writing – good level of english

Content –

Comment 4: In seveal sections the authors refer to "luminal tumours" and it should be clear that you are referrring to ER or PR positive and HER2 negative, once you are aware HER2-positive could still be included on luminal subtypes. If appropriate, the authros could consider change the description to HR+ Her2-.

Reply 4: We were aware of this concept, however, the definitions of the three subtypes were described in the method section of the article, we think it would not cause readers to misunderstand. So, we did not made changes for the time being.

Changes in the text: None. Definition was in line 119-112 marked in red.

Comment 5: Would patients receiving vinorelbine require a separated analisys or potentially be excluded from the final analysis?

Reply 5: The NCCN guideline of breast cancer recommend that patients with operable breast cancer experiencing progression of disease during preoperative therapy may be given an alternate systemic regimen or proceed to surgery if deemed resectable. Though there is currently no standard recommendation, with few literature reports. In TNBC,25% (8/32) patients achieved pCR; in luminal subtype, in 18 patients with tumors of luminal subtype, 1 patients achieved pCR; however, none of 15 patients with tumors of HER2 positive achieved pCR. Our experience shows that alternate systemic regimen of vinorelbine was effective, especially for triple-negative breast cancer. So, we tend to keep these cases. The proportion of patients receiving vinorelbine was relatively small, and aim of this study was to assess the feasibility of using RCB to stratify prognoses of patients after NAC treatment, therefore, we did not discuss it separately. After accumulating enough cases, we will make further research of this issue.

As a supplement, we added a description of the treatment effect of these patients in the form of supplementary documents

Changes in the text: Line 170-172 and appendix 1.

Comment 6: Line 157 – should the 7 patients lost during follow-up be included in the analysis until the data is available? If not, please include on the methodology the minimum period of follow-up accepted to include the patient on the analisys.

Reply 6: We have added the definition of lost to follow-up. The 7 patients lost during follow-up had none prognostic information, we have to exclude these 7 cases.

Changes in the text: Line 135-136

Comment 7: Line 189 – should this information be adressed on the discussion section?
Reply 7: We have added description of the MP system in the results section and explanations for this result in the discussion section.
Changes in the text: Line 196-197 &Line 234-238

Discussion:
Structure – well structured
Writing – good level of english
Content – overall good.
Comment 8: Line 282 – I am not sure if you can state this given the desing of this study (you are not investigating treatment adjuvant in patients with RCB I on this study).
Reply 8: After thorough consideration, we decided to delete this statement. This statement was a hypothesis based on the results of the RCB system, and should not appear in the conclusion section.
Changes in the text: Line 292

Table 1:
Comment 9:
•11.8% of patients with non-ductal tumours receiving neoadjuvant treatment seems very high. It would be interesting to clarify on the results section which subtype they are referring to (lobular?)
• Pathological category Tis and T 0 (I assume this is pos-treatment and should be clear on the table.
Reply 9: We rechecked the data and found that 11 missing data, which were not suitable for classification under labels named "other", and we were sorry for our carelessness. These non-ductal tumors are listed: 10 invasive lobular carcinoma;9 invasive micropapillary carcinoma; 5 carcinoma with apocrine differentiation; 7 mixed carcinoma; 2 mucinous carcinoma; 2 neuroendocrine tumors and 4 metaplastic carcinoma. We thought it was to long, and was not suitable for listing one by one in the text.
We modified table1 as advised.
Changes in the text: Table 1

Table 2-4 and figures 1-2: satisfactory.

Finally, I would be happy to recommend this article for publication after the authors consideration of this minor review points.