Peer Review File

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Reviewer A

The title and the abstract are pertinent to the design and results of study. The abstract accurately summarize the manuscript and keywords are relevant. However, the introduction does not provide an appropriate background to the study and deserves to be developed (demographic data, disease characteristics, genetic alterations, endocrine risk, treatment options, clinical trials...)
Reply: We have modified our Introduction as advised (see Page 3, line 88-101)"

Materials and Methods:
Timeframes, locations, population, sample size, inclusion and exclusion criteria are clearly stated.
Outcome measures seems to be clearly stated but a lot of important data are missing: ECOG-PS, TNM, tumour stage, genetic data, …
The study design seems not to be appropriate to fully answer the question that is being posed that is "to relate factors affecting the prognosis of metastatic patients" and "to provide a reference for the diagnosis and treatment of MBC patients".
The statistical analysis explanation are coherent.
Reply: Thank you for your kind advice, the object of this research try to obtain the elementary results of clinicopathological features of MBC, so we didn't take ECOG-PS, TNM, tumour stage, genetic data into account . We will add more detail and complex data in the next research.

Results:
Results are not clearly presented. For example, the median age is missing. Why the 60-year-old threshold was chosen? Statistical analysis was wrong, chi2 validity condition was not respected for many analyses, but were made anyway. So, the results are wrong. For example, "location of primary tumour" the Chi2 test is not possible so a fisher test was made? Between which location?
Other example: Chi2 test is possible for "operation" factor but the p-value result is 0.33. So, operation is not a significant factor.
Another one: What is "Bilateral factor"? With left, right and other? What is other? They speak about unilateral? Never mind, the statistical results are wrong too. The p-value with Chi2 test is 0.33 so it is not significant factor.
Another one: Degree of tumour differentiation is also wrong. Chi2 test is not possible

because condition test is not ok (data <5). Fisher test could be used but the results will never be statistically significant in view of data.
So, to conclude, all the results checked are wrong. And it is not possible to check the survival results with the data provided.
Reply: Patients were stratified by age into 2 groups: <60 or ≥60 years according to the data from SEER database.
$\chi 2$ or Fisher's exact test were utilized to test the fit between a theoretical frequency distribution and a frequency distribution. The comparision of "Location of primary tumour" were made by Mann-Whitney U Test, which will add in the section of Method (see Page 5, line 137). The p-value result is <0.001 as shown in Table 1.
The p-value result for "Bilateral" factor is <0.001 as shown in Table 1.
The p-value result for "operation" factor is <0.001 as shown in Table 1.
Mann-Whitney U Test was used to compare "Degree of tumour differentiation" factor.

Reviewer B

The paper titled "Analysis of distant organ metastasis of male breast cancer and its effect on overall survival based on the SEER database" is interesting. Metastatic MBC has unique clinicopathological disease features and patterns of metastasis. No significant difference between the survival of metastatic MBC and FBC patients was observed. Distant metastasis was an independent risk factor impacting the prognosis of MBC patients. However, there are several minor issues that if addressed would significantly improve the manuscript.
1) In the introduction of the manuscript, it is necessary to clearly indicate the knowledge gaps and limitations of prior study and the clinical significance of this study.
Reply: We have added the limitations of prior study and the clinical significance of this study.
(see Page 7, line 214-217)

2) What are the possible roles of survival issues for male patients? What are the unique psychological and social impacts of this disease on its overall survival rate? Suggest adding relevant content.
Reply: We have added in the Introduction section, as follows: "The MBCs were usually diagnosed at a later stage than FBCs, and exhibited more advanced disease features, such as larger tumor size, lymph node involvement, and distant metastases. The distinct gene mutations have not been determined. Currently, no standard of care exists for MBC.The objective of this study is to compare MBC and FBC patients with distant metastasis to identify the clinical characteristics of MBC and the related factors

affecting the prognosis of metastatic patients to provide a reference for the diagnosis and treatment of MBC patients."

3) The data selection period for this study is from 2012 to 2017. Is there a certain deviation from the current data as this time is relatively early? How to avoid the deviation of results caused by this factor?
Reply: Your advice is of great help. The data from SEER is within the limits of authority, however, we will update our data in the future study.

4) What is the author's next research plan? It is recommended to add relevant content to the discussion.
Reply: We added our plan at the end of discussion.
(see Page 7, line 216-217)

5) The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as "Prognostic significance of preoperative serum inflammation markers in patients with male breast cancer, Transl Cancer Res, PMID: 35116698". It is recommended to quote this article.
Reply: We have added the recommended paper in the Reference.

6) Suggest providing the latest overview of the biology, genetics, and histology of MBC.
Reply: We have added the latest overview of the biology, genetics, and histology of MBC in the section of Introduction.
(see Page 3, line 88-101)

Reviewer C

1) First, the title needs to indicate the comparisons between MBC and FBC and the clinical research design of this study such as a retrospective cohort study.
Reply: We have modified the title as "Analysis of the distinct features of metastasis male breast cancer and its effect on overall survival based on the SEER database compared with female breast cancer".

2) Second, the abstract is not adequate and needs some revisions. The background did not describe the knowledge gap on MBC and the questions to be answered in this study. The methods need to describe the inclusion of MBC and FBC patients, clinical variables and prognosis outcomes collected, and the follow up procedures of SEER patients. The results need to first briefly summarize the clinical characteristics of the

MBC and FBC patient samples. The conclusion needs comments for the clinical implications of the findings.

Reply: We have added the knowledge gap on MBC in the section of Introduction. We have summarized the statistically significant results such as age, location of primary tumor, degree of tumor differentiation, operation or not and molecular subtype.

(see Page 3, line 88-101)

3) Third, the introduction of the main text is far inadequate. The authors need to review what has been known on the clinical characteristics, prognostic factors, and prognosis of MBC patients, what the unique characteristics, prognostic factors, and prognosis of MBC patients in comparison to FBC patients are, and analyse the knowledge gaps and limitations of prior studies, to indicate the clinical needs for this research focus.

Reply: We have added the knowledge gap on MBC in the section of Introduction.

(see Page 3, line 88-101)

4) Fourth, the methodology of the main text needs to describe the clinical research design, inclusion criteria for both MBC and FBC samples, follow up procedures, and prognosis outcomes from the SEER dataset. In statistics, the authors need to do adjust the potential confounding factors when comparing the prognosis outcomes of MBC and FBC patients. Please consider multiple Cox regression analysis.

Reply: All the information obtained from SEER database was strictly followed the inclusion criteria and follow up procedures. We have modified the "Kaplan-Meier curve and logarithmic rank sum test" to "Cox regression analysis" when comparing the prognosis outcomes of MBC and FBC patients.

(see Page 4, line 138)

5) Finally, please consider to review and cite some potentially relevant papers: 1. Chen Y, Wu J, Hu T, Wang J, Su F. Male breast cancer with ureteral metastasis: a case report. Ann Palliat Med 2021;10(7):8346-8351. doi: 10.21037/apm-20-2374. 2. Wang M, Liu D, Zhang Z, Dai X, Chen G, Zhu L. Molecular subtypes predict the prognosis of male breast cancer: a retrospective cohort study. Transl Breast Cancer Res 2023;4:4. 3. Sang G, Pan H, Lu C, Sun R, Zha X, Wang S, Zhu D. Clinical features and prognostic factors of male breast cancer vs. female breast cancer. Transl Cancer Res 2021;10(5):2199-2209. doi: 10.21037/tcr-21-1.

Reply: OK, but we have not cited Chen Y et al. because it's unrelated to this paper.

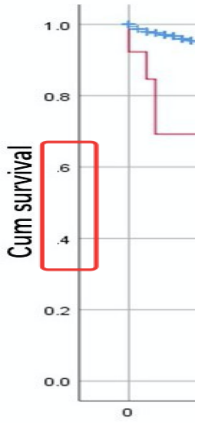
Reviewer D

1. Figure 2
Should “None” be “Non”? Please check and revise.

Reply: We have checked, and it’s right.

2. Figure 5
“.4” and “.6” should be changed to “0.4” and “0.6”. Please check and revise.

Reply: It is the “0.4” and “0.6”, it maybe the unmated software for viewing images.



3. Figure 6
“None” or “Non”? which one is correct? Please check and revise.

Reply: “None” is right. It is the “0.4” and “0.6”, it maybe the unmated software for viewing images.