

Peer review file

Article information: <http://dx.doi.org/10.21037/jtd-20-2826>

Comment 1: The authors should give consideration for describing risk factors for metastasis vs. none. Table 1 should describe the cohort overall with those who have metastasis vs those who do not. This will give insights into characteristics of those who develop metastasis at all. The authors can then go on to describe characteristics based on metastasis site in table 2.

Reply 1: We have added a table for comparison of clinicopathological characteristics between non-metastasis and metastasis PSC patients of the overall cohort (table 1), the previous table 1 was changed to the table 2.

Changes in the text: See page 7, line 127, line 134-143.

Comment 2: The authors frequently jump to identifying a characteristic as a “risk factor” as oppose to an association. The authors should not jump to conclusions. I also caution on using the term “chose radiation” when these are associations.

Reply 2: Thanks for the comments of reviewers, we try our best to change the "risk factors" that may be involved in the manuscript to "associated factors".

Changes in the text: See page 2, line 40, page 8, line 156, page 9, line 169, page 10, line 202.

Comment 3: The language can be difficult to follow at time. The following language issues should be clarified, with other minor spelling errors that were too numerous to list below that must be addressed prior to acceptance.

Reply 3: We’re sorry that the reviewer had difficulty in reading due to language problems. We have solved the following problems one by one, and asked a native English speaker to help us revise the article again before the resubmit.

Line 62-65. The authors state the SEER database contains 28% of the American population with recorded PSC diagnosis since 2010. Is there a citation for this fact? Is this a part of the methodology/results that the database was queried to identify the

proportion of the American population with PSC included in the SEER database?

Reply 4: Sorry for the misunderstanding caused by the unclear expression. What we want to show is that the SEER database covers 28% of the total population of the US (according to <https://seer.cancer.gov/about/overview.html>, and now has been updated to the latest 35%). The database has been recorded the information of patients with PSC since 1975, and the information of common metastasis site has been documented since 2010.

Changes in the text: See page 4, line 65-69.

Line 72. Please clarify what was meant by “population study”. It appears this is a registry/database study, not a population-based study.

Reply 5: We accept the reviewer's suggestion that the “population study” has been changed into “database study”.

Changes in the text: See page 5, line 77.

Line 76. Please clarify ICD-1-0. Do you mean ICD-O histology codes?

Reply 6: Sorry for the misunderstanding caused by the incorrect expression. We have amended it in the manuscript.

Changes in the text: See page 5, line 81.

Line 106: Please clarify. You state your IRB approved this study but then gave ethics exemption? Does this mean it did not require approval or there was a waiver to consent?

Reply 7: This was an open database study that involved no identifiable information for individuals throughout the analyses, and does not require approval by an ethics committee.

Changes in the text: See page 6, line 108-111.

Line 114: Please change to “final analysis”

Reply 8: We have changed it to final analysis.

Changes in the text: See page 7, line 121.

Line 116: This reads as 59% of patients in the SEER database are males, do you mean 59% of patients in the final inclusion population of 934 patients? Maybe exclude the

term SEER database.

Reply 9: We remove the term “SEER database” from the manuscript.

Changes in the text: See page 6, line 123.

Line 118: include SD and IQR for mean and median.

Reply 10: We have added the values of SD and IQR in the manuscript.

Changes in the text: See page 7, line 125.

Line 119: place % after 422.

Reply 11: We have added the percentage of non-metastatic cases after the number 422.

Changes in the text: See page 7, line 127.

Line 122: Include n with percentages.

Reply 12: We have corrected it.

Changes in the text: See page 7, line 130-131.

Line 126: This paragraph does not read well. It is difficult to understand the message the authors are trying to convey. I would caution the authors that if a higher proportion of patients undergo radiotherapy instead of surgery, it may not be patient choice. Please rewrite to state the subset of patients of interest “among patients with bone metastasis” followed by the characteristics of interest in the subset. Keep consistent organization of presentation of results throughout the paragraph for ease of reading. Please state which histological subtype is associated with brain metastasis.

Reply 13: Thank the reviewers for their suggestions. We carefully replaced "chose" with "proportion". And we redescribed the clinical characteristics of different metastatic sites.

Changes in the text: See page 7-8, line 134-151.

Line 136: It might make more sense to have the risk factors for metastasis presented prior to long-term survival results (reverse tables 3 and 2 in order and in text)

Reply 14: We accept the reviewer's suggestion, and have adjusted the order of risk factors for metastasis to before long-term survival results, then, we have changed

previous table 2 into table 4.

Changes in the text: See page 8-9, line 153-136. See table 3 and table 4.

Line 150: Place variables in brackets.

Reply 15: Reviewers' comment have been accepted.

Changes in the text: See page 9, line 165.

Line 193: Line does not makes sense. What does “which is equally poor” refer to?

Reply 16: We have changed the previous sentence to “survival time remained short”.

Changes in the text: See page 11, line 212.

Figure 3: title should state in patients with single site metastasis.

Reply 17: "Single site metastasis" has been included in the original title of figure 3. However, due to too many words in the title, it can't be completely displayed during the submission process. In order to avoid the mistake to happen again, we collect all the figures and tables in a word document and submit them as supplementary materials.

Changes in the text: See the supplementary materials of “figures and tables”.

Table 1: Place N and percent in the first row of table

Reply 18: Reviewers' comment have been accepted. Besides, we replaced the horizontal percentage of each cell with the vertical percentage for a more intuitive analysis.

Changes in the text: See the table 2(the previous table 1).

Table 2: place spaces between numbers and brackets

Reply 19: Reviewers' comment have been accepted.

Changes in the text: See the table 4(the previous table 2).