

Peer Review File

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Reviewer A

Cancer Reconstruction: A Population-Based Analysis

I have highlighted and commented on some areas I feel would benefit from re-wording.

- Line 61: Overuse of the word “noted” revised
- Line 112-114: added percentages of unknown race to equal 100%
- Line 118: AJCC abbreviation spelled out
- Line 173: rephrased
- Line 184: citation added
- Line 220: typo corrected
- Line 225: sentence deleted
- Line 234: changed “generalizable” to “representative”

Reviewer B

This study uses breast cancer data from the SEER database for 2004-2014 to compare mastectomy types and breast cancer reconstruction for successive cohorts classified by year of diagnosis. Types of mastectomies analyzed were classified as nipple sparing, total simple mastectomy, modified radical mastectomy, and radical mastectomy. The paper is interesting, the SEER data source is a suitable choice, and the statistical methodology basically sound, but the following questions arise where comments from the researchers would be appreciated:

Comment 1: Is the use of chi square tests the best option to assess difference in categorical variables when the variables are not distributed on a nominal scale? For example, in this study, could the mastectomy categories be construed as lying on an ordinal scale ranging from nipple sparing mastectomy through to radical mastectomy? Would testing for differences better be done using ordinal methods?

Reply 1: Thank you for this excellent point. However, we believe that treatments listed do not lie on a true ordinal scale. There are several other mastectomy types and subtypes which were not included in our study and thus our data cannot be listed in a true ordinal fashion as all types of mastectomies were not listed within the SEER database. Thus, we believe our chi-square test suited this variable better. We will add this to our limitations section. Furthermore, to our knowledge, the use of the chi square test applies to categorical variables of either nominal or ordinal distribution. See citation below, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3900058/>.

Changes in text: We have added in Limitations, Line 227, “There are several other mastectomy types and subtypes which were not listed in the SEER database

and thus not included in this study”.

Comment 2: Multiple logistic regression is used to determine predictors of modified radical vs. simple mastectomy. Would it have been preferable to analyze all mastectomy categories using ordinal regression?

Reply 2: Thank you for the question. Please see the response above and thus we believe a multiple logistic regression was better suited.

Changes in text: We have added in Limitations, Line 227, “There are several other mastectomy types and subtypes which were not listed in the SEER database and thus not included in this study”.

Comment 3: Due to large numbers in the SEER database, many statistically significant differences ($p < 0.05$) were likely when actual differences were small. Examples include differences in Table 1 regarding distributions over time in age, racial background, and TNM stage. I think greater emphasis could have been placed in the paper on differences observed in a multivariate context where 95% CIs did not include 1.00 (Table 3). This may have helped the reader to focus on the more meaningful differences such as surgery type, trends in breast reconstruction, age, racial background, stage and treatment combinations.

Reply 3: Thank you for this comment. We acknowledge that there are limitations in our interpretation of such a large database and that some variables were statistically significant however may not be clinically relevant. We chose to highlight the variables listed in Table 3 as those were the primary end points of our paper.

Changes in text: we have added in Limitations, Line 228, “Additionally, the SEER database includes a large sample size and, as such, multiple variables were found to be clinically significant in the multivariate analysis although differences may not be clinically relevant.”

Comment 4: How many mastectomy types could not be classified and what was the potential for their exclusion to have biased results?

Reply 4: Thank you for this comment. Per our inclusion criteria patients were only included if they had a documented mastectomy status of the mastectomies we included. We did not include patients with unknown mastectomy results. Furthermore, we have added to our limitations that the SEER database does not further detail mastectomy subtypes and thus only the mastectomy types listed above were studied.

Changes in text: We have added in Limitations, Line 227, “There are several other mastectomy types and subtypes which were not listed in the SEER database and thus not included in this study”.

Comment 5: Did the researchers explore interaction terms to assess whether the increases in simple compared with modified radical mastectomies, increases in post mastectomy breast reconstructions, increases in implant compared with tissue

reconstruction, and trends towards lower stages of mastectomy cases differed by age, racial background, and other characteristics? Would this have added value?

I don't see these matters as showstoppers but rather as aspects that could have been given more attention.

Reply 5: Thank you for this comment. We attempted to control for further variables for our primary outcome per our multi-variable logistic regression.

However, we did not further assess possible interactions in this manuscript as this was beyond the scope of this study. This is an excellent point and will be considered for our further research. We sought to explore our current results and plan to further expand on them with further research. We have added this as an area for further research exploration in the article.

Changes in text: added in Discussion, Line 232, "Additionally, future studies may wish to assess the interactions of age and racial background on the types of mastectomies and reconstructions performed, but this was beyond the scope of this publication."