

Peer Review File

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Reviewer A

Comment 1: The authors must describe the type of study, retrospective, prospective, etc.

Reply 1: We have described the retrospective nature of the study in methods.
Changes in the text: We have modified the text as revised, see page 3, line120.

Comment 2: Exclusion criteria 1. Patients receiving neoadjuvant chemotherapy requires explanation, may bias the result.

Reply 2: Meta-analysis on long term outcome for neo-adjuvant chemotherapy versus adjuvant chemotherapy in early breast cancer has shown that tumors downsized by NACT had a higher local recurrence rate. We believe that the response to NACT is an important prognostic factor for the NACT group and should be explored in detail and separately from the CT group.

Comment 3: BCSS and DFS have to be defined, state of last review or state at some point, also follow-up requires description (test and exploration)

Reply 3: We have added the definition of our endpoints and description of follow-up.

Changes in the text: We have modified the text as revised, see page3 line122-124, page4 line 151-153.

Comment 4: Some aspect of his cohort should be commented on.

BCS rate is very low when compared to Western publications, 29.4%

ALND rate is too high 83.6%

BCS without RT 29.6% is too high and requires explanation

This feature made your cohort special and added value to the study (you named real world study).

Reply 4: The high rate of BCS without RT rate is the characteristic of this cohort. This could be attributed to unevenly distribution of medical resources in China. Since our hospital is one of the top medical facilities, patients from regions with scarce medical resources would come here to receive surgery. However, when they return home they may not be able to receive follow up RT due to financial reasons and the limited local medical resources, thus causing unsatisfactory patient compliance.

Reviewer B

Comment 1: For example, in the abstract, page 2, lines 48-49, there is mention of 'risk factor for recurrence-free survival'. It might provide more clarity if one were to phrase this as 'risk factor for recurrence' or 'risk factor for higher recurrence' and alter the sentence structure as such.

Reply 1: We have rephrased it as 'risk factor for recurrence' to provide more clarity as the reviewer suggested.

Changes in the text: We have revised text as revised, see page 2 line61-63, page7 line289-293, page8 line365-366, page9 line379-390, page9 line417, page10 line430. We have replace LRFS with local-recurrence and LRRFS with local-regional recurrence.

Comment 2: In page 2, line 65, the authors speak of a few studies demonstrating improved survival with breast conservation compared to mastectomy. They proceed to say that this may be due to confounding factors not being addressed. There is a recent article published in JAMA surgery which takes into adjusted for previously unmeasured confounders and found that breast conservation treatment resulted in better survival outcomes than mastectomy. Please explain what impact this study would have on this assertion?

Reply 2: The recent JAMA article had included socioeconomic status and comorbidity which were previously unmeasured confounders. Their results were certainly meaningful. However, difference in patient selection has caught our attention: 1. They have included 1940(4.0%) patients who has underwent neo-adjuvant systematic treatment. 2. 4298(8.8%) patients in their cohort had received targeted treatment. 3. The details on radiotherapy, chemotherapy and endocrine treatment are missing. 4. When adjusting for confounding factors, the study did not include chemotherapy, endocrine therapy, targeted treatment and neo-adjuvant therapy. These factors could account for the better survival in BCS group.

Changes in the text: We have included this study in our reference. We have added these confounding factors in our limitation, see page10 line 442.

Comment 3: Page 4. In the methods section, 3 men were included in this study. Could the authors kindly explain why they were included? Is breast conservation treatment considered a standard option for breast cancer treatment in men? Would this be a confounding factor?

Reply 3: 3 men included in our study all had invasive cancer and underwent mastectomy, so they did not concern conclusions regarding the BCS group. We

originally included their data in the MT group as a contrast. However, after consideration into the reviewer's opinion, we feel that gender could be a confounding factor, however small. So we excluded the 3 men and changed the statistics accordingly.

Changes in the text: We have revised table 1,6,7 and all the related statistics in the text.

Comment 4: Page 4, lines 130-131. How do the authors explain the local recurrence rate of 25% for breast conservation in their cohort when other studies cite recurrence risk of 2.38% for breast conservation and 3.48% for mastectomy?

Reply 4: Other studies are western publications which may differ from us in terms of genetic background, social-economic factors and treatment routines. Our study is a real-world study conducted in China centering a special cohort characterized by low BC rate and high local recurrence rate. Currently, we think the most likely reason for high recurrence is the difference in systematic treatment. A relatively large proportion of our patients did not follow through their treatment after the surgery and the dosage of systematic treatment were low compared with western medical routines. However, this was not the focus of this study since we didn't specify on the treatment plan. Nevertheless, this discrepancy in recurrence rate do warrant further exploration.

Comment 5: There appears to be contradictory statements which would benefit from clarification. On page 4, lines 147-151, the authors state that for stage I & II disease, 10-year BCSS for women with IBC treated with breast conservation was significantly higher than those who underwent mastectomy. For IBC of Stage III & IV, the 10-yr LRFS rate was higher for the BCS group than that of the MT group. Yet, in their conclusion on page 8, lines 287-288, they state that there is no significant difference in BCSS between patients undergoing BCS and MT. Could they please clarify and be more specific?

Reply 5: We have rephrased the sentence in our conclusion in order to deliver our message more clearly. Surgery type was not an independent prognostic factor for BCSS for patients with IBC. Before adjusting for confounding factors, BCS group displayed better BCSS over MT group. After adjusting for confounding factors, the advantage in BCSS was gone.

Changes in the text: See page 2 line 52,68-69.

Comment 6: In another publication, Dr Murphy stated that many studies with

cumulative patient numbers in excess of 1 million patients have shown a consistent benefit in overall survival and BCSS in favour of BCS.3 Could the relatively low breast conservation rate be a confounding factor in this study as was suggested by research led by Dr Brooks?4

Reply 6: The low breast conservation rate could be a confounding factor which undermines BCT's survival benefit over MT.

Reviewer C

Comment 1: I wonder in the methods section or in the introduction to let the reader know whether the BCS is both level 1 and level 2 BCS surgery?, if just level 2 surgery this needs to be highlighted

Reply 1: All of the surgery performed is level 2 surgery.

Changes in the text: We have highlighted the surgery style as advised in page3 line125-126.

Comment 2: Wording and grammar:

In Discussion line 237 " What's more " change the wording here to open this sentence e.g However..

In Discussion line 283 "... speaking from a technically point of view " - suggest changing wording/ grammar here

Reply 2: We have changed the grammar and wording as advised.

Changes in the text: See page8 line359, page10 line438.