Peer Review File

Article information: https://dx.doi.org/10.21037/abs-23-48

Reviewer A

This is a manuscript documenting the analysis of factors associated with reconstruction in women aged 40 or younger who underwent mastectomy for breast cancer. The data was drawn from NCDB.

It is interesting that such a detailed analysis of women who underwent mastectomy has been undertaken by the authors at a time when there is a growing body of compelling evidence which demonstrates that women who undergo breast conservation treatment (BCT) have superior survival outcomes when compared with mastectomy.1 This is true for younger women, and those with Stage I & II disease.2-4 In patients with stage III breast cancer, survival is similar whether undergoing BCT or mastectomy.5 Furthermore, rates of re-operation and complications were the highest in women who underwent mastectomy and IBR, compared with those who underwent BCT or mastectomy alone.6,7 Concomitantly, costs for mastectomy with reconstruction are substantially higher than for BCT.7 In addition, there is no evidence to show that the use of bilateral mastectomy for unilateral breast cancer confers survival benefit.8 The authors correctly state that patients who choose contralateral prophylactic mastectomy (CPM) may have misplaced anxiety about breast cancer recurrence. This reasoning can be applicable to the use of mastectomy over BCT in younger women with unilateral operable breast cancer as well.

I note that the authors state in their analysis that receipt of CPM and MR were associated with OS benefit. However, it is unclear whether this was compared with BCT or just with mastectomy alone.

With the convincing data in favour of BCT in the literature aside from this study, the focus should be on appropriate counselling. Women should be informed that there possibly could be a survival advantage with BCT compared to mastectomy, with or without reconstruction or contralateral prophylactic mastectomy.

Hence, it behoves the authors to argue their case as to why there is a need for data comparing mastectomy with or without reconstruction and contralateral prophylactic mastectomy without reference to BCT. Kindly highlight if this has been done, for it is not evident to me in your manuscript.

References

1. De La Cruz Ku G, Karamchandani M, Chambergo-Michilot D, et al. Does breast-conserving surgery with radiotherapy have a better survival than mastectomy? A meta-

analysis of more than 1,500,000 patients. Ann Surg Oncol 2022;29:6163-6188.
2. Li P, Li L, Xiu B, et al. The prognoses of young women with breast cancer (<35 year) with different surgical options: a propensity score matching retrospective cohort study. Front Oncol 2022;12:795023
3. Hartmann-Johnsen OJ, Karesen R, Schlichting E, Nygard JF. Better survival after breast-conserving therapy compared to mastectomy when axillary node status is positive in early-stage breast cancer: a registry-based follow-up study of 6387 Norwegian women participating in screening, primarily operated between 1998 and 2009. World J Surg Oncol 2017;15:118
4. Xiang W, Wo C, Wu H, et al. Survival comparisons between breast conservation surgery and mastectomy followed by postoperative radiotherapy in stage I-III breast cancer patients: analysis of the Surveillance, Epidemiology and End Results (Seer) program database. Curr Oncol 2022;29:5731-5747
5. Mazor AM, Mateo AM, Demora L, et al. Breast conservation versus mastectomy in patients with T3 breast cancer (>5 cm): an analysis of 37,268 patients from the National Cancer Database. Breast Ca Res Treat 2019;173:301-311
6. Al-Hilli Z, Thomsen KM, Habermann EB, et al. Reoperation for complications after lumpectomy and mastectomy for breast cancer from the 2012 National Surgical Quality Iprovemnet Program (ACS-NSQIP). Ann Surg Oncol 2015;22 Suppl 3:S459-69.
7. Smith BD, Jiang J, Shih YCT, et al. Cost and complications of local therapies for early-stage breast cancer. J Natl Cancer Inst 2017;109:djw178
8. Kurian AW, Lichtensztajn DY, Keegan THM et al. Use of and mortality after bilateral mastectomy compared with other surgical treatments for breast cancer in California, 1998-2011. JAMA 2014;312:902-914

Reply: Thank you for your review and comment. We agree with your excellent points about the many oncologic, surgical, and financial benefits if BCT, in particular for younger women with breast cancer. However, many young women still choose mastectomy for a variety of reasons (i.e. concern regarding breast asymmetry following BCT, tumor to breast size ratio, desire to omit radiation or avoid future imaging surveillance, etc.), and rates of CPM are alarmingly high in this population as well. Therefore, our analysis focused on the use of post-mastectomy reconstruction and CPM in women ≤ 40, with comparisons between those who received reconstruction and/or CPM, and those who did not. BCT was not included as a comparison group, for the very reason stated above that several recent studies have already examined the benefit of BCT in this age group. We were interested in determining factors associated with reconstruction and CPM in young women having mastectomy for unilateral breast cancer, rather than factors associated with BCT vs. mastectomy. In particular, we sought to examine the relationship between reconstruction and CPM (which were closely and positively associated) since neither procedure confers a survival benefit and choice for to undergo additional surgery is often based on factors unrelated to oncologic outcome, particularly in young women.

Regarding your question about our OS analysis, the comparison groups were mastectomy alone (MA), MR, and CPM. BCT was not included in our analysis.

We agree that more emphasis should be placed on appropriate counselling for young women who are candidates for BCT or mastectomy. However, since our cohort included Stage I-III breast cancer and the NCDB does not include information on breast-to-tumor size ratio or genetic mutation status, it is possible that some patients were not candidates for BCT.

Changes in text: We added a sentence and several references in the introduction to outline the evidence supporting the survival advantage of BCT and the lack of data for a survival benefit with CPM for average risk women with unilateral breast cancer (paragraph 2, page 3). We also included comments in the discussion highlighting the importance of counselling patients as stated above (paragraph 1, page 13).

Reviewer B

Good paper which explores the reasons behind variation in immediate reconstruction uptake following mastectomy in younger women. Similar study in women between 55-65 would also be interesting to help provide better understanding about the barriers to IR.

Advantage of CPM in this age group with high-risk cancers (even in the absence of gene mutation) with better OS; is informative.

Reply: Thank you for your review and comment. We will consider that idea for a future study.

Reviewer C

Thank you for your submission shedding light on breast reconstruction in patients under the age of 40.

1. Given that that NCDB does not allow for differentiation of immediate vs delayed reconstruction, can the authors please comment on how combining immediate and delayed reconstruction might be biasing some of their findings, specifically as relates to OS seen in patients undergoing MR and CPM.

Reply: Thank you for your comment. In general, patients are unlikely to be offered reconstruction either in the immediate or delayed setting if their prognosis is poor, surgical risks are high, or there is concern that it would impede other oncologic care. The same applies to CPM. It is possible that patients undergoing immediate reconstruction had superior prognosis (and therefore survival) compared to those undergoing delayed reconstruction, assuming that delayed reconstruction was necessary due to advanced disease requiring adjuvant chemotherapy or radiation. Therefore, while the inclusion of all patients who underwent reconstruction in the same group could have biased our survival analysis, it is difficult to predict in which direction. However, there are probably fewer differences between the two groups who received reconstruction (immediate vs. delayed) than the groups that received any reconstruction

vs no reconstruction, which is why we felt it was reasonable to report these results.
Changes in the text: We expanded our comments in the limitations section of the discussion about how the inability to differentiate immediate and delayed reconstruction may bias our findings, particularly regarding OS (paragraph 2, page 14-15).

Reviewer D
Dear Authors, I really appreciated your paper: clear, simple concepts well expressed, well written. It's interesting the evaluation of how socio-economical aspects can affect health-related choices and outcomes.

Reply: Thank you for your review and comment.