

Peer Review File

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Reviewer # A:

manuscript needs major revision as it is full of wrong concepts, which will give a completely wrong idea to the reader about breast cancer management. I am going to list some of these:

- . However, radiation therapy after breast-conserving surgery can lead to non-satisfactory cosmetic results. Therefore, breast reconstruction after mastectomy is considered for patients who are eligible for breast conserving surgery.

This concept is completely wrong as mastectomy and reconstruction does not replace breast conserving surgery which remain the main treatment for most breast cancers.

-> **Answer) Thank you for good comments. As the reviewer recommended, We changed it to**

It is difficult to perform BCS if the breast cancer is large or multicentric or contraindication of radiation treatment or persistently positive margins. etc. In these cases, breast reconstruction after mastectomy is considered instead of BCS.

- There is no mention of the indications for mastectomy and how this can be different from breast conserving surgery.

-> **Answer) Thank you for good comments. We added indications for mastectomy in line 75-77**

- In addition, as an important part of current breast cancer treatment, neoadjuvant chemotherapy (NACT) is widely used in the treatment of early stage breast cancer, as well as locally advanced and inflammatory breast cancer. Most patients receiving NACT undergo mastectomy as a surgical treatment if breast conserving surgery is not possible or depends on the patient's preference. Therefore, IBR after mastectomy may be an important alternative surgical option for NACT (3).

- This statement has not been put properly, as it gives the reader that NCT should be followed by mastectomy and reconstruction, which is not true

Answer) Thank you for good comments. As the reviewer recommended, we changed it to

If breast-conserving surgery is not possible after NACT, breast cancer patients undergo mastectomy as a surgical treatment. In this case, Breast reconstruction after mastectomy may be an important alternative surgical option

Reviewer # B:

This manuscript demonstrated the results of a systemic review and meta-analysis for investigating the oncologic outcome of immediate breast reconstruction (IBR) followed by mastectomy (Bt) in patients (pts) with breast cancer (BC). And, they showed that the clinical outcome was no significant difference between IBR and mastectomy, and IBR followed by Bt may even has better OS than that of mastectomy alone. Despite the

study is interesting, there seems to be several concerns and following key comments should be addressed.

1. Authors reviewed and analyzed a total of 15 retrospective studies for IBR followed by Bt in pts with breast cancer. Because these studies most based on the public health database included National Cancer Database, SEER etc., that usually do not capture the timing of breast reconstruction surgery, the immediate or delayed reconstruction are difficultly be indicated from this kind of database. So, “IBR after mastectomy” in this manuscript should be defined.

Answer) Thank you for good comments. As the reviewer recommended we changed it “IBR after mastectomy” to “breast reconstruction after mastectomy”

2. The pts had clinical stage I to stage IV BC, or pts with early BC to advanced T4 BC were also included in this study as shown in Table1. Delayed reconstruction surgery with autologous tissues is recommended as a preferred option by practice guidelines for pts with local advanced BC or inflammatory BC after radical mastectomy and radiation, even who had received the effective neo-adjuvant chemotherapies. Weather all these pts with advanced BC in this systemic review received “IBR after mastectomy” should be indicated and the difference or possibility of bias should be discussed.

Answer) Thank you for good comments.

As you pointed out, since many patients of various stages were included in this study, heterogeneity was considered in the forest plot analysis and calculated using a random effect model instead of a fixed effect model

3. Authors described that some studies reported no differences in oncological outcomes of EFS and BC specific survival (BCSS) between IBR+Bt group and Bt alone group, but in contrast, some studies including this manuscript showed that IBR+ Bt group had better BCSS than Bt alone group. The reasons of these difference between the studies should be discussed.

Answer) Thank you for good comments. As the reviewer recommended we added the reasons in line 210-220, 234-242

4. No outcome data of local recurrence and distant metastasis were provided. Whether pts received IBR followed by Bt and Bt alone showed similarly recurrence profiles?

Answer) Thank you for good comments.

Some of the studies included in this meta-analysis provide local recurrence and distant metastasis. But some provided only survival rates. We set hazard ratio (HR) as effect size and performed a meta-analysis by calculating the HR of EFS, BCSS, and OS in this study. Studies where local recurrence and distant metastasis were provided showed similar result between two groups.

5. No information was provided for the detail in Table 1, line 1.

Answer) Thank you for good comments. As the reviewer recommended we changed it.