Peer Review File

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Reviewer A

General impression

There is valuable data inside hidden in this article. Decent size patient groups. However, it needs major revisions to bring up this information.

The aim of the article is not well described. While reading line 4 and 5, it seems to me that the left breast is compared to the right and visa versa. In my opinion it would be better to described the aim with the population, intervention, comparison and primary outcome included. For example, “we assessed complications in patients undergoing/following…..” or “we compared complication rates in X vs X”. Regarding the title, I know from reading the abstract that complications/revisions are assessed. In my opinion it would be more clear what the manuscript is about when “complications” instead of “surgical outcomes” is used.

Reply: Thank you for taking the time to review our article and for giving your valuable feedback on our manuscript. We re-wrote the Background section of the Abstract to describe the aim of this study more clearly according to your comments. “Surgical outcomes” was changed to “Postoperative Complications” through the entire manuscript.

Changes in the text: The sentences “Both implant-based reconstruction and contralateral augmentation mammoplasty could potentially cause deterioration of the thickness of the mastectomy skin flap and increase postoperative complications. We assessed the effect of contralateral augmentation mammoplasty on the outcomes of tissue expander/implant breast reconstruction.”

were changed to

“Contralateral augmentation mammoplasty in implant-based reconstruction could potentially lead to deterioration of the thickness of the mastectomy skin flap and increase postoperative complications of the reconstructed breast. We compared the complication rates of the reconstructed breast in the augmentation and no-augmentation groups among patients undergoing tissue expander/implant breast

reconstruction."

(See Page 3, lines 2-8, line number is based on the state that the track changes function in Microsoft Word is activated).

"Surgical outcomes" was changed to "Postoperative Complications"

(See page 1, lines 2-3, page 4, line 1, page 12, line 19, page 13, lines 6-7, and page 13, lines 22-23).

The research question and hypotheses and conclusion do not match

Break up long sentences in to shorter, more-readable, sentences. Use the correct terminology.

Improve on data presentation

Reply: Several modifications were made according to your specific questions, and these are provided below. We think most problems pertaining to mismatch between the research question, the hypotheses, and the conclusion, run-on sentences, and data presentation issues have been solved or improved. Thank you for your specific questions that helped us polish our manuscript.

Background:

The sentence, line 12-14, page 5, in which the hypothesis is stated, is unclear and should be rewritten. It now suggests that a tissue expander is inflated in the (contralateral) breast before augmentation. I assume that is meant that "the potential lack of sufficient skin in combination with inflation of this skin (in the mastectomy breast) to reach the size of the contralateral breast, which is indicated for augmentation, may be associated with adverse outcomes".

In general, sentences could be shorter, to make the introduction more easy to read.

Reply: Thank you for pointing out an important mistake in the description of the hypothesis. We modified the sentence according to your comment.

Changes in the text: The text "caused by the additional inflation of the tissue expander for the contralateral augmentation might be associated with postoperative adverse outcomes after the exchange of the tissue expander for the permanent implant in the two-stage expander/implant breast reconstruction." was changed to

"in combination with the inflation of the tissue expander to reach the size of the contralateral breast (which is indicated for contralateral augmentation), may be

associated with postoperative complications of the reconstructed breast”
in the last paragraph of the INTRODUCTION section (see Page 6, lines 21-24).

“immediate two-stage” is a confusing term. Use mastectomy followed by tissue expander placement.
Reply: The term “immediate two-stage breast reconstruction” was changed to “mastectomy followed by tissue expander implant breast reconstruction” throughout the entire manuscript.
Changes in the text: The text “immediate two stage” was changed to “mastectomy followed by tissue expander/implant”.
(See Page 3, lines 9-10, Page 4, line 3, Page 7, line 9, and Page 10, line 19).

Introduction
The skin flap thickness is not well introduced (page 5 line 1-3).
Reply: The sentence was re-written according to your comment.
Changes in the text: The sentence “The decrease in skin flap thickness that occurs in a mastectomy with breast reconstruction is thought to be associated with compromised circulation in the skin flap and increased postoperative complications”
was changed to
“A decrease in skin flap thickness was demonstrated to be associated with postoperative complications after mastectomy.”
(See Page 6, lines 7-8)

Line 10-12: Evolution of mastectomy makes breast reconstruction easy to perform? In cases of autologous option makes no difference. Add more references as well please.
Reply: I agree with you that we cannot say that the evolution of methods of mastectomy makes autologous reconstruction easy to perform. So, we modified the appropriate text accordingly.
Changes in the text: The sentence “This evolution in mastectomy methods has made breast reconstruction easy to perform and thus is performed more frequently after a mastectomy”
was changed to
“The incidence of breast reconstruction surgery after mastectomy has increased due to

advances in the field".
(See Page 5, lines 10-12).

Line 14: matching procedure. Use contra-lateral matching procedure
Reply: We added the word "contralateral" according to your comment.
Changes in the text: The term "matching procedure" was changed to "contralateral matching procedure".
(See Page 5, line 15).

Line 22: weak argumentation on the problem/niche. Discuss more on 2-stage procedure. Autologous completely different ballgame than implant reconstruction, please clarify on the distinction between these forms of breast reconstruction.
Reply: We agree with you that the argument pertaining to the research problem needs to be bolstered. We re-wrote the corresponding sentence to describe the problem more clearly.
Changes in the text: The sentence "Therefore, the effect of each matching procedure on the surgical outcomes of each reconstruction method is still not well understood."
was changed to
"However, the effect of each matching procedure on the surgical outcomes of breast reconstruction can be different because contralateral augmentation causes the volume of the reconstructed breast to increase, while contralateral reduction causes the volume of the reconstructed breast to decrease. Regarding the reconstruction method, implant-based reconstruction can compromise blood supply to the mastectomy skin flap, and serial inflation of the tissue expander can cause thinning of the mastectomy skin flap."
(See Pages 6, lines 1-6).

page 5 Line 3; weak argumentation. I assume authors do not perform prepectoral placement?
Reply: We performed subpectoral placement of implants in this study. I apologize, but I am not able to understand your comment that the argument pertaining to the insertion plane of the implant was weak. I request that you clarify this aspect with additional explanation.

Changes in the text: N/A

7 to 10; skin envelope to cover breast mound; wrong; skin envelop is part of breast mound

Reply: Thank you for pointing out the error.

Changes in the text: The term “breast mount” was changed to “implant” (see Page 6, line 15).

Clarify on the “no-augmentation” group.

Reply & Changes in the text: The text “Except for mastopexy which was performed on the contralateral breast for 28 patients, no procedure was performed in the contralateral breast of patients in the no-augmentation group.” was added to the Results section to clarify about the “no-augmentation” group.

(See Page 10, 11, lines 21-22, 1).

Contralateral augmentation does NOT yield in a skin flap. Currently the manuscript reads as the contralateral side is also ablated.

Please the rewrite introduction.

Reply: In addition to the changes in the introduction section according to your prior comments, we changed the text “in contralateral augmentation” in the 3rd paragraph of the introduction section to “in patients undergoing contralateral augmentation” to prevent any confusion as you pointed out.

Changes in the text: The text “in contralateral augmentation” was changed to “in patients undergoing contralateral augmentation”.

(See Page 6, line 18).

Methods:

Patient selection is explained in the text, however, a flow chart is missing. It is unclear how many patients were excluded, because of, for example, delayed reconstruction or earlier contralateral reduction. Also, which types of mastectomy were performed? Nipple sparing? Skin sparing? Ablated? Did all patients included complete the follow up? Adding a flow chart would clarify patient selection.

Reply: We added a flow chart to present the patient selection process. We feel that

your comment helped us to better demonstrate the design of this study.
Changes in the text: Figure 1 and legend were added.
The sentence “The final cohort consisted of 751 patients (Figure 1).” was added to the first paragraph of the Methods section.
(See Page 7, lines 21-22).

Missing: surgery technique; where is the tissue expander placed? How long before secondary surgery? How is the contralateral side augmented? What is the selection criterium for breast size? ADM used? Are there other surgeries performed to contralateral mamma besides implant placement?
Reply: A paragraph was added to describe the surgical technique with the subheading “Surgical technique” in the Methods section. We did not perform any surgical procedure for contralateral augmentation besides implant placement.
Changes in the text: A paragraph was added with the subheading “Surgical technique” in the Methods section.
(See Pages 8, lines 1-16).

Complications include “capsular contracture” and follow up is at least 6 months (average 25.2 months). It is known that capsular contraction usually occurs after a follow up of several years and is even rare to occur in such a short postoperative period. The same accounts for “implant rupture”, except for the few implants that are damaged during surgery. Conclusions regarding this complication should be drawn with care.
Reply: We agree with you that capsular contracture and implant rupture could be underestimated in this study. So, we have mentioned this issue as a limitation of this study.
Changes in the text: The sentence “Fourth, capsular contracture and implant rupture may not have been fully evaluated in the study population because these complications usually occur several years after surgery.” was added to the last paragraph of the Discussion section.
(See Page 16, lines 13-15).

Besides, it is not explained how “implant rupture” is diagnosed. Also,

hematoma/seroma vary in degrees of severity. It should be further explained if any seroma/hematoma was registered, or only the ones requiring intervention?

Reply: We added text to define an implant rupture. We only included seroma/hematoma cases which were treated by surgical intervention. Descriptions regarding seroma/hematoma and implant rupture were added to the Methods section.

Changes in the text: The sentences “Seroma/hematoma was defined as an abnormal collection of fluid or blood, which was treated by surgical intervention.” (see Page 9, lines 17-18) and “An implant rupture was defined as a tear in the outer shell of the implant diagnosed using magnetic resonance imaging.” were added to the Methods section.

(See Page 9, lines 20-21).

Validity; complications/revision are measured in both breasts and compared between two matched groups.

Reliability is doubtful; it is described that capsular contracture is assessed by one surgeon. Regarding other complications, definition/assessment is unclear. Patient selection is not completely clarified. This makes repeating this study difficult.

Reply: According to your previous comments, we added definitions for seroma/hematoma and implant rupture under the subheading “Outcome measurement” and also added a flow chart to describe patient selection as Figure 1. Assessment of complications was performed using our prospectively recorded database as described in the first sentence under the subheading “Study design and patients” in the Methods section.

(See Page 7, lines 8-10).

Results:

Please review your table:

Table 2: Smooth implant n=85, textured 113 = 198 (but says n=200 in total)

Table 3: “All patients N=(n=751)” same as “unmatched cases (n 751-400 = 351)? Augmentation = 234 en no augmentation = 517. Please clarify.

Reply: We apologize for the mistake regarding implant type in the Table 2. We found that the data regarding implant type were not revised based on the results of preliminary analysis performed using the initial data. We corrected the error and

checked the entire manuscript to correct any such errors. No additional errors were found. Thank you very much for pointing out an important mistake in this manuscript. In Table 3, the number of patients was added.
Changes in the text: Data regarding implant type in Table 2 were revised. The number of patients was added to Table 3.

page 8
line 15 -> augmentation group had smaller breasts to begin with than no augmentation
line 22 -> they end up with larger breasts than no augmentation
line 20 tissue expander size is mostly chosen on breast width; was a different projection chosen?
Reply: Projection of the tissue expander was not considered in this study. In patients who wanted contralateral augmentation, we selected an expander that was larger in width than the patient's original breast to match the width of the augmented breast (which is larger than the original breast). We added the description regarding selection of the tissue expander under the subheading "Surgical technique" in the Methods section.
Changes in the text: The text "The tissue expander was chosen based on breast width, height, and mastectomy weight. For patients who wanted contralateral augmentation, an expander with a width larger than that of the original breast was chosen." was added under the subheading "Surgical technique" in the Methods section.
(See Page 8, lines 2-5).

page 9 line 6: revision surgery for the ablated or augmented side? More info needed! Which complications?
Reply: Outcome variables included in this study were complications and revision operation rates pertaining to the ablated side only. We modified a sentence describing outcome variables in the Methods section. We also added the text "of the reconstructed breast" in the Results section when indicating outcome variables, to prevent possible confusion.
Changes in the text: The text "Outcome variables for the reconstructed breasts were complication and revision operation rates"
was changed to

“Outcome variables were complications and revision operation rates of the reconstructed breasts” under the subheading “Outcomes measurement” in the Methods section (see Page 9, lines 12-13).
The text “of the reconstructed breast” was added to the Abstract and the second and third paragraphs of the Results section.
(See Page 3, lines 4-5, Page 3, line 4, Page 3, line 23, Page 4, lines 1-2, Page 11, line 21, Page 12, line 4, and Page 12, line 13).

Do not compare unmatched vs matched groups please.
Reply: We believe that we did not compare unmatched and matched groups in the current manuscript. Please let us know if we have overlooked something on the issue.

Discussion
The structure of the discussion is fine.

The aim is still unclear: Page 11: We hypothesized that contralateral augmentation mammoplasty had the potential to cause a lack of local soft tissue for breast reconstruction
>> What does the contralateral side have to do with it? There is no breastreconstruction there, only augmentation!
Reply: We agree with you that the sentence does not describe our hypothesis well. We modified the sentence as below.
Changes in the text: The text “We hypothesized that contralateral augmentation mammoplasty had the potential to cause a lack of local soft tissue for breast reconstruction”
was changed to
“We hypothesized that contralateral augmentation mammoplasty can cause a lack of skin envelope on the reconstruction side to cover an implant larger in size than the original breast”.
(See Page 13, 14, lines 23-24, 1-2).

However, on page 12, a new subject is introduced. Aesthetic outcome, psychological well-being and patient satisfaction is described based on another, previously

published, study. The comparison with the authors study “However, the results of out study indicated that contralateral augmentation mammoplasty significantly increases the risk of the need for a revision”, line 17-19, page 12, suggests patients with a revision are less satisfied, have a worse aesthetic outcome/less psychological well-being. Is this based on previous research? Add references. Otherwise, I would not make this comparison.

Reply: We did not intend to suggest that patients with a revision are less satisfied, have a worse aesthetic outcome/less psychological well-being, but intended to suggest that increased rates of revision operations in the reconstructed breast can themselves be a risk of contralateral augmentation. We revised the following sentence to describe our intended meaning more clearly.

Changes in the text: The sentence “Both risks and benefits of contralateral augmentation need to be carefully assessed in preoperative planning and addressed during patient counseling.”

was changed to

“In addition to the benefits of contralateral augmentation, the associated risks need to be carefully assessed in preoperative planning and should be addressed during patient counseling. (See Page 15, lines 19-21)”

In the conclusion, line 1-3, page 14, the above mentioned new outcomes are mentioned as well. I would suggest to conclude on the aim/key results, of this study.

Reply: We agree with you that the sentence is not necessary in the Conclusion section, so we removed the sentence from the revised manuscript.

Changes in the text: The sentence “Given that contralateral augmentation mammoplasty has the obvious benefits of improved aesthetic outcome and patient satisfaction and the potential risk for the surgical outcomes demonstrated in this study,” was removed from the Conclusion section.

(See Page 17, lines 3-5).

In the limitations section, line 21-23, page 12, it is mentioned that this is a retrospective study. What is the specific limitation of this design in this study? This is not explained and the following sentence “We did not exclude contralateral mastopexy… “ is about a new subject, meaning this is the second limitation. So, the word “second” in line 1, page 13, should be replaced.

Reply: We used the sentence “First, this was a retrospective study based on the hypothesis mentioned above.” to indicate that our hypothesis needs to be validated. We removed the sentence because the sentence is not necessary.

Changes in the text: The text “this was a retrospective study based on the hypothesis mentioned above.” was removed from the last paragraph of the Discussion section.

(See Page 15, lines 22-23).

Page 11 line 13: why is ischemic complications so important? Isn't it the problem with placing a too large implant in too small pocket, straining the skin and causing dehiscense because of it?

Reply: The relevant factors associated with mastectomy skin flap necrosis in implant-based breast reconstruction have been investigated by many studies (reference numbers 27-34 in the revised manuscript). A study by Frey et al.(1) suggested a possible association between postoperative skin flap thickness and ischemic complications after nipple-sparing mastectomy. Our hypothesis was based on these previous studies, so we discussed the issue of ischemic complications. We added “such as mastectomy skin flap necrosis” to the third paragraph of the Discussion section to clarify the meaning of “ischemic complication”.

Changes in the text: The text “such as mastectomy skin flap necrosis” was added to the third paragraph of the Discussion section.

(See Page 14, line 9).

Page 11 line 17: “In our study, we hypothesized that the additional inflation volume of the tissue expander for contralateral augmentation mammoplasty can cause the mastectomy skin flap to become thinner, which will eventually increase postoperative adverse outcomes for the reconstructed breast. However, we cannot confirm our hypothesis because this retrospective study did not include quantitative and objective

analyses of mastectomy skin flap thickness."

The hypothesis has not been investigated: no flap thickness measured. Surgical techniques are not well written. It looks like a tissue expander is placed in the contralateral side, but this makes no sense from clinical perspective.

Authors should study how much volume was increased in percentage compared to the contralateral side in matched groups.

Reply: We have added data pertaining to the implant size used for contralateral augmentation. The percentage increase in volume was not presented because the volume of each side of the breast can be different and the preoperative volume of the breast on the augmentation side was not evaluated in this study.

Changes in the text: The average size of the implant for augmentation of all patients was added using the following text:

"The mean volume of the implant for augmentation was 182.9 ± 37.2 cc (range, 90-410 cc)."

This text was added to the Results section (see Page 11, lines 11-12).

The average size of the implant for augmentation of propensity-score matched patients was added using the following text:

"The mean volume of the implant for augmentation was 183.1 ± 35.0 cc (range, 90-295 cc)"

This text was added to the Results section.

(See Page 11, lines 19-20). Data were also added to Tables 1 and 2.

Currently, the study in presented form is not very informative. All we can draw from this, is that the authors have had significant complications. But there should be more investigation on what causes this, so it is more generizable to the public.

Reply: In this study, we hypothesized that additional inflation of the tissue expander to reconstruct a breast larger than the original breast to perform contralateral augmentation may cause the mastectomy skin flap to be thinner. We speculated that consequently, postoperative adverse outcomes for the reconstructed breast may be increased. This was discussed in the 3rd paragraph of the Discussion section. We cannot confirm that the thinning of the mastectomy skin flap really caused complications because the skin flap was not measured by objective measurements in this study. So, we discussed this issue in the 3rd paragraph of the Discussion section

and mentioned that further studies would be warranted to reveal the cause of increased complications in the augmentation group.

Reviewer B

This is a retrospective study to evaluate surgical outcomes of TE/implant breast reconstruction.
I think some revision are needed.
1.what type of breast augmentation do you use? Please clarify it
Reply: Thank you for taking the time to review our article and for giving your valuable feedback. When performing contralateral augmentation, we inserted the implant in the subpectoral space via an inframammary fold incision. We added details of the surgical technique used in this study under the subheading “Surgical technique” in the Methods section.
Changes in the text: The following text was added:
“For contralateral augmentation, inframammary incisions were used, and the implant was inserted in the sub-pectoral spaces.”
This text was added under the subheading “Surgical technique” in the Methods section.
(See Page 8, lines 12-14, line number is based on the state that the track changes function in Microsoft Word is activated).

2.About complications: in the group augmentation you put together the TE side with the augmentation side.i think it is useful to know if for example the wound dehiscence is from the TE side or augmented side.
Reply: We did not evaluate complications in the augmentation side because the purpose of this study was to evaluate the effect of contralateral augmentation on the postoperative complications of the reconstructed breast. We modified a sentence describing the outcome variables in the Methods section and added the text “of the reconstructed breast” in the Results section to prevent possible confusion.
Changes in the text: “Outcome variables for the reconstructed breasts were complications and revision operation rates” was changed to “Outcome variables were complications and revision operation rates of the reconstructed breasts” under the

subheading “Outcomes measurement” in the Methods section.
(See Page 9, lines 12-13).
The text “of the reconstructed breast” was added to the Abstract and the second and third paragraphs of the Results section.
(See Page 3, lines 4-5, Page 3, line 4, Page 3, line 23, Page 4, lines 1-2, Page 11, line 21, Page 12, line 4, and Page 12, line 13).

3.i think it is useful in your discussion cite this retrospective study:Extra-projected Implants as an Alternative Surgical Model for Breast Reconstruction. Implantation Strategy and Early Results.
Reply: Thank you for your detailed suggestion. The suggested study was added as reference number 38 to support the argument that contralateral augmentation can improve symmetry.
Changes in the text: Reference number 38 was added to the Discussion section.
(See Page 15, line 9).

Reviewer C

This is a good article and it provides interesting data. The authors assessed the effect of contralateral augmentation mammoplasty on the outcomes of tissue expander/implant breast reconstruction by conducting a retrospective chart review. The groups underwent propensity score-matched analysis and the matched cases underwent multivariable logistic regression analysis. They found that the augmentation group had a higher revision operation rate than did the no-augmentation group. I have a couple clarification questions:
1) What was the brassiere cup size of patients before and after the procedure?
Reply: Thank you for your encouraging comments about our manuscript. Unfortunately, data regarding brassiere cup size was not available in the database used in this retrospective study. Instead, we added implant size used for contralateral augmentation as below.
Changes in the text: The average size of the implant for augmentation of all patients was added using the following text:

“The mean volume of the implant for augmentation was 182.9 ± 37.2 cc (range, 90-410 cc).”

This text was added to the Results section.

(See Page 11, lines 11-12, line number is based on the state that the track changes function in Microsoft Word is activated).

The average size of the implant for augmentation of propensity-score matched patients was added using the following text:

“The mean volume of the implant for augmentation was 183.1 ± 35.0 cc (range, 90-295 cc)”

This text was added to the Results section.

(See Page 11, lines 19-20). Data were also added to Tables 1 and 2.

2) Please clarify if within the same patient in the augmentation group, whether the implant used for augmentation had the same volume as the implant used for reconstruction. In most of my cases, there has been a significant volume difference between the implant in the reconstructed side and the implant in the augmentation side, since the augmentation side still has breast tissue. Based on your table, the average weight was 259±115g, so even in the small 150mL natural unoperated breast, if one uses a 250mL implant on one side and 250mL implant in the other side, there would be a considerable difference (250mL versus 400mL)

Reply: There was a significant volume difference between the implant in the reconstructed side and the implant in the augmentation side in the patients included in our study as well. We added data regarding the implant size used for contralateral augmentation in this study. Changes in the text: The average size of the implant for augmentation was added to the Results section.

(See also Tables 1 and 2).

3) If the implants were different, what was the average implant size for reconstruction and the average size for augmentation?

Reply: Additional data were added according to question #2. Data pertaining to age, BMI, mastectomy, expander size, and reconstruction implant size were also added to the Results section to maintain consistency for description of data.

Changes in the text: Data pertaining to age, BMI, mastectomy, expander size, and

reconstruction implant size were added to the Results section.

4) How did you determine the size of the implant to be used in the augmentation side?
Reply: The implant size of the augmentation side was decided before the surgery, based on patients' desire and clinical examination of the mastectomy skin flap by attending surgeons. We added a sentence pertaining to this aspect under the subheading "Surgical technique" in the Methods section.
Changes in the text: The sentence "The implant size of the augmentation side was decided before surgery based on patients' desire and clinical examination of the mastectomy skin flap by the attending surgeons." was added under the subheading "Surgical technique" in the Methods section.
(See Page 8, lines 14-16).

Reference

1. Frey JD, Salibian AA, Choi M, et al. Mastectomy flap thickness and complications in nipple-sparing mastectomy: objective evaluation using magnetic resonance imaging. Plast Reconstr Surg Glob Open 2017;5:e1439.