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Peer Review File

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Reviewer A

Methodological concerns:

1. do you have experience with expandable implants, if yes, why were these excluded?

- Reply: We perform breast reconstruction surgery with expanders as well as breast implants. However, an expander was used instead of an implant due to high wound complications such as skin necrosis in case of patient who decided to undergo postop-radiotherapy or who had high possibility of it. In this study, patients who received radiotherapy after breast reconstruction were excluded. (description added in Method section/Para 1)

2. did all the patients get implant+adm? Subpectoral? Prepectoral, any? drains used, when removed?

- Reply: All patients used implants and ADM. Implants located in subpectoral plane. Also, all patients used drainage. (described in Method section/Para 1)

3. it is unclear why none of the patients in the study received radiotherapy- were those with radiotherapy excluded from the study?

-Reply: Radiation therapy causes chronic inflammation of the skin tissue, causing gradual changes in the skin. Radiation complications cause dryness, epilation, pigmentation tissue fibrosis, tenlangiextasia, delayed wound healing, ulceration, and histologically induce micoangiopathic change of microvessels, resulting in tissue ischemic, increasing the rate of complication. Therefore, in our hospital, patients who need or are likely to receive radiation therapy, insert an expander and perform delayed breast reconstruction after radiation and chemotherapy are completed. For this reason, it has been excluded from this study. (Described on Method section/Para 1)

4. were all the patients operated during that period exclusively unilateral or bilateral cases were excluded?

- Reply: During the period, all patients were unilateral breasts.

5. did any of the patients receive neoadjuvant treatment? If yes, how did it affect the analyses/complications?

- Reply: The sample patients included only those who received postoperative chemotherapy. Patients who did received postoperative radiotherapy, neoadjuvant chemotherapy (preoperative CTx), or chemotherapy were excluded. Also

6. Did I get it correctly that the cohort described is a selection of patients who did not receive any neoadjuvant treatment and no radiotherapy? If yes, it should be stated and explained why this selection was made.

Were there really no smokers or were they excluded?

- Reply: All sample patients were non-smokers. The cohort is described in detail in the Method section.

7. Please, define hypertension and diabetes criteriae. How many had both diabetes and hypertension?

- Reply: In this study, hypertension was defined to have systolic blood pressure higher than 140~159mmHg. Diabetes was defined to Diabetes was defined if any one of the following three conditions was satisfied.

① Symptoms of drinking a lot of water and urinating a lot, which are characteristic symptoms of diabetes, appear. Weight loss appears that cannot be explained by any other specific cause. The measured blood sugar was 200mg/dL or higher regardless of the meal time.

② Fasting blood sugar measured in a fasting state without caloric intake for 8 hours is 126mg/dL or more

③ In the oral glucose tolerance test, the blood sugar measured 2 hours after ingesting 75mg of glucose is 200mg/dL or more.

However, I don't think it's important enough to explain the definitions of hypertension and diabetes separately in the text. We corrected the term 'hypertensive', 'diabetic' to proper word. (Results section/Para1)

8. It's paramount to describe in detail the chemotherapy protocols, i.e. when and which chemotherapy agents were given. 4 weeks postreconstruction? Did you use drains? Did patients have a checkup with plastic surgeon before the start of adjuvant treatment? Did you postpone adjuvant treatment in patients with wound-healing problems?

- Reply: Postop-chemotherapy was postponed according to the status of wound healing. Chemotherapy underwent after enough recovery of surgical site or complication such as skin necrosis or wound dehiscence. Chemotherapy was performed with the consent of the plastic surgeon and the breast surgeon. After surgery, it took an average of 33.04 days in the non-CIN group to start chemotherapy and 17.66 days in the CIN group. Drainage removal took 16.79 days in the non-CIN group and 15.81 days in the CIN group. (Described on Table 1, Result section/Para 1)

9. Discussion

You need to cite and refer to more articles on this topic. Do you think that you have acceptable results? Compared to what is known in the literature? How can you improve the results? Use of expander-implants with inflation depending on the flap circulation and infection risks? Please, extend your hypothesis and share your experience and thoughts. Do the literature search.

- Reply: We modified our Discussion section, added new paragraph.

10. Support your paper with the images of good and bad results. Did it go well for patients with neutropenia? What could be other confounding factors- smaller implants? No ADM?

- Reply: We added clinical photographs of patients who had major infection, underwent implant removal, and minor infection, which healed with IV antibiotic treatment. (Figure 1.)

Reviewer B:

There are major issues with this manuscript.

1. Firstly, the study design is over a 10-year period. In this period, the management of patients has drastically changed, with changes in chemotherapy protocols, radiotherapy protocols, implant types and techniques.

The authors do not address this at all.

- Reply: We described the implant type and surgical technique (subpectoral method) and more details of study design in method section. We added the adjuvant chemotherapy regimens in Table 1. Demographics. As explained in the discussion section, this study aims to analyze the relationship between CIN and breast complication. There are minor differences in the type of ADM used, cancer stage, adjuvant chemotherapy regimen type between the two groups, but this does not seem to act as a major bias in the association between CIN and breast complication. In addition, there were no significant differences in breast cancer stage and adjuvant chemotherapy regimen between the two groups.

2. The authors would need to show changes over the course of the study - were outcomes worse early or late in the study period?

- Reply: In this study, major and minor infections among breast complications were of major interest. In both groups, there were 3 and 5 patients with major and minor infections, respectively, accounting for a small percentage of the population. Changes in the occurrence of complications during the study period could not be compared.

3. what were the chemotherapy regimes

- Reply: We described patients first line chemotherapy regimes in Table 1.

4. what were the radiotherapy regimes. Did these differences have different outcomes?

- Reply: There was no significant difference of complication according to the chemotherapy regimens. And patients who had radiotherapy were excluded in this study. (Method section/Para 1)

5. what were the implants used? textured or non textured? Did these change over the course of the study?

- Reply: During the study period, all breast implants used in our patient groups were textured type. (There were very few cases of BIA-ALCL in Asia compared to Western countries, and the problem has recently emerged, so our institution replaced it with a smooth type from the last two years. In this study, only the textured type was used in patient samples which performed by senior surgeon (JH Lee).)

6. why was DTI used only and not expander/implant options?

- Reply: We performed breast reconstruction surgery with expander as well as breast implant. However, expander was used in case of patient planning to under go radiation treatment because radiotherapy cause dryness, epilation, pigmentation tissue fibrosis, tenlangiextasia, delayed wound healing, ulceration, and histologically induce micoangiopathic change of microvessels, resulting in tissue ischemic, increasing the rate of complication. In this study, patients who received radiotherapy after breast reconstruction were excluded.

7. were biologics used? meshes? flaps?

- Reply: No, only breast implant and ADM were used.

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8. what surgical approach? which plane? sub pec? pre-pec?

- Reply: All surgical approaches were performed through the incision site where the breast surgeon performed mastectomy. In most cases, incisions were made to transverse in the lateral direction in the nipple areolar complex. The implant was located on the subpectoral plane. (Method section/ Para 1)