Title

Efficacy of rhomboid flap reconstruction after mastectomy for locally advanced breast cancer

Running Title

Rhomboid Flap Reconstruction for Breast Cancer

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Abstract

Background: In cases of mastectomy for locally advanced breast cancer (LABC), surgical skin flap reconstruction is sometimes required to cover large skin defects. In this study of patients with LABC, the patient group that required local flap reconstruction after mastectomy and the patient group that underwent mastectomy alone were compared to evaluate the efficacy of local, cutaneous (rhomboid) flap reconstruction after mastectomy.

Methods: Sixty-eight patients with LABC who underwent mastectomy were reviewed retrospectively.

Fourteen patients underwent local (rhomboid) flap reconstruction after mastectomy (local flap group) and 54 patients underwent direct closure after mastectomy (direct closure group). A pinch test was performed to determine the closure method. Data regarding the operation and post-operative complications and quality of life (QOL) were compared between both groups.

Results: It was possible to close defects in the local flap group that were significantly larger than those in the direct closure group (p=0.0002), and there were no significant differences in post-operative complications between the groups. Although the operative duration was significantly longer in the local flap group than in the direct closure group (p=0.016), the average difference was only 25 minutes. There were no significant differences in factors pertaining to post-operative QOL.

Conclusions: Rhomboid flap reconstruction is effective for covering large defects after mastectomy in patients with LABC.
Key words

locally advanced breast cancer, breast reconstruction, local flap, postoperative complication
Main text

Introduction

The standard therapy for locally advanced breast cancer (LABC) is multidisciplinary therapy, and the most common treatment combination is neoadjuvant systemic therapy (NST) followed by local therapy such as surgery and irradiation. The NST response rate in patients with LABC has recently been increasing. If NST is effective and tumor invasion signs such as ulcers, scars, and red spots on the breast skin decrease, the skin resection area becomes small such that conventional mastectomy can be performed without reconstruction. However, if the tumor invasion signs persist despite NST, it becomes necessary to resect a large skin area and employ some kind of reconstruction method.

Skin grafts and several types of myocutaneous flaps have reportedly been used for reconstruction in such cases, but in an earlier report, we presented the merits of local, cutaneous (rhomboid) flap reconstruction for large skin defects and the favorable outcomes with regard to post-operative complications and wound healing \(^1\). However, there are no comparative studies on mastectomy requiring local flap reconstruction and mastectomy alone in patients with LABC. Therefore, to evaluate the efficacy of local (rhomboid) flap reconstruction after mastectomy in patients with LABC, operation data and post-operative complications between the patient group requiring local flap reconstruction after mastectomy and the patient group that underwent mastectomy alone were compared in this study.
Materials and Methods

Patients diagnosed with LABC using the criteria for primary breast cancer diagnosis, of clinical stage T4, any N, M0 (according to the eighth edition of the Union for International Cancer Control [UICC] tumor-node-metastasis [TNM] classification of malignant tumors), and who had undergone mastectomy from August 2011 to September 2016 were retrospectively reviewed at the Saitama Cancer Center. All breast cancer surgeries and reconstructions were performed or supervised by first author. The study was approved by the Ethics Committee Board of the Saitama Cancer Center.

The patients were divided into 2 groups according to the skin defect closure method used after mastectomy as follows: local flap group and direct closure group for the local flap reconstruction and direct closure methods, respectively. The selection of closure methods is shown in Figure 1. A round skin resection line including the sign of tumor invasion such as an ulcer, scar, or red spot on the breast skin and the nipple-areolar complex is drawn. After tumor resection, a pinch test³ is performed to indicate the skin tension (Figure 1, left figure). If the pinch test reveals that the skin tension is low and the skin defect is assessed to be closed using the direct closure method, the skin is trimmed to a spindle shape and closed directly after tumor resection (Figure 1, right, top figure). If the skin tension is high and direct closure is considered unsuitable, the local flap closure method is selected (Figure 1, right, bottom figure).

Rhomboid flap reconstruction was performed according to the description in our earlier report.
The fundamental design of the rhomboid flap is shown in Figure 2. The skin defect is considered rhomboid in shape. A flap with sides equal in length to those of the rhomboid shape of the defect is designed (Figure 2, left figure). The flap is moved and transposed with the edges marked with a circle and a triangle matched to the edges of the rhomboid shape of the defect (Figure 2, right figure). Although the flaps were fundamentally designed according to the above description, the flap for each individual patient was modified depending on the shape and size of the skin defect and the degree of skin softness. The area of the actual skin defect can sometimes be slightly larger than the skin resection area marked before tumor resection because skin contracture caused by the tumor is released after tumor resection. Therefore, the local flap is designed to be slightly larger than the local flap area estimated from the marked skin resection area before tumor resection. Dog ear deformities are appeared at the base of the flap after the flap and the axillary area is moved to the defect (Figure 2, right figure circle). Although dog ear deformities can be repaired by various methods, dog ear deformity at the base of the flap should be repaired as a secondary surgery, that is, after complete healing of the flap. Repair the dog ear deformity during the initial surgery (resection of LABC and rhomboid flap reconstruction) would encroach on the base of the flap and endanger the blood circulation of the flap. The dog ear deformity at the axillary area can be repaired during the initial surgery as it will not compromise the blood circulation of the flap.

Patient characteristics were collected. They included age, body mass index (BMI), body surface area (BSA: Du Bois formula: \( \text{weight}^{0.425} \times \text{height}^{0.725} \times 0.007184 \)), smoking status, diabetes
mellitus, administration of corticosteroids, clinical stage according to the eighth edition of the UICC TNM classification, NST data including NST rate and pathological response according to the Japanese Breast Cancer Society (JBCS) classification, adjuvant therapy data including type of therapy and delay of adjuvant therapy due to surgical complications with systemic therapy started more than 12 weeks after surgery or irradiation started after more than 8 weeks after surgery, and operation data, including skin resection area, duration of operation, amount of blood loss, type of axillary operation, and length of hospital stay after operation. The skin resection area was calculated using the formula for the area of an ellipse, which is: 
\[(\text{major axis} \times 1/2) \times (\text{minor axis} \times 1/2) \times \pi.\]
Ratios of the skin resection area to BMI and BSA were calculated. Data on post-operative complications including wound dehiscence (requiring re-suture), hematoma (requiring reoperation), infection (requiring antibiotics and surgical debridement or irrigation), and skin necrosis (requiring surgical debridement) were collected. Data on factors influencing post-operative quality of life (QOL) including limitation of shoulder joint movement (requiring physical therapy), lymphedema (requiring compression bandage), and revision surgery (to correct the cosmetic deformity) were also collected.

The Fisher’s exact test, Student’s t-test, and Mann-Whitney’s U test were used to compare the patient and tumor characteristics, clinical stage, NST data, adjuvant therapy data, operation data, and post-operative complications. \(P<0.05\) was considered statistically significant. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a
graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R Commander designed to add statistical functions frequently used in biostatistics.

Results

Of the 68 patients who underwent mastectomy for LABC, 14 were in the local flap group and 54 were in the direct closure group. The patient and tumor characteristics are summarized in Table 1. The rate of human epidermal growth factor 2 (HER2)-positive tumor was significantly lower in the local flap group than in the direct closure group (0% versus 33.3%; \( P = 0.014 \)). There were no statistically significant differences in age, BMI, BSA, smoking status, diabetes mellitus, administration of corticosteroids, clinical stage, and estrogen receptor (ER) status between the groups.

Table 2 shows the NST and adjuvant therapy data. There were no statistically significant differences in NST rate and pathological response to NST, type of adjuvant therapy, and delay of adjuvant therapy between the groups. A 53-year-old woman in the direct closure group could not start her post-operative irradiation until 11 weeks after surgery because of wound infection and skin dehiscence that required irrigation, surgical debridement, and re-suture. Although she had no complications, she was a current smoker. Her BMI was 18.5, BSA was 1.78 m\(^2\) and her skin resection area was 33 cm\(^2\).

Table 3 shows operation data and post-operative complication data and QOL data. The skin
Resection area was significantly larger in the local flap group than in the direct closure group (112.7±71.4 cm² versus 45.4±26.8 cm²; $P=0.0002$). Ratios of skin resection area to BMI and BSA were also higher in the local flap group than in the direct closure group (5.1±3.6 versus 2.0±1.3, $p=0.0001$ and 77.8±51.3 versus 30.2±17.2, $p=0.0003$). However, the skin resection area and it’s ratio to BMI and BSA varied widely in both groups. The duration of operation was significantly longer in the local flap group than in the direct closure group (142.5±40 minutes versus 117±22.6 minutes; $P=0.016$). There were no statistically significant differences in the amount of blood loss, type of axillary operation, length of hospital stay, and incidence of post-operative complications or factors affecting QOL. There were 2 cases of skin necrosis in the local flap group that were treated quickly and did not cause delay of adjuvant therapy. There was no revision surgery including repair of dog ear deformities in either groups.

**Clinical Case**

A 69-year-old woman presented with a right breast tumor with skin ulcer and redness of the surrounding skin. The patient was diagnosed with right LABC (cT4bN1M0 clinical stage IIIB according to the eighth edition of the UICC TNM classification) that was ER positive and HER2 negative. The patient underwent NST (doxorubicin, cyclophosphamide and docetaxel) After NST, the tumor showed partial response. Surgery was scheduled for 4 weeks after the completion of systemic therapy.

Mastectomy with $12 \times 8$ cm (75.4 cm²) skin resection, including the ulcer and red spot on the
skin, and axillary lymph node dissection were performed (Figure 3A). After tumor resection, the size of the skin defect became larger due to the release of the skin contracture (Figure 3B). Pinch test revealed that the skin tension was high, and the defect could not be closed directly; therefore, it was closed using the local flap closure method. A rhomboid flap with 8 cm limbs was dissected and used to cover the skin defect (Figures 3C). The total duration of the operation was 171 minutes, and the amount of blood loss was 114 mL. There were no post-operative wound complications. The patient was discharged from the hospital on post-operative day 7. Pathological examination revealed a ypT4bN1a (according to the eighth edition of the UICC TNM classification) invasive ductal carcinoma with a grade 1a pathological response (according to the JBCS classification). The patient underwent post-operative chest wall and supraclavicular lymph node irradiation and hormonal therapy (aromatase inhibitor). 24 months after surgery, there were no local or distant metastasis and limitations of shoulder joint movement (Figures 3D and 3E). There was also no lymphedema. The patient was satisfied with the result of the operation and did not want a revision surgery.

Discussion

Patients with LABC who undergo a combination of systemic and local therapy have better prognoses than patients who undergo systemic therapy or local therapy alone. Thus, the current standard therapy for LABC is multidisciplinary therapy, which combines surgery, systemic therapy, and
irradiation. Many studies have reported a lack of a difference in overall survival between pre-operative and post-operative systemic therapy. However, when upfront surgery is selected for LABC, curative resection is sometimes difficult because of tumor invasion to the surrounding skin and/or chest wall or massive metastasis to the regional lymph nodes. Therefore, combination NST is considered the first choice treatment protocol for LABC followed by surgery.

Surgery and irradiation play important roles in the local treatment strategy for patients with LABC. In concert with irradiation, surgery improves the prognosis of patients with LABC. Wide local resection and reconstructive surgery are required if skin invasion signs persist after NST. In these cases, the skin graft method or various myocutaneous flaps are the traditionally selected reconstructive methods for patients. However, they each have advantages and disadvantages.

Although the skin graft can cover the relatively larger skin defect, pain is felt at the donor site and wound control is necessary until the wound heals. Further, we feel the skin graft site is unsightly, especially in the mesh skin graft method. Moreover, resection of LABC sometimes results in partial exposure of the sternum or rib, and the skin graft can hardly take on cortical bone. Since graft survival is dependent on the condition of the recipient site, poor wound healing of the skin graft may constitute grounds to delay post-mastectomy irradiation and adjuvant systemic therapy. Significant delay of post-mastectomy irradiation and adjuvant systemic therapy may negatively impact overall survival.

Pedicled myocutaneous flaps including the latissimus dorsi, external oblique, and rectus
abdominis myocutaneous flaps have also been reportedly used in reconstruction techniques\(^{14-18}\). Even though these techniques can be used to cover large skin defects and even exposed bone surfaces, they also have particular disadvantages such as donor site morbidity, including muscle dysfunction, and relatively long operation time.

As an alternative method to the skin graft and myocutaneous flaps, we described the usefulness of rhomboid flap (local, cutaneous flap) reconstruction for skin defects after malignant breast tumor resection in an earlier report\(^1\). The rhomboid flap reconstruction method has been frequently used since Limberg described it in 1946\(^{19}\), and some modified methods have been reported\(^{20-22}\).

Compared with the skin graft, rhomboid flap reconstruction has a better aesthetic outcome. The local flap has a similar texture and color to the surrounding normal skin as well as the thickness of the skin compared to the skin graft\(^{23}\). Consequently, the local flap has a better aesthetic outcome and patient satisfaction than the skin graft in past reports\(^{23,24}\). In addition, the rhomboid flap can cover skin defects with bone exposure. LABC carries a high risk of local recurrence, therefore, salvage surgery for a recurred tumor must be considered. As opposed to the skin graft, a rhomboid flap contains the subcutaneous tissue and has the softness of the tissue. Therefore, resection and primary closure or irradiation for a locally recurrent tumor may be possible even in the case of local recurrence within the flap. Compared with myocutaneous flap reconstruction, rhomboid flap reconstruction is a less invasive technique. The rhomboid flap does not require any vessels or muscles in the flap. Consequently, the
rhomboid flap can be implemented with a shorter operation time and does not result in muscle dysfunction.

While the rhomboid flap has such advantages over the skin graft or the myocutaneous flap, it has its’ disadvantages. The coverable skin defect area is relatively small compared with the skin graft or myocutaneous flaps. The limit of the skin defect area that can be covered with a rhomboid flap must be selected on a case-by-case basis. Skin grafts or myocutaneous flaps were not required for defects after resection for LABC in this study’s duration. In this study, skin defects did not significantly extend over the area between the second and sixth ribs in the vertical axis and the sternal edge and the midaxillary line in the horizontal axis in which mammary gland is located. We considered that a rhomboid flap can cover a defect within this area.

Considering the selection of rhomboid flap reconstruction or direct closure method, the skin defect size may be an important factor. However, in the present study, the skin resection area varied widely in both groups. Even though in patients with the same size defects, one underwent a direct closure method and the other underwent a rhomboid flap reconstruction. The ratio of the skin resection area to BSA or BMI also varied widely. Thus, the application of a rhomboid flap reconstruction should be determined by not only the defect size or the patient’s physical constitution such as their BSA or BMI but also include several other factors such as the softness of the skin or the volume of subcutaneous tissue. In addition, the size of the actual skin defect can sometimes become larger after tumor resection due to skin...
contracture after the tumor is released. Thus, it is difficult to determine the application of rhomboid flap reconstruction prior to operation, and it is more appropriate to make this decision after tumor resection and consider the skin tension of the defect. Wound closure with over-tension could disturb the blood circulation of the skin edge and result in wound dehiscence or skin necrosis. A pinch test is a simple method and has a correlation to the actual skin tension of the defect which is measured by a tension gauge. In the present study, there was only one severe wound complication that delayed adjuvant therapy caused by high tension of the sutured skin in both groups. The test is thought to be a reasonable and reliable method to evaluate the skin tension of the defect and to determine the most appropriate approach between the rhomboid flap reconstruction and the direct closure method.

In this retrospective study, operation data and post-operative complications and factors of post-operative QOL were compared to evaluate the efficacy of the rhomboid flap reconstruction method after mastectomy for LABC. It was possible to reconstruct significantly larger skin defects in the local flap group using rhomboid flaps. Although the duration of operation was significantly longer in the local flap group, the average difference in operation duration between the 2 groups was only 25 minutes. There were no significant differences in other factors, including the amount of blood loss, length of hospital stay, incidence of post-operative complication, and delay of adjuvant therapy between the groups. There were 2 cases of skin necrosis in the local flap group. They were cases of small flap tip necrosis, and they were quickly treated by debridement and application of ointments. There was also no significant
difference in factors that deteriorate post-operative QOL, such as limitation of shoulder joint movement or lymphedema. Cosmetic deformity that required revision surgery was not observed in either group. Therefore, the rhomboid flap method can be considered a safe reconstruction method for large skin defects after mastectomy for LABC, and local flap reconstruction after mastectomy is relatively less invasive for patients.

Conclusion

In the local flap group, significantly larger skin defects than those in the direct closure group could be reconstructed with rhomboid flaps, and there were no significant differences in post-operative complications between the 2 groups. Although the duration of operation was significantly longer in the local flap group than in the direct closure group, the average difference between the groups was only 25 minutes. There were no significant differences in the factors influencing post-operative QOL. A pinch test is thought to be a useful method to determine the suitability of rhomboid flap reconstruction. The rhomboid flap method is an effective reconstruction method for large defects after mastectomy for LABC.

Conflict of interest

We declare no conflicts of interest.
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Figure legends

Figure 1 Selection of the closure method

A round skin resection line including the area of tumor invasion and the nipple-areolar complex is drawn.

After tumor resection, pinch test is performed (left figure).

If the skin tension is low, the skin is trimmed to a spindle shape and closed directly (right, top figure).

If the skin tension is high, the local flap closure method is selected (right, bottom figure).

Figure 2 The fundamental design of the rhomboid flap

A flap with sides equal in length to those of the rhomboid shape of the defect is designed (left figure).

The flap is moved and transposed with the edges marked with a circle and a triangle matched to the edges of the rhomboid shape of the defect (right figure).

Dog ear deformities appear at the base of the flap and the axillary area (right figure, circle).

Figure 3 Clinical case

Skin resection line was designed including the skin ulcer and a red spot (A).

After tumor resection, the size of the skin defect became larger (B).

Rhomboid flap reconstruction was performed (C).
There were no limitations of shoulder joint movement after surgery (D.E).
Figure 1

1. Tumor resection
2. Pinch test
3. The direct closure group
4. The local flap group
Figure 2

[Diagram showing a defect and its flap]
Figure 3
Table 1. Patient and tumor characteristics

|                          | The local flap group n=14 (%) | The direct closure group n=54 (%) | P    |
|--------------------------|-------------------------------|----------------------------------|------|
| Mean age ± SD (years)    | 63.5 ± 13.1                   | 57.2 ± 11.3                      | 0.07 |
| BMI ± SD                 | 22.9 ± 2.9                    | 23.6 ± 4.6                       | 0.58 |
| BSA ± SD (m²)            | 1.46 ± 0.14                   | 1.52 ± 0.13                      | 0.31 |
| Smoking                  | 3 (21.4)                      | 15 (27.8)                        |      |
| Diabetes mellitus        | 1 (7.1)                       | 7 (13)                           | 1    |
| Administration of Corticosteroids | 0                           | 1 (1.9)                          | 1    |
| Clinical Stage           |                               |                                  |      |
| T4a                      | 11 (78.6)                     | 46 (85.2)                        | 0.68 |
| T4b                      | 2 (14.3)                      | 3 (5.6)                          | 0.27 |
| T4c                      | 1 (7.1)                       | 5 (9.3)                          | 1    |
| N0                       | 2 (14.3)                      | 8 (14.8)                         | 1    |
| N1                       | 7 (50)                        | 25 (46.3)                        | 1    |
| N2                       | 2 (14.3)                      | 11 (20.4)                        | 1    |
| N3                       | 3 (21.4)                      | 10 (18.5)                        | 1    |
| Estrogen receptor positive | 10 (71.4)                    | 34 (63)                          | 0.76 |
| HER2 positive            | 0                             | 18 (33.3)                        | 0.014|
Table 2. Neoadjuvant and adjuvant therapy data

| Pathological response | The local flap group n=14 (%) | The direct closure group n=54 (%) | P |
|-----------------------|-----------------------------|-----------------------------------|---|
| Grade 0               | 0                           | 0                                 | 1 |
| 1                     | 8 (66.7)                    | 31 (67.4)                         | 1 |
| 2                     | 2 (16.7)                    | 10 (21.7)                         | 1 |
| 3                     | 2 (16.7)                    | 5 (10.9)                          | 0.62 |
| Adjuvant therapy      | 14 (100)                    | 52 (96.3)                         | 1 |
| Systemic therapy      | 12 (85.7)                   | 42 (80.8)                         | 1 |
| Irradiation           | 9 (64.3)                    | 31 (60)                           | 1 |
| Delay of adjuvant therapy | 0                           | 1 (1.9)                           | 1 |
|                                | The local flap group n=14 (%) | The direct closure group n=54 (%) | P     |
|--------------------------------|--------------------------------|----------------------------------|-------|
| Skin resection area ± SD (cm²) | 112.7 ± 71.4                  | 45.4 ± 26.8                      | 0.0002|
| Skin resection area / BMI      | 5.1 ± 3.6                     | 2.0 ± 1.3                        | 0.0001|
| Skin resection area / BSA      | 77.8 ± 51.3                   | 30.2 ± 17.2                      | 0.00003|
| Duration of operation ± SD (min) | 142.5 ± 40                    | 117.7 ± 22.6                     | 0.016 |
| Blood loss ± SD (ml)           | 124.4 ± 63.1                  | 184.3 ± 172.1                    | 0.57  |
| Axillary operation             |                                |                                  |       |
| Sentinel lymph node biopsy     | 2 (14.3)                      | 7 (13)                           |       |
| Axillary lymph node dissection | 12 (85.7)                     | 47 (87)                          | 1     |
| Hospital stay ± SD (day)       | 7.6 ± 2.2                     | 7.1 ± 3.1                        | 0.18  |
| Wound dehiscence               | 0                             | 4 (7.4)                          | 0.57  |
| Hematoma                       | 0                             | 2 (3.7)                          | 1     |
| Infection                      | 0                             | 4 (7.4)                          | 0.57  |
| Skin necrosis                  | 2 (14.3)                      | 3 (5.6)                          | 0.27  |
| Limitation of                 |                                |                                  |       |
| shoulder joint movement        | 1 (7.1)                       | 3 (5.6)                          | 1     |
| Lymphedema                     | 1 (7.1)                       | 2 (3.7)                          | 0.505 |
| Revision surgery               | 0                             | 0                               |       |