Is there a difference in the diagnosis and prognosis of local recurrence between autologous tissue and implant-based breast reconstruction?

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Abstract

Purpose

Breast reconstruction has become common after total mastectomy; however, certain types of breast reconstruction may be associated with delayed local recurrence or poor survival. Here we investigated whether there are differences in the diagnosis and prognosis of local recurrence between autologous reconstruction and implant reconstruction.

Methods

A retrospective analysis was performed on patients undergoing breast cancer surgery with autologous tissue or immediate implant reconstruction in a single center (January 2003–December 2017). Patient data including the period from cancer surgery to local recurrence diagnosis, tumor size at the time of recurrence, and survival times after cancer surgery and recurrence detection were analyzed.

Results

There was a significant difference ($p = 0.021$) in the time from surgery to recurrence between the autologous tissue (1,246 days) and implant (909 days) groups. Recurrence tumor size did not differ (autologous: 1.00 cm^2 vs. implant: 0.90 cm^2; $p = 0.813$). Survival time after surgery ($p = 0.63$) and recurrence detection ($p = 0.74$) did not statistically vary.

Conclusions

Local recurrence detection takes longer following autologous reconstruction. However, there is no difference in recurrence tumor size or survival, suggesting no variation in the prognosis of local recurrence according to the reconstruction method.

Introduction

According to American Cancer Society data, 252,710 cases of invasive breast cancer were diagnosed in 2017. Also, 63,410 cases of carcinoma *in situ* detection and 101,657 cases of breast reconstruction were performed in 2018 [1]. These statistics reveal an increase in the incidence by more than 20,000 cases relative to those reported in 2000 [1].

Postmastectomy breast reconstruction offers the options of reconstruction with either autologous tissue or an implant. In cases undergoing autologous tissue reconstruction, the quality of the material is similar to natural glandular tissue, and flap tailoring is possible considering the patient's breast shape. Moreover, there is no immune response such as capsule formation and there is a reduced likelihood of infection. However, the method usually disrupts the normal anatomy; leaves long, undesirable scars on the donor site; and is more damaging in cases of reconstruction failure.

Conversely, the advantages of implants include simple surgical procedures, reconstruction without damaging other normal tissues, and rapid recovery. However, implant malposition may occur. Furthermore, implant products cannot be customized for each patient; therefore, asymmetry occurs more frequently than autologous reconstruction. Unpredictable capsular contracture, seroma, and breast implant–associated anaplastic large-cell lymphoma are also well known potential risks [2, 3]. Moreover, postoperative complications such as wound dehiscence and subsequent exposure can be increased by the postoperative radiotherapy [4].

As each reconstruction method has distinct advantages and disadvantages, reconstruction choices can differ according to the doctor's preferences, medical insurance system, and patient's socioeconomic status and decision [5]. However, it remains controversial whether to consider implants or autologous reconstruction first.

Further, a more important consideration to adopt in choosing the modality of reconstruction is whether the reconstruction itself influences patient prognosis after cancer treatment. Autologous tissue below the mastectomy skin flap may interfere with the detection of newly formed nodules, and fat necrosis can confuse the discriminating mode used to detect recurrent cancer [6, 7]. Recurrence after implant insertion can cause the mass to be touched more easily on the surface. However, when using screening modalities such as ultrasound, it may be challenging to detect recurring masses beneath the implant (Figure 1) [8]. In this regard, there is a concern that either reconstruction may be disadvantageous in allowing precise detection of the local recurrence in the breast.

The purpose of this study was to determine whether there is a difference in the diagnosis, treatment process, and prognosis of local recurrence between autologous tissue reconstruction and implant reconstruction.

Materials And Methods

A retrospective analysis was performed on patients undergoing breast cancer surgery in a single center between January 1, 2003 and December 31, 2017 after institutional review board approval (IRB 2020-0035). All eligible patients were classified as those undergoing reconstruction by autologous tissue or immediate implantation, respectively. Among them, only those with local recurrence were further included in this study. Patients who received breast-preserving surgery, breast reconstruction before the diagnosis of breast cancer, or breast reconstruction using both autologous tissue and implant were excluded from data

analysis. Additionally, patients who had cancer stage IIIB or higher, those with a serious history (e.g., primary malignancy in other sites, severe cardiac/pulmonary disease), or those who died owing to a reason other than the recurrence of breast cancer were excluded from the study.

Inclusion criteria for local recurrence

We included patients only diagnosed with local recurrence that could be detected superficially in the skin and nipple–areolar complex or in deep tissues such as the subcutaneous layer or chest wall of mastectomy (Figure 2). Therefore, patients with regional recurrences such as axillary lymph node metastasis or distant metastasis were excluded from the present study regardless of the presence of local recurrence. This exclusion was conducted is because regional and distant metastases can be found in areas that are far apart, independently of the reconstruction. Moreover, when any metastasis was combined with local recurrence, the sequence of recurrence could not be clearly identified.

Collecting data

Demographics, such as age, body mass index (BMI), history of diabetes, hypertension, and smoking, were assessed. Furthermore, the stage, hormonal status (estrogen receptor (ER), progesterone receptor (PR), and Her2), and preoperative/preoperative treatment of cancer diagnosed at the time of surgery were reviewed, and the tumor size and location depth at the time of the initial recurrence were noted. We investigated whether the outpatients suspected of recurrence had scheduled visits or unplanned visits. Finally, we compared periods of time from breast cancer surgery to recurrence diagnosis, salvage of reconstructive reconstruction after recurrence, and breast reshaping in salvaged cases between two reconstructions. The definition of salvage in the autologous group was that more than 50% of the reconstructed tissue was preserved.

Statistical analysis

The Statistical Package for the Social Sciences version 26.0 software (IBM Co., Armonk, NY) was used to confirm the statistical significance of data collected from the groups. Chi-square test, Student's t-test, and Mann–Whitney U test were employed for comparing continuous and categorical variables between two groups. A linear regression analysis was conducted to clarify the variable which affect the cancer surgery to recurrence detection period. Log-transformation was necessary because the data were skewed to the right side. The fitness was tested through the Kolmogorov-Smirnov test, Cramer-von Mises test, and Anderson-Darling test to examine whether the cancer surgery to recurrence detection rate period, which appeared to be similar to the Gamma distribution, was affected by the hormone receptor and Her2. The effect of hormone receptor and Her2 was also confirmed using a linear regression model. In addition, a Kaplan–Meier curve was used to compare recurrence with the time of death and cancer surgery with the time of death. Statistical significance was confirmed using the log-rank test.

Results

Over 15 years, a total of 2,361 autologous tissue reconstructions and 551 immediate implants were performed. In total, 93 (3.94%) patients were diagnosed as having local recurrence in the autologous tissue group and 25 (4.54%) patients were diagnosed with the same in the immediate implant group (p = 0.521). The mean age of the autologous group (40.03 ± 7.59 years) was older than that of the immediate implant group (35.12 ± 6.75 years; p = 0.004). Also, there was a difference in the mean BMI (Autologous tissue: 22.68 ± 2.69 kg/m^2 vs. immediate implant: 21.14 ± 2.80 kg/m^2; p = 0.013). History of Diabetes, hypertension and smoking was not different between two groups.

The cancer stage distribution of patients was not statistically significant between the autologous tissue and implant groups (p = 0.261). Neither the history of neoadjuvant chemotherapy, or adjuvant chemo- and radiotherapy was not significant (Table I).

Comparing the periods from breast cancer surgery to recurrence diagnosis showed that the autologous tissue group experienced a longer period at 1,246 (742–1,820) days, while the immediate implant group exhibited the shorter period at 909 (384–1,231) days, with statistical significance found among the two groups (p = 0.021).

The detected tumor size at the time of recurrence was 1.09 cm^2 (0.94–1.23) in the autologous tissue group and 1.11 cm^2 (0.82–1.4) in the immediate implant group, indicating that there was no difference in this regard among the two groups (p = 0.868).

In the classification of the location of recurrence, implant patients were diagnosed with a higher rate of deep tissue recurrence compare to that of the autologous group (implant: 9 of 36, 36% vs. autologous tissue: 24 of 93, 25.8%). However, there was no statistical significance (p = 0.449).

Considering the type of outpatient visits in those cases where the patient was diagnosed with recurrence, the immediate implant group had a higher rate of unplanned visits (13 patients; 52.0%); however, no statistical significance was found between the two groups (p = 0.203).

Three patients diagnosed with local recurrence underwent local advancement flap after surgical removal, while one patient underwent reconstruction with a mini latissimus dorsi musculocutaneous flap. Initially, all patients underwent reconstruction using autologous tissue. Failure to salvage existing autologous reconstruction occurred in no patient. In one patient who underwent reconstruction with an implant, the device was removed and replaced with an expander because of the difficulty of salvage (Table 2). The rest of the both group patients underwent simple wide excision with primary closure.

According to linear regression analyses, for the period of time between cancer surgery and the detection of recurrence, the type of reconstruction, patient age, and reception of neoadjuvant chemotherapy were significant in the univariate analysis, while only reception of neoadjuvant chemotherapy was statistically significant in the multivariable analysis (best point estimate: -0.553; 95% CI -0.928- -0.178; p=0.001, Table 3).

Based on ER/PR/Her2 expression, it was classified into four subgroups. When ER/PR/Her2 was (positive/positive or negative/negative), the cancer surgery to recurrence detection period was the longest in both autologous and implant groups, and no statistical significance was observed between the two groups; autologous group: 1,471 (1,003-1,827) days; implant group: 1,351.5 (1,127-1,707) days, and p = 0.7128. In contrast, the cancer surgery to recurrence detection period was the shortest when ER/PR/Her2 was (negative/ negative / negative, known as triple-negative type); autologous group: 743 (225-1,246) days; implant group: 535.5 (194-877) days, and p = 0.7728. However, no statistical significance was observed when comparing the four groups of the cancer surgery to recurrence detection period (autologous group: p = 0.0877, implant group: p = 0.2812, Table 4).

As a result of exploratively confirming the effect of the interaction between the autologous group and ER, PR, and Her2 on the cancer surgery to recurrence detection period using a linear regression model, the period was shorter in the case of the implant group than in the case of the autologous group (Estimate: -0.3615, Standard error: 0.1501, p = 0.0177). A relatively long period was confirmed in the case of ER-positive breast cancer, but the statistical significance was on the boundary line (Estimate: 0.4242, Standard error: 0.2198, p = 0.0562). PR and Her2 did not showed statistical significance.

Finally, the survival times after surgery and after the detection of recurrence, respectively, were not significantly different (time from first surgery to death: p = 0.63 vs. time from recurrence to death: p = 0.74) in the two groups (Figures 3 and 4).

Discussion

Since pedicled transverse rectus abdominis (TRAM) flap was first introduced by Hartrampf in 1982, options for breast reconstruction based on autologous tissue insertion have expanded into free TRAM flap, free deep inferior epigastric perforator flap, and procedures involving gluteal or thigh tissues [9-11]. Separately, implant-based reconstruction has evolved since it was first introduced by Snyderman in 1971 and, today, more implant-based breast reconstruction surgery is being performed [12]. In addition, the invention of an instrument such as an indocyanine green camera, which is capable of directly identifying the tissue circulation, had played a major role in reducing the number of surgical complications [13, 14], while the development of acellular dermal matrix and a new generation of implants has minimized the incidence of capsular contracture and seroma [15]. In this regard, rates of breast reconstruction are expanding alongside continued advances in equipment, technology, and materials.

Because both advantages and disadvantages, though different depending upon the choice of breast reconstruction method, remain in existence overall, doctors must discuss with individual patients the reconstruction method to be used in each case. Results of previous studies on breast cancer recurrence and survival rates have supported that reconstruction does not increase the recurrence of breast cancer and cannot affect the survival rate of these patients [16-27]. However, some surgeons still have concerns that autologous tissues or implants may act as obstacles in the diagnosis of the local recurrence of breast cancer [28].

Siotos et al. studied differences in survival rates between reconstructed and non-reconstructed cases among 1,517 patients with breast cancer. According to their study, there was a 20% higher overall survival benefit in the reconstruction group [29]. Factors contributing to survival, such as differences in race, income, and socioeconomic status, and the varying effects of instruction and counseling on reconstruction outcomes among those who might appreciate such (i.e., those with a higher education level) versus those who may not are not yet fully understood.

Kanchwala et al. studied 41 patients with locoregional recurrence. The time required to pinpoint recurrence did not differ between the immediate implant and autologous tissue groups. The average tumor size in patients with recurrent cancer was 1.5 cm in the immediate implant group and 2.9 cm in the autologous tissue group, with the immediate implant group showing nearly double the rate of index reconstruction loss [30]. However, it was hard to elucidate the incidence of locoregional recurrence because the authors did not report the total numbers of mastectomy and reconstruction procedures. Furthermore, when assessing reconstruction salvage, the implant can be clearly distinguished because device explantation is considered as a failure, while in cases of autologous reconstruction, the salvage definition might be more vague, which potentially affected the credibility of their data.

In this study, attempting to assess the local recurrence is consistent with our research, we clarified the definition of salvage in the autologous group. Furthermore, medical treatment was conducted through a single and equivalent public insurance system. These can bring us the benefit of data accuracy because these kinds of social systems automatically control variables and factors that may bias statistics.

According to our data analysis, the period from cancer surgery to recurrence detection was shorter in the immediate implant group. Two interpretations are possible in the result: First thing is the local recurrence may be found late or the tumor may relapse late. Given that the tendency of unplanned visits was low among patients with autologous tissues, it may be more difficult to palpate an existing lesion among patients in the autologous tissue group. Second thing is that the autologous tissue group had earlier cancer stages and a small number of patients in this group received neoadjuvant chemotherapy, which can lead to late tumor growth. The finding that there was no difference in the tumor size at the time of detection supports those hypotheses. If relapse had occurred earlier and the tumor had been allowed to grow for a longer period, the tumor would have been larger-sized.

The finding that there was no difference in the tumor size at the time of detection supports those hypotheses. If relapse had occurred earlier and the tumor had been allowed to grow for a longer period, the tumor would have been larger-sized.

Based on the linear regression test that was completed to determine the factors affecting the time from initial breast cancer resection to the diagnosis of local recurrence, only neoadjuvant chemotherapy was found to have an effect. As mentioned earlier, the autologous tissue group, which included fewer patients who received neoadjuvant chemotherapy, had more cases of early-stage cancer, and it is likely that tumor growth began later.

Another factor that can have a significant effect on the cancer surgery to local recurrence detection period is the hormone receptor and Her2 expression. According to previous studies, the prognosis is the best for ER-positive, any PR, and Her2-negative breast cancer and poor for triple-negative breast cancer [31, 32]. As a result of the classification by hormone receptor and Her2 expression, results similar to those of previous studies were obtained in absolute values,

although statistical significance could not be observed. When the hormone receptor and Her2 distributions in the autologous and implant group patients were summarized, 39.78 percent of patients were ER positive and Her2 negative patients in the autologous group; however, only 24 percent of patients were diagnosed ER positive and Her2 negative in the implant group; whereas 11 (44%) patients were ER and Her2 positive patients. A total of 3 (3.23%) patients were triple-negative breast cancer patients in the autologous group; however, the percentage of triple-negative breast cancer was more than twice as much in the case of the implant group.(2 (8%) patients, p = 0.636) These data also indicate that local recurrence occurred later in the autologous group than in the implant group.

Survival rate is the most important factor to distinguish the difference of local recurrence prognosis. Ultimately, in this study, the postoperative survival period and survival period after recurrence detection were not statistically significantly different between the two groups. Contrary to the concerns of some surgeons, there was no difference in local recurrence findings between autologous tissue reconstruction and implants nor any statistical difference in terms of survival.

Separately, the incidence of the local recurrence of breast cancer in this study was less than 5%; therefore, the study population may be too small in this regard to draw certain conclusions from in this study. However, the present study drew conclusions based on the accumulation of 15 years of data. Furthermore, unlike in previous papers of locoregional recurrence which include the recurrence of lymph nodes or distant metastasis, our study clarified the definition of local recurrence while excluding lymph node recurrence or metastasis. And distant metastasis cases were also excluded for this same reason. Therefore, the present study offers good practical evidence regarding the direct effect of the two reconstruction methods on the diagnosis of local recurrence.

Because the study was conducted with patients belonging to a single race who benefited from the national health care service, the environmental factor was automatically controlled to increase the reliability of the study. Altogether, this study followed a systematic approach to determine whether there exist variations in the recurrence detection and survival period of patients when treated with different breast reconstruction methods. It is expected that this will be a reasonable basis for the assumption that breast implant or autologous tissue reconstruction does not cause harmful effects in the diagnosis and the treatment of local recurrence.

There are some limitations to this study. First, the immediate reconstruction method involving the use of implants was initiated in 2008, resulting in a relatively small number of reconstructions and a short follow-up period. Second, although no significance was observed in both the univariate and multivariate analyses, patient age and BMI values were different between the two groups. This may be a limitation because of the small number of patients who only developed local recurrence after breast cancer surgery. We expect that more accurate results will be obtained if we examined the matched patients throughout a longer follow-up period.

Conclusions

The period of detection of local recurrence is longer in patients who underwent autologous reconstruction. However, there is no difference in tumor size at the time of recurrence and survival rate between patients treated with autologous tissue and those given implants. Therefore, reconstruction using autologous tissue or implants does not interfere with the diagnosis of local recurrence, and there is no inferiority in the survival prognosis.

Declarations

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Tables

Table 1. Patients' demographics, past histories, stage, and pre-/post-operative therapy

	Autologous	Implant	p-value
All patients	2361	551	
Local recurrence (%)	93 (3.94)	25 (4.54)	0.521
Age (mean (SD))	40.03 (7.59)	35.12 (6.75)	0.004
Stage (%)			0.261
0	13 (14.0)	2 (8.0)	
1	44 (47.3)	9 (36.0)	
2	33 (35.5)	14 (56.0)	
3	3 (3.2)	0 (0.0)	
ER positive (%)	71 (76.3)	17 (68.0)	0.554
PR positive (%)	65 (69.9)	13 (52.0)	0.150
HER positive (%)	52 (55.9)	17 (68.0)	0.390
BMI (mean (SD))	22.68 (2.69)	21.14 (2.80)	0.013
Diabetes (DM) (%)	1 (1.1)	0 (0.0)	1.000
Hypertension (HTN) (%)	3 (3.2)	0 (0.0)	0.846
Smoking (%)	5 (5.4)	1 (4.0)	1.000
NeoCTx. (%)	7 (7.5)	5 (20.0)	0.145
RTx. (%)	6 (6.5)	1 (4.0)	1.000
Post.CTx. (%)	30 (32.3)	8 (32.0)	1.000
Hormone.Tx. (%)	62 (66.7)	14 (56.0)	0.451
Herceptin (%)	7 (7.5)	5 (20.0)	0.145

SD, standard deviation; IQR, interquartile range; NeoCTx., neoadjuvant chemotherapy; RTx., adjuvant radiotherapy; Post CTx., adjuvant chemotherapy; Hormone Tx., hormone therapy

Table 2. Local recurrence profiles

	Autologous	Implant	p-value
Cancer surgery to recurrence detection	1246	909	0.021
(days, median [IQR])	[742.00, 1820.00]	[384.00, 1231.00]	
Tumor size (cm^2, mean (95% CI))	1.09 (0.94, 1.23)	1.11 (0.82, 1.4)	0.868
Deep tissue recurrence (%)	24 (25.8)	9 (36.0)	0.449
(%, 95% CI)	17.3, 35.9	18.0, 57.5	
The number of unplanned visit	33	13	0.203
(%, (95% CI))	35.5 (17.3, 35.9)	52.0 (18.0, 57.5)	
Reconstruction after recurrent breast cancer operation (%)	4 (4.30)	1 (4)	1.000
Failed to salvage of previous reconstruction (%)	0 (0)	1 (4)	0.052

IQR. Interquartile range; CI. confidence interval

Table 3. Cancer surgery to recurrence detection rate period: univariate and multivariable analyses

	Univariate				Multivariable			
	Beta Point Estimate	95% CI		p-value	Beta Point Estimate	95% CI		p-value
		LB	UB			LB	UB	
Group (reference: Implant)	−0.411	−0.749	−0.074	0.017	−0.286	−0.625	0.054	0.098
Age	0.018	0.000	0.037	0.047	0.009	−0.010	0.028	0.373
BMI	0.005	−0.046	0.056	0.854	−0.011	−0.062	0.040	0.670
NeoCTx.	−0.707	−1.045	−0.369	< 0.001	−0.553	−0.928	−0.178	0.001

CI, confidence interval; LB, lower bound of uncertainty interval; UB, upper bound of uncertainty interval; NeoCTx., neoadjuvant chemotherapy

Table 4. Subgroup analysis by ER, PR, and Her2 expression

Subgroup	ER (+), PR (+ or -), Her2 (+)					ER (+), PR (+ or -), Her2 (-)					ER (-), PR (-), Her2	
	Autologous		Implant			Autologous		Implant			Autologous	
	n =34		n = 11		p-value	n = 37		n = 6		p-value	n = 18	
Age (mean (SD))	40.21	7.73	34.18	7.29	0.0279	40.14	7.96	36.00	4.15	0.2232	40.56	7.22
Age (median [IQR])	40	[35.00,46.00]	31	[29.00,36.00]	0.0139	40	[36.00,44.00]	34.50	[33.00,40.00]	0.1654	40.00	[34.00,48
Stage (%)					0.5618					0.5871		
0	4	11.76	2	18.18		6	16.22	0	0.00		3	16.67
1	15	44.12	3	27.27		16	43.24	2	33.33		11	61.11
2	12	35.29	6	54.55		15	40.54	4	66.67		4	22.22
3	3	8.82	0	0.00								
BMI (mean (SD))	22.7	2.2	21.81	2.42	0.2624	22.11	2.27	19.31	2.67	0.0091	23.85	3.96
BMI (median [IQR])	22.58	[21.19,23.81]	21.2	[19.69,23.07]	0.2399	22.11	[20.51,23.28]	19.84	[17.59,20.69]	0.0217	23.42	[20.08,26
DM = 1 (%)	0	0.00	0	0.00	-	1	2.70	0	0.00	1.0000	0	0.00
HTN = 1 (%)	1	2.94	0	0.00	1.0000	2	5.41	0	0.00	1.0000	0	0.00
Smoking = 1 (%)	3	8.82	0	0.00	1.0000	1	2.70	1	16.67	0.2625	1	5.56
Tumor size (cm^2, mean (95% CI))	0.99	(0.80,1.17)	1.1	(0.59,1.61)	0.5817	1.14	(0.85,1.46)	0.75	(0.45,1.05)	0.0408	1.08	(0.63,2.3
Tumor size (cm^2, median [IQR])	0.95	[0.6,1.2]	0.9	[0.60,1.40]	0.905	0.90	[0.70,1.20]	0.75	[0.50,1.00]	0.1931	1.10	[0.60,1.5
Cancer surgery to recurrence detection (days, median [IQR])	1242.5	[762,2378]	818	[369,1172]	0.0314	1471	[1003,1827]	1351.5	[1127,1707]	0.7128	848	[687,133

Table 5. Linear regression analysis: Group, ER, PR, and Her2

	Estimate	SE	p-value
Group (Implant vs. Autologous)	−0.3615	0.1501	0.0177
ER	0.4242	0.2198	0.0562
PR	−0.1059	0.2079	0.6116
Her2	−0.08543	0.1334	0.5232

SE: standard error

Figures

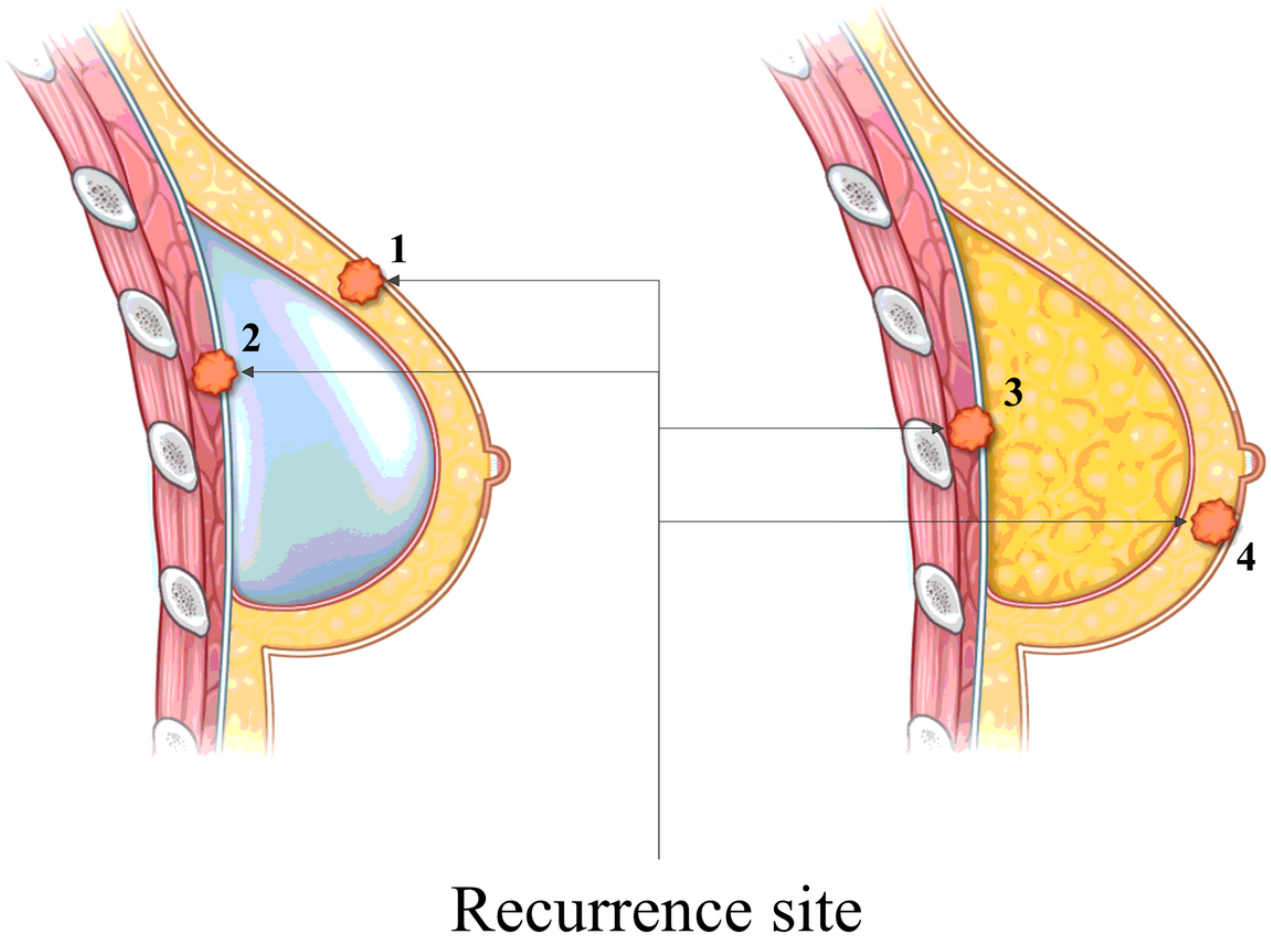

Figure 1

Site of local recurrence detection. 1. Implant insertion can cause the mass to be touched more easily on the surface. 2. However, when screening modalities such as ultrasound are used, it may be difficult to detect recurring masses in the bottom layer beneath the implant. 3, 4. Autologous tissue below the mastectomy skin flap may interfere with the detection of a newly formed nodule, and fat necrosis can confuse the detection and discrimination of recurrent cancer.

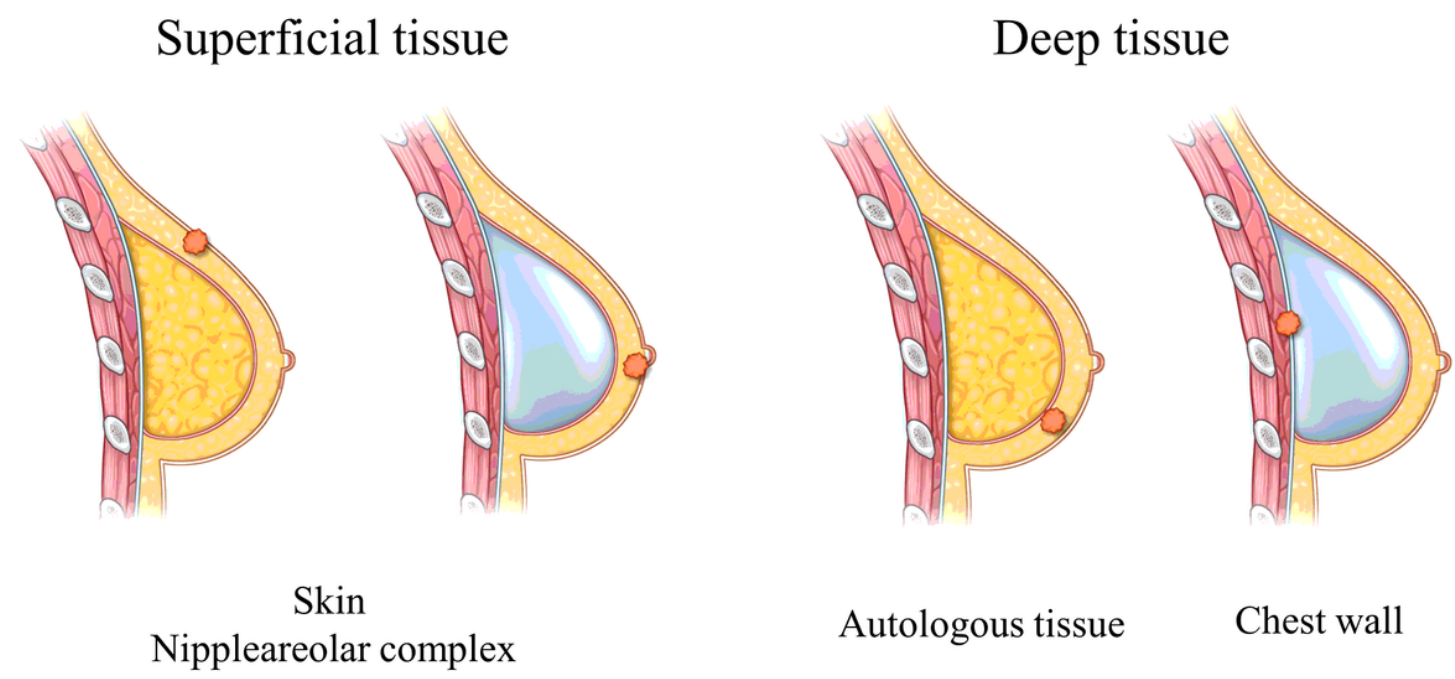

Figure 2

Type of local recurrence. A. Superficial tissue recurrence; B. deep tissue recurrence. Cases of local recurrence with any regional recurrence or distant metastasis were excluded.

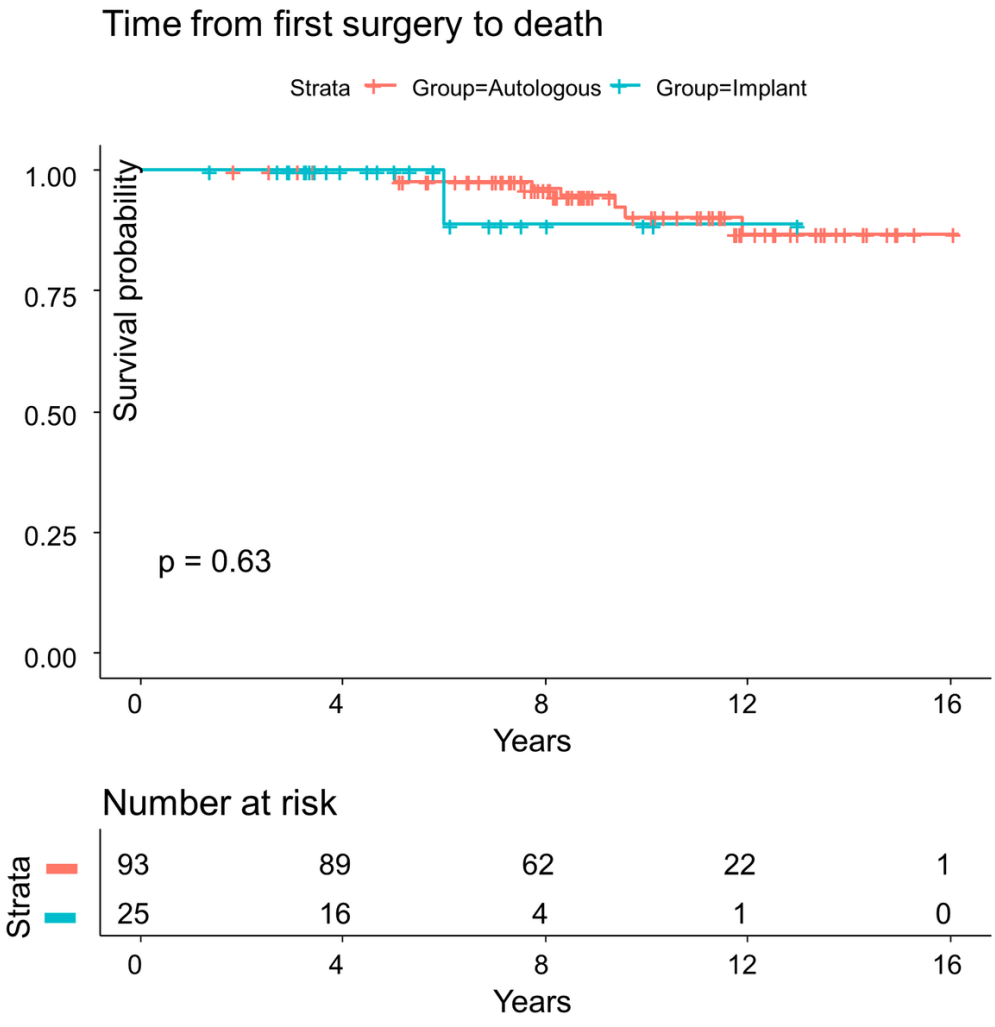

Figure 3

Survival analysis: cancer surgery to the time of death.

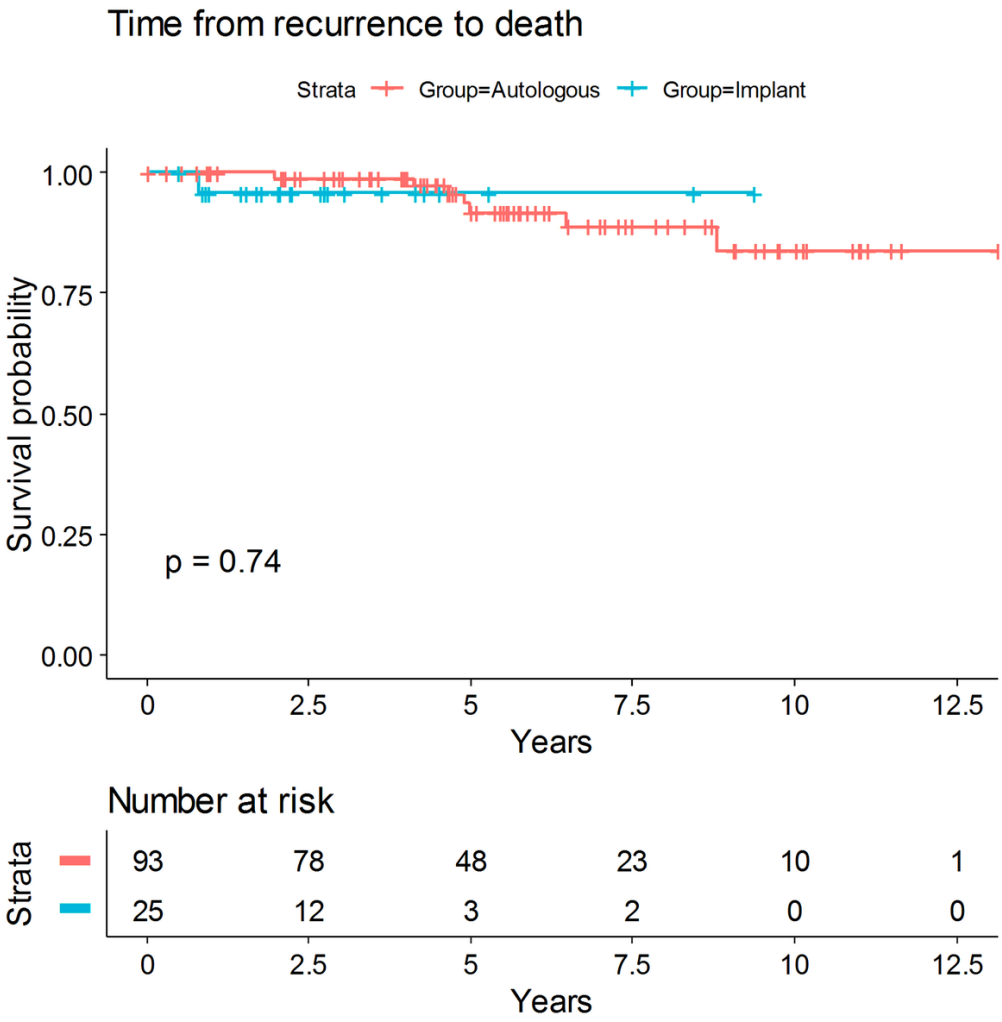

Figure 4

Survival analysis: local recurrence to the time of death.