Radiotherapy Increases Major Complications and Complication-related Reconstruction Failures in Patients with Implant-based Breast Reconstruction

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Research Article

**Keywords:** breast cancer, breast reconstruction, radiotherapy, complications, and reconstruction failure

**DOI:** https://doi.org/10.21203/rs.3.rs-551671/v1

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Abstract

**Purpose** This study was designed to assess the impact of post-mastectomy radiation therapy (PMRT) on reconstruction complications and failures in patients undergoing mastectomy and different types of breast reconstruction.

**Methods** We retrospectively identified 832 breast cancer patients who underwent mastectomy and breast reconstruction at Fudan University Shanghai Cancer Center between June 2001 and December 2015. Of these, 159 patients received PMRT, and 673 patients did not receive PMRT. The endpoints of the reconstruction outcomes included any complications, major complications, overall reconstruction failures and complication-related reconstruction failures. Multivariate analysis was applied to identify independent predictors of reconstruction outcomes in patients with different types of breast reconstruction. The nomogram model was built on the basis of the multivariate analysis to predict complication-related reconstruction failures.

**Results** The median follow-up time was 58.5 months. Of all 832 patients, 394 patients received implant-based reconstruction, and 438 patients received autologous reconstruction. For patients with implant-based reconstruction, multivariate analysis showed that PMRT was associated with 3.16 times (95% CI 1.17-8.54, p=0.023) higher odds of major complications and 3.22 times (95% CI 1.01-10.20, p=0.047) higher odds of complication-related reconstruction failures but was not associated with any complications (OR 1.73, 95% CI 0.88-3.38, p=0.113) or overall reconstruction failures (OR 2.09, 95% CI 0.76-5.73, p=0.152). The nomogram model for implant-based reconstruction showed good predictive performance for complication-related reconstruction failures (AUC =0.714).

**Conclusions** PMRT appears to be associated with an increased risk of major complications and complication-related reconstruction failures in patients with implant-based reconstruction.

**Introduction**

Breast reconstruction has greatly improved different aspects of quality of life, including psychosocial, sexual and physical factors, for patients with breast cancer treated by mastectomy [1]. The rate of breast reconstruction has increased over the past decade both in the United States and in China [2,3]. Breast reconstruction includes diverse options in terms of the sources of reconstructive tissue (such as autologous tissues, implants, or a combination of an implant and a flap) or the timing of the reconstruction (e.g., immediate, delayed, or delayed-immediate). Many factors should be taken into account when choosing the appropriate types of reconstruction, including patient anatomical characteristics and preferences, socioeconomic costs and planned adjuvant therapies.

Postmastectomy radiation therapy (PMRT) plays an imperative role in the management of breast cancer. An Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis demonstrated that PMRT can reduce both local recurrence and breast cancer mortality in patients with positive lymph nodes [4]. However, for patients undergoing breast reconstruction and PMRT, the situation has become complicated since PMRT might increase the frequency of complications and affect the outcomes of breast reconstruction [5-
The typical approach to integrating PMRT with different types of breast reconstruction remains an important and controversial question.

In our previous study, we found that PMRT was associated with an increased risk of unanticipated reoperations among patients receiving implant-based reconstruction, but no such risk with those receiving autologous reconstruction\(^9\)\(^9\). The prospective multicenter Mastectomy Reconstruction Outcomes Consortium (MROC) study also demonstrated that radiotherapy was associated with higher odds of any complications and of major complications in the implant reconstruction cohort but showed no difference in the autologous reconstruction cohort\(^10\). These data indicated that the impact of PMRT on reconstruction outcomes might differ between autologous reconstruction and implant-based reconstruction. In addition, the MROC study did not report the impact of PMRT on reconstruction failures in the multivariable analysis.

In this study, we retrospectively reviewed patients who underwent mastectomy and autologous and implant-based breast reconstruction with or without PMRT in our cancer center. We tried to assess the impact of PMRT on both reconstruction complications and reconstruction failures in patients with autologous reconstruction and implant-based breast reconstruction. In addition, implant-based reconstruction and autologous reconstruction nomograms were built on the basis of multivariate analysis to predict complication-related reconstruction failures.

**Materials And Methods**

Patients From June 2001 to December 2015, the results from 832 breast cancer patients who underwent mastectomy and breast reconstruction with or without PMRT in our cancer center were retrospectively analyzed. Breast reconstruction options included autologous tissues, implants, or a combination of autologous tissue and an implant. Autologous tissues were obtained from the latissimus dorsi muscle, a pedicle transverse rectus abdominis musculocutaneous (TRAM) flap or a deep inferior epigastric perforator (DIEP) flap. Implant reconstruction included single-stage direct-to-implant reconstruction or two-stage expander-implant reconstruction (also called delayed-immediate reconstruction). Patients with bilateral reconstruction, patients who received radiotherapy for local-regional recurrences, or patients with less than one year of follow-up were excluded. A review of the data for this study was approved by the Ethical Committee and Institutional Review Board of Fudan University Shanghai Cancer Center. Radiotherapy was delivered after completion of adjuvant chemotherapy. The dose prescription for the chest wall and regional nodes (supraclavicular, infraclavicular with or without internal mammary nodes) was 50 Gy in 25 fractions. Before 2009, the chest wall was irradiated with two tangential fields with a field-in-field technique using 6-MV X-ray. The supraclavicular and infraclavicular regions were treated with a single field calculated at a 3.5 cm depth. The internal mammary nodes were irradiated at the first 3 intercostal spaces. Those regional nodes were irradiated with a mixture of photons and electron beams at a ratio of 1:1 or 1:2. The intensity-modulated radiation therapy (IMRT) technique has been applied for patients with breast cancer in our institution since 2009. Clinical target volumes (CTVs) of the chest wall and regional nodes were delineated according to the Radiation Therapy Oncology Group (RTOG) guidelines\(^11\). The CTV of the chest wall included all reconstruction autologous tissues and tissue expanders/implants. A chest wall bolus of 0.3 cm was placed for all patients. No patient received a boost to the chest wall. Definition of
reconstruction outcomes Information on complications and reconstruction failures following breast reconstruction was collected from patients’ electronic medical records and/or telephone follow-up. “Any complications” were defined as all complications associated with reconstructed breast or donor sites. “Major complications” were defined as complications that required rehospitalization or reoperation. “Overall reconstruction failures” were defined as the complete loss or necrosis of an autologous flap, implant explanation or unplanned tissue expander removal with or without salvage reconstruction. “Complication-related reconstruction failures” were defined as reconstruction failure that resulted from complications or dissatisfaction related to reconstructed breasts. Development of prediction nomogram The nomogram model of implant-based reconstruction and autologous reconstruction was constructed on the basis of multivariate analysis. The AUC was measured for both nomogram models. In addition, the calibration curve was applied. Statistical analyses For the current analysis, we categorized both implant reconstruction and autologous plus implant reconstruction as implant-based reconstruction. The patient baseline characteristics and treatment information between the PMRT and no-PMRT groups were compared using the chi-square test or Fisher’s exact test. Multivariable analysis (logistic regression models) was performed to test the impact of radiotherapy and other factors on reconstruction outcomes in the autologous reconstruction cohort and the implant-based reconstruction cohort, respectively. All tests were two-sided, and a p value less than 0.05 was considered statistically significant. SPSS software version 20.0 and R software (version 3.5, www.Rproject.org) were used for data analysis.

**Results**

**Patient and treatment characteristics**

Patient and treatment characteristics regarding the PMRT receipt status in the autologous and implant-based reconstruction cohorts are listed in detail in Table 1. In total, 438 patients received autologous reconstruction, of whom 107 (24.4%) patients were treated with PMRT, and 52 (13.2%) of 394 patients who received implant-based reconstruction were treated with PMRT. In the autologous reconstruction cohort, patients with age younger than 40 years and BMI ≥ 24 were more common in the PMRT group than in the no-PMRT group (p=0.007 and p=0.004, respectively). Delayed reconstruction was more common in the PMRT group (p=0.044). Systemic therapy was more common in the PMRT group than in the no-PMRT group (p=0.044). In the implant-based reconstruction cohort, systemic therapy was also more common in the PMRT group than in the no-PMRT group (p<0.001), and other factors were well balanced.

**Details of the reconstruction complications and failures**

The median follow-up time was 58.5 months (range, 12.3~176.0 months). The rates of any complications, major complications, overall reconstruction failures and complication-related reconstruction failures were 17.4%, 5.0%, 2.1% and 1.6% in the autologous reconstruction cohort and 23.6%, 5.8%, 7.1% and 4.6% in the implant-based reconstruction cohort.

The details of the reconstruction complications are presented in Table 2. The most common complications were volume loss (6.6%), infection (3.4%) and fat necrosis (1.8%) in the autologous reconstruction cohort.
and implant malposition (6.6%), infection (5.1%) and implant contraction (4.6%) in the implant-based reconstruction cohort. In the autologous reconstruction cohort, there were 9 reconstruction failures (3 in the PMRT group and 6 in the no-PMRT group); of these, 7 reconstruction failures were caused by complications or dissatisfaction related to reconstructed breasts, and 2 reconstruction failures were due to disease recurrence or other reasons. In the implant-based reconstruction cohort, there were 28 reconstruction failures (6 in the PMRT group and 22 in the no-PMRT group); of these, 18 reconstruction failures were caused by complications or dissatisfaction related to reconstructed breasts, and 10 reconstruction failures were due to disease recurrence or other reasons.

Univariate and multivariate analysis of reconstruction complications and failures

The univariate analysis is shown in Table 3. In the autologous reconstruction cohort, PMRT was not associated with any complications (20.6% vs. 16.3%, p=0.313), major complications (5.6% vs. 4.8%, p=0.750), overall reconstruction failures (2.8% vs. 1.8%, p=0.813) or reconstruction-related reconstruction failures (2.8% vs. 1.2%, p=0.484). Reconstruction timing was not significantly associated with any of these four endpoints. In the implant-based reconstruction cohort, PMRT was associated with major complications (13.5% vs. 4.7%, p=0.028) but not with any complications (30.8% vs. 22.5%, p=0.192), overall reconstruction failures (11.5% vs. 6.4%, p=0.296) or reconstruction-related reconstruction failures (9.6% vs. 3.6%, p=0.130). Reconstruction timing was significantly associated with all four endpoints.

The multivariable analysis showed that PMRT was associated with 3.16 times (95% CI 1.17-8.54, p=0.023) higher odds of major complications and 3.22 times (95% CI 1.01-10.20, p=0.047) higher odds of complication-related reconstruction failures but was not associated with any complications (OR 1.73, 95% CI 0.88-3.38, p=0.113) or overall reconstruction failures (OR 2.09, 95% CI 0.76-5.73, p=0.152) in implant-based reconstruction (Table 4). Reconstruction timing was still significantly associated with all four endpoints. In the autologous reconstruction cohort, PMRT was not associated with any complications (OR 1.25, 95% CI 0.70-2.24, p=0.448), major complications (OR 1.10, 95% CI 0.39-3.05, p=0.863), overall reconstruction failures (OR 1.19, 95% CI 0.28-5.19, p=0.813) or reconstruction-related reconstruction failures (OR 1.92, 95% CI 0.39-9.41, p=0.421).

The performance of the predictive nomogram

The AUC of the implant-based reconstruction nomogram was 0.714 (95% CI 0.589-0.838), and the AUC of the autologous reconstruction nomogram was 0.686 (95% CI: 0.476-0.897). The calibration plot showed good accuracy in both nomograms.

Discussion

The current study investigated the impact of PMRT on reconstruction outcomes in patients undergoing mastectomy and different types of breast reconstruction. To our knowledge, this was the largest sample size in China used to identify the relationship between PMRT and breast reconstruction in patients with breast cancer. We observed that PMRT increased the risk of major complications and complication-related reconstruction failures in patients with implant-based reconstruction but did not increase the risk of any
complications, major complications, overall reconstruction failures or complication-related reconstruction failures in patients with autologous reconstructions. Although various factors should be weighed when selecting the appropriate type of breast reconstruction, our findings have important clinical implications for patients with PMRT indications selecting a particular type of breast reconstruction: For patients who preferred autologous reconstruction, PMRT might not impair reconstruction outcomes, but for those preferring implant-based reconstruction, PMRT would increase the risk of major complications and complication-related reconstruction failures.

The approach of integrating PMRT with breast reconstruction, including the selection of different reconstruction types in the setting of PMRT, the relative sequence of PMRT and breast reconstruction and the optimization of radiotherapy techniques, has been studied widely and remains controversial [6,12-15]. The largest and highest level of evidence published to date is the prospective, multicenter MROC study [10]. The MROC study enrolled 2247 patients diagnosed with breast cancer who received breast reconstruction from 11 centers between 2012 and 2015 and assessed the impact of radiotherapy on any complications and major complications in patients with different types of breast reconstruction. Among those patients, 1604 received implant-based reconstruction, and 643 received autologous reconstruction. Multivariable analysis showed that radiotherapy was not associated with any complications or major complications in the autologous reconstruction cohort but was associated with higher odds of any complications and major complications in the implant-based reconstruction cohort both at one and two years postoperation.

The results of the current investigation in the autologous reconstruction cohort were consistent with the MROC study and other studies [6,16], which all showed that PMRT did not increase the risk of any complications or major complications. However, there were some inconsistencies among patients with implant-based reconstruction, and our study showed that PMRT increased the risk of major complications but not the risk of any complications. A possible explanation for this outcome might be that the definition of major complications was the same between the MROC study and ours, while the definitions and approaches of collecting any complications were different. Our study included more complications than the MROC study, such as fat necrosis, volume loss, donor site issues and nipple atrophy. In addition, most patients included in our study were treated after 2009 and received the IMRT technique, as we knew that the radiotherapy technique was an important factor impacting reconstruction outcomes [17-20]. This could also explain why the major complications and reconstruction failures in our study were much lower in both the PMRT and no-PMRT groups than in the corresponding groups in the MROC study.

In addition, the current study design differed in several aspects from the MROC study. First, the participating centers in the MROC study were mostly from America (with one from Canada), and our study provides further evidence from Asian patients. Second, the MROC study assessed the impact of radiotherapy on any complications and major complications in the multivariable analysis but did not include reconstruction failures. Our study assessed the impact of radiotherapy on reconstruction failures and provided supplemental data for MROC studies. Third, we focused here on complication-related reconstruction failures, which were more directly related to reconstruction complications. We found that a considerable number of patients experienced reconstruction failure because of disease recurrence or other reasons, such as patients refusing further reconstruction, especially for implant-based reconstruction. Excluding non-
complication-related reconstruction failure, the rate of reconstruction-related failures was much lower (9.6% in the PMRT group vs. 3.8% in the no-PMRT group) than that in the MROC study (18.7% vs. 3.7%) and other previous studies [13,21,22] in implant-based reconstruction patients. We believe that complication-related reconstruction failure deserves more attention in further studies since it directly reflects reconstruction failures associated with complications, such as breast cancer-related mortality, when we report survival outcomes.

To our knowledge, reports of predictive models designed especially for breast reconstruction failure are limited. Therefore, two nomogram models were built on the basis of multivariate analysis and were tested for predictive accuracy to evaluate the risk of complication-related reconstruction failures and guide clinical practice. The ROC curve and calibration plot were applied. Consistent with the results of the calibration plot, the AUC of the implant-based model was 0.714, indicating good predictive accuracy. Based on the implant-based model, patients with different risks of complication-related reconstruction failure can be identified. The stratification of reconstruction failure may help doctors and patients decide whether the latter should receive breast reconstruction and what reconstructive material is suitable.

Because of its retrospective nature, this study had several limitations. First, an imbalance existed in the sample size, patient baseline characteristics and treatment assignment between the PMRT and no-PMRT groups, which might have decreased the statistical power. Although we performed multivariate analyses to mitigate the impact of potential confounding risk factors, other unmeasured or unknown factors might have affected the results. Second, information on reconstruction complications and failures was retrospectively collected from the electronic medical record system and telephone-call follow-up, and the assessment of complications was relatively subjective, especially regarding any complications.

**Conclusion**

The current study demonstrated that the impact of PMRT on reconstruction outcomes might differ by the type of breast reconstruction. PMRT increases the risk of major complications and complication-related reconstruction failures in patients with implant-based reconstruction but does not impair these reconstruction outcomes in patients with autologous reconstruction. This information should be considered for patients who desire breast reconstruction and have PMRT indications. Prospective studies are warranted to optimize the integration of PMRT and breast reconstruction, especially for implant-based reconstruction.

**Abbreviations**

PMRT Post-mastectomy radiation therapy

IMRT Intensity-modulated radiation therapy

CTV Clinical target volume

TRAM Transverse rectus abdominis musculocutaneous
Declarations

Funding Not applicable

Conflicts of interest/Competing interests The authors declare no competing interests.

Availability of data and material The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability The code of nomograms is available from the corresponding author on reasonable request.

Authors' contributions XMG, XLY, ZZ, ZMS and JW designed the study. LZ, XYW, KRJ, ZZY, JQW, SW, XM and XXC conducted the study and collected the data. LZ, XFW, JM and JLM analyzed the data and interpreted the results. LZ, XYW Consent to participate and KRJ wrote the manuscript. All authors read and approved the final manuscript.

Ethics approval A review of the data for the current study was approved by the Ethical Committee and Institutional Review Board of Fudan University Shanghai Cancer Center

Consent to participate A review of the data for the current study was approved by all individual patients included in the study.

Consent for publication All authors read and approved the final manuscript.

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Tables

Table 1 Patient and treatment characteristics in patients with autologous reconstruction and implant-based reconstruction
| Variable                        | Autologous reconstruction | Implant-based reconstruction |
|--------------------------------|---------------------------|-----------------------------|
|                                | (N=438)                   | (N=394)                     |
|                                | All patients              | All patients                |
|                                | PMRT (N=107)              | PMRT (N=52)                 |
|                                | No. (%)                   | No. (%)                     |
|                                | P value                   | P value                     |
| Age, y                         |                           |                             |
| < 40                           | 225                       | 274                         |
| No. (%)                        | 67 (62.6)                 | 42 (80.8)                   |
| P value                        | 0.007                     |                             |
| ≥ 40                           | 213                       | 120                         |
| No. (%)                        | 40 (37.4)                 | 10 (19.2)                   |
| BMI, kg/m²                     |                           |                             |
| < 24                           | 356                       | 343                         |
| No. (%)                        | 77 (72.0)                 | 41 (78.8)                   |
| P value                        | 0.004                     |                             |
| ≥ 24                           | 82                        | 51                          |
| No. (%)                        | 30 (28.0)                 | 11 (21.2)                   |
| Smoking                        |                           |                             |
| Yes                            | 1                         | 2                           |
| No. (%)                        | 1 (0.9)                   | 0 (0.0)                     |
| P value                        | 0.551                     |                             |
| No                             | 437                       | 392                         |
| No. (%)                        | 106 (99.1)                | 52 (100.0)                  |
| Diabetes                       |                           |                             |
| Yes                            | 3                         | 3                           |
| No. (%)                        | 1 (0.9)                   | 1 (1.9)                     |
| P value                        | 0.728                     |                             |
| No                             | 435                       | 391                         |
| No. (%)                        | 106 (99.1)                | 51 (98.1)                   |
| Menopause status               |                           |                             |
| Premenopausal                  | 408                       | 382                         |
| No. (%)                        | 101 (94.4)                | 51 (98.1)                   |
| P value                        | 0.559                     |                             |
| Postmenopausal                 | 30                        | 12                          |
| No. (%)                        | 6 (5.6)                   | 1 (1.9)                     |
| Prior breast radiotherapy      |                           |                             |
| Yes                            | 9                         | 2                           |
| No. (%)                        | 1 (0.9)                   | 0 (0.0)                     |
| P value                        | 0.584                     |                             |
| No                             | 429                       | 392                         |
| No. (%)                        | 106 (99.1)                | 52 (100.0)                  |
| Reconstruction timing          |                           |                             |
| Yes                            | 0.044                     |                             |
| No                             | 0.764                     |                             |
| Immediate | 403 | 92 (86.0) | 311 (94.0) | 214 | 30 (57.7) | 184 (53.8) |
| Delayed    | 30  | 13 (12.1) | 17 (5.1)   | 1   | 0 (0.0)  | 1 (0.3)   |
| Delayed-immediate | 5   | 2 (1.9)   | 3 (0.9)    | 179 | 22 (42.3) | 157 (45.9) |
| **Systemic therapy** |     |           |            |     |          |           |
| Yes        | 385 | 106 (99.1) | 279 (85.3) | 52  | 100.0    | 285 (84.6) |
| No         | 49  | 1 (0.9)   | 48 (14.7)  | 0   | 0.0      | 52 (15.4)  |

Table 2 Complication details after mastectomy and breast reconstruction
| Complications               | Total | PMRT | No-PMRT | Complications               | Total | PMRT | No-PMRT |
|-----------------------------|-------|------|---------|-----------------------------|-------|------|---------|
|                             | No. (%) | No. (%) | No. (%) |                             | No. (%) | No. (%) | No. (%) |
| **Seroma**                  | 3 (0.7) | 2 (1.9) | 1 (0.3) | **Seroma**                  | 1 (0.3) | 0 (0.0) | 1 (0.3) |
| **Hematoma**                | 4 (0.9) | 2 (1.9) | 2 (0.6) | **Hematoma**                | 3 (0.8) | 0 (0.0) | 3 (0.9) |
| **Infection**               | 15 (3.4) | 2 (1.9) | 13 (3.9) | **Infection**               | 20 (5.1) | 7 (13.5) | 13 (3.8) |
| **Delayed/poor wound healing** | 7 (1.6) | 0 (0.0) | 7 (2.1) | **Delayed/poor wound healing** | 3 (0.8) | 1 (1.9) | 2 (0.6) |
| **Fibrosis**                | 3 (0.7) | 1 (0.9) | 2 (0.6) | **Implant contraction**     | 18 (4.6) | 4 (7.7) | 14 (4.1) |
| **Volume loss**             | 29 (6.6) | 8 (7.5) | 21 (6.3) | **Implant dehiscence/leak** | 11 (2.8) | 5 (9.6) | 6 (1.8) |
| **Fat necrosis**            | 8 (1.8) | 2 (1.9) | 6 (1.8) | **Implant malposition**     | 24 (6.1) | 3 (5.8) | 21 (6.1) |
| **Flap necrosis**           | 7 (1.6) | 3 (2.8) | 4 (1.2) | **Capsular contracture**   | 13 (3.3) | 1 (1.9) | 12 (3.5) |
| **Donor site issues**       | 2 (0.5) | 0 (0.0) | 2 (0.6) | **Nipple atrophy**         | 4 (1.0) | 0 (0.0) | 4 (1.2) |
| **Malposition**             | 3 (0.7) | 2 (1.9) | 1 (0.3) |                             |       |      |         |
| **Nipple atrophy**          | 3 (0.7) | 0 (0.0) | 1 (0.9) |                             |       |      |         |

Table 3 Univariate analyses of reconstruction outcomes according to PMRT status
| Variable                        | Any complication | Major complication | Overall reconstruction failure | Complication-related reconstruction failure |
|--------------------------------|------------------|--------------------|-------------------------------|---------------------------------------------|
|                                | N (%)            | N (%)              | N (%)                         | N (%)                                      |
|                                | P value          | P value            | P value                       | P value                                    |
| Autologous reconstruction cohort |                  |                    |                               |                                             |
| All patients                   | 76 (17.4)        | 22 (5.0)           | 9 (2.1)                       | 7 (1.6)                                    |
| PMRT                           | 0.313            | 0.750              | 0.813                         | 0.484                                      |
| Yes                            | 22 (20.6)        | 6 (5.6)            | 3 (2.8)                       | 3 (2.8)                                    |
| No                             | 54 (16.3)        | 16 (4.8)           | 6 (1.8)                       | 4 (1.2)                                    |
| Age                            | 0.606            | 0.314              | 0.934                         | 0.942                                      |
| ≥40                            | 39 (18.3)        | 13 (6.1)           | 5 (2.3)                       | 4 (1.9)                                    |
| <40                            | 37 (16.4)        | 9 (4.0)            | 4 (1.8)                       | 3 (1.3)                                    |
| BMI                            | 0.803            | 0.947              | 0.790                         | 0.754                                      |
| ≥24                            | 15 (18.3)        | 4 (4.9)            | 2 (2.4)                       | 1 (1.2)                                    |
| <24                            | 61 (17.1)        | 18 (5.1)           | 7 (2.0)                       | 6 (1.7)                                    |
| Menopause status               | 0.918            | 0.682              | 0.256                         | 0.317                                      |
| Postmenopausal                 | 5 (16.7)         | 2 (6.7)            | 0 (0.0)                       | 0 (0.0)                                    |
| Premenopausal                  | 71 (17.4)        | 20 (4.9)           | 9 (2.2)                       | 7 (1.7)                                    |
| Reconstruction timing          | 0.173            | 0.160              | 0.332                         | 0.186                                      |
| Immediate                      | 67 (16.6)        | 18 (4.5)           | 7 (1.7)                       | 5 (1.2)                                    |
| Delayed and Delayed-immediate  | 9 (25.7)         | 4 (11.4)           | 2 (5.7)                       | 2 (5.7)                                    |
| Systemic therapy               | 0.528            | 0.731              | 0.140                         | 0.727                                      |
| Yes                            | 69 (17.9)        | 20 (5.2)           | 9 (2.3)                       | 7 (1.8)                                    |
| No                             | 7                | 2                  | 0                             | 0 (0.0)                                    |
| Implant-based reconstruction cohort | | | |
|-------------------------------------|-------------------|------------------|-------------------|
| All patients                         | 93 (23.6)         | 23 (5.8)         | 28 (7.1)         |
| PMRT                                 | 0.192             | 0.028            | 0.296            | 0.130 |
| Yes                                  | 16 (30.8)         | 7 (13.5)         | 6 (11.5)         | 5 (9.6) |
| No                                   | 77 (22.5)         | 16 (4.7)         | 22 (6.4)         | 13 (3.8) |
| Age                                  | 0.933             | 0.349            | 0.822            | 0.800 |
| ≥40                                  | 28 (23.3)         | 5 (4.2)          | 8 (6.7)          | 5 (4.2) |
| <40                                  | 65 (23.7)         | 18 (6.6)         | 20 (7.3)         | 13 (4.7) |
| BMI                                  | 0.734             | 0.760            | 0.511            | 0.551 |
| ≥24                                  | 13 (25.5)         | 2 (3.9)          | 2 (3.9)          | 1 (2.0) |
| <24                                  | 80 (23.3)         | 21 (6.1)         | 26 (7.6)         | 17 (5.0) |
| Menopause status                     | 0.909             | 0.802            | 0.687            | 0.946 |
| Postmenopausal                       | 3 (25.0)          | 0 (0.0)          | 0 (0.0)          | 0 (0.0) |
| Premenopausal                        | 90 (23.6)         | 23 (6.0)         | 28 (7.3)         | 18 (4.7) |
| Reconstruction timing                | 0.001             | 0.005            | 0.001            | 0.005 |
| Immediate                            | 36 (16.8)         | 6 (2.8)          | 7 (3.3)          | 4 (1.9) |
| Delayed and Delayed-immediate        | 57 (31.7)         | 17 (9.4)         | 21 (11.7)        | 14 (7.8) |
| Systemic therapy                     | 0.717             | 0.883            | 0.947            |
| Yes                                  | 75 (22.3)         | 0.294            | 21 (6.2)         | 4 (7.1) |
| No                                   | 15 (28.8)         | 2 (3.8)          | 4 (7.7)          | 3 (5.8) |
Table 4. Multivariate analyses of reconstruction outcomes.

| Variable                        | Any complication | Major complication | Overall reconstruction failure | Complication-related reconstruction failure |
|---------------------------------|------------------|---------------------|-------------------------------|---------------------------------------------|
|                                 | OR (95%CI)       | P value             | OR (95%CI)                    | P value                                    |
| Autologous reconstruction cohort|                  |                     |                              |                                             |
| PMRT, yes vs. no                | 1.25 (0.70-2.24) | 0.448               | 1.10 (0.39-3.05)              | 0.863 (0.28-5.19)                          |
| Age, ≥40 vs. <40                | 1.17 (0.71-1.94) | 0.546               | 1.54 (0.63-3.75)              | 0.341 (0.33-4.97)                          |
| BMI, ≥24 vs. <24                | 1.02 (0.54-1.93) | 0.962               | 0.89 (0.29-2.79)              | 0.843 (0.21-5.46)                          |
| Reconstruction timing,          | 1.59 (0.70-3.60) | 0.265               | 2.53 (0.78-8.16)              | 0.121 (0.57-15.57)                         |
| Delayed and Delayed-immediate vs.| 2.42 (1.48-3.94) | 0.000               | 3.86 (1.47-10.15)             | 0.006 (1.61-9.49)                          |
| Systemic therapy, yes vs. No    | 1.19 (0.51-2.54) | 0.679               | 1.19 (0.26-5.45)              | -                                           |
|                                |                  |                     |                               |                                             |
| Implant-based reconstruction cohort|                |                     |                              |                                             |
| PMRT, yes vs. no                | 1.73 (0.88-3.38) | 0.113               | 3.16 (1.17-8.54)              | 0.023 (0.76-5.73)                          |
| Age, ≥40 vs. <40                | 0.91 (0.53-1.54) | 0.719               | 0.66 (0.23-1.87)              | 0.433 (0.39-2.22)                          |
| BMI, ≥24 vs. <24                | 1.23 (0.61-2.47) | 0.570               | 0.61 (0.13-2.74)              | 0.514 (0.11-2.24)                          |
| Reconstruction timing,          | 2.42 (1.48-3.94) | 0.000               | 3.86 (1.47-10.15)             | 0.006 (1.61-9.49)                          |
| Delayed and Delayed-immediate vs.| 2.42 (1.48-3.94) | 0.000               | 3.86 (1.47-10.15)             | 0.006 (1.61-9.49)                          |
| Systemic therapy, yes vs. no    | 0.69 (0.35-1.37) | 0.289               | 1.51 (0.33-6.93)              | 0.598 (0.30-2.98)                          |
|                                |                  |                     |                               |                                             |
Figures

Figure 1

Nomograms and calibration plots for implant-based and autologous reconstruction. a, autologous model for patients receiving autologous reconstruction model; b, implant-based model for patients receiving implant-based reconstruction. Abbreviation, RT, radiotherapy.
Figure 2

ROC curves of autologous model and implant-based model. a, ROC curve of autologous model; b, ROC curve of implant-based model