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CLINICAL TRIAL

# Post-mastectomy immediate breast reconstruction is oncologically safe in well-selected T4 locally advanced breast cancer: a large population-based study and matched case–control analysis

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**Abstract**

**Purpose** Although it is well accepted that the survival outcome is most probably unaffected by immediate breast reconstruction (IBR) for T1–T3 tumors, the safety of IBR in T4 locally advanced breast cancer (LABC) remains unclear.

**Methods** By using data from the Surveillance, Epidemiology, and End Results (SEER) database, the trend of IBR for female T4 LABC patients undergoing mastectomy, chemotherapy and radiotherapy was explored. The predictors of IBR in T4 LABC were evaluated by multivariate logistic regression. The survival outcomes were compared by means of Cox hazards models adjusting for known clinicopathological variables and stratifying on the T stage and contralateral prophylactic mastectomy (CPM).

**Results** Altogether 714 cases underwent IBR between 1998 and 2015. The IBR cohort had a lower percentage of cases with T4d disease whereas higher percentage with CPM. The IBR rate was 10.1% and increased from 4.1% in 1998 to 17.7% in 2015. Since 2009, the rate of implant-based IBR exceeded that of the autologous tissue method. An age less than 45 years (OR 2.930, 95% CI 2.299–3.735) and CPM (OR 2.758, 95% CI 2.306–3.299) were the strongest predictors of IBR. In the 1:2 matched case–control analysis, IBR was not an independent prognostic factor for breast cancer specific-survival (BCSS) (HR 0.893, $p=0.236$, 95% CI 0.741–1.077) and overall survival (OS) (HR 0.886, $p=0.183$, 95% CI 0.741–1.059). BCSS and OS were similar among patients undergoing IBR whether they underwent CPM or not and whether they were inflammatory breast cancer (IBC) or not.

**Conclusions** IBR is oncologically safe in well-selected T4 LABC.

**Keywords** Immediate breast reconstruction · T4 · Locally advanced breast cancer · Oncological safety

## Introduction

Immediate breast reconstruction (IBR) after mastectomy of breast cancer is on the rise as it has a positive impact on patients' life quality [1]. IBR helps to improve psychosocial and sexual well-being in breast cancer survivors [2]. It is well accepted that the oncological safety is most probably unaffected by IBR for T1–T3 tumors [3, 4]. The utilization of IBR has increased significantly over the last decade but is significantly lower for higher tumor stages ($p<0.0001$) [5].

Only a limited number of studies focused on IBR in locally advanced breast cancer (LABC) [6–10], although LABC may not be an absolute contradiction to IBR. As a subset of LABC, T4 stage breast cancer includes tumors that exhibit chest wall invasion (T4a), skin invasion consisting of ulceration or nodules (T4b) or both (T4c), inflammatory breast cancer (IBC) (T4d) and is classified as AJCC stage IIIB–IIIC. Multimodal therapy, such as neoadjuvant chemotherapy (NAC) and post-mastectomy radiotherapy (RT) is recommended. High-risk surgical and oncological features contribute to make IBR a great challenge for T4 LABC, not only due to technological feasibility but also oncological safety. To date, few reports have been published on IBR in T4 LABC.

Given lack of data on IBR in T4 LABC, we conducted a retrospective study to investigate the trend of IBR in T4 LABC and to evaluate its oncological safety based on the surveillance, epidemiology, and end results (SEER) 18 databases and a further matched case–control analysis.

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## Patients and methods

### Patient population

This retrospective study employed data derived from the National Cancer Institute's limited use SEER 18 registry databases that were released in November 2017. We identified unilateral invasive T4 stage breast cancer in less than 80-year-old female patients undergoing mastectomy, radiotherapy and chemotherapy. Patients with more than one primary cancer, having metastatic disease at diagnosis, or diagnosed at death or autopsy only were excluded from the study. Because a surgery code was first established in the SEER in 1998, we selected cases diagnosed between 1 January 1998 and 31 December 2015. Borderline ER or PR status was considered as unknown status. Poorly differentiated and anaplastic histological grades were considered as grade III disease. Using the database coding, IBR was defined as breast reconstruction performed within 4 months after the primary oncologic surgery. Implant only and combined methods IBR were categorized into implant-based IBR. Patients undergoing IBR and mastectomy were categorized into the IBR cohort and those who underwent mastectomy only were categorized into the control cohort.

We obtained the permission to access the files of SEER program custom data with additional treatment fields such as radiation therapy and chemotherapy. An informed consent was not required because personal identifying information was not involved. This study was reviewed and approved by the Institutional Review Board of Obstetrics and Gynecology Hospital of Fudan University.

### Statistical analysis

Differences in patient and tumor characteristics were evaluated using Chi square tests. Multivariate logistic regression was used to measure the relationship between various predictive variables and the use of IBR while adjusting for potentially confounding variables. The follow-up cut-off was 31 December 2015. Overall survival (OS) was computed from the time of diagnosis until the time of death from any cause or the last follow-up with patients still alive at the last censored follow-up. Breast cancer-specific survival (BCSS) was computed from the time of diagnosis of breast cancer to the time of death from breast cancer or the last follow-up with patients still alive at the last censored follow-up. Survival outcomes were estimated using the Kaplan–Meier plot and compared across groups using the log-rank test. Adjusted hazard ratios (HRs) with 95% confidence intervals (95% CI) were calculated using the Cox proportional hazards model to fit demographic and disease characteristics for BCSS and OS. To diminish the effects of baseline differences on outcome differences in the IBR and control groups, the propensity score matching method was applied by matching each IBR case to two control cases. They were exactly matched for the T stage, N stage, histologic grade, and ER status. All the other parameters, such as histology type, contralateral prophylactic mastectomy (CPM), year

**Table 1** Comparison of patient and tumor characteristics between the IBR and control cohort

| | IBR cohort | | Control cohort | | *p* |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Year | | | | | < 0.001 |
| 1998–2003 | 149 | 20.9 | 1885 | 29.8 | |
| 2004–2009 | 208 | 29.1 | 2311 | 36.5 | |
| 2010–2015 | 357 | 50.0 | 2136 | 33.7 | |
| Age, (year) | | | | | < 0.001 |
| < 45 | 224 | 31.4 | 1248 | 19.7 | |
| 45–59 | 369 | 51.7 | 2912 | 46.0 | |
| 60–79 | 121 | 16.9 | 2172 | 34.3 | |
| Race | | | | | 0.190 |
| White | 566 | 79.3 | 4789 | 75.6 | |
| Black | 98 | 13.7 | 1008 | 15.9 | |
| Asian or Indian | 49 | 6.9 | 521 | 8.2 | |
| Unknown | 1 | 0.1 | 14 | 0.2 | |
| Histology | | | | | 0.016 |
| IDC | 467 | 65.4 | 3953 | 62.4 | |
| ILC | 44 | 6.2 | 291 | 4.6 | |
| Others | 203 | 28.4 | 2088 | 33.0 | |
| Grade | | | | | 0.072 |
| I | 36 | 5.0 | 218 | 3.4 | |
| II | 207 | 29.0 | 1704 | 26.9 | |
| III | 410 | 57.4 | 3809 | 60.2 | |
| Unknown | 61 | 8.5 | 601 | 9.5 | |
| T stage | | | | | < 0.001 |
| T4a | 88 | 12.3 | 464 | 7.3 | |
| T4b | 296 | 41.5 | 2556 | 40.4 | |
| T4c | 10 | 1.4 | 98 | 1.5 | |
| T4d | 310 | 43.4 | 3164 | 50.0 | |
| Unknown | 10 | 1.4 | 50 | 0.8 | |
| N stage | | | | | 0.312 |
| N0 | 107 | 15.0 | 850 | 13.4 | |
| N1 | 383 | 39.6 | 2367 | 37.4 | |
| N2 | 178 | 24.9 | 1692 | 26.7 | |
| N3 | 136 | 19.0 | 1351 | 21.3 | |
| Unknown | 10 | 1.4 | 72 | 1.1 | |
| ER | | | | | 0.084 |
| Negative | 274 | 38.4 | 2504 | 39.5 | |
| Positive | 410 | 57.4 | 3446 | 54.4 | |
| Unknown | 30 | 4.2 | 382 | 6.0 | |
| PR | | | | | 0.150 |
| Negative | 355 | 49.7 | 3174 | 50.1 | |
| Positive | 323 | 45.2 | 2726 | 43.1 | |
| Unknown | 36 | 5.0 | 432 | 6.8 | |
| CPM | | | | | < 0.001 |
| None | 438 | 61.3 | 5367 | 84.8 | |
| Yes | 276 | 38.7 | 965 | 15.2 | |

of diagnosis, age at diagnosis, PR status and race, were matched as exactly as possible. Two-sided *p* values less than 0.05 were considered statistically significant. The complete statistical analysis was performed using the SPSS 22.0 software package (SPSS, Chicago, IL, USA).

## Results

### IBR trend among T4 LABC and clinical characteristics of the IBR and control cohorts

According to the inclusion criteria, 7046 T4 LABC patients who received mastectomy, radiotherapy and chemotherapy were enrolled in this study. Altogether, 714 cases underwent IBR, which constituted the IBR cohort. The clinical characteristics of the IBR and control cohorts were summarized in Table 1. IBR was performed more frequently since 2010. Younger patients, patients with invasive lobular carcinoma (ILC) histology, and patient who received CPM were more likely to receive IBR. In addition, the IBR cohort had a lower percentage of cases with T4d disease compared with the control cohort.

The total IBR rate among T4 LABC was 10.1%. This rate has increased from 4.1% in 1998 to 17.7% in 2015. Since 2010, it has increased significantly, which is in line with the rapid increase in CPM. The rates of autologous tissue only and implant-based IBR increased both with the time. At first, autologous tissue IBR dominated the IBR methods. Since 2009, the rate of implant-based IBR exceeded that of the autologous tissue method by increasing from 1.2% in 1998 to 8.0% in 2015, whereas the autologous tissue IBR rate only increased from 2.4 to 6.0% (Fig. 1).

### Predictive factors of IBR among T4 LABC

Multivariate logistic regressions confirmed that year of diagnosis after 2010, patient age of less than 60 years, married status, T4a–c, and CPM were independently associated with IBR in T4 LABC (Table 2, Hosmer–Lemeshow test $p = 0.814$). Significantly higher odds of IBR were found in younger women, those aged less than 45 years (OR 2.930, 95% CI 2.299–3.735) and those aged 45–59 years (OR 2.228, 95% CI 1.791–2.773). Patients who underwent CPM had significantly higher odds of IBR compared with those who did not undergo CPM (OR 2.758, 95% CI 2.306–3.299).

### Survival significance of IBR among T4 LABC

In order to precisely evaluate the prognosis and perform an adequate follow-up, T4 LABC cases with definite histologic grade, T stage, N stage and ER status who were diagnosed between 1998 and 2013 were enrolled in the analysis. The T stage was divided into T4a–c and T4d, and the histologic grade was divided into I + II and III.

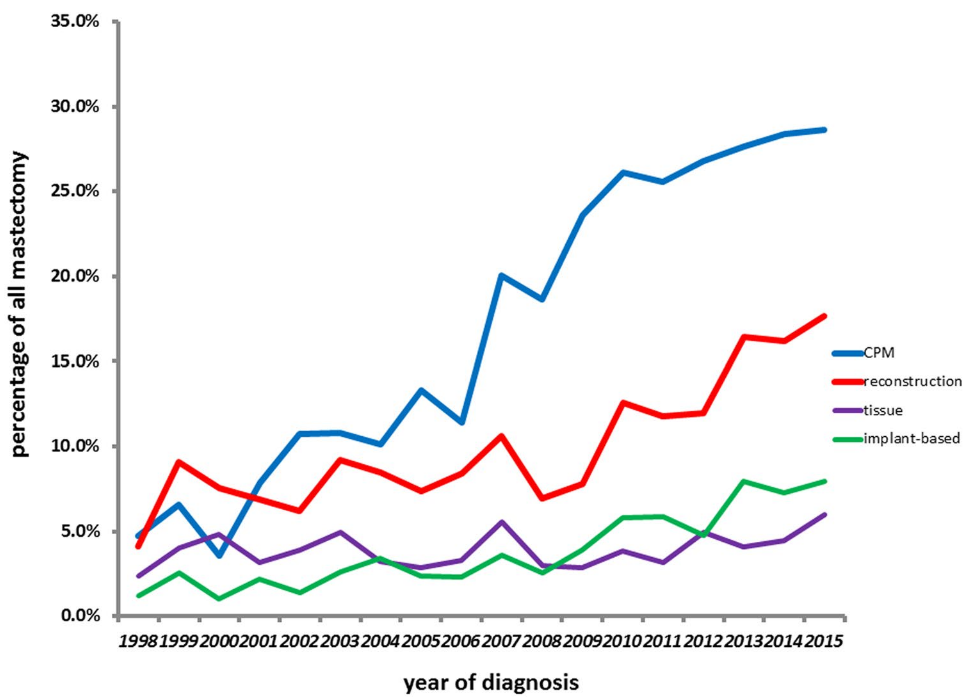


**Fig. 1** Immediate breast reconstruction rates in T4 locally advanced breast cancer diagnosed between 1998 and 2015

**Table 2** Multivariate analysis of factors associated with IBR in T4 locally advanced breast cancer

| Factor | OR | 95% CI | *p* |
|---|---|---|---|
| Year | | | < 0.001 |
| 1998–2003 | 1.000 | Reference | |
| 2004–2009 | 0.996 | 0.789–1.256 | |
| 2010–2015 | 1.708 | 1.359–2.148 | |
| Age, (year) | | | < 0.001 |
| < 45 | 2.930 | 2.299–3.735 | |
| 45–59 | 2.228 | 1.791–2.773 | |
| 60–79 | 1.000 | Reference | |
| Marital status | | | 0.003 |
| Married | 1.333 | 1.121–1.584 | |
| Unmarried | 1.000 | Reference | |
| Race | | | 0.404 |
| White | 1.000 | Reference | |
| Back | 0.869 | 0.684–1.105 | |
| Asian or Indian | 0.807 | 0.588–1.109 | |
| Histology | | | 0.329 |
| IDC | 1.000 | Reference | |
| ILC | 1.310 | 0.913–1.879 | |
| Others | 1.052 | 0.867–1.278 | |
| Grade | | | 0.548 |
| I | 1.000 | Reference | |
| II | 0.807 | 0.539–1.208 | |
| III | 0.771 | 0.516–1.151 | |
| T stage | | | < 0.001 |
| T4a | 2.033 | 1.535–2.692 | |
| T4b | 1.353 | 1.225–1.628 | |
| T4c | 1.698 | 0.860–3.354 | |
| T4d | 1.000 | Reference | |
| N stage | | | 0.250 |
| N0 | 1.180 | 0.891–1.562 | |
| N1 | 1.037 | 0.828–1.297 | |
| N2 | 1.032 | 0.809–1.315 | |
| N3 | 1.000 | Reference | |
| CPM | | | <0.001 |
| No | 1.000 | Reference | |
| Yes | 2.758 | 2.306–3.299 | |
| ER | | | 0.853 |
| Negative | 1.000 | Reference | |
| Positive | 1.038 | 0.822–1.309 | |
| PR | | | 0.724 |
| Negative | 1.000 | Reference | |
| Positive | 0.920 | 0.733–1.155 | |

The median follow-up time was 53 months (4–210) for the IBR cohort and 55 months (2–215) for the control cohort. The IBR group had a higher BCSS ($p = 0.001$) and OS ($p < 0.001$) compared with the control cohort (Fig. 2). According to the multivariate COX analysis, IBR was an independent favorable prognostic factor for BCSS (HR 0.843, $p = 0.041$, 95% CI 0.716–0.993) and OS (HR 0.834, $p = 0.024$, 95% CI 0.713–0.976).

Due to the great baseline differences between the IBR and control groups (Table 1), a 1:2 matched case–control analysis was conducted, in which 491 IBR cases were matched to 982 control cases. The matching analysis was considered successful, as no significant difference was observed in any characteristic (Table 3). In the matched case–control analysis, IBR lost significance as an independent favorable prognostic factor for BCSS (HR 0.893, $p = 0.236$, 95% CI 0.741–1.077) or OS (HR 0.886, $p = 0.183$, 95% CI 0.741–1.059) (Fig. 3). Different IBR methods caused no significant difference in BCSS (implant-based IBR as reference, HR 1.189, $p = 0.345$, 95% CI 0.830–1.703) and OS (HR 1.119, $p = 0.521$, 95% CI 0.794–1.577).

In the subgroup analysis based on the matched study cohort, the IBR cohort had a similar BCSS and OS compared with the control cohort inT4a–c ($p = 0.463$ for BCSS, $p = 0.368$ for OS) and T4d ($p = 0.344$ for BCSS, $p = 0.311$ for OS) (Fig. 4). Besides, the IBR cohort also had a similar BCSS and OS compared with the control cohort whether CPM was performed ($p = 0.124$ for BCSS, $p = 0.080$ for OS) or not ($p = 0.751$ for BCSS, $p = 0.727$ for OS) (Fig. 5).

## Discussion

An increasing number of studies suggested that IBR in LABC patients is a safe and acceptable option [6–10]. However, these studies only contained a limited number of T4 stage cases. Skin or chest wall invasion and multimodal therapy present obstacles for IBR in this subgroup. Many surgeons hesitate to perform IBR in T4 LABC. To the best of our knowledge, our study explored IBR especially in T4 LABC, which had by far the largest sample size and integrated both a large population study and a matched case–control analysis.

Oncological safety is of first prior in the treatment of T4 LABC. Only cases receiving multimodal therapy such as mastectomy, radiotherapy and chemotherapy were included in our study. It should be pointed out that the information of adjuvant chemotherapy or NAC is not available for breast cancer in SEER database. Although IBR following NAC raises concerns about increased perioperative complications, there were mixed results

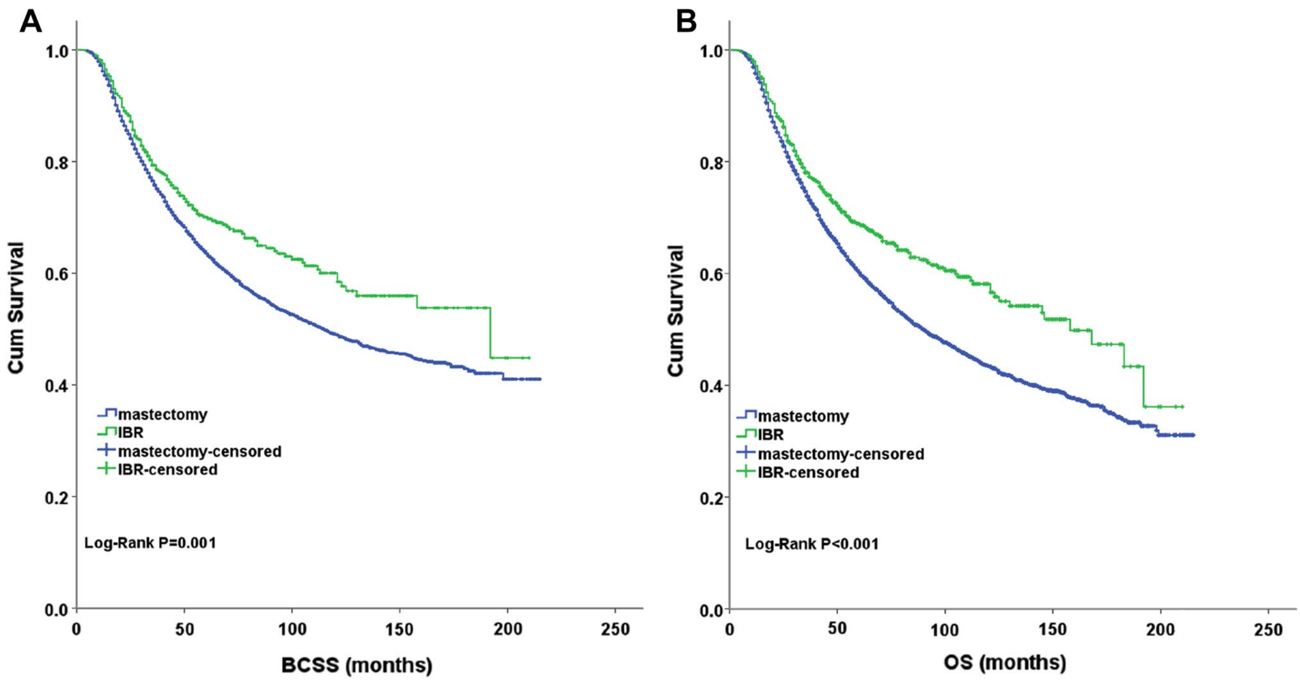


**Fig. 2** Kaplan–Meier survival curves of breast cancer-specific survival (BCSS) and overall survival (OS) stratified by the immediate breast reconstruction and control cohorts in a large population database (**a** BCSS; **b** OS)

concerning complication rates in IBR following NAC [7, 11–14]. Adjuvant RT increases the complexity of IBR planning in T4 LABC. Traditionally, when post-operative RT may be required, implant-based IBR is discouraged, whereas autologous flaps can be performed safely regardless of pre-operative or post-operative RT [13, 15]. However, multiple studies in recent years have endorsed favorable outcomes of implant reconstruction of the radiated breast [16, 17]. Implant-based IBR rate increased in the setting of planned post-mastectomy RT [18, 19]. In our study, the autologous tissue and implant-based IBR demonstrated quite different trends with the time. At first, the autologous tissue IBR dominated the IBR methods. More aggressive resection used to be essential for the surgery in most T4 LABC. The autologous tissue IBR had the power to reconstruct the defect left by the oncological surgery. As a result, the plastic surgery was more in the service of coverage. But since 2009, the rate of implant-based IBR exceeded that of the autologous tissue method by increasing from 1.2% in 1998 to 8.0% in 2015. Probably the improvement in neoadjuvant therapies resulted in improved tumor response in more and more patients with T4 LABC, which made it possible to de-escalate oncological surgery. Under such circumstances, more emphasis could be placed on aesthetics in the plastic surgery for LABC. Patients with advanced disease favor implant-based IBR, probably because it means a potential for shorter recovery and greater satisfaction within the first two post-operative years compared with the autologous tissue transfer [20, 21].

In our study, the IBR rate in T4 LABC increased from 4.1% in 1998 to 17.7% in 2015, which was in accord with the greater increase in the IBR rate in the high-risk patients compared with that in the low-risk patients (9% vs. 6% per year) [22]. Although IBR during chemotherapy and radiotherapy in such patients causes greater risk of surgical complications and oncological safety, they appear to show an increased willingness to accept this potential risk in exchange for its benefits including enhanced body image. Although SEER database did not provide information about satisfaction or cosmetic outcomes as well as complications in this cohort, there were researches related to patient-reported outcomes after IBR in LABC, especially in patients undergoing IBR followed by RT. Brennan et al. demonstrated acceptable cosmetic results, high patient satisfaction and low complication rates in patients with high-risk breast cancer by means of good outcomes for quality of life (FACTB), satisfaction (Breast-Q), distress (Impact of Events scale) and body image (Body Image scale) and low score on the Decisional Regret scale

**Table 3** Comparisons of patient and tumor characteristics between the IBR and control cohort in 1:2 matched case–control analysis

| | IBR cohort | | Control cohort | | *p* |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Year | | | | | 0.952 |
| 1998–2001 | 62 | 12.6 | 130 | 13.2 | |
| 2002–2005 | 113 | 23.0 | 223 | 22.7 | |
| 2006–2009 | 122 | 24.8 | 253 | 25.8 | |
| 2010–2013 | 194 | 39.5 | 376 | 38.3 | |
| Age | | | | | 0.180 |
| < 45 | 151 | 30.8 | 264 | 26.9 | |
| 45–59 | 264 | 53.8 | 537 | 54.7 | |
| 60–79 | 76 | 15.5 | 181 | 18.4 | |
| Race | | | | | 0.693 |
| White | 388 | 79.0 | 794 | 80.9 | |
| Black | 66 | 13.4 | 129 | 13.1 | |
| Asian or Indian | 36 | 7.3 | 58 | 5.9 | |
| Unknown | 1 | 0.2 | 1 | 0.1 | |
| Histology | | | | | 0.787 |
| IDC | 330 | 67.2 | 666 | 67.8 | |
| ILC | 26 | 5.3 | 44 | 4.5 | |
| Others | 135 | 27.5 | 272 | 27.7 | |
| Grade | | | | | 1.000 |
| I + II | 172 | 35.0 | 344 | 35.0 | |
| III | 319 | 65.0 | 638 | 65.0 | |
| T stage | | | | | 1.000 |
| T4a–c | 276 | 56.2 | 552 | 56.2 | |
| T4d | 215 | 43.8 | 430 | 43.8 | |
| N stage | | | | | 1.000 |
| N0 | 73 | 14.9 | 146 | 14.9 | |
| N1 | 185 | 37.7 | 370 | 37.7 | |
| N2 | 135 | 27.5 | 270 | 27.5 | |
| N3 | 98 | 20.0 | 196 | 20.0 | |
| ER | | | | | 1.000 |
| Negative | 213 | 43.4 | 426 | 43.4 | |
| Positive | 278 | 56.6 | 556 | 56.6 | |
| PR | | | | | 0.194 |
| Negative | 265 | 54.0 | 528 | 53.8 | |
| Positive | 220 | 44.8 | 450 | 45.8 | |
| Unknown | 6 | 1.2 | 4 | 0.4 | |
| CPM | | | | | 0.280 |
| None | 309 | 62.9 | 646 | 65.8 | |
| Yes | 182 | 37.1 | 336 | 34.2 | |

reported by questionnaires [23]. Carnevale et al. showed that 86% LABC patients who underwent reconstruction followed by radiotherapy were very satisfied or satisfied with the cosmetic outcome of reconstruction [24]. All these might reflect a great unmet demand and a trade-off for the benefits of IBR [3, 25].

It is well acknowledged that younger women are more likely to undergo IBR [26]. Our study indicated that CPM was also a strong predictor of IBR in T4 LABC apart from younger age. The rapid increase in the IBR rate was in line with the increase in the CPM rate since 2010, with the implant-based IBR dominating the IBR methods. It has been postulated that the increase in bilateral reconstruction associated with CPM is correlated with an increase in the use of the implant-based reconstruction [27–30]. Although CPM has been proven to not improve the survival even for high-risk patients [31, 32], the patients' desire for a peace of mind and preference for symmetry are the leading reasons for CPM, especially for patients undergoing IBR. However, the benefits must be weighed against the added morbidity [33, 34].

The safety of IBR in T4 LABC remains unclear due to limited cases. Our study had the largest sample size and confirmed the oncological safety of IBR in T4 LABC. In the population study, the IBR cohort had a higher BCSS and OS compared with the control cohort. However, this survival benefit should be interpreted with caution, because the IBR group contained fewer cases with IBC whereas more cases undergoing CPM. Perhaps healthier patients with not so serious disease could tolerate a second surgical procedure and this part of patients was considered to have a longer lifespan. As a result, based on the matched analysis, IBR was no longer an independent prognostic factor for BCSS and OS. Moreover, IBR exhibited similar survival outcome whether patients underwent CPM or not and whether the patients had IBC or not, which was in accord with the conclusion in our previous study [35]. Improved tumor response through more effective neoadjuvant therapies makes possible IBR in T4 LABC. Although information about response to the systemic therapy was not available in SEER database, it could be true that well-selected patients with T4 LABC, who are healthy enough to tolerate a second surgical procedure, respond well to the initial systemic therapy, have a negative surgical margin, and have a strong willing for reconstruction, could be offered IBR safely.

We recognized several limitations of this study. Firstly, this study was a retrospective study, and intrinsic defects existed. Secondly, information on hormone therapy or HER2 status before 2010 is not available, so their effects on IBR could not be evaluated. Thirdly, information about complications, satisfaction and cosmetic outcomes

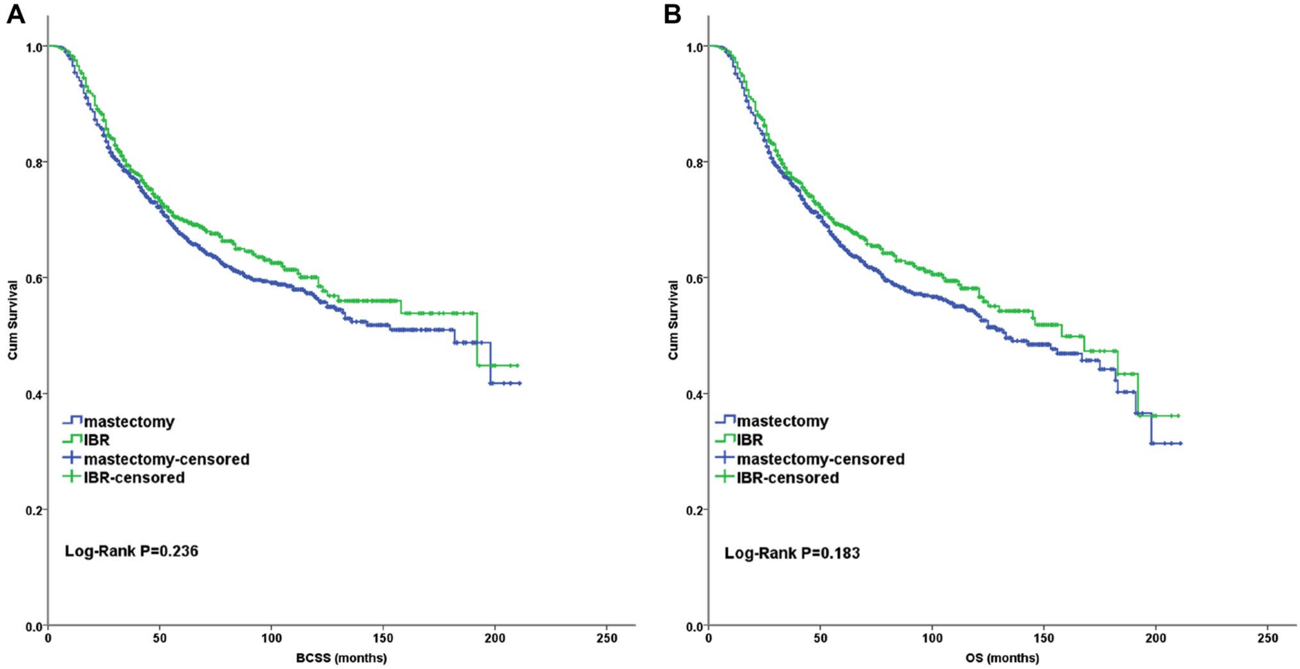


**Fig. 3** Kaplan–Meier survival curves of breast cancer-specific survival (BCSS) and overall survival (OS) stratified by the immediate breast reconstruction and control cohorts in the matched case–control analysis (**a** BCSS; **b** OS)

following IBR in our study was not available as discussed above. Fourthly, although reconstruction performed within this 4-month period is most likely performed at the time of mastectomy surgery, distinction between immediate and delayed immediate reconstruction is not possible due to the data collection methods [36]. It could bias the results, because patients with early recurrence might have poor survival outcomes and they would not be reconstructed. However, very early recurrence within 4 months appears part of wide spread recurrent disease rather than inadequate local treatment [37]. In the matched cohort, the main predictive factors for recurrence were well balanced. Furthermore, only 14 patients in 982 cases receiving mastectomy alone had breast cancer specific survival less than 12 months and none less than 8 months. So it could be supposed that such bias had limited impact on the conclusion of a similar survival outcome. Fifthly, T4 is a heterogeneous disease with great difference in disease extent which could make IBR quite feasible or much more challenging. However, it is impossible to obtain the information of the true extent of skin/muscle involvement from the SEER database. Lastly, SEER database does not capture information on socioeconomic and baseline health statuses, which may distort the relationship between reconstruction and survival. In the absence of prospective evidence, our current retrospective study represents an important step in evaluating the oncological safety of IBR among T4 LABC patients.

In conclusion, the rate of IBR, especially implant-based IBR, increased among T4 LABC patients. Young age and CPM were the strongest predictors of IBR. IBR could be safely performed in well-selected T4 LABC cases.

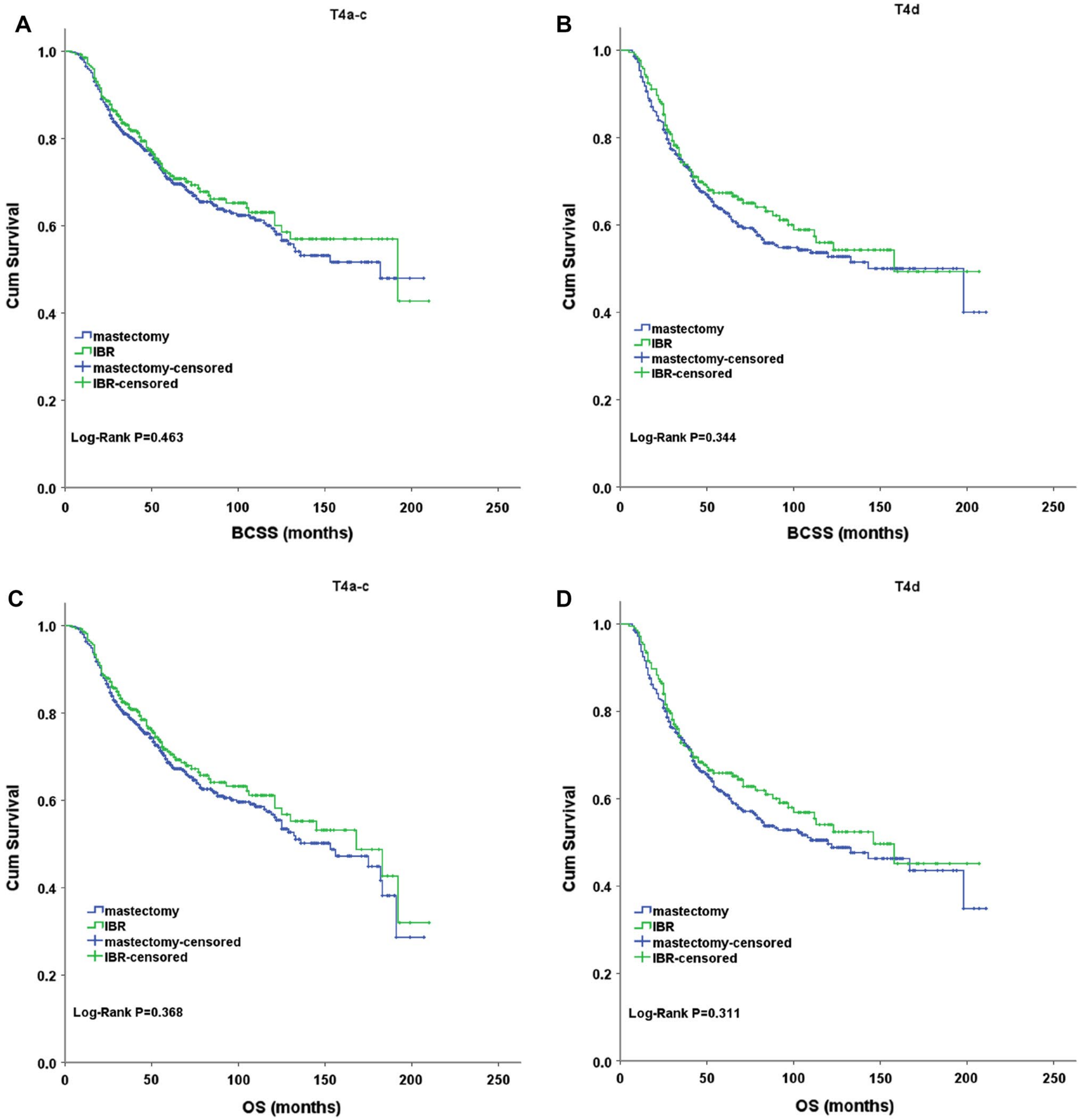


**Fig. 4** Kaplan–Meier survival curves of breast cancer-specific survival (BCSS) and overall survival (OS) for the immediate breast reconstruction and control cohorts stratified by the T stage in matched case–control analysis (**a** BCSS in T4a–c; **b** BCSS in T4d; **c** OS in T4a–c; **d** OS in T4d)

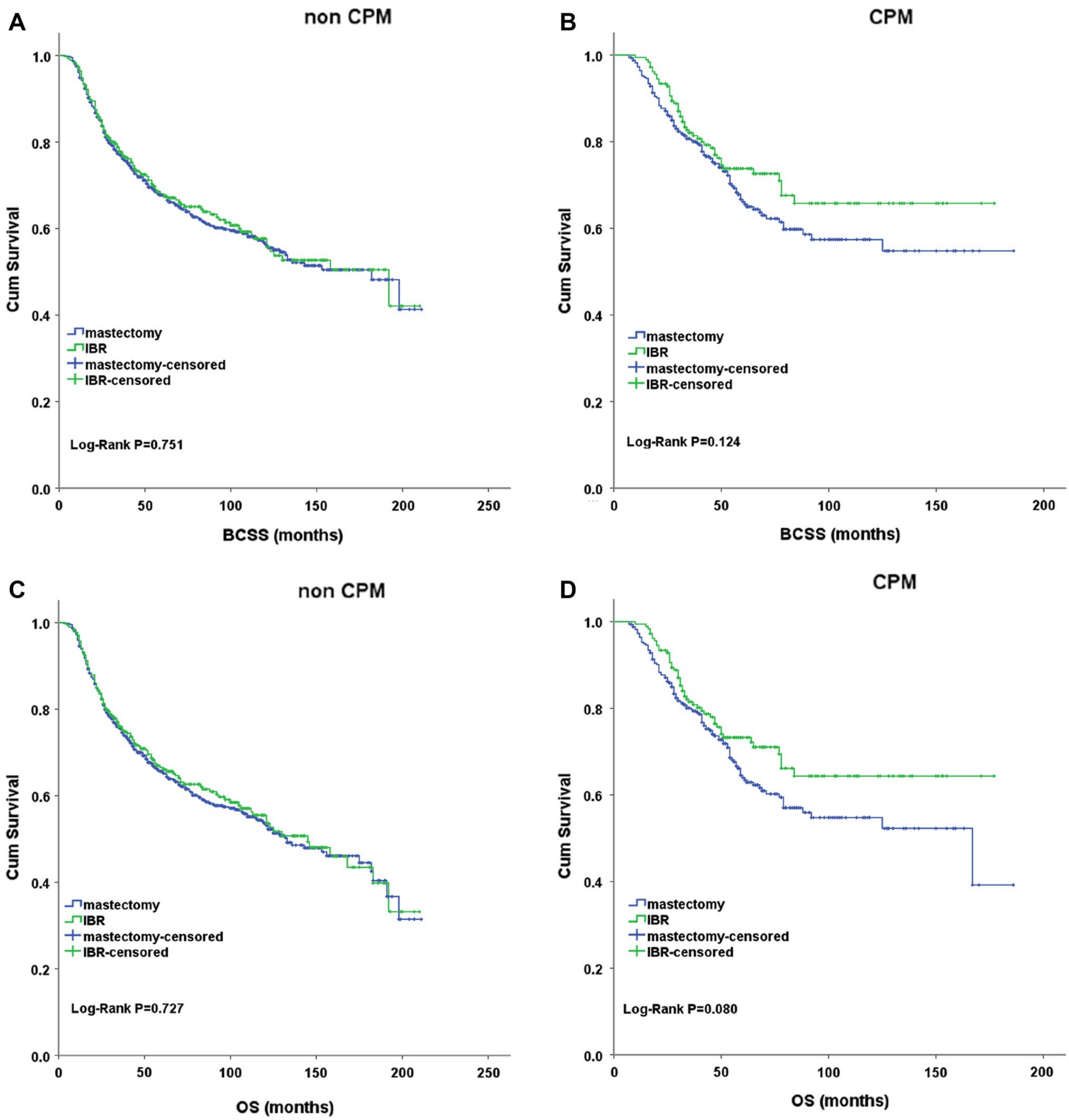


**Fig. 5** Kaplan–Meier survival curves of breast cancer-specific survival (BCSS) and overall survival (OS) for the immediate breast reconstruction and control cohorts stratified by the contralateral prophylactic mastectomy (CPM) status in matched case–control analysis (**a** BCSS in non-CPM; **b** BCSS in CPM; **c** OS in non-CPM; **d** OS in CPM)

## Compliance with ethical standards

**Conflict of interest** All the authors declared that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

**Informed consent** The informed consent was not required because personal identifying information was not involved.

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