Immediate Breast Reconstruction in De Novo Metastatic Breast Cancer: An Analysis of 563 Cases Based on the SEER Database

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Abstract

Controversy exists regarding the appropriateness of immediate breast reconstruction (IBR) in patients with metastatic breast cancer (MBC). An analysis of the SEER database found that 5.2% of patients with de novo MBC undergoing mastectomy received IBR between 1998 and 2015, and that the rate of IBR increased significantly. There were no statistically significant differences in survival outcomes between IBR and mastectomy in the well-matched analysis.

Background: Controversy exists regarding the appropriateness of immediate breast reconstruction (IBR) in patients with metastatic breast cancer (MBC). **Patients and Methods:** By using the Surveillance, Epidemiology, and End Results (SEER) database, data of patients with de novo MBC undergoing mastectomy with or without IBR were assessed. The trend of IBR in de novo MBC was explored. Comparisons of the distribution of clinicopathologic characteristics were evaluated by chi-square and Fisher exact tests. The predictors of IBR in de novo MBC were evaluated by multivariate logistic regression. The survival outcomes were compared by Cox hazards models adjusting for known clinicopathologic variables in both the entire population and in the matched cohorts. **Results:** Between 1998 and 2015, 5.2% of patients with de novo MBC undergoing mastectomy received IBR. The rate of IBR increased significantly, from 6.3% in 1998 to 16.8% in 2015. Patients undergoing IBR were younger and had smaller tumor size, fewer positive lymph nodes, lower proportion of hormone receptor–negative disease and lung metastasis, and better economic status. They were also more likely to receive radiotherapy and chemotherapy. Although IBR was an independent favorable prognostic factor for breast cancer–specific survival and overall survival in the whole population, there were no statistically significant differences between IBR and mastectomy for breast cancer–specific survival ($P = .892$) and overall survival ($P = .708$) in the well-matched analysis. **Conclusion:** IBR in selected de novo MBC could be an acceptable practice when balancing quality of life, underlying health care burden, and oncologic risks.

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Keywords: Immediate breast reconstruction, De novo metastatic breast cancer, Survival, Population-based

Introduction

Patients with de novo metastatic breast cancer (MBC) make up approximately 6% of newly diagnosed cases.[1] MBC is considered incurable and results in a short life expectancy. Although the prognosis is poor, it is improving.[2] Over the past 2 decades, there have been many new treatment options shown to improve survival among patients with de novo metastases,[3] including newer endocrine therapies, human epidermal growth factor receptor 2 (HER2)-targeted agents, and new chemotherapy combinations. Between 1978 and 2013, the 5-year survival rate of patients with de novo MBC improved from 17.4% to 24.7%.[4]

The improvement in survival has made the mode of primary tumor surgery more important. Retrospective reports and meta-analyses have suggested survival benefit of primary tumor surgery in de novo MBC,[2,5-11] but randomized clinical trials showed mixed results.[12,13] As a result, it is still unclear whether locoregional surgery is of value.

Immediate breast reconstruction (IBR) in de novo MBC is controversial. Although metastatic disease is not a contraindication to IBR, MBC patients do not seem to be good candidates. Doubts exist whether survival of MBC is long enough to warrant further IBR and whether complications associated with IBR would have a

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negative impact on oncologic outcome. The significant improvement in survival of MBC and in IBR techniques now allows IBR in those patients with de novo MBC who request it.

There is paucity of literature and lack of consensus on this subject. We therefore conducted a retrospective study to investigate the trend of IBR in de novo MBC and its survival outcome based on the Surveillance, Epidemiology, and End Results (SEER) 18 database.

Patients and Methods

This retrospective study used data derived from the National Cancer Institute's limited-use SEER 18 registry databases, which were released in November 2017. We identified unilateral invasive de novo stage IV breast cancer. Patients with more than one primary cancer, those missing during follow-up, or those with disease diagnosed only at death or autopsy were excluded. Because a surgery code was first established in the SEER in 1998, we selected cases diagnosed between January 1, 1998, and December 31, 2015, for investigation of the IBR trend. Borderline estrogen receptor (ER) or progesterone receptor (PR) status was considered as unknown status. Poorly differentiated and anaplastic histologic grades were considered as grade III disease. Family income above median income was defined as high and below median as low. 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. Tumor size category (T) and positive lymph node category (N) were based on a derived American Joint Committee on Cancer (AJCC) 6th edition (2004-2009) or 7th edition (2010-2015) of tumor, node, metastasis classification system. Because the SEER database did not provide information of T and N in most MBC cases between 1998 and 2003, and because it did not provide information of HER2 status and distant metastasis location before 2010, only cases from 2004 with definite information of race, grade, T, N, ER and PR status, and receipt of mastectomy were considered for further analysis.

We obtained permission to access the SEER program custom data files with additional treatment fields, such as radiotherapy and chemotherapy. Informed consent was not required because personal identifying information was not involved. This study was reviewed and approved by the institutional review board of the Obstetrics and Gynecology Hospital of Fudan University.

Comparisons of the distribution of clinicopathologic characteristics were evaluated by chi-square and Fisher exact 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 cutoff was December 31, 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. BCSS and OS were estimated using the Kaplan-Meier method and compared across groups by the log-rank statistic. Adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated using the Cox model to assess factors independently associated with survival. To diminish the effects of baseline differences on survival outcome in the IBR and control groups, the propensity score matching method was applied by matching each IBR case to one control case. The following covariates were included: year of diagnosis, age at diagnosis, race, marital status, histologic type, histologic grade, T, N, ER, PR, and HER2 status, radiotherapy, chemotherapy, distant metastasis location, and income level. Two-sided $P < .05$ was considered statistically significant. The complete statistical analysis was performed by SPSS 22.0 software (IBM, Armonk, NY).

Results

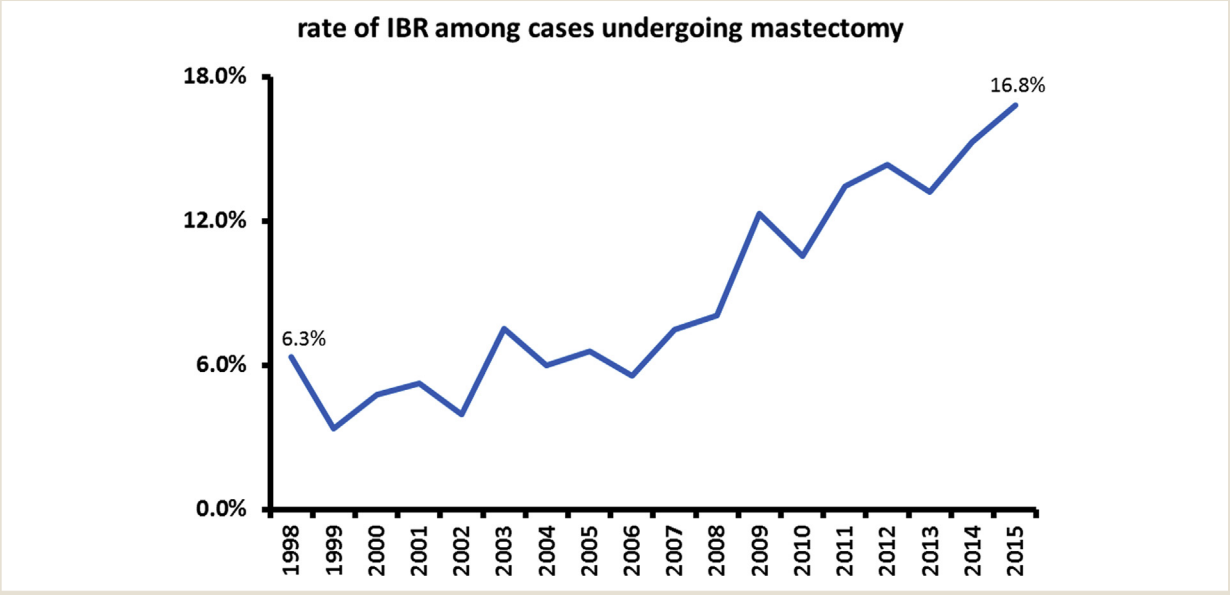
Between 1998 and 2015, there were 37,497 primary breast cancer cases classified by AJCC as stage IV, 33.5% of which underwent some kind of surgery. The rate of surgery decreased from 45.4% in 1998 to 21.0% in 2015, and the rate of mastectomy also decreased from 27.7% in 1998 to 15.0% in 2015. However, among patients undergoing mastectomy, 5.2% received IBR. The rate of IBR increased significantly from 6.3% in 1998 to 16.8% in 2015 (Figure 1).

Altogether, 563 patients received IBR since 2004 who had definite information on race, grade, and T, N, ER, and PR status. There were large baseline differences between patients undergoing mastectomy only and mastectomy plus IBR. A higher proportion of patients undergoing IBR were observed in recent years. Patients undergoing IBR were more often younger and married, and had better economic status. They were more likely to receive radiotherapy and chemotherapy. Furthermore, IBR was performed less frequently in T4 and N2-3 cases, and in cases of negative ER or PR status (Table 1). Two hundred patients underwent autologous IBR, and 250 underwent implant-based IBR. Among reconstructed patients, the proportion of autologous IBR decreased from 54.2% in 2004 to 25.8% in 2015, while the proportion of implant-based IBR increased from 25.0% in 2004 to 56.5% in 2015. In T4 reconstructed patients, 42.6% chose autologous IBR, while 48.8% chose implant-based IBR in T1-3 reconstructed patients ($P = .001$). There were no differences among distribution of other tumor characteristics between the two IBR methods.

The median follow-up was 28 months. In univariate analysis, IBR was associated with favorable BCSS and OS ($P < .001$) (Figure 2). According to Cox multivariate analysis, IBR was an independent favorable prognostic factor for BCSS (HR = 0.820; 95% CI, 0.712-0.943; $P = .005$) and OS (HR = 0.797; 95% CI, 0.695-0.914; $P = .001$). Among different IBR methods, autologous IBR had similar BCSS (HR = 1.056; 95% CI, 0.867-1.287; $P = .587$) and OS (HR = 0.999; 95% CI, 0.821-1.216; $P = .995$) compared to mastectomy, while implant-based IBR had a better BCSS (HR = 0.633; 95% CI, 0.501-0.801; $P < .001$) and OS (HR = 0.624; 95% CI, 0.496-0.785; $P < .001$) compared to mastectomy.

Because of the great baseline differences between the IBR and mastectomy cohorts (Table 1), a 1:1 matched case–control analysis was conducted by the propensity score matching method. There were a total of 1126 cases in the matched analysis. The matching analysis was considered successful, as no significant difference was

Figure 1 Immediate Breast Reconstruction Rates in Patients With De Novo Metastatic Breast Cancer Undergoing Mastectomy, 1998-2015



observed for any characteristic (Table 1). In the matched analysis, the median BCSS of the IBR and control cohorts was 62 and 67 months, respectively; median OS of IBR and control cohorts was 60 and 61 months. There were no statistically significantly differences between IBR and mastectomy for BCSS ($P = .892$) and OS ($P = .708$) (Figure 3).

Since 2010, a total of 363 patients underwent IBR who had definite information on HER2 status and on distant metastasis at bone, liver, lung, and brain. According to the multivariate logistic regressions, recent year of diagnosis, age < 60 years, married status, higher income, invasive ductal carcinoma histology, T1-3 disease, receipt of chemotherapy, and lack of lung metastasis were independently associated with IBR in patients with stage IV disease undergoing mastectomy ($P = .226$, Hosmer-Lemeshow test; Table 2).

Discussion

The standard care for MBC is systemic therapy. Surgery in MBC used to be performed solely for symptom control and palliation. However, systemic therapy advances provide better control of distant disease.[14,15] Furthermore, patients with de novo disease had a decreased risk of death compared to those with a metastatic relapse.[16,17] The question is thus prompted whether more aggressive locoregional surgery could improve survival outcomes for de novo MBC. To date, many retrospective studies and population-based analyses have suggested an OS benefit for primary tumor surgery in the setting of de novo MBC compared to systemic therapy alone.[2,5-10,18] However, these results must be considered carefully in the context of potential bias. Randomized controlled trials, such as the Tata Memorial trial, ABCSG-28, and MF07-01, showed conflicting results relative to OS benefit for surgical resection of primary breast cancer.[12,13,19] As a result, surgical decisions may be considered in selected individuals who had all sites of distant disease well controlled, a long disease-free interval after treatment of the primary tumor, and a good performance status.[20-22]

Reconstruction in MBC patients is also controversial. Reconstruction in the metastatic setting used to be recognized as not "worthwhile." However, with more effective therapy, metastatic survival can be markedly extended with quality of life (QoL) maintained.[23] Patients with de novo MBC were more likely to have high informational needs and decreased overall QoL.[24] As the life expectancy of MBC patient increases, QoL may be a growing concern and deserves full consideration. Patients with breast reconstruction have better satisfaction and QoL than those without,[25] so this challenging clinical question may become more common.[26]

In the current study, we found that the proportion of IBR was increasing among patients with de novo MBC undergoing mastectomy while the rate of surgery was decreasing. A similar trend of slightly decreasing surgery rate over time was also shown by studies of the National Cancer Data Base (NCDB),[18] which may partially be explained by more metastatic patients with a lower tumor burden detected through increasingly sensitive imaging technology.[10] Weiss et al[27] utilized the NCDB and demonstrated that more than 10% of patients with MBC have received breast reconstruction surgery, a finding similar to ours. The increasing proportion of IBR showed a demand for high QoL among some MBC patients. The survey by Durrant et al[28] showed that more and more patients with stage IV disease would require breast reconstruction as systemic therapies improve survival. In this survey, more than half of the plastic surgeons showed a propensity for IBR to patients with longer disease-free intervals and good response to systemic therapy.

Patients undergoing IBR in this study were younger, with smaller tumor size, fewer lymph nodes involved, and lower

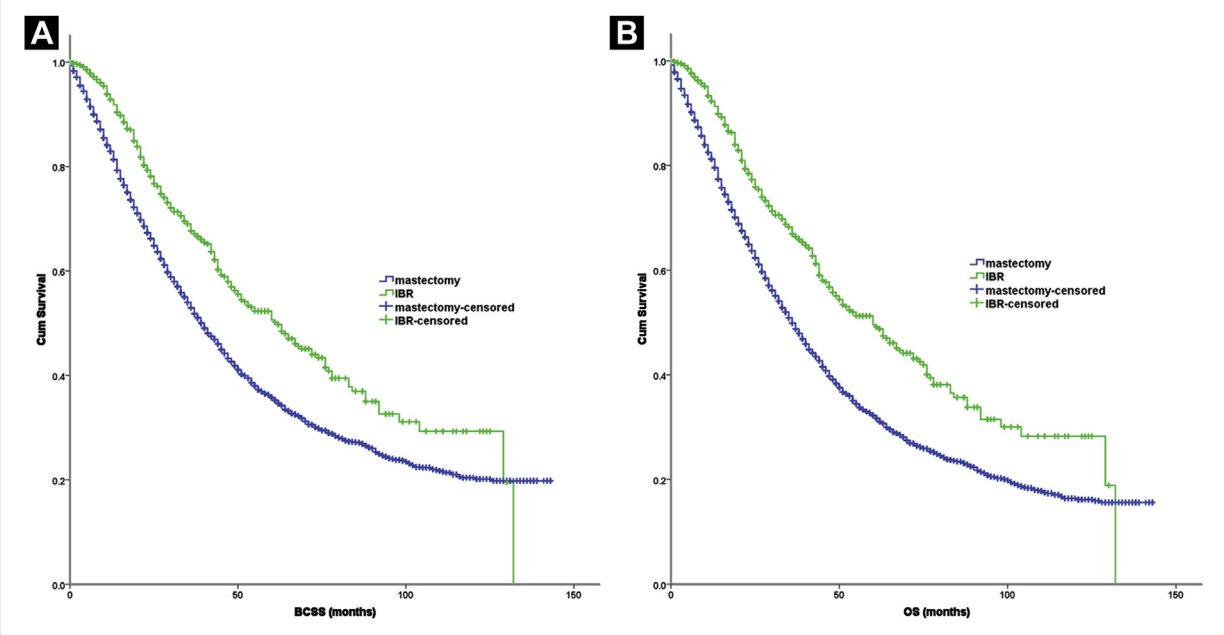
Table 1 Clinicopathologic Characteristic Comparison Between Patients Undergoing Mastectomy Only and Mastectomy + IBR and Further Matched Case–Control Analysis

Characteristic	Mastectomy Cohort	IBR Cohort	Mastectomy (Matched Cohort)	*P* (All Cohorts)	*P* (Matched Cohorts)
Year				<.001	.995
2004-2006	956 (24.3)	70 (12.4)	71 (12.4)		
2007-2009	1092 (27.8)	130 (23.1)	132 (23.1)		
2010-2012	1056 (26.9)	187 (33.2)	183 (33.2)		
2013-2015	824 (21.0)	176 (31.3)	177 (31.3)		
Age, y				<.001	.381
<60	1927 (49.1)	450 (79.9)	438 (77.8)		
≥60	2001 (50.9)	113 (20.1)	125 (22.2)		
Race				.078	.209
White	2881 (73.3)	438 (77.8)	458 (81.3)		
Black	686 (17.5)	83 (14.7)	76 (13.5)		
Other	361 (9.2)	42 (7.5)	29 (5.2)		
Marital Status				<.001	.187
Unmarried	1987 (50.6)	214 (38.0)	230 (40.9)		
Married	1795 (45.7)	331 (58.8)	306 (54.4)		
Unknown	146 (3.7)	18 (3.2)	27 (4.8)		
Histology				<.001	.081
IDC	2866 (73.0)	456 (81.0)	478 (84.9)		
Other	1062 (27.0)	107 (19.0)	85 (15.1)		
Grade				.871	.537
I + II	1507 (38.4)	214 (38.0)	204 (36.2)		
III	2421 (61.6)	349 (62.0)	359 (63.8)		
T				<.001	.784
T1-3	2325 (59.2)	422 (75.0)	418 (74.2)		
T4	1603 (40.8)	141 (25.0)	145 (25.8)		
N				.003	1.000
N0-1	1858 (47.3)	304 (54.0)	304 (54.0)		
N2-3	2070 (52.7)	259 (46.0)	259 (46.0)		
Radiotherapy				.024	.952
Yes	1651 (42.0)	265 (47.1)	266 (47.2)		
No or unknown	2277 (58.0)	298 (52.9)	297 (52.8)		
Chemotherapy				<.001	.461
Yes	2632 (67.0)	470 (83.5)	479 (85.1)		
No or unknown	1296 (33.0)	93 (16.5)	84 (14.9)		
ER				.032	.558
Negative	1323 (33.7)	164 (29.1)	173 (30.7)		
Positive	2605 (66.3)	399 (70.9)	390 (69.3)		
PR				.001	.467
Negative	1935 (49.3)	236 (41.9)	224 (39.8)		
Positive	1993 (50.7)	327 (58.1)	327 (58.1)		
Income				<.001	.752
Low	2147 (54.7)	185 (32.9)	190 (33.7)		
High	1781 (45.3)	378 (67.1)	373 (66.3)		

Data are presented as n (%).
Abbreviations: ER = estrogen receptor; IBR = immediate breast reconstruction; IDC = invasive ductal carcinoma; PR = progesterone receptor.

proportion of hormone receptor–negative disease. They were also more likely to receive radiotherapy and chemotherapy. Further multivariate logistic regressions showed patients with better economic status and no lung metastasis were more likely to receive IBR. More favorable characteristics and median survival of over 60 months observed in the IBR cohort indicated that such patients

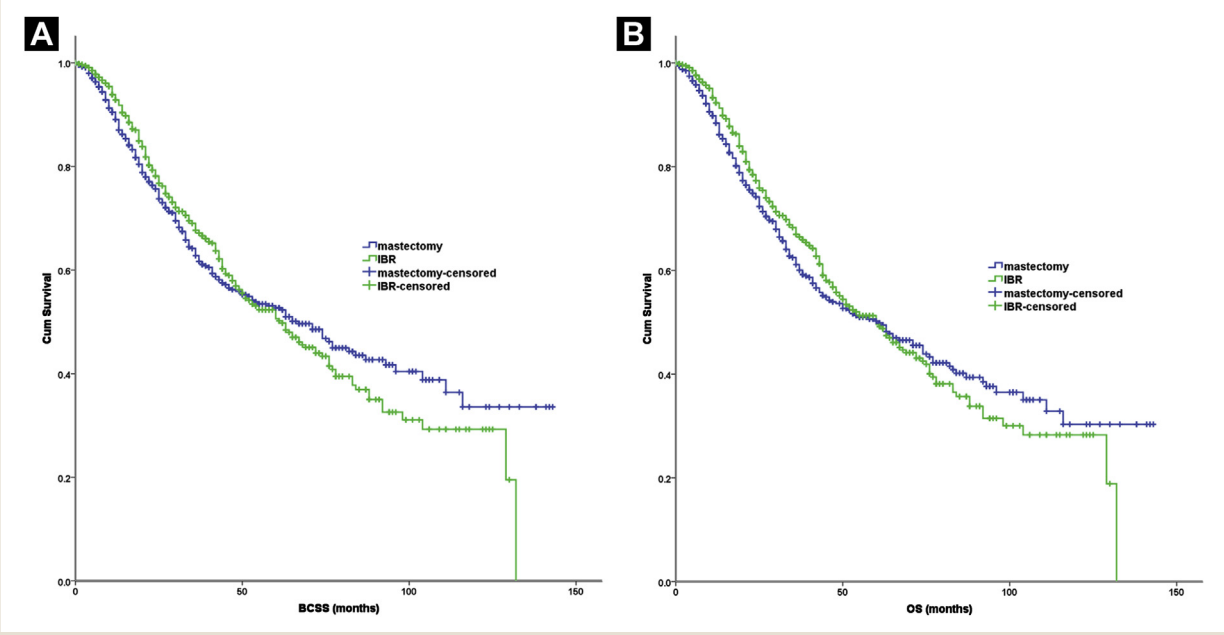
Figure 2 Kaplan-Meier Survival Curves Stratified by Immediate Breast Reconstruction and Control Cohorts in Whole Population. (A) BCSS ($P < .001$). (B) OS ($P < .001$)



Abbreviations: BCSS = breast cancer–specific survival; OS = overall survival.

were carefully selected. For a patient with reduced life expectancy, the need for extensive and potentially morbid treatment requires careful and detailed discussion. An association between T4 disease and autologous reconstruction was observed in our study, which may be indicative of surgical palliation with coverage for advanced disease. Resection of lung metastases from breast cancer may offer

Figure 3 Kaplan-Meier Survival Curves Stratified by Immediate Breast Reconstruction and Control Cohorts in Matched Cohorts. (A) BCSS ($P = .892$). (B) OS ($P = .708$)



Abbreviations: BCSS = breast cancer–specific survival; OS = overall survival.

Table 2 Multivariate Analysis of Factors Associated With IBR in Patients Undergoing Mastectomy With De Novo Metastatic Disease

Factor	OR	95% CI	*P*
Year	1.115	1.036-1.199	.004
Age, y			<.001
<60	3.388	2.539-4.520	
≥60	1.000	Reference	
Marital Status			.092
Married	1.321	1.017-1.715	.037
unknown	0.959	0.518-1.774	.893
Unmarried	1.000	Reference	
Race			.055
Back	0.836	0.598-1.170	.297
Other	0.547	0.351-0.853	.008
White	1.000	Reference	
Histology			<.001
IDC	1.883	1.374-2.580	
Other	1.000	Reference	
Grade			.949
III	1.009	0.771-1.320	
I + II	1.000	Reference	
T			<.001
T1-3	2.220	1.679-2.934	
T4	1.000	Reference	
N			.074
N2-3	0.799	0.625-1.022	
N0-1	1.000	Reference	
Radiotherapy			.277
Yes	1.152	0.893-1.486	
No	1.000	Reference	
Chemotherapy			.003
Yes	1.654	1.180-2.318	
No	1.000	Reference	
ER			.065
Positive	1.407	0.978-2.022	
Negative	1.000	Reference	
PR			.183
Positive	1.246	0.902-1.722	
Negative	1.000	Reference	
HER2			.655
Positive	1.132	0.860-1.490	.377
Unknown	0.942	0.452-1.964	.874
Negative	1.000	Reference	
Bone Metastasis			.108
No	1.244	0.953-1.623	
Yes	1.000	Reference	
Brain Metastasis			.348
No	1.444	0.670-3.113	
Yes	1.000	Reference	
Liver Metastasis			.585
No	0.981	0.674-1.250	
Yes	1.000	Reference	
Lung Metastasis			.004
No	1.643	1.176-2.296	
Yes	1.000	Reference	
Income			.004
High	1.115	1.036-1.199	
Low	1.000	Reference	

Abbreviations: CI = confidence interval; ER = estrogen receptor; HER2 = human epidermal growth factor receptor 2; IDC = invasive ductal carcinoma; OR = odds ratio; PR = progesterone receptor.

a significant survival benefit for selected patients.[29] Because breast reconstruction might interfere with the surgery on lung metastases and vice versa, IBR was performed less frequently in cases of lung metastasis.

In our study, we compared the survival outcome between IBR and mastectomy. IBR was an independent favorable prognostic factor for BCSS and OS in the whole cohort. However, we believe this association is more likely attributable to imbalances in tumor characteristics, disease severity, and socioeconomic factors between the two cohorts. Autologous reconstruction had similar survival compared to mastectomy, while implant-based reconstruction had better survival. Patients with advanced disease favored implant-based IBR, probably because it means shorter operative times, less technically demanding operations, and potential for shorter recovery relative to autologous transfer. The opposite trends of the proportion of autologous and implant-based IBR in our study reflected the choice. Autologous reconstruction served as coverage in many cases. Patients who had more favorable characteristics, who were in better health condition, and who had low-burden metastatic disease were more likely to choose implant-based IBR for the sake of QoL. There were great differences in these factors between the whole cohort. As a result, there were no significant survival differences between matched cohorts where these known confounding factors were well balanced.

De novo MBC is in itself not a contraindication to reconstruction,[30] but complication rate is an important point. Cordeiro et al[31] analyzed the American College of Surgeons National Surgery Quality Improvement Program database and found that patients with metastatic disease were more likely to experience complications. Complications and recovery associated with reconstruction may interrupt systemic treatments and have a detrimental effect on survival. Although information of complications was unavailable in the SEER database, recent research has indicated that patients with advanced breast cancer do not have an increased rate of postoperative complications, poor QoL, or financial burden, and IBR was safe and well tolerated in the setting of advanced-stage breast cancer without significant delays in adjuvant therapy. Furthermore, radiation impaired the reconstructed breast less significantly than previously reported.[30,32,33] It would appear that reconstruction in selected cases is an accepted practice with case-by-case discussions.

Several limitations of the present study should be acknowledged. Although known sources of bias can be adjusted for in multivariable

analysis and additional propensity score matching, unidentified prognostic factors including performance status, information on systemic treatment, and volume and location of metastases could not be adjusted for in most cases. Cases of diagnosis of stage IV disease made after surgery also added bias. Patients who found metastases unexpectedly after initial surgery tended to have a lower burden of metastatic disease.

Conclusion

IBR in MBC patients is a challenging clinical question. More and more patients with de novo MBC would choose IBR. Those with longer life expectancy, favorable characteristics, better performance status, and better social economic status were more likely to undergo IBR. Although IBR did not seem to impair survival compared to mastectomy, it should be performed in well-selected patients while balancing QoL, underlying health care burden, and oncologic risks. Further prospective research on this subject is warranted to fully understand its true risks and benefits.

Clinical Practice Points

- Although controversy exists regarding the appropriateness of IBR in MBC patients, 5.2% of patients with de novo MBC undergoing mastectomy received IBR between 1998 and 2015. The rate of IBR increased significantly from 6.3% in 1998 to 16.8% in 2015.
- Patients undergoing IBR were younger and had smaller tumor size, fewer lymph nodes involved, lower proportion of negative hormone receptor and lung metastasis, and better economic status. They were also more likely to receive radiotherapy and chemotherapy.
- There were no statistically significant differences between IBR and mastectomy for BCSS and OS in the well-matched survival analysis.
- IBR in selected de novo MBC should be balanced between QoL and oncologic risks.

Disclosure

The authors have stated that they have no conflict of interest.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin* 2018; 68: 7-30.
2. Thomas A, Khan SA, Chrischilles EA, Schroeder MC. Initial surgery and survival in stage IV breast cancer in the United States, 1988-2011. *JAMA Surg* 2016; 151:424-31.
3. Zeichner SB, Herna S, Mani A, et al. Survival of patients with de-novo metastatic breast cancer: analysis of data from a large breast cancer-specific private practice, a university-based cancer center and review of the literature. *Breast Cancer Res Treat* 2015; 153:617-24.
4. Holzel D, Eckel R, Bauerfeind I, et al. Survival of de novo stage IV breast cancer patients over three decades. *J Cancer Res Clin Oncol* 2017; 143:509-19.
5. Rapiti E, Verkooijen HM, Vlastos G, et al. Complete excision of primary breast tumor improves survival of patients with metastatic breast cancer at diagnosis. *J Clin Oncol* 2006; 24:2743-9.
6. Neuman HB, Morrogh M, Gonen M, Van Zee KJ, Morrow M, King TA. Stage IV breast cancer in the era of targeted therapy: does surgery of the primary tumor matter? *Cancer* 2010; 116:1226-33.
7. Blanchard DK, Shetty PB, Hilsenbeck SG, Elledge RM. Association of surgery with improved survival in stage IV breast cancer patients. *Ann Surg* 2008; 247: 732-8.
8. Nguyen DH, Truong PT, Alexander C, et al. Can locoregional treatment of the primary tumor improve outcomes for women with stage IV breast cancer at diagnosis? *Int J Radiat Oncol Biol Phys* 2012; 84:39-45.
9. Perez-Fidalgo JA, Pimentel P, Caballero A, et al. Removal of primary tumor improves survival in metastatic breast cancer. Does timing of surgery influence outcomes? *Breast* 2011; 20:548-54.
10. Warschkow R, Guller U, Tarantino I, et al. Improved survival after primary tumor surgery in metastatic breast cancer: a propensity-adjusted, population-based SEER trend analysis. *Ann Surg* 2016; 263:1188-98.
11. Petrelli F, Barni S. Surgery of primary tumors in stage IV breast cancer: an updated meta-analysis of published studies with meta-regression. *Med Oncol* 2012; 29: 3282-90.
12. Badwe R, Hawaldar R, Nair N, et al. Locoregional treatment versus no treatment of the primary tumour in metastatic breast cancer: an open-label randomised controlled trial. *Lancet Oncol* 2015; 16:1380-8.
13. Soran A, Ozmen V, Ozbas S, et al. Randomized trial comparing resection of primary tumor with no surgery in stage IV breast cancer at presentation: protocol MF07-01. *Ann Surg Oncol* 2018; 25:3141-9.
14. Chia SK, Speers CH, D'Yachkova Y, et al. The impact of new chemotherapeutic and hormone agents on survival in a population-based cohort of women with metastatic breast cancer. *Cancer* 2007; 110:973-9.
15. Sundquist M, Brudin L, Tejler G. Improved survival in metastatic breast cancer, 1985-2016. *Breast* 2017; 31:46-50.
16. den Brok WD, Speers CH, Gondara L, Baxter E, Tyldesley SK, Lohrisch CA. Survival with metastatic breast cancer based on initial presentation, de novo versus relapsed. *Breast Cancer Res Treat* 2017; 161:549-56.
17. Lobbezoo DJ, van Kampen RJ, Voogd AC, et al. Prognosis of metastatic breast cancer: are there differences between patients with de novo and recurrent metastatic breast cancer? *Br J Cancer* 2015; 112:1445-51.
18. Lane WO, Thomas SM, Blitzblau RC, et al. Surgical resection of the primary tumor in women with de novo stage IV breast cancer: contemporary practice patterns and survival analysis [e-pub ahead of print]. *Ann Surg*. https://doi.org/10.1097/SLA.0000000000002621. Accessed December 7, 2017.
19. Fitzal F, Bjelic-Radisic V, Knauer M, et al. Impact of breast surgery in primary metastasized breast cancer: outcomes of the prospective randomized phase III ABCSG-28 POSYTIVE trial [e-pub ahead of print]. *Ann Surg*. https://doi.org/10.1097/SLA.0000000000002771. Accessed April 24, 2018.
20. Singletary SE, Walsh G, Vauthey JN, et al. A role for curative surgery in the treatment of selected patients with metastatic breast cancer. *Oncologist* 2003; 8: 241-51.
21. Khan SA, DesJardin ESM. Readdressing the role of surgery of the primary tumor in de novo stage IV breast cancer. *Cancer Treat Res* 2018; 173:73-88.
22. Patrick J, Khan SA. Surgical management of de novo stage IV breast cancer. *J Natl Compr Canc Netw* 2015; 13:487-93.
23. Cardoso F, Senkus E, Costa A, et al. 4th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 4). *Ann Oncol* 2018; 29:1634-57.
24. Seah DS, Lin NU, Curley C, Weiner EP, Partridge AH. Informational needs and the quality of life of patients in their first year after metastatic breast cancer diagnosis. *J Commun Support Oncol* 2014; 12:347-54.
25. Dauplat J, Kwiatkowski F. Quality of life after mastectomy with or without immediate breast reconstruction. *Br J Surg* 2017; 104:1197-206.
26. Danesh M, Belkora J, Volz S, Rugo HS. Informational needs of patients with metastatic breast cancer: what questions do they ask, and are physicians answering them? *J Cancer Educ* 2014; 29:175-80.
27. Weiss A, Chu CK, Lin H, et al. Reconstruction in the metastatic breast cancer patient: results from the National Cancer Data Base. *Ann Surg Oncol* 2018; 25: 3125-33.
28. Durrant CA, Khatib M, Macneill F, James S, Harris P. Mastectomy and reconstruction in stage IV breast cancer: a survey of UK breast and plastic surgeons. *Breast* 2011; 20:373-9.
29. Kycler W, Laski P. Surgical approach to pulmonary metastases from breast cancer. *Breast J* 2012; 18:52-7.
30. Behnam AB, Nguyen D, Moran SL, Serletti JM. TRAM flap breast reconstruction for patients with advanced breast disease. *Ann Plastic Surg* 2003; 50:567-71.
31. Cordeiro E, Jackson TD, Elnahas A, Cil T. Higher rate of breast surgery complications in patients with metastatic breast cancer: an analysis of the NSQIP database. *Ann Surg Oncol* 2014; 21:3167-72.
32. Crisera CA, Chang EI, Da Lio AL, Festekjian JH, Mehrara BJ. Immediate free flap reconstruction for advanced-stage breast cancer: is it safe? *Plastic Reconstr Surg* 2011; 128:32-41.
33. Chang EI, Chang EI, Ito R, et al. Challenging a traditional paradigm: 12-year experience with autologous free flap breast reconstruction for inflammatory breast cancer. *Plastic Reconstr Surg* 2015; 135:262e-9e.