Original Article

A retrospective cohort study comparing reconstructive techniques and outcomes in post-mastectomy triple negative breast cancer patients

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Background: Up to 42% of all breast cancer patients undergo post-mastectomy reconstruction, however reconstructive techniques have not been widely studied in patients with triple negative breast cancer (TNBC). Reconstructive complications may delay adjuvant treatments; in TNBC, which inherently carries an increased risk of locoregional recurrence, this can greatly affect oncological outcomes. Therefore, we evaluate factors influencing choice of reconstructive techniques following mastectomy in TNBC patients and assess operative and oncologic safety outcomes.

Methods: A single institution retrospective chart review identified TNBC patients who underwent post-mastectomy reconstruction between 2010 to 2020. Clinical characteristics collected included demographics, cancer history, reconstructive techniques [autologous-based reconstruction (ABR) *vs.* implant-based reconstruction (IBR)] and surgical and oncologic outcomes such as complications, recurrence, and mortality. Factors impacting whether patients underwent ABR versus IBR were assessed, as well as differences in outcomes between the two procedures. Statistical significance was defined as $P<0.05$.

Results: During the 10-year period, 52.9% (n=127) of all post-mastectomy TNBC patients (n=240) underwent breast reconstruction, most frequently immediately after mastectomy (97.0%). Most patients underwent IBR compared to ABR (82.4% *vs.* 14.5%). Patients undergoing ABR were older than IBR patients (54.3 *vs.* 46.4 years; P=0.040) and had a higher body mass index (BMI; 30.0 *vs.* 26.1 kg/m^2; P=0.007). Patients more often pursued ABR if they had a prior breast cancer history (36.8% *vs.* 16.7%; P=0.041) or experienced TNBC recurrence (26.3% *vs.* 9.3%; P=0.034), while primary TNBC patients more often opted for IBR. Reconstructive type did not impact complications (ABR 31.6% *vs.* IBR 16.8%, P=0.131), recurrence (ABR 15.8% *vs.* IBR 13.0%, P=0.719), or mortality (ABR 0.0% *vs.* IBR 6.5%, P=0.593) rates.

Conclusions: Factors such as age, BMI, and breast cancer history impacted choice of reconstructive technique among TNBC women. No differences in complications, recurrence, or mortality occur in these high-risk patients regardless of reconstructive technique, highlighting that neither ABR nor IBR is superior in regard to surgical and oncologic safety in post-mastectomy TNBC patients.

Keywords: Triple negative breast cancer (TNBC); post-mastectomy reconstruction; autologous-based reconstruction (ABR); free tissue transfer; implant-based reconstruction (IBR)

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Introduction

Triple negative breast cancers (TNBC), defined by the lack of expression of estrogen receptor (ER), progesterone receptor (PR), and overexpression of human epidermal growth factor receptor 2 (HER2) gene, account for 10% to 20% of invasive breast cancers (1). This breast cancer subtype more commonly occurs in patients under the age of 40 years and of African American or Hispanic ethnicity (2). Compared to other breast cancer types, TNBC is associated with the worst prognosis as there are no targeted systemic therapies given the lack of receptor expression (3,4). Prior studies have suggested a higher risk of locoregional recurrence and distant metastasis in TNBC patients who undergo breast-conserving surgery (BCS) (5,6). Previous reports have stated that patients with TNBC who were candidates for BCS opted to undergo mastectomy instead, although there is no evidence that biomolecular subtype of breast cancer should influence type of surgical treatment (4,7,8). Furthermore, a recent systematic review found no evidence of a detrimental effect of BCS compared with mastectomy on locoregional recurrence or distant metastasis in TNBC patients (4).

Immediate or delayed breast reconstruction confers psychological benefits and improvements in quality of life, and has become increasingly common following mastectomy for breast cancer (9). Recent reports suggest that immediate breast reconstruction is oncologically safe following resection of invasive breast cancer (10,11), with no differences in cancer burden in TNBC versus non TNBC patients (12). Interestingly, Kneubil *et al.* reported triple-negative receptor status to be an independent risk factor for locoregional recurrence in TNBC patients who elected for mastectomy with breast reconstruction (13).

Implant-based breast reconstruction (IBR) is a safe technique with favorable outcomes, minimal morbidity, and short operative times (14). Alternatively, autologous breast reconstruction (ABR) can safely be performed using microvascular free tissue transfer or pedicled locoregional flap transfer. Multiple factors are considered to determine reconstructive technique following mastectomy, such as need for adjuvant radiotherapy, breast size, degree of breast ptosis, comorbidities, age, and patient preference are used to determine the ideal post-mastectomy reconstructive approach in each patient (15-18). Some patients may even choose not to undergo post-mastectomy breast reconstruction given the risks of additional complications that a second surgery may impose. Reconstructive complications may delay adjuvant treatments; in TNBC, which inherently carries an increased risk of locoregional recurrence, this can greatly affect oncological outcomes (12). Overall, little is known about the outcomes of TNBC patients undergoing reconstruction, and no study to date has evaluated and compared the objective clinical factors associated with the decision to undergo implant versus autologous reconstruction in the TNBC population. Thus, the aim of this study is to evaluate the clinical factors that impact choice of post-mastectomy reconstructive technique in patients with TNBC, as well as to assess post-reconstruction surgical and oncologic outcomes in these high-risk patients. We present the following article in accordance with the STROBE reporting checklist (available at https://tbcr.amegroups.com/article/view/10.21037/tbcr-22-42/rc).

Methods

Following institutional review board approval (MHRI No. 00004330), a single institution retrospective chart review was performed for patients with TNBC who underwent post-mastectomy breast reconstruction from 2010 to 2020. TNBC patients who did not undergo post-mastectomy breast reconstruction were excluded. Patients over the age of 18 with biopsy-confirmed TNBC who underwent total mastectomy with reconstruction were included. Collected patient characteristics included demographics such as age, race, body mass index (BMI), smoking history, and other comorbidities such as diabetes or connective tissue disease. Breast cancer history was additionally collected, including details regarding cancer histology, tumor size and stage, and receipt of treatments such as chemotherapy or radiation therapy. Reconstruction was performed by multiple surgeons at this single institution. Patients were categorized depending on the initial post-mastectomy reconstructive technique they underwent: ABR or IBR. ABR included free tissue transfer or rotational/local flap reconstruction, while IBR included tissue expanders (TE) and saline or silicone implants. Additional details regarding follow-up procedures were also collected, such as mean months between TE and final reconstruction and the type of final reconstruction (ABR *vs.* IBR) that the patient received. Mean follow-up was described for ABR and IBR patients. Collected outcomes data comprised of rates of TNBC recurrence, postoperative complications, and mortality in the included patients.

Comparative analyses included patients who underwent ABR or IBR. STATA version 17.0 (StataCorp, College

Station, TX) was used to conduct univariate Chi-square, Fisher's exact, and paired *t*-tests to analyze the data for statistical significance, defined at values of P<0.05. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional review board of MedStar Health Research Institute (No. 00004330) and individual consent for this retrospective analysis was waived.

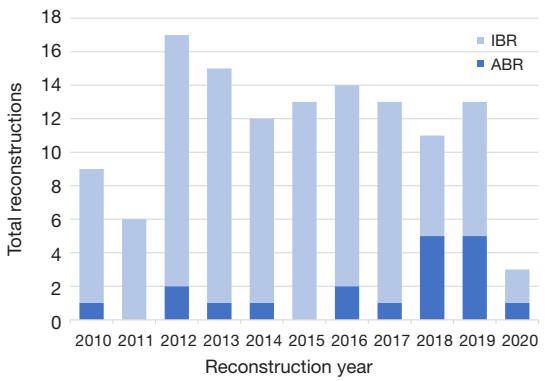

Figure 1 Frequency of reconstruction types from 2010–2020. IBR, implant-based reconstruction; ABR, autologous-based reconstruction.

Results

A total of 465 female patients were diagnosed with TNBC during the 10-year study period, of which 240 underwent total mastectomy. From these patients, 52.9% (n=127) underwent breast reconstruction. Reconstructive techniques most commonly included IBR (n=108, 85.0%), followed by ABR (n=19, 15.0%). Trends in reconstructive techniques performed for patients treated at our institution can be seen plotted over the past decade in *Figure 1*, which demonstrates an increase in ABR procedures over recent years. On average, patients who elected for ABR were older than patients undergoing IBR (54.3±10.4 *vs.* 46.4±10.9 years; P=0.040). There was no difference in race for patients who underwent ABR versus IBR (P=0.566), with 51.2% of those undergoing the procedures being Caucasian (n=64), 34.4% African American (n=43), 5.6% Asian (n=7), and 2.4% Hispanic or Latino (n=3). Patients with a higher BMI were more likely to undergo ABR compared to IBR (30.0 *vs.* 26.1 kg/m^2; P=0.007). Patients with a current or prior smoking history were more likely to undergo ABR compared to IBR, though this was not significant (42.1% *vs.* 23.6%, P=0.092). Comorbidities, such as diabetes or connective tissue disease did not significantly influence choice of reconstruction type. Patient demographics for those who underwent ABR or IBR are summarized in *Table 1*.

Table 1 Patient demographics and comorbidities in TNBC patients

Variable	ABR + IBR reconstructions	ABR	IBR	P value
Total	127	19 (15.0)	108 (85.0)	–
Age, years	47.8±11.3	54.3±10.4	46.4±10.9	0.040
Race[a]				0.566
Caucasian	64 (51.2)	8 (44.4)	56 (52.3)	
African American	43 (34.4)	9 (50.0)	34 (31.8)	
Asian	7 (5.6)	1 (5.6)	6 (5.6)	
Hispanic or Latino	3 (2.4)	0 (0.0)	3 (2.8)	
Other	8 (6.4)	0 (0.0)	8 (7.5)	
BMI, kg/m^2	26.6±6.1	30.0±4.0	26.1±6.2	0.007
Smoking history[a]	33 (26.4)	8 (42.1)	25 (23.6)	0.092
Comorbidities				
Diabetes[b]	4 (3.4)	1 (5.3)	3 (2.8)	0.484
Connective tissue disease[a]	4 (3.2)	0 (0.0)	4 (3.8)	1.000

Data are shown as mean ± standard deviation or number (percentage). [a], n=125; [b], n=126. ABR, autologous-based reconstruction; IBR, implant-based reconstruction; BMI, body mass index.

Table 2 Cancer characteristics

Variable	ABR + IBR reconstructions (n=127)	ABR (n=19)	IBR (n=108)	P value
Prior BC history	25 (19.7)	7 (36.8)	18 (16.7)	0.041
Occurrence				0.034
Primary TNBC	112 (88.2)	14 (73.7)	98 (90.7)	
Recurrence	15 (11.8)	5 (26.3)	10 (9.3)	
Prior breast surgery	33 (26.0)	8 (42.1)	25 (23.1)	0.087
Cancer histology				0.066
DCIS	4 (3.2)	0 (0.0)	4 (3.7)	
Invasive ductal CA	115 (90.6)	16 (84. 2)	99 (91.7)	
Invasive lobular CA	2 (1.6)	0 (0.0)	2 (1.9)	
Mammary CA	4 (3.2)	3 (15.8)	1 (0.9)	
Other	2 (1.6)	0 (0.0)	2 (1.9)	
Tumor size (cm^2)[a]	2.3±1.6	1.7±1.2	2.4±1.6	0.085
Tumor stage[b]				0.640
0	2 (1.8)	0 (0.0)	2 (2.0)	
1	39 (34.5)	6 (40.0)	33 (33.7)	
2	58 (51.3)	6 (40.0)	52 (53.1)	
3	13 (11.5)	3 (20.0)	10 (10.2)	
4	1 (0.9)	0 (0.0)	1 (1.0)	
Chemotherapy[c]				0.430
Neoadjuvant	47 (40.2)	7 (46.7)	40 (39.2)	
Adjuvant	66 (56.4)	7 (46.7)	59 (57.8)	
Both	4 (3.4)	1 (6.7)	3 (2.9)	
Radiation				–
Neoadjuvant	0 (0.0)	0 (0.0)	0 (0.0)	
Adjuvant	40 (31.5)	6 (33.3)	34 (31.5)	

Data are shown as mean ± standard deviation or number (percentage). [a], n=121; [b], n=113; [c], n=117. ABR, autologous-based reconstruction; IBR, implant-based reconstruction; BC, breast cancer; TNBC, triple negative breast cancers; CA, carcinoma.

Patients were more likely to undergo ABR compared to IBR if they had prior history of any type of breast cancer (36.8% *vs.* 16.7%; P=0.041) or if they experienced a TNBC recurrence (26.3% *vs.* 9.3%; P=0.034), while patients experiencing a primary occurrence of TNBC more often underwent IBR (90.7% *vs.* 73.7%; P=0.034). The trend to undergo ABR over IBR in patients with a prior history of breast surgery (i.e., lumpectomy, partial mastectomy, or cosmetic breast implant surgery) was not significant (42.1% *vs.* 23.1%; P=0.087). Patients with larger tumors tended to undergo IBR (2.4±1.6 cm^2) compared to ABR (1.7±1.2 cm^2), though this was not significant (P=0.085). Cancer histology and tumor stage at presentation had no influence on reconstruction choice. History of neoadjuvant versus adjuvant chemotherapy or radiation also had no effect on type of breast reconstruction chosen. Cancer characteristics stratified by type of reconstruction can be found in *Table 2*.

At the time of primary oncologic surgery, 73.3% of patients (n=96) underwent contralateral mastectomy. Of these 96 patients, 3.1% (n=3) underwent mastectomy due

Table 3 Reconstructive details and outcomes

Variable	ABR + IBR reconstructions (n=127)	ABR (n=19)	IBR (n=108)	P value
Operative details				
Contralateral reconstruction technique	96	13	83	<0.001
ABR	12 (12.5)	12 (92.3)	0 (0.0)	
IBR	81 (84.4)	1 (7.7)	80 (96.4)	
Implant-based reconstruction	–	–		–
Tissue expander			77 (71.3)	
Silicone or saline implant			31 (28.7)	
Final reconstruction following TE	–	–		–
<3 months			10 (14.5)	
3–6 months			26 (37.7)	
6–9 months			12 (17.4)	
9–12 months			12 (17.4)	
12–15 months			6 (8.7)	
>15 months			3 (4.4)	
Type of final reconstruction following TE	–	–		–
ABR			11 (15.9)	
IBR			58 (84.1)	
Follow-up, months	51.3±33.5	32.9±24.9	54.7±33.7	0.006
Reconstructive and oncologic outcomes				
Recurrence	17 (15.9)	3 (15.8)	14 (13.0)	0.719
Complications	24 (19.1)	6 (31.6)	18 (16.8)	0.131
Mortality	7 (5.6)	0 (0.0)	7 (6.5)	0.593

Data are shown as mean ± standard deviation or number (percentage). ABR, autologous-based reconstruction; IBR, implant-based reconstruction; TE, tissue expander.

to breast cancer in the contralateral breast, while 96.9% (n=93) underwent prophylactic contralateral mastectomy. All patients underwent reconstruction in the contralateral breast following mastectomy, with the majority undergoing the same reconstructive technique as in the primary breast (P<0.001). Patients undergoing IBR had longer follow-up compared to those undergoing ABR (54.7±33.7 *vs.* 32.9±24.9 months; P=0.006). Reconstructive outcomes such as complication rates were similar between cohorts. At mean follow-up of 51.4 months (range, 2.7–131.4 months), oncologic outcomes, such as TNBC recurrence and mortality rate, did not significantly differ between the two groups. Surgical outcomes and reconstructive details such as implant type used and time to final reconstruction following TE use are outlined in *Table 3*.

Discussion

This is the first study to evaluate post-mastectomy reconstruction methods specific to TNBC patients. Compared to an overall post-mastectomy reconstruction rate of 42% for all breast cancer patients (19), we report a higher rate of 52.9% within patients with TNBC. We found that compared to patients who underwent IBR, TNBC patients who underwent ABR were significantly older, had a higher BMI, and either had a prior history of breast cancer or experienced TNBC recurrence. Despite concerns for increased complication rates or locoregional recurrence in

TNBC patients undergoing ABR, there was no significant difference in recurrence or mortality outcomes following ABR versus IBR techniques.

Butz *et al*. previously reported a significantly higher risk of 30-day postoperative complications in older patients receiving ABR compared to younger patients (20). Although ABR may confer greater operative risks in older patients due to longer operative times under general anesthesia, there are also reports that demonstrate no increased risk of complications in this cohort, which parallels our findings (21). Additionally, previous data has suggested that older women who opted for autologous reconstruction reported significantly higher satisfaction than women of the same age who underwent implant-based methods, in part because autologous reconstruction provides better symmetry (21). This may explain why a higher proportion of older patients chose to undergo ABR following mastectomy in our study (P=0.040).

Patients receiving autologous reconstruction had significantly higher BMI than those receiving IBR (P=0.007), suggesting that those with higher fat content may opt to use their own adipose tissue for breast reconstruction for the benefit of improving their body contour. Interestingly, there is mixed data regarding outcomes following ABR versus IBR in obese women, with some sources demonstrating increased complication rates in autologous reconstruction and other sources suggesting decreased complications and higher patient satisfaction with ABR (22,23). Furthermore, our data demonstrates no significant difference in complication rates between all women receiving ABR versus IBR. While an increase in BMI does pose a greater risk of postsurgical complications in general, this heterogeneity in reported outcomes from ABR warrants further investigation, and the decision to undergo certain reconstructive procedures should be based on clinical decision-making on a case-by-case basis.

It is well-known that smoking has an important deleterious impact on wound healing, and several reports have shown that nicotine use contributes to poor outcomes in both autologous and implant-based breast reconstruction (24-26). While not significant, there was a trend towards undergoing ABR in patients with a smoking history compared to those who underwent IBR (P=0.092). While the reason for this tendency is not entirely clear, it may prompt clinical providers to consider smoking history in reconstructive choice, given that the microvascular disease found in smokers may result in complications such as abdominal dehiscence. Larger studies are warranted to compare outcomes in smokers receiving ABR versus IBR in TNBC patients receiving breast reconstruction.

We found that patients with a personal history of breast cancer or recurrence were more likely to undergo ABR over IBR (P=0.041 and P=0.034, respectively). This corresponded to the trend towards undergoing ABR more commonly in those with a prior history of breast surgery (P=0.087), such as in cases of patients who underwent oncologic procedures for prior breast cancer. It has been previously reported that ABR is associated with higher cancer recurrence rates compared to those who undergo mastectomy alone, possibly due to extensive surgery activating dormant micrometastases, but more recent reports suggest that there is no increased recurrence risk (27). Importantly, our results suggest no difference in TNBC-specific recurrence following either ABR or IBR, paralleling other reports that have shown no association between breast reconstruction type and cancer recurrence (28). Our findings support that the relationship between personal breast cancer history, recurrence, and reconstructive choice is not causative. We also show that there is neither an increased risk of complications or mortality in patients who receive either autologous or implant-based reconstruction. These findings can provide invaluable information to patients who are often uncertain when choosing a particular reconstructive option, helping to ease the decision-making process by reducing concern for surgical or oncologic complications.

We report a greater percentage of TNBC patients undergoing reconstruction (52.9%) compared to what has previously been reported in the literature for all BC patients (42%) (19). This could be the result of patients being seen at a high-volume, tertiary academic center, and therefore may not reflect access to reconstruction nationally for TNBC patients, particularly in rural areas. Our institution saw an increase in the proportion of TNBC patients who received ABR in recent years compared to IBR. In 2018, 45.5% of TNBC breast reconstructions performed were autologous (*Figure 1*). This is compared to the period of 2010 to 2017, during which the average rate of ABR was only 7.7%. This significant increase in ABR is due to greater surgical experience and the addition of reconstructive microsurgeons who perform ABR at our center. Furthermore, the increase in ABR in the last few years may be due, in part, to recent reports linking textured breast implants to anaplastic large cell lymphoma (ALCL) and a greater awareness of illness related to breast implants, although currently unsubstantiated by evidence (29-31). Women have previously reported a fear of implants as a

reason to forego reconstruction, despite the proven safety of this reconstructive method (32-34).

Strengths of this study include the 10-year study duration, allowing for a widespread evaluation of cases and trends at our institution. Inherent limitations of this study include a relatively small sample size. Thus, a larger study possibly utilizing a national dataset may provide a deeper understanding of demographic and medical factors that influence TNBC patients' decision-making for post-mastectomy reconstruction. Second, our retrospective chart review study design depends on the quality of data reported within patients' medical records. Additionally, an understanding of factors influencing TNBC patients' decisions to undergo post-mastectomy reconstruction could not be achieved, due to non-reconstruction patients not being included in this study. While the aim of this study was to provide an overview of reconstructive methods and resulting outcomes in TNBC patients, a major limitation is the lack of details regarding the discussions and decisions made between surgeons and patients on choosing either autologous or implant-based reconstruction. Because both surgeon-sided and patient-sided factors influence this decision, further details would improve the conclusions found in this study; however, the long duration of this study and the heterogeneity in reconstructive surgeons make finding surgeon-sided decision-making rationales difficult to identify. Regardless of this limitation, no other study has identified the objective clinical factors that are associated with different modalities of breast reconstruction in TNBC patients, and this data could help guide physicians and patients better understand reconstructive options and outcomes. It would also be valuable to assess patient preferences to undergo reconstruction using a prospective survey of those who did and did not undergo the procedure to assess aspects affecting their decisions. Additionally, it would be interesting to compare TNBC reconstructive techniques to patients with other cancer subtypes to better appreciate any differences. Finally, based on our original classification of patients into ABR versus IBR groups, many patients who initially received TEs were included within IBR. Of these patients, 11 (15.9%) underwent eventual ABR, but were still considered within the IBR group due the patient classification system used for this study.

Conclusions

In patients with TNBC, the decision to undergo breast reconstruction should be based on the primary goal of a safe operative and oncologic outcome. In TNBC women undergoing reconstruction, older age, higher BMI, and a prior history of breast cancer were factors associated with undergoing ABR. Regardless of the reconstructive option undergone, we found no differences in recurrence, complications, or mortality in these high-risk TNBC patients. These findings provide valuable information to patients and physicians and may assist in the risk stratification component of the decision-making process.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tbcr.amegroups.com/article/view/10.21037/tbcr-22-42/rc

Data Sharing Statement: Available at https://tbcr.amegroups.com/article/view/10.21037/tbcr-22-42/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tbcr.amegroups.com/article/view/10.21037/tbcr-22-42/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional review board of MedStar Health Research Institute (No. 00004330) and individual consent for this retrospective analysis was waived.

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