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Comparative Study between Breast Conserving Surgery and Modified Radical Mastectomy in Management of Triple Negative Breast Cancer

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Abstract: Background: Breast cancer is the most common cancer in women around the world. Modified radical mastectomy (MRM) is a radical procedure of surgery usually used in the treatment of breast cancer. Breast conserving surgery (BCS) and radiotherapy have been shown to provide similar local control and survival rates to radical procedures in the surgical treatment of early breast cancer. Patients with breast cancer are managed using clinical, histological parameters, hormone receptors like Estrogen, Progesterone, and human epidermal growth factor receptors and radiological investigations. **Objective:** The aim of this study is to assess and compare the oncologic and cosmetic outcomes of breast conserving surgery (BCS) and Modified Radical Mastectomy (MRM) regarding in triple-negative breast cancer patients. **Patients and Methods:** This retrospective study included 20 breast cancer patients presented in many hospitals in Egypt divided into two groups, breast conserving surgery group, and modified radical mastectomy group. *Inclusion criteria* have proven histopathology of early (stage I-II) breast cancer, a triple-negative receptors test (Estrogen receptor, Progesterone receptor and Human epidermal growth factor receptor 2 (HER2)) and with no other lesions in the same or contralateral breast. *Exclusion criteria:* patients with advanced breast cancer, medically unfit for surgery, patient with a past history of breast cancer and patients with contraindication of BCS or radiation. **Results:** We investigated Overall Survival (OS) in patients with Triple-negative breast cancer (TNBC) treated with mastectomy compared with those receiving BCS, patients with BCS had better survival than patients with mastectomy. Multivariate analysis revealed an excellent survival rated in the BCS group comparing to the mastectomy group. **Conclusion**: our results reported superior overall survival in the BCS group compared to mastectomy. Patients managed using mastectomy suffered from cosmetic impairments, worse outcomes and an avoidable deterioration in quality life during the surgical decision-making process. Therefore, we recommend BCS is a preferable line of management in patients with TNBC tumors when given adequate adjuvant treatment.

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1. Introduction

Breast cancer is the commonest cancer affecting women around the globe. For controlling breast cancer, both radiotherapy and Conserving breast surgery (BCS) have been reporting similar results regarding local control and survival comparing to more radical procedures used in the treatment of breast cancer ***(1).*** In 1994, a new type of operation was defined where the surgeons perform lumpectomy with simultaneous bilateral reduction mammoplasty in a breast cancer patient with macromastia and oncoplastic ***(2).***

Usually, Brest cancer patients are managed through multiple histological and clinical parameters including the size of the tumor, the condition of lymph nodes (LN), and assessment of the hormonal receptors such as estrogen receptor [ER] and progesterone receptor [PR] and most recently testing for human epidermal growth factor receptor 2 (HER2) ***(3)***.

The previously mentioned loco-regional lines in managing cases of breast cancer were implemented according to the results of many RCTs compared between the breast-conserving methods and more radical methods like modified radical mastectomy (MRM) ***(4-6).***

Most of the recent studies have ditched the previously used molecular and/or biological classifications, and adopted a new molecular classification with at least three major molecular subtypes of breast cancer, associated with different response to the treatment and different survival rates ***(5-6).*** Most of these studies classified the tumors according to biologic subtyping using ER, PR,

and HER2 as biomarkers ***(7).*** One of the commonest breast cancer types is the triple-negative breast cancers (TNBCs) accounts for 10% to 17% of breast cancer cases ***(3)*** is considered to be more aggressive than other subtypes, and characterized by high proliferation rates. (TNBC) tumors are usually presented as poorly differentiated tumors lacking expression of ER, PR, and HER2 biomarkers ***(8-9).***

(TNBC) are usually managed using conventional cytotoxic chemotherapy followed by adjuvant RT, as other lines of management such as endocrine and HER2-targeted treatment cannot be used (**10).**

Many previous studies have retrospectively assessed the risk of cancer loco-regional recurrence (LRR) in breast cancer patients. Patients with TNBC tumors were associated with a higher risk of LRR than patients with tumors with other biological subtypes ***(11)***.

2. Patients and methods

This retrospective study included breast cancer patients presented in Ain Shams University Hospital, Military production specialized medical center, Al-Azhar university hospitals, and El-Monira general hospital. Our inclusion criteria was for the patients to have proven histopathology of early (stage I-II) breast cancer, a triple-negative receptors test (Estrogen receptor, Progesterone receptor and Human epidermal growth factor receptor 2 HER2) and with no other lesions in the same or contralateral breast. Patients were excluded from the study if they were patient with advanced breast cancer, medically unfit for surgery, patients with a past history of breast cancer and patients with contraindication of BCS or radiation. Patients who refused to be enrolled in the study were excluded from the study, and an inform consent was taken from the patients.

After applying our inclusion\exclusion criteria, the final sample size was 20 patients divided into two groups; 10 patients were treated by conservative breast surgery, while the other 10 patients were treated by modified radical mastectomy.

Each patient was subjected to a Comprehensive medical history taking, a careful clinical examination. Full laboratory investigations were done for all the patients enrolled in the study including (CBC, R.B.S, PT, PTT, INR, S. Urea, S. Creat., liver enzymes).

All the required imaging techniques were acquired from the patients including bilateral sonomammography, plain chest-X-ray, pelvi-abdominal US, bone scan, and further radiology whether local or systemic according to indication.

For diagnostic pathology, Core biopsy or wedge biopsy from the patients.

In BCS operation, the tumor with adequate safety margin as well as axillary L.Ns. was removed, while In MRM technique, the whole breast, pectoral fascia and axillary L.Ns. were removed.

Postoperative, follow up for 6 months was done using U\S, sonomammography, or other radiology, in addition to cosmetic follow up and recurrence monitoring.

Statistical Analysis

The collected data was revised, coded, tabulated and introduced to a PC using SPSS 23.0. Data were presented and suitable analysis was done according to the type of data obtained for each parameter. Quantitative variables were described using mean, SD and range. While qualitative variables were described using number and percentage.

Chi-square test was used to compare qualitative variables, and Two-sample t-test was used to compare quantitative variables between independent groups in parametric data.

Paired t-test was used to assess the statistical significance of the difference between two means measured twice for the same study group.

McNemar test was used to assess the statistical significance of the difference between a qualitative variable measured twice for the same study group.

P- Value was considered significant if $P < 0.05$.

3. Results

For demographic and Clinical Characteristics, the sample size was 20 patients, 10 of them were treated with MRM, while the other 10 patients were treated with BCS.

The age of the patients ranged between 41-65 years in the BCS group compared with 45-70 years with a mean age.

In BCS group 6 (60 %) of patients were married compared with 4 (40 %) in the MRM group of patients. There was no statistically significant difference in this distribution.

In BCS group 6 (60 %) of patients were affected on the left side compared with 5 (50 %) in the MRM group of patients. There was no statistically significant difference in this distribution. **(Table 1).**

Table 1: Distribution of the studied patients regarding their demographic and Clinical Characteristics.

	BCS	MRM	p-value
Number of patients	10	10	
Age (Mean S.D)	57.2 12.33	58.2 11.24	**> 0.05**
≤ 50	4 (40 %)	5 (50 %)	**> 0.05**
> 50	6 (60 %)	5 (50 %)	
Marital status			
Married	6 (60 %)	4 (40 %)	**> 0.05**
Not Married a	4 (40 %)	6 (60 %)	
Laterality (affected side)			
Left	6 (60 %)	5 (50 %)	**> 0.05**
Right	4 (40 %)	5 (50 %)	

a. Not married includes divorced, separated, single (never married), unmarried or domestic partner and widowed.

Regarding lesion characterization, in BCS group tumor size was < 2 cm in 6 (60 %) of patients w compared with 5 (50 %) in the MRM group of patients. (2-5) cm in 4 (40%) and 4 (40%) in BCS and MRM groups respectively. One patient in MRM had a (> 5) cm tumor size. This was a statistically significant difference (p-value: 0.047).

In BCS group tumor size was < 2 cm in 6 (60 %) of patients w compared with 5 (50 %) in MRM group of patients. (2-5) cm in 4 (40%) and 4 (40%) in BCS and MRM groups respectively. One patient in MRM had a (> 5) cm tumor size. This was a statistically significant difference (p-value: 0.047).

In BCS group tumor grade II was in 3 (30 %) of patients compared with 2 (20 %) in the MRM group of patients. tumor grade III and IV were in 7 (70%) and 8 (80%) in BCS and MRM groups respectively. This was a statistically significant difference (p-value: 0.001).

In BCS group N0 presented in 7 (70 %) of patients compared with 8 (80 %) in the MRM group of patients. N1 was in 3 (20%) and 2 (20%) in BCS and MRM groups respectively. N2 presented in only one patient in the BCS group. This was a statistically significant difference (p-value: 0.022). **(Table 2)**

Table 2: Distribution of the studied patients regarding tumor size, tumor stage, tumor grade, and Lymph node involvement.

	BCS	MRM	p-value
T-size			
T1 (< 2)	6 (60%)	5 (50%)	**0.047**
T2 (2-5)	4 (40%)	4 (40%)	
T3 (> 5)	0 (0%)	1 (10%)	
T-stage			
Tmic/T1a/T1b	2	2	**0.035**
T1c	5	6	
T2	3	2	
Grade			
I	0	0	**0.001**
II	3	2	
III and IV	7	8	
Lymph node involvement			
N0	7	8	**0.022**
N1	2	2	
N2	1	0	

The hospital stay ranged from 1 to 3 days in the BCS group and from 2 days to 4 days in the MRM group.

Regarding metastasis development, in BCS group Loco-regional recurrence occurred in 1 (10 %) of patients and 1 (10 %) in the MRM group of patients. Distant metastases occurred in 1 (10 %) and 1 (10 %) in BCS and MRM groups respectively. Loco-regional and distant metastases occurred in only one patient in the BCS group. This was statistically non-significant (p-value: > 0.05).

Regarding wound healing time, In BCS group Wound healing time was 6.1 ± 2.34 days compared

with 7.4 ± 3.36 in MRM group of patients. This was statistically non-significant (p-value: > 0.05).

As for Wound complications, In BCS group seroma formation occurred in 1 (10%) of patients and 1 (10%) in the MRM group of patients equally. Wound infection occurred in only one patient in the MRM group of patients. Considering a small sample size, this was statistically non-significant (p-value: > 0.05). **(Table 3).**

Table 3: Distribution of the studied patients regarding Wound healing time, complications

	BCS	MRM	p-value
Wound healing time			
Mean ± SD	6.1 ± 2.34	7.4 ± 3.36	**> 0.05**
Wound complications			
Seroma formation	1	1	**> 0.05**
Wound infection	0	1	

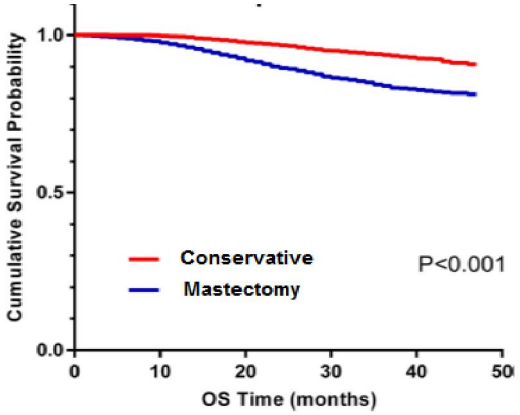

Figure 1: Comparison of survival between mastectomy and BCS

We compared the Overall Survival in patients with TNBC tumors managed by BCS with those managed by mastectomy. The Kaplan-Meier analysis showed that BCS was associated with better Overall Survival than mastectomy (P < 0.001) **(Figure 1).**

In the Multivariate analysis, the BCS group was associated with superior survival comparing to the mastectomy group (HR, 0.579; 95%CI, 0.488 to 0.687; P < 0.001, for Overall Survival). **(Table 4).**

Table 4: Multivariate Cox proportional hazard regression model of overall survival (OS)

Variables	OS	
	HRs (95% CI)	***Pc***
Marital status		
Married	Reference	Reference
Not Married	1.308 (1.129–1.516)	**< 0.001**
Grade		
I	0.263 (0.085–0.820)	***0.021***
II	**0.879 (0.707–1.093)**	**0.246**
III and IV	Reference	Reference
Lymph node envolvement		
N0	Reference	Reference
N1	1.902 (1.540–2.349)	**< 0.001**
N2	3.858 (2.527–5.889)	**< 0.001**
Tumor Size (cm)		
T1 (< 2)	Reference	Reference
T2 (2-5)	1.534 (1.163–2.022)	**0.002**
T3 (> 5)	2.862 (2.069–3.958)	**< 0.001**

After multivariate adjustment, no significant difference between loco-regional treatments in grade I (HR, 0.529; 95% CI, 0.032 to 8.626; P = 0.655, for OS) and stage I (HR, 0.737; 95% CI, 0.497 to 1.095; P = 0.131, for OS) was reported **(Table 5).**

Table 5: Stratified according to clinical variables

Variables	BCS VS mastectomy	
	HRs (95% CI)	***Pc***
Age at Diagnosis (y)		
20–49	0.756 (0.556–1.026)	0.073
50–79	0.492 (0.400–0.606)	**< 0.001**
Histologic Grade		
I	0.529 (0.032–8.626)	0.655
II	0.558 (0.346–0.898)	**0.016**
III and IV	0.553 (0.460–0.666)	**< 0.001**
T-stage		
Tmic/T1a/T1b	0.737 (0.497–1.095)	0.131
T1c	0.560 (0.443–0.708)	**< 0.001**
T2	0.483 (0.340–0.686)	**< 0.001**
Tumor Size (cm)		
T1 (< 2)	0.690 (0.504–0.946)	**0.021**
T2 (2-5)	0.528 (0.420–0.664)	**< 0.001**
T3 (> 5)	0.525 (0.317–0.869)	**0.012**
LN Status		
N0	0.626 (0.487–0.804)	**< 0.001**
N1	0.532 (0.389–0.727)	**< 0.001**
N2	0.536 (0.325–0.885)	**0.015**

4. Discussion

Breast cancer is considered the most common cancer in women throughout the world ***(12).*** Both radiotherapy and breast conserving surgery (BCS) have been reporting similar results regarding local control and survival comparing to more radical procedures used in the treatment of breast cancer ***(1).***

In this study, we compared between BCS and MRM in TNBC patients in 20 patients form different Egyptian hospitals, 10 patients treated with MRM and 10 patients treated with BCS. The patient's age in both groups were between 40-70 years.

There was no statistical difference regarding the marital status between both groups where 60 % of BCS patients were married comparing to 40 % in the MRM group.

Regarding the site of the tumor, no statistical difference was recorded between both groups where60 % of patients in the BCS group were affected on the left side compared with 50 % in the MRM group.

The size of the tumor in the BCS group was < 2 cm 60 % of patients, compared with 50 % in the MRM group. 40% of patients had (2-5) cm tumors in both groups. One patient in the MRM group had a tumor larger than cm (p-value: 0.047).

In a previous study, TNBC tumors larger than 5 cm in size treated with BCS were associated with better survival rates compared to tumors managed by mastectomy.

The National Comprehensive Cancer Network (NCCN) reported different results where TNBC tumors larger than 5 cm in size managed with BCS were associated with a higher risk of recurrence ***(13)***.

The results of another previous study reported that TNBC tumors were associated with a greater risk of distant relapse than other hormone receptor-positive tumors. Although TNBC tumors are currently classified to have a lower risk of LRR. The authors recommend for such tumors to be managed with adjuvant chemotherapy ***(14)***.

On the other hand, another study reported that TNBC tumors were associated with lower risk of axillary LN involvement, and reported the size of the tumor to be an unreliable factor in predicting the involvement of the lymph nodes ***(15)***.

Taking into consideration the results of all of the previously mentioned studies, and the recent

recommendations suggesting that the size of the tumor cannot predict the involvement of the LNs, and the higher risk of LRR associated with TNBC tumors managed with MRM compared with BCS, many studies suggest that the plan of loco-regional treatment after MRM should not be set according to the previously mentioned prognostic factors ***(16).***

In our results, 30 % of patients in the BCS group had grade II was compared to 20 % in the MRM group. While 70% of patients in the BCS group had grade III and IV tumors compared to 80% MRM group (p-value: 0.001).

In BCS group N0 was presented in 70 %of patients compared with 80 % in the MRM group. While 20% of patients of both groups were presented with N1 tumors. Only one patient in the BCS group was presented with an N2 tumor (p-value: 0.022).

Although previous studies suggested that adjuvant radiotherapy after MRM can be beneficial in T1-2N0 patients, guidelines show that this treatment plan is offered only to patients with LN-positive or T3N0 tumors ***(17,18)***. In our results, the only factor associated with a higher risk of loco-regional recurrence (LRR) in patients with T1-2N0 TNBC tumors was MRM when compared with BCS.

Our results showed that the BCS group was associated with shorter hospital [1-3 days] comparing hot [2-4 days] in the MRM group.

In our results, loco-regional recurrence was recorded only in 10% of patients of both BCS and MRM group. Distant metastases also occurred in 10% of both groups. No statistically significant difference was recorded (p-value: > 0.05).

A previously published study found that MRM in patients with T1-2N0 TNBC were associated with a significantly higher risk of LRR compared with patients managed with BCS where 6% reduction of LRR was recorded compared with patients managed with MRM, no significant difference was reported regarding OS between the BCS and MRM groups ***(19)***.

Similar results were reported by the Early Breast Cancer Trialists' Collaborative Group, where they reported a 20% lower risk of LRR after 5 years and a 5.2% improvement in the15 years overall survival ***(5).***

Our results showed no significant difference in the wound healing time between the BCS and MRM groups (p-value: > 0.05).

Only 10% of both groups developed seroma formation. One patient from the MRM group developed a wound infection. Considering a small sample size, this was statistically non-significant (p-value: > 0.05).

In this study, we investigated the Overall Survival in TNBC tumor managed with MRM comparing to patients managed with BCS. Kaplan-Meier analysis showed BCS was associated with better overall survival comparing to MRM group (P < 0.001). In the Multivariate analysis, excellent survival was reported in the BCS group when compared with the mastectomy group (HR, 0.579; 95%CI, 0.488 to 0.687; P < 0.001, for Overall Survival).

After multivariate adjustment, there was no significant difference between loco-regional treatments in grade I (HR, 0.529; 95% CI, 0.032 to 8.626; P = 0.655, for OS) and stage I (HR, 0.737; 95% CI, 0.497 to 1.095; P = 0.131, for OS). Many previous prospective and retrospective randomized controlled trials reported similar results where long-term survival of early-stage breast cancer patients managed with BCS was superior to patients managed with mastectomy (***13)***.

Recently, a Dutch population-based study compared between BCS and MRM regarding the 10-year overall survival and breast relative survival in early breast cancer patients (T1–2, N0–1, M0), reported the superiority of BCS ***(20).***

A previous study published in 2011 reported that T1-2N0 TNBC tumors managed with mastectomy without further radiotherapy were associated with increased risk of LRR compared with cases managed with BCS ***(21).***

Additionally, most of the studies investigating the loco-regional treatment of TNBC patients had relatively small sample sizes and were associated with inconsistent outcomes. In 2011, Adkins et al. compared between BCS and MRM regarding the five-year LRR survival and distant metastasis survival rates in 1325 TNBC patients, and reported better survival rates associated with the BCS group ***(22).***

Furthermore, a cohort study of 1,138 Asian TNBC patients managed using BCS, mastectomy alone or mastectomy plus RT reported no significant difference between the three groups regarding the adjusted risks of mortality ***(23).***

Our study had several limitations. In terms of sample size, follow-up data, it is a well-known fact that documentation is not accurate in our institutions. In addition to the poor compliance of our patients. Therefore, we were compelled to focus on the short-term survival outcomes after initial diagnosis and to identify any outcome-related factors.

Conclusion

In conclusion, our results reported superior overall survival in the BCS group compared to mastectomy. Patients managed using mastectomy suffered from cosmetic impairments, worse outcomes and an avoidable deterioration in quality life during the surgical decision-making process.

Therefore, we recommend BCS is a preferable line of management in patients with TNBC tumors when given adequate adjuvant treatment.

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