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ORIGINAL ARTICLE

Breast – conserving Surgery in Early – Stage Triple – Negative Breast Cancer: Is There a Higher Risk of Locoregional Recurrence?

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Summary
Introduction. Triple- negative breast cancer (TNBC) is an aggressive disease with poor prognosis and high risk of locoregional recurrence (LRR).
Aim of the Study. Is to examine the impact of type of surgery on locoregional recurrence in women with early- stage invasive triple-negative breast cancer (TNBC).
Materials and Methods. A total of 68 women with stage I- II (T1N0M0, T2N0M0, T1N1M0, or T2N1M0) invasive, unifocal TNBC with hitologically tumor- free surgical margins were included. Patients were stratified into two groups according to surgical treatment, breast- conserving therapy (BCT) in 36 of 68 patients versus mastectomy in 32 of 68 patients. The two common founder mutations in *BRCA1 (4153delA and 5382insC)* in Latvia were tested using a multiplex- specific polymerase chain reaction(PCR) assay. Clinicopathological data and survival outcomes were analyzed.
Results. There were no statistically significant differences in relation to age, stage, tumor size, histological type, tumor grade and nodal status between two groups. 24 patients (77.4%) in the mastectomy group and 27(75%) patients in the BCT group received chemotherapy, these difference was not statistically significant. 10(32.2%) of 32 patients in the mastectomy group and 34(94%) of 36 patients in the BCT group received postoperative radiation (P< 0.0001). There was no statistically significant difference noted in rates of distant metastases (5 cases (16.1%) in the mastectomy group versus 4 cases (11.1%) in the BCT group; P < 0.725)). A higher proportion of patients in the BCT group experienced locoregional recurrence compared with patients in the mastectomy group (3 cases (8.3%) versus 0 case (0%), respectively), but this did not reach statistical significance (P< 0.241). It was found that the tumor histology, grade, age at presentation and *BRCA1* mutation status were not significant predictors of local recurrence. There was no significant difference in 5- year breast cancer- related survival between two groups (P>0.05).
Conclusions. Patients after BCT have a higher locoregional recurrence rates compared to mastectomy, but this did not reach statistical significance. According to our study data BCT is not a contraindication in the TNBC.
Key words: triple- negative, breast- conserving therapy, locoregional recurrence.

INTRODUCTION

Triple- negative breast cancer (TNBC) accounts for approximately 15% of all breast cancer subtypes and is characterized by the lack of expression of estrogen receptor (ER), progesterone receptor (PR), and the human epidermal growth factor receptor 2 (HER2). TNBC serves as an immunohistochemical surrogate of basal- like breast cancer subtype, with the accuracy of identification for approximately 80- 97% (7). TNBC is biologically aggressive, BRCA1- related disease associated with poor prognosis, early relapse and shorter survival (1, 2, 4, 7). In the TNBC group distant recurrence risk rises rapidly in the first 3 years after diagnosis. Most distant recurrences and deaths occur within 5 years after diagnosis. There are conflicting data about locoregional recurrence rate in TNBC. Njugen et al. reported significantly higher risk of local recurrence rate in patients with TNBC who underwent BCT versus non- TNBC (adjusted HR 7.1; P= 0.009) (6). In contrast, other groups demonstrated no statistically significant difference in locoregional recurrence between TNBC and other cancer subtypes (3, 5).

AIM OF THE STUDY

The aim of this study is to examine the impact of type of surgery on locoregional recurrence in women with early- stage invasive TNBC.

MATERIALS AND METHODS

Materials

A total of 68 women with stage I- II(T1N0M0, T2N0M0, T1N1M0, or T2N1M0) invasive, unifocal TNBC with hitologically tumor- free surgical margins were included. Patients were stratified into two groups according to surgical treatment, breast- conserving therapy(BCT) in 36 of 68 patients versus mastectomy in 32 of 68 patients. Clinicopathological data and survival outcomes were analyzed.

Microscopic investigation

Histological parameters of all cases were reviewed by a pathologist. Histological type and grade of ductal breast cancers was determined for each case according to the Bloom-Richardson system. The specimens were selected based on the formalin-fixed, paraffin-embedded breast carcinoma tissue blocks from the primary tumors obtained from the archives of the RAKUS Department

of Pathology and Pauls Stradins Clinical University Hospital. Tumor at surgical margins was considered positive.

Immunohistochemical analysis

For this study, triple-negative breast cancers were defined as those that were ER negative, PR negative, and HER2 negative.

ER and PR status were determined using immunochemistry. For ER and PR, monoclonal antibodies were from *DakoCytomation, Glostrup*, Denmark, with cutoff levels for receptor positivity of more than 0%.

The assessment of HER-2/neu expression was carried out using the *HercepTest* kit according to the manufacturer's instructions.

Genetic testing

The two common founder mutations in *BRCA1* (4153delA *and 5382insC)* in Latvia were tested using a multiplex- specific polymerase chain reaction (PCR) assay.

Results interpretation

ER and PR are considered negative if immunoperoxidase staining of tumor cell nuclei is 0 %. HER2 was assessed through immunohistochemistry (IHC). IHC is scored on a qualitative scale from 0 to 3+, based on interpretation of staining intensity, with 0 and 1+ classified as negative (0- are considered, if staining of tumor cell membrane are less than 10%, and 1+, if more than 10% of tumor cell membrane stains partly).

The outcomes were analysed in all 68 patients. Follow up has been maintained by reviewing clinical charts. Relapses after 90 days were considered events. Local recurrence was considered as clinical and histological documented relapse in ipsilateral breast or regional lymphnodes.

Distant recurrence was considered as clinical disease distant evidence detected clinically and radiographically.

Statistical analysis: a SPSS statistical software version 12 and Microsoft Excell programm were used for statistical data analysis. Following data were analysed:

1) frequency analysis – were analysed frequencies,
2) descriptive statistics – were analysed minimal, maximal and average value, as well as standart deviation,
3) pair correlation analysis (Spearmans test), having detected p- value and correlation coefficient –r.
4) 5- year breast cancer- related survival- were conducted using the Kaplan- Meier curves.

RESULTS

Median age at presentation was 59.1 years (range, 27-84 years) in the mastectomy patient group and 53.4 years (range, 31-82 years) in the BCT patient group. There were no statistically significant differences in relation to age, stage, tumor size, histological type, tumor grade and nodal status between two groups (Table 1). 24 patients (77.4%) in the mastectomy group and 27(75%) patients in the BCT group received chemotherapy, these difference was not statistically significant (Table 2). 10(32.2%) of 32 patients in the mastectomy group and 34(94%) of 36 patients in the BCT group received postoperative radiation (P< 0.0001). The median dose to the whole breast was 46 Gy in the mastectomy group and 50 Gy in the BCT group at 1.8- 2.0 Gy/fraction. The median cavity boost in the BCT was 10 Gy at 2 Gy/fraction. 4 patients from 15 tested in the mastectomy patient group were positive for *BRCA1* mutation, compared with 3 patients from 26 tested in the BCT group. The median follow-up period was 42.2 months (range, 9- 84 months). There was no statistically significant difference noted in rates of distant metastases (5 cases (16.1%) in the mastectomy group versus 4 cases (11.1%) in the BCT group; P < 0.725)). All patients with distant metastases in the mastectomy group received previous adjuvant chemotherapy (in 4 cases (80%) - anthracycline- based regimen, in 1 case (20%) - standard CMF). In the BCT group 1 patient (25%) with distant metastases received previous anthracycline- based regimen, 2 patients (50%) - standard CMF regimen and 1 patient (25%) received no chemotherapy. A higher proportion of patients in the BCT group experienced locoregional recurrence compared with patients in the mastectomy group (3 cases (8.3%) versus 0 case (0%), respectively), but this did not reach statistical significance (P< 0.241). It was found that the tumor histology, grade, age at presentation and *BRCA1* mutation status were not significant predictors of local recurrence. All patients in the BCT group who experienced local recurrence had received prior radiotherapy. There were 6(18.7%) deaths in the mastectomy group and 6(16.7%) deaths in the BCT (P=1). There was no significant difference in 5- year breast cancer- related survival between two groups (P>0.05) (Fig.1).

DISCUSSION

To date, a limited number of studies have compared outcomes of TNBC patients after BCT and mastectomy. Parker et al. reported higher local recurrence rate in the mastectomy group versus BCT, but this did not reach statistical significance. The 5-year overall survival, in this study, was better for the BCT group than for the mastectomy group (89% versus 69%; P = 0.018). This was likely due to unsatisfactory balanced groups, the mastectomy group had larger neoplasm size (T3/T4: 4% BCT versus 27% mastectomy; P = 0.0002), advanced N-disease (N2/3: 8% BCT versus 25% mastectomy; P = 0.0003), and advanced stage of disease (stage 3: 8% BCT versus 35% mastectomy; P < 0.0001)(8). According to our study results patients after BCT have shown a tendency of increased risk of LRR compared to mastectomy, but this did not reach statistical significance and had no impact on 5- year breast cancer- related survival. It was found that the tumor histology, grade, age at presentation and *BRCA1* mutation status were not significant predictors of local recurrence. Both groups, in our study, were good balanced with no statistically significant differences in relation to age, stage, tumor size, histological type, tumor grade and nodal status

and number of patients treated with chemotherapy between two groups. All patients in the BCT group who experienced local recurrence had received prior radiotherapy. Although, in the mastectomy group there were a relatively low proportion of patients who received adjuvant radiotherapy, there were no local recurrences during follow- up period (51.8 months, range 9- 84 months).

As with many studies, there some limitations. Although, our study size is relatively small, both groups are good balanced.

Our follow- up period of 3.5 years is relatively short. Dent et al. reported that the risk of any recurrence in the TNBC is high in 1-3 years after diagnosis with majority occuring within the first 5 years(2). Thus, our follow- up period is quite adequate to distinquish the majority of treatment outcomes.

CONCLUSIONS

Patients after BCT have a higher locoregional recurrence rates compared to mastectomy, but this did not reach statistical significance. According to our study data BCT is not a contraindication in the TNBC.

Figures and tables.

Table 1. Patient and clinical characteristics by operative treatment

Variable	BCT (N= 36), n (%)	Mastectomy group (N= 32), n (%)	P- value
Mean age at diagnosis	53.4 years	51.8 years	P=0.119
Mean follow-up (m)	33.8 months	51.8 months	
Tumor size	21 mm	23.7 mm	P=0.375
T stage			
T1	19(52.8%)	13(40.6%)	P=0.739
T2	17(47.2%)	19(59.4%)	
Lymph node status			
N0	27(75%)	19(59.4%)	P=0.394
N1	9(25%)	13(40.6%)	
Histology			
Ductal	27(75%)	17(53.1%)	
Lobular	4(11.1%)	9(28.1%)	P=0.166
Other	5(13.9%)	6(18.8%)	
Tumor grade			
I	2(7.4%)	1(5.9%)	
II	5(18.5%)	1(3.1%)	
III	16(59.3%)	15(88.2%)	P=0.411
Unknown	4(14.8%)	0(0%)	

Table 2. Characteristics of received chemotherapy in the mastectomy group and BCT group

Chara-cteristic	All patients (N= 68), n (%)	BCT (N= 36), n (%)	Maste-ctomy group (N= 32), n (%)	P- value
Adjuvant chemo-therapy Anthra-cycline based	33(48.5%)	21(58.3%)	12(37.5%)	P=0.674
Anthra-cycline + Taxane based	2(2.9%)	1(2.8%)	1(3.1%)	
CMF	13(19.2%)	5(13.9%)	8(25%)	
Cisplatin-based	2(2.9%)	0(0%)	2(6.2%)	
No chemo-therapy	18(26.5%)	9(25%)	9(28.2%)	

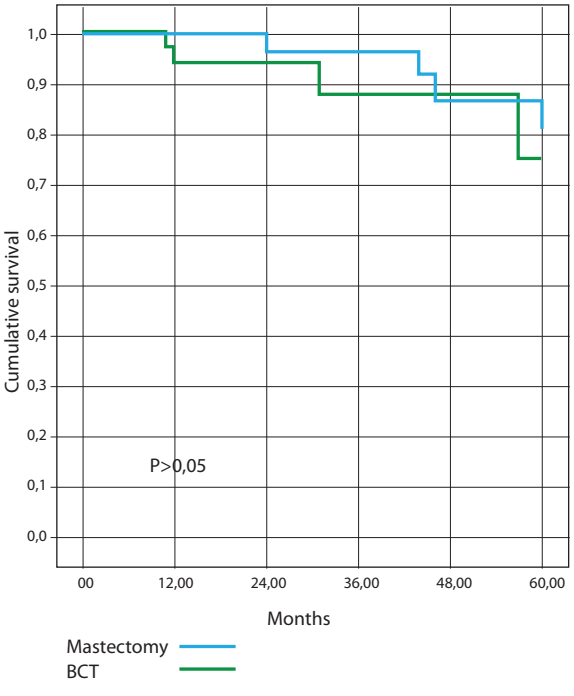

Fig. 1. Breast cancer- related survival curves of patients after mastectomy and BCT.

Conflict of interest: None

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