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ORIGINAL ARTICLE

Overall Survival Among Breast Cancer Patients After Surgery: A Retrospective Observational Analysis

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ABSTRACT

Background: Breast cancer is the most common cancer in women. Early diagnosis of breast cancer is challenging. We aimed to identify breast cancer patients' overall survival after conservative surgery or modified radical mastectomy.

Methods: We conducted a retrospective observational study of breast cancer patients treated with conservative surgery or modified radical mastectomy between 2012 and 2019. We performed Cox regression and Kaplan-Meier survival analyses, using Statistical Package for the Social Sciences (SPSS) software version 23.0.

Results: Of the 70 women treated for breast cancer, 29 women aged ≥50, and 22 women had a tumor size of ≥20. Negative lymph node involvement was noted in 54 women (77.1%) and multifocality in 33 women (47.1%). Neoadjuvant chemotherapy was reported in about one-third of the included women, and the commonest histological type was ductal (87.1%). Positive estrogen, progesterone, and HER2 receptors were reported in 84%, 70%, and 6%, respectively. Seven patients had a local relapse; six of them had it in the first 24 months. The mean recurrence-free survival was 47.06 months. The Cox regression analysis showed that histological grade <G2, negative HER2 receptors, and metastasis were insignificant independent risk factors for overall survival (all p> 0.05). Negative progesterone receptors and positive margins significantly increased the risk by 15.183 and 30.012 folds, with a p-value of 0.028 and 0.003, respectively.

Conclusions: Proper monitoring of breast cancer patients is critical to prevent local relapse and subsequent metastasis and death after surgical operations. Determining the risk factors may provide a proper management plan, good clinical outcome, and improved quality of life and overall survival.

Keywords: Predictive; Survival; Recurrence; Breast Cancer.

INTRODUCTION

Breast cancer is the most common cancer and the second leading cause of cancer-related death in women. Early diagnosis of breast cancer is challenging because it evolves silently and is discovered during the routine examination, or it may present with a palpable breast mass, breast shape or size changes, or nipple discharge [1,2].

Local relapse is a serious complication that occurs after the surgical removal of breast cancer. Its incidence varies between 3% to 15%, mostly in the first follow-up years, and it is associated with poor prognosis and reduced overall survival. The local relapse after mastectomy significantly increases mortality rate and distant metastasis [3,4].

The published literature has documented that after breast cancer surgeries (breast-conserving ones), there is strong evidence of the tumor's distant metastasis and, subsequently, death among the recurrent cases [5]. Identifying the possible risk factors that predict distant metathesis and, subsequently, mortality after surgery may help guide

proper management and guidelines to decrease such sequences and better understand the tumor prognosis and progression.

This study aimed to identify the overall survival among breast cancer patients after conservative surgery or modified radical mastectomy surgeries.

METHODS

The study protocol was approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Zagazig University, Egypt (Approval number: ZU-IRB#5697/19-11-2019). The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

We conducted this retrospective cohort study at the Surgical Oncology Unit at Zagazig University Hospitals, Egypt. Data of female patients of any age treated with conservative surgery or modified radical mastectomy for breast cancer during the study period were collected during the period between 2012 and 2019. We excluded data of male patients or female patients with missing data.

Routinely in our institution, all patients are subjected to (1) complete history taking, (2) demographic data including name, age, residence, occupation, marital status, particular habits of medical importance, and menstrual history, (3) full local and general clinical examination including both axillae for any clinical palpable axillary lymph nodes, (4) mammography and ultrasound of present breast, (5) FNAC or Tru-cut biopsy from breast mass, (6) routine laboratory investigations including complete blood picture, coagulation profile, liver function test, kidney function test, and viral markers, (7) plain X-ray chest and CT chest if needed, and (8) abdominal ultrasonography & CT abdomen & pelvis if needed. The patients' disease-free interval, as well as the relation between local relapse and other variables, were defined.

Statistical Analysis

All analyses were undertaken using Statistical Package for the Social Sciences (SPSS) software version 23.0. Qualitative data were represented as frequency and percentages, while the quantitative data were represented as mean ± standard deviation (SD). Differences between continuous variables were tested using a student t-test or Mann-Whitney test as appropriate. The Chi-square test was used to assess the difference and association of qualitative variables. We used the Kaplan–Meier method to estimate the overall survival time curves; also, we used the cox proportional-hazards models to calculate the hazard ratios (HR) and its 95% confidence intervals. We carried out a univariate analysis to investigate the association between overall survival and baseline patient characteristics. Statistically significant variables were selected for the multivariate logistic regression model. An alpha level below 0.05 was considered for statistical significance.

RESULTS

Seventy women were included in our study. Of them, 58.6% were less than 50 years old, and 68.6 had tumor size <20. Most of the included women had negative LN involvement (77.1%), ductal histological type (87.1%), carcinoma in situ (64.3%), with no lymphovascular involvement (74.3%). About 84%, 70%, and 6% had positive estrogen receptors (ER), progesterone receptors (PR), and HER2 receptors. Metastasis and positive margins were reported in seven and 10 patients out of the 70 patients. The distribution of the studied patients according to demographic and disease-specific characteristics is shown in **Table 1.**

local relapse

Seven patients (10%) had a local relapse; six patients experienced it in the first 24 months. The time for recurrence-free survival (RFS) ranged from 9 to 79 months, with a mean of 47.06 months**.**

Overall survival

Cox regression analysis

Histological grade <G2 and negative HER2 receptors were nonsignificant independent risk factors for survival (HR=0). Metastasis non-significantly increases risk by 24.34 folds. Negative PR and positive margins significantly increased the risk by 15.183 and 30.012 folds, with a p-value of 0.028 and 0.003, respectively **(Table 2).**

Kaplan–Meier Plots

Figures 1-5 shows the Kaplan–Meier plots of the relation between RFS and histological grade (p=0.483), PR (p= 0.015), HER2 receptor (p<0.001), positive margins (p<0.001), and metastasis (p<0.001). The mean RFS was 75.167 months in histological grade <G2 versus 71.564 months in histological grade ≥G2, was 76.163 months in PR positive versus 64.143 months in PR negative, was 37.25 months in HER2 positive versus 74.206 months in HER2 negative, was 52.6 months in patients whose tumors had positive margins versus 75.805 months in patients without positive margins, and was 17.429 months in patients with metastasis versus 75.114 months in patients without metastasis.

Table 1: Distribution of the studied patients according to demographic and disease-specific characteristics

		n= 70 (%)
Age	<50 years	41 (58.6)
	≥ 50 years	29 (41.4)
Tumor size	<20	48 (68.6)
	≥ 20	22 (31.4)
Clinical LN involvement	Positive	16 (22.9)
	Negative	54 (77.1)
Multifocality	Yes	33 (47.1)
	No	37 (52.9)
Neoadjuvant chemotherapy	Yes	22 (31.4)
	No	48 (68.6)
Histological type	Ductal	61 (87.1)
	Lobular	9 (12.9)
Carcinoma in situ	Yes	45 (64.3)
	No	25 (35.7)
Lymphovascular involvement	Yes	18 (25.7)
	No	52 (74.3)
Histological grade	<G2	18 (25.7)
	≥G2	52 (74.3)
Metastasis	Present	7 (10)
	Absent	63 (90)
Positive margins	Present	10 (14.3)
	Absent	60 (85.7)
Estrogen receptor	Positive	59 (84.3)
	Negative	11 (15.7)
Progesterone receptor	Positive	49 (70)
	Negative	21 (30)
HER2	Positive	4 (5.7)
	Negative	66 (94.3)

Table 2: The Cox regression analysis of survival in patients with locally recurrent breast cancer

	β	p-value	Hazard ratio	95.0% CI	
				Lower	Upper
Histological grade	-14.814-	0.930	0.000	0.000	6.147E+137
Progesterone receptors	2.720	0.028*	15.183	1.348	171.000
HER2	-16.936-	0.920	0.000	0.000	7.405E+136
Positive margin	3.402	0.003*	30.012	3.080	292.425
Metastasis	3.192	0.088	24.340	0.620	955.542

FIGURES

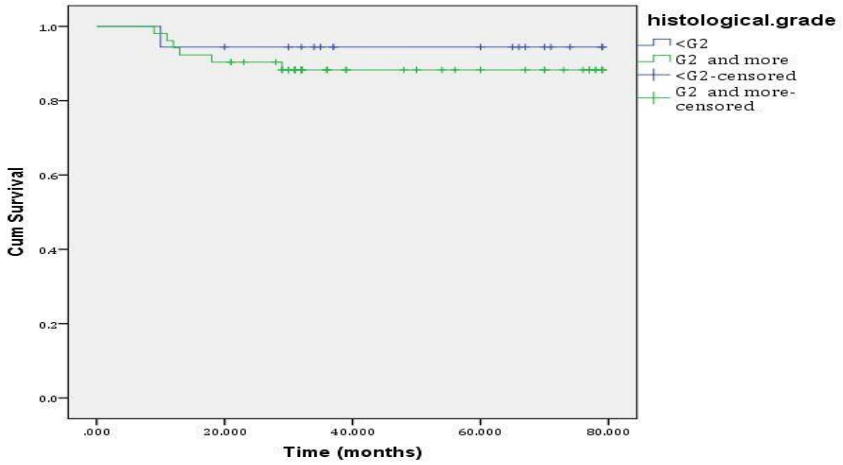

Figure 1: Kaplan Meier plot showing the relation between RFS and histological grade (p=0.483).

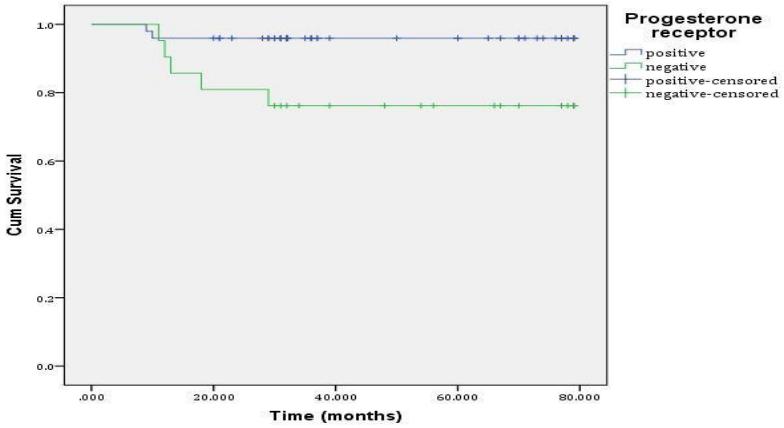

Figure 2: Kaplan Meier plot showing the relation between RFS and PR (p=0.015).

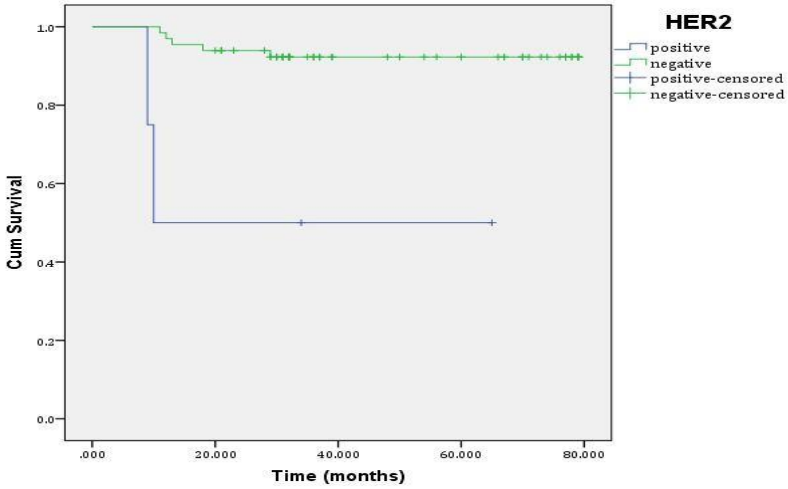

Figure 3: Kaplan Meier plot showing the relation between RFS and HER2 receptor (p<0.001).

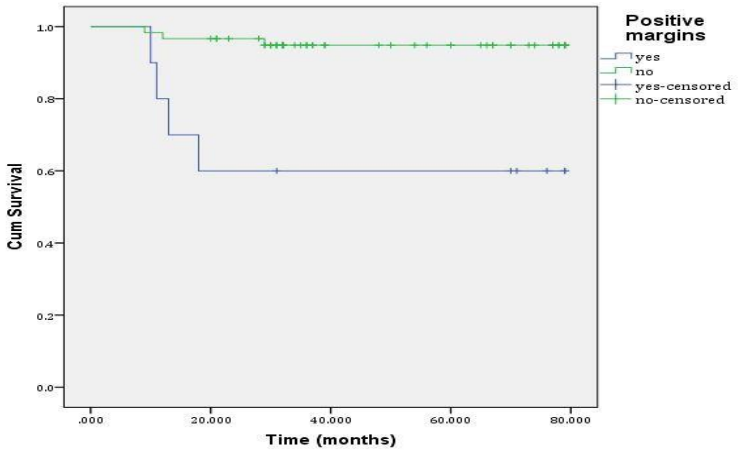

Figure 4: Kaplan Meier plot showing the relation between RFS and positive margins (p<0.001).

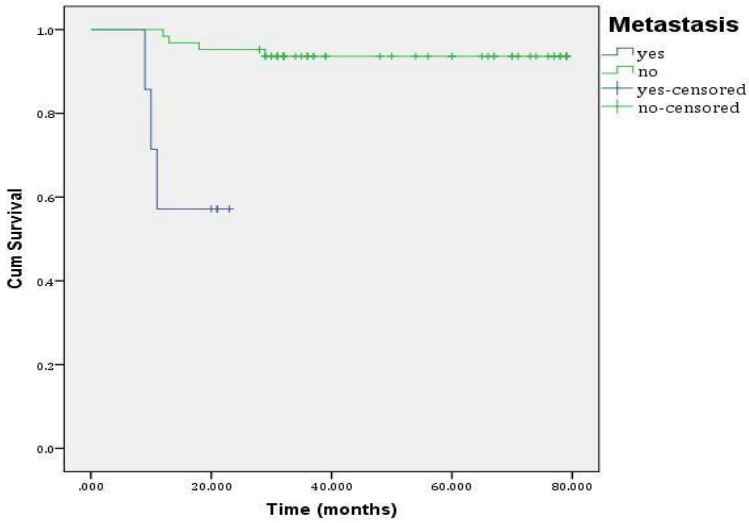

Figure 5: Kaplan Meier plot showing the relation between RFS and metastasis (p<0.001)

DISCUSSION

Breast cancer is the most common cancer diagnosed among women [4]. All patients who have been treated for breast cancer have concerns about the disease recurrence, either local or distal. In our study, we evaluated the recurrence and overall survival through the follow-up of 70 patients. The local relapse occurred in 7 patients, with a rate of 10%. The recurrence occurred during the first 24 months in 6 patients. According to Engelhardt et al., the range for local relapse risk was from 3 up to 15% [3].

In 2016, Roué et al. documented that, in younger patients and patients with triple-negative, the recurrence mainly occurs during the first few years after surgery 6. Strasser-Weippl and Goss, 2013, documented that the rate of 5-year free-of-disease in these patients is >80% [7]. Recently in 2017, Liu et al. reported that the recurrence rate among patients with carcinoma in situ was 45%; also, they reported that two factors (location of the tumor as well as its histopathological characteristics) are critical to differentiate recurrence from the newly formed tumors, that holds better outcomes and prognosis [8].

Our study included 45 patients with carcinoma in situ; of the seven recurrent cases, four patients had a local relapse (57.14%). This percentage is slightly high due to the small number of carcinoma cases in situ included in our study compared to their study. We included 18 patients with a histological degree of less than 2; of them, only one patient had a local relapse (14.3%) and 52 patients with a histological degree of more than 2; 6 patients had a local relapse (85.7%). In Tamura et al., 2016, the authors reported that younger patients present a widely studied hormonal component, facilitating tumor recurrence. According to their study, local relapse occurred in 65% of the patients below 50 years old, and they

survived a longer duration and had an influenced disease-free interval [9].

Additionally, Roué et al., 2016 reported that local relapse occurred in 70% of patients below 50 years old [6]. In our study, patients below 50 years old were 41; 5 of them had a local relapse with a percentage of 71.4%, while patients above 50 years old were 29, 2 of them had a local relapse with a percentage of 28.6% of the recurrent cases. Steward et al., 2014 documented that the patients present with large tumors, with axillary involvement or triple-negative ones, would probably have unfavorable outcomes rather than the treatment [10]. They reported that triple-negative patients have a high risk of distant metastasis rather than local recurrence, affecting the overall survival and mortality rate.

Evidence has highlighted the relationship between local recurrence and metastasis, subsequently reduced overall survival [10,11]. In their study, Rezai et al., 2015 documented that the survival rate was lower depending on the time of onset and the location, with the poorest rates for brain metastases [12]. We observed such a relationship in our study. Of the seven recurrent cases, three of them had local recurrence. Of the 63 patients who did not have metastasis, four patients had a local recurrence. These results should be considered with caution because, from a statistical point of view, this experience corresponded to only one center and was conducted on a limited number of patients; however, most of our outcomes agreed with those reported in the literature. Moreover, the retrospective study design restricts the generalization of these data.

In conclusion, because of the recent early diagnosis techniques and screening programs for the population at risk, local relapse rates have decreased. Moreover, the selective surgical approach to manage the small-sized non-palpable lesions and the advanced adjuvant treatments played a critical role in such decline. However, there will always be factors influencing a patient's prognosis, and these should be taken into account in planning the follow-up. A close follow-up should be provided for women who underwent surgery for breast cancer during the first years, which holds a high possibility for recurrence. Half of the recurrent cases will have distant metastases and less overall survival; this should be considered, and the factors affecting these outcomes should be evaluated.

REFERENCES

1. Mahvi DA, Liu R, Grinstaff MW, Colson YL, Raut CP. Local Cancer Recurrence: The Realities, Challenges, and Opportunities for New Therapies. CA Cancer J Clin. 2018;68(6):488-505

2. Narod SA. Personalised medicine and population health: breast and ovarian cancer. Hum Genet. 2018 Oct;137(10):769-78.

3. Engelhardt, E. G., Garvelink, M. M., de Haes, J. H., van der Hoeven, J. J., Smets, E. M., Pieterse, A. H., et al. Predicting and communicating the risk of recurrence and death in women with early-stage breast cancer: A systematic review of risk prediction models. Journal of Clinical Oncology 2014 32:3, 238-50

4. Kolben, T., Schwarz, T. M., Goess, C., Blume, C., Degenhardt, T., Engel, J., et al. Surgical management of ipsilateral breast tumor recurrence, International Journal of Surgery Int J Surg. 2015 Nov;23(Pt A):141-6.

5. Anderson, S. J., Wapnir, I., Dignam, J. J., Fisher, B., Mamounas, E. P., Jeong, J. H., et al. Prognosis after ipsilateral breast tumor recurrence and locoregional recurrences in patients treated by breast-conserving therapy in five National Surgical Adjuvant Breast and Bowel Project protocols of node-negative breast cancer. Journal of clinical oncology. J Clin Oncol. 2009 May 20;27(15):2466-73.

6. Roué T, Labbé S, Belliardo S, Plenet J, Douine M, Nacher M. Predictive Factors of the Survival of Women With Invasive Breast Cancer in French Guiana: The Burden of Health Inequalities. Clin Breast Cancer. 2016 Aug;16(4):e113-8.

7. Strasser-Weippl K, Goss PE. Competing risks in low-risk breast cancer. American Society of Clinical Oncology educational book. ASCO Educational Book 2013:32-9.

8. Liu Y, Dong C, Chen L. The clinicopathological features of second primary cancer in patients with prior breast cancer. Medicine (Baltimore). 2017 Apr;96(16):e6675.

9. Tamura, N., Tsuda, H., Yoshida, M., Hojo, T., Akashi-Tanaka, S., Kinoshita, T., et al. Clinicopathological predictive factors for ipsilateral and contralateral events following initial surgery to treat ductal carcinoma in situ. Breast Cancer. 2016 May;23(3):510-8.

10. Steward L, Conant L, Gao F, Margenthaler JA. Predictive factors and patterns of recurrence in patients with triple negative breast cancer. Annals of Surgical Oncology. 2014 Jul;21(7):2165-71.

11. Bogina, G., Lunardi, G., Coati, F., Zamboni, G., Gori, S., Bortesi, L., et al. Progesterone receptor status and clinical outcome in breast cancer patients

with estrogen receptor-positive locoregional recurrence. Tumori. 2015 Jul-Aug;101(4):398-403.

12. Rezai M, Kraemer S, Kimmig R, Kern P. Breast conservative surgery and local recurrence. Breast. 2015 Nov;24 Suppl 2:S100-7.

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