Suez Canal University Medical Journal Vol. 26 (6), 2023
Pages 20-31

Comparison of Survival Rate of Triple Negative *versus* Luminal B HER2 neu-positive Breast Cancer Patients in Oncology Medicine Center in Suez Canal University Hospital

Mai M. Mandor*, Mahinour M. Atef, Fifi M. El-Sayed, Soheir E. Abdel-Mohsen

Department of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Suez Canal University, Egypt

Abstract

Background: **Triple-negative breast cancer (TNBC) and Triple-positive breast cancer (TPBC) pose a greater likelihood to recur both locally, regionally, and metastatically affecting patients' survival.** ***Aim:*** **To compare clinicopathological differences between TNBC and TPBC and assess possible associations of the parameters with recurrence and survival.** ***Methods:*** **Retrospective cohort study, and medical records present at the Clinical Oncology and Nuclear Medicine Department SCUH between January 2010 and December 2018 were used to compare clinicopathological variables and DFS between both groups.** ***Results:*** **Hundred breast cancer patients, fifty in each group. There was a significant difference regarding tumor stage (T) where 74% of TNBC had T2 stage and 44% of TPBC. 88% of TNBC had IDC compared to 68% of TPBC. Liver metastasis was the most common site in both groups followed by bone and lung. Three-year DFS was 73.5% and 77.5% in TNBC and TPBC respectively. Seven-year DFS was higher in patients with TNBC (60.5%) than in patients with TPBC (45%) but wasn't statistically significant. Regression analysis showed that patients without LVI had significantly 2.6 years higher in DFS time than patients with LVI in the TNBC group.** ***Conclusion:*** **Diabetes and hypertension were the most reported comorbidities in both groups. There were significant differences regarding IDC, ENE, LVI, and PNI. However, there was no significant difference between both groups regarding the net disease progression. However, LVI was found to have a significant impact on this progression in each group separately.**

***Keywords*:** Breast Cancer, TPBC, TNBC, Clinicopathological, DFS

Introduction

Breast cancer (BC), which is considered the most widespread malignancy present in women, exhibits significant heterogeneity. The molecular type of BC is important to guide different treatment modalities and to alter the survival of patients' treatable stage, breast cancer has a 97% probability of surviving 5 years. However, women's likelihood of surviving 5 years decreases to 20% once it spreads to other body parts[1]. Regarding molecular classification, breast cancer is classified into 4 subtypes based on the expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 neu (HER2 neu). Positive expression of ER/PR and/or HER2 neu determines the ER-positive and/or HER2-positive subtype, while the absence of ER, PR, and HER2 neu expression defines triple-negative breast

*Corresponding Author: maimandor18@gmail.com

cancer (TNBC), known also as a basal-like subtype[2]. Both ER-positive and HER2-positive subtypes are routinely and effectively treated with specific targeted therapy. In contrast, TNBCs lack targeted therapy and are still being treated with systemic chemotherapy drugs[3]. Triple-negative breast cancer (TNBC) accounts for 15%–20% of breast cancer patients[4]. Triple-positive breast cancer (TPBC) is thought that roughly 20% to 25% of breast cancers are HER2-positive[5]. TNBC patients are younger in age, with increased tumor size, higher recurrence incidence, and metastasis[6]. It tends to be present with more aggressive clinical features and tends to recur earlier, which makes it one of the most aggressive subtypes of breast cancer[7]. TNBC has a higher response rate than luminal but with shorter disease-free survival (DFS) and overall survival (OS). While luminal B HER2 neu-positive breast cancer patient (TPBC) also has higher tumor grade, larger tumor size, and exhibits worse prognosis with a distinct profile of response to hormonal therapy and chemotherapy in view of Her2 neu overexpression[8]. So, this study aimed to identify clinicopathological features and patient survival in a cohort of Egyptian women diagnosed with breast cancer, comparing triple-negative breast cancer (TNBC) with luminal B HER2 neu-positive breast cancer tumors (triple-positive breast cancer -TPBC-), and assess possible associations of the parameters with recurrence and survival.

Patient and Methods

Research design and setting: An analytical, record-based retrospective cohort study was conducted at the Clinical Oncology and Nuclear Medicine Department of Suez Canal University Hospital (SCUH), Ismailia, Egypt. The patients were identified through the department Registry, and data was obtained through a standardized form from the medical records.

Study population: Breast cancer patients, attending the Clinical Oncology and Nuclear Medicine department in Suez Canal University Hospital in the period between January 2010 and December 2018 and fulfilling the Inclusion Criteria. They were stratified into two groups according to the pattern of hormonal receptors then selection of patients from each group as following: *Group-A: Triple-negative Breast Cancer (TNBC):* Patients with immunohistochemical staining negative for estrogen receptor (ER-), progesterone receptor (PgR-) and Her-2 neu negative and *Group-B: Luminal B HER2 neu-positive breast cancer / Triple Positive Breast Cancer (TPBC):* Patients with immunohistochemical staining positive for estrogen receptor (ER+), progesterone receptor (PgR+) and Her-2 neu positive.

Inclusion criteria: Age between 18-75 years. Patients who underwent surgical resection either by modified radical mastectomy (MRM) or breast conservative surgery (BCS) and histopathologically proven to have cancer breast. *Exclusion criteria:* Luminal A patients (ER+, PR+, Her-2 neu -ve). Double pathology patients. Comorbidities such as ischemic heart disease could affect choosing the appropriate protocol.

Sample size

The study sample was selected by simple random sampling from all cancer patients who were diagnosed with cancer breast by pathology and fulfilled the inclusion and exclusion criteria who attended to Clinical Oncology and Nuclear Medicine department of Suez Canal University Hospital from January 2010 to December 2018. A list of the two groups was done then simple random sampling was selected. The sample size was determined using the

following equation:[9]

$$p_2 = p_1 RR$$

$$p = \frac{p_1 + r p_2}{1+r}$$

$$n' = \frac{\left[Z_{1-\alpha/2}\sqrt{(r+1)p(1-p)} + Z_{1-\beta}\sqrt{rp_1(1-p_1)+p_2(1-p_2)} \right]^2}{r(p_2-p_1)^2}$$

$$n_{exposure} \geq \frac{n'}{4}\left(1+\sqrt{1+\frac{2(r+1)}{n' r |p_2-p_1|}}\right)^2$$

n = Sample size, r = Sample size ratio = 1, Alpha (α): Type 1 error rate = 0.05, Beta (β:) Type 2 error rate = 0.2, P1 = Prevalence of outcome (patient survival) in Non-exposure (Triple negative group) = 0.62 [4], RR: Expected Risk Ratio = 0.5 [4], Therefore, the calculated sample size was 50 participants per group.

Study variables, and data collection

A list of all eligible patients in the specified period from January 2010 to December 2018 was retrieved from the department Registry. The obtained data included: *Background variables:* patient age, and chronic illness (diabetes, hypertension, cardiac and renal disease). *Independent variables:* TNM staging, grade of the tumor, histopathological features, and molecular type. *Dependent variables:* Disease-free survival (DFS): was defined as the interval between the surgery and recurrence (locoregional recurrence) or metastasis, proven by imaging or pathology[4].

Results

The present study was designed as a retrospective cohort study that included 100 breast cancer patients, attending the Oncology and Nuclear Medicine department, SCUH in the period from 2010 to 2018. The study included two groups TNBC and TPBC. This study aimed to compare disease-free survival (DFS), and clinicopathological data between the two study groups. Table 1 shows that there was no statistically significant difference between patients in TNBC and TPBC regarding age group with about 68% of patients were ≤50 years. Meanwhile, about 34% of total population had different comorbidities, with no statistically significant difference between both groups. Diabetes and hypertension were the most reported comorbidities in both groups. Moreover, table 1 also shows that there is a statistically significant difference between the two groups regarding tumor stage (T) where 74% of TNBC had T2 stage compared to 44% of TPBC (p= 0.003). On the other hand, there was no statistically significant difference between both groups and other staging parameters. Meanwhile, there was no statistically significant difference between the two groups regarding the staging of the disease. The most reported stage in TNBC was IIA (24%) and the most reported stage in TPBC was IIIA (32%). Table 2. shows that there is a statistically significant difference between the two groups regarding histopathological type, ENE, LVI, and PVI. Where 88% of TNBC had invasive duct carcinoma (IDC) compared to 68% of TPBC (p= 0.02), Extra-nodal extension (ENE) where 28% of TNBC were positive compared to 52% of TPBC (p= 0.024), Lymphovascular invasion (LVI) where 12% of TNBC were positive compared to 44% of TPBC (p= 0.001) and Peri-neural invasion (PNI) where no patient (0%) with TNBC was positive compared to 20% of TPBC (p= 0.001). On the other hand, there was no statistically significant difference between both groups and other histopathological variables. Regarding the site of metastasis, 34% had metastasis to different sites, with no statistically significant difference between both groups (p=0.53). The liver was reported as the most common site for 1st metastasis location (in both groups) followed by bone and lung. Table 4. shows 3-year and 7-year survival analysis for disease progression; (DFS) of TNBC and TPBC patients.

Table 1. Comparison of Baseline clinical characteristics, laboratory data and staging parameters of study groups				
Variables	**Total** n (%) (n=100)	**Study groups**, n (%) TNBC (n=50)	TPBC (n=50)	**p-value**
Age at diagnosis				
≤50 years	68 (68)	30 (60)	38 (76)	0.13 [b]
>50 years	32 (32)	20 (40)	12 (24)	
Co-morbidities				
Absent	66 (66)	34 (68)	32 (64)	
Present	34 (34)	16 (32)	18 (36)	0.83 [b]
Hypertension	22 (22)	12 (24)	10 (20)	
Diabetes	26 (26)	11 (22)	15 (30)	
TNM staging*				
(T): Tumor				
1	19 (19)	4 (8)	15 (30)	
2	59 (59)	37 (74)	22 (44)	**0.003** [a]
3	16 (16)	5 (10)	11 (22)	
4	6 (6)	4 (8)	2 (4)	
(N): Nodal				
0	29 (29)	20 (40)	9 (18)	
1	25 (25)	11 (22)	14 (28)	0.11 [b]
2	24 (24)	9 (18)	15 (30)	
3	22 (22)	10 (20)	12 (24)	
(M): metastasis				
0	100 (100)	50 (100)	50 (100)	-
Grade				
1	1 (1)	0 (0)	1 (2)	
2	77 (77)	37 (74)	40 (80)	0.47 [a]
3	22 (22)	13 (26)	9 (18)	
TNM staging*				
I (n=10)				
IA	10 (10)	3 (6)	7 (14)	
II (n=36)				
IIA	17 (17)	12 (24)	5 (10)	
IIB	19 (19)	11 (22)	8 (16)	0.2 [a]
III (n=54)				
IIIA	26 (26)	10 (20)	16 (32)	
IIIB	6 (6)	4 (8)	2 (4)	
IIIC	22 (22)	10 (20)	12 (24)	

TNBC; Triple Negative Breast Cancer, TPBC; Triple Positive Breast Cancer.
[a] p-values are based on Fisher's Exact test. Statistical significance at P < 0.05
[b] p-values are based on Chi-square test. Statistical significance at P < 0.05

The 3-year cumulative survival rate was 73.5% and 77.5% of patients with TNBC and TPBC, respectively (Figure 1a). Moreover, there was no statistically significant difference (p =0.6) between both groups regarding their 3-year DFS with a mean

survival time of 2.63 years for TNBC and 2.78 years for TPBC. Regarding 7-year survival analysis for disease-free survival (DFS) of TNBC and TPBC patients, the cumulative survival rates reach 60.5% in TNBC group and drop to 45% for TPBC group (Figure 1b).

Table 2. Comparison of histopathological variable and study groups.

Variables	Total n (%) (n=100)	Study groups, n (%) TNBC (n=50)	Study groups, n (%) TPBC (n=50)	p-value
Histopathological type, n (%)				
Invasive ductal carcinoma (IDC)	78 (78)	44 (88)	34 (68)	
Invasive lobular carcinoma (ILC)	14 (14)	5 (10)	9 (18)	
Mixed	6 (6)	0	6 (12)	**0.02** [a]
Others*	2 (2)	1 (2)	1 (2)	
Site, n (%)				
Right	60 (60)	33 (66)	27 (54)	0.31[b]
Left	40 (40)	17 (34)	23 (46)	
Number, n (%)				
Solitary	75 (75)	40 (80)	35 (70)	0.35 [b]
Multiple	25 (25)	10 (20)	15 (30)	
Lymph nodes, mean ± SD	4.97 ± 6.5	4.38 ± 6.6	5.62 ± 6.2	0.34 [c]
Extra-nodal extension (ENE), n (%)				
Negative	60 (60)	36 (72)	24 (48)	**0.024** [b]
Positive	40 (40)	14 (28)	26 (52)	
Lympho-vascular invasion (LVI), n (%)				
Negative	72 (72)	44 (88)	28 (56)	**0.001** [b]
Positive	28 (28)	6 (12)	22 (44)	
Peri-neural invasion (PNI), n (%)				
Negative	90 (90)	50 (100)	40 (80)	**0.001** [b]
Positive	10 (10)	0	10 (20)	
Margins, n (%)				
Free	94 (94)	46 (92)	48 (96)	0.34 [a]
Positive	6 (6)	4 (8)	2 (4)	

* *Others: phyloid, Ductal Carcinoma In Sito (DCIS) and Lobular Carcinoma In Sito (LCIS)*

[a] p-values are based on Fisher's Exact test. Statistical significance at P < 0.05

[b] p-values are based on Chi-square test. Statistical significance at P < 0.05

[c] p-values are based on an independent t-test. Statistical significance at P < 0.05

However, there was no statistically significant difference between both groups regarding their mean survival time. Multivariable linear regression analysis was used to assess predictors of disease progression among triple-negative breast cancer patients (TNBC) and (TPBC) (Table 5). It was found that patients without Lympho-vascular invasion (LVI) had significantly 2.624 years higher disease-free survival time than patients with LVI (p=0.007) in TNBC while none of the tested predictors was found to have a significant impact on DFS in TPBC.

Discussion

Breast cancer is a heterogeneous disease, with substantial genotypic and phenotypic diversity. (TNBC) accounts for 15–20% of diagnosed breast tumors, with a higher incidence in young women.

Table 3. Comparison of study groups and disease progression.				
Variables	**Total** (n=100)	**Study groups,** n (%)		**p-value**
		TNBC (n=50)	TPBC(n=50)	
Local recurrence				
Absent	90 (90)	45 (90)	45 (90)	0.93 [a]
Present	10 (10)	5 (10)	5 (10)	
Metastasis				
Absent	66 (66)	35 (70)	31 (62)	0.53 [a]
Present	34 (34)	15 (30)	19 (38)	
Location of 1st metastasis:				
Liver	15 (15)	6 (12)	9 (18)	0.5 [a]
Bone	11 (11)	5 (10)	6 (12)	0.7 [a]
Lung	10 (10)	5 (10)	5 (10)	0.9 [a]
Brain	2 (2)	1 (2)	1 (2)	0.9 [a]
Nodal metastasis	7 (7)	2 (4)	5 (10)	0.4 [a]
Location of 2nd metastasis:				
Lung	2 (2)	0 (0)	2 (4)	0.5 [a]
Brain	4 (4)	2 (4)	2 (4)	0.9 [a]
Bone	6 (6)	1 (2)	5 (10)	0.3 [a]
Liver	1 (1)	1 (2)	0 (0)	0.2 [a]

[a] *p-values are based on Chi square test. Statistical significance at P < 0.05*

Table 4. Comparison between the study groups regarding their 3-year and 7-year disease-free survival (DFS).					
Survival duration	**Total**	**Study groups**		**Log rank**	**p-value**
		TNBC	**TPBC**		
3-year DFS					
Cumulative survival rate	**75.7%**	**73.5%**	**77.5%**		
Total survival rate	75.7%	73.5%	77.5%		
Mean survival time	2.71	2.63	2.78	0.25	0.62 [a]
Standard error (SE)	0.072	0.12	0.083		
95% Confidence interval	(2.57 – 2.85)	(2.39 – 2.86)	(2.62 – 2.95)		
7-year DFS					
Cumulative survival rate	**55.4%**	**60.5%**	**45%**	0.68	0.41 [a]
Total survival rate	60.8%	60%	60.8%		
Mean survival time	5.29	5.32	5.15		
Standard error (SE)	0.26	0.41	0.36		
95% Confidence interval	(4.77 – 5.81)	(4.52 – 6.12)	(4.45 – 5.85)		

[a] *p-values are based on the Log-Rank (Mantel-Cox) U test. Statistical significance at P < 0.05*

Also, HER-2 protein overexpression is reported in about 15–20% of primary breast carcinomas and is associated with decreased disease-free survival (DFS) and overall survival (OS)[5,10]. In the past, different studies highlighted the difference in clinic-pathological features and prognosis of patients with TNBC and non-TNBC with diverse results[6]. Thus, this study aimed to identify clinical, and pathological features and compare disease-free survival (DFS) of patients with triple-negative breast cancer (TNBC) and triple-positive breast cancer (TPBC) patients attending Oncology and

Nuclear Medicine Department, Suez Canal University Hospital which is a regional reference for cancer care. Regarding clinical characteristics, 68% of patients were ≤50 years among both groups. An observational study by Sajid et al. showed that TNBC was noted in 65.88% of patients with age<50 years [11].

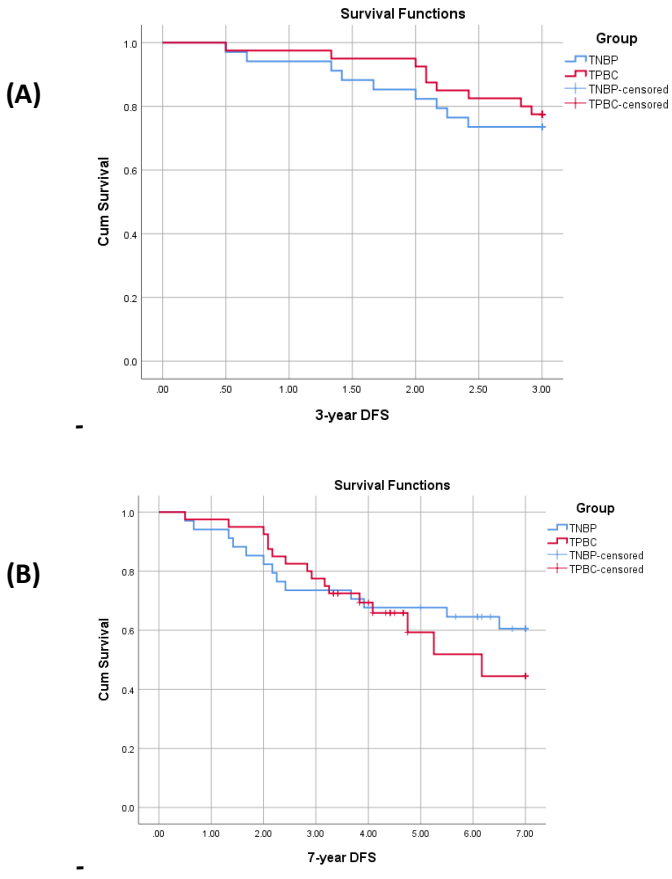

Figure 1. Kaplan Meier curve for (a) 3-year and (b) 7-year disease-free survival (DFS) of triple-negative breast cancer patient (TNPC) vs triple positive breast cancer patient (TPBC) (p-value=0.6).

That was similar to a Mouh et al., study that showed both TNBC and non-TNBC cases occur in younger women, with no statistical difference between the two groups. Some results showed that in all ethnic/racial groups, the incidence of TNBC increased among young patients [12]. For comorbidity, diabetes (26% of the target population) and hypertension (22% of the target population) were the most reported comorbidities in both groups which is similar to the study by Sharma et al., where they reported the incidence of hypertension among BC patients to be 21.8%, and they stated that hypertension is the most prevalent comorbidity associated with BC and similar to a Alzahrani et al. study where half of the patients had co-morbidities and the commonest was hypertension (25.8%) [13,14].

Table 5. Multivariate linear regression for time of disease progression among TNBC and TPBC					
Predictors	**Unstandardized Coefficients**		**Standardized Coefficients Beta**	**95% CI**	**P value**
	B	Std. Error			
TNBC					
(Constant)	0.97	2.066			0.64
ENE					
Negative Vs Positive (R)	-0.457	0.67	-0.092	-1.804 – 0.891	0.49
LVI					
Negative Vs Positive (R)	2.624	0.926	0.381	0.762 – 4.486	**0.007** [a]
TPBC					
(Constant)	3.201	1.169			0.009
ENE					
Negative Vs Positive (R)	0.361	0.616	0.107	-0.878 – 1.6	0.561
LVI					
Negative Vs Positive (R)	0.336	0.694	0.099	-1.061 – 1.733	0.63
PNI					
Negative Vs Positive (R)	-0.058	0.738	-0.014	-1.544 – 1.427	0.93

*****ENE: Extra-nodal extension, LVI; Lympho-vascular invasion,*
PNI: Peri-neural invasion, R; reference group. [a] Statistical significance at P <0.05

Regarding staging parameters, there is a statistically significant difference between the two groups regarding tumor stage where 74% of TNBC had T2 stage compared to 44% of TPBC with no other significance between the two groups regarding other TNM staging parameters and no metastasis present at the time of diagnosis. Worldwide, published data showed that TNBC cases are characterized by bigger tumor sizes and high-grade histology [15]. However, in Mouh et al., there was no statistical difference between the TNBC and non-TNBC groups study. Of particular interest, in a study that conducted a long-term follow-up of 1608 BC patients and found that the recurrence of TNBC did not correlate with the tumor size [12]. Despite the insignificance in nodal parameters in our study, Mouh et al. showed that large tumors and high grade are in favor of a high lymph node metastases incidence. However, the incidence of positive nodes with TNBC is considerably less than non-TNBC [16,17]. Conversely, some other studies showed that there is no statistical correlation of lymph node status between TNBC and non-TNBC groups[18,19]. Moreover, the most reported stage in TNBC was IIA (24%) and the most reported stage in TPBC was IIIA (advanced stage) (32%). In a Chinese cohort, 28% of TNBC and 14% of non-TNBC were diagnosed at stage III whereas in Gonçalves et al. study, these rates were 38% and 28%, respectively[4]. Regarding histopathological variables, about 78% of total patients are Invasive ductal carcinoma (IDC) with statistical significance between two groups where IDC is 88% in TNBC and 68% in TPBC. Reports have not been consistent regarding differences in outcomes after IDC and ILC, with some evidence of better short-term survival in ILC than IDC, but worse outcomes in ILC than IDC after 10 years of follow-up [20]. However, in Timbres et al. study, there were no differences between ILC and IDC in disease-free survival[21]. Regarding disease progression, only 10 cases (10%) from all study populations developed local recurrence, 5 cases per group and 34% from all studies had metastasis to different sites, with no statistically significant

difference between both groups. This may be due to the performance of MRM in almost all of our study population (91%) with free surgical margins in 95% of all patients. Also, may be returned that all patients in TPBC and 86% of TNBC patients had radiotherapy after surgery, decreasing the local recurrence rate. In contrary, in Gonçalves et al., study, recurrences were observed in 43% of patients with TNBC, compared with 25% in non-TNBC patients[4]. In addition, in Negi et al., study, patients with TPBC were less likely to develop a locoregional recurrence (8% versus 12.8%) and distant metastasis after surgery (15.8% versus 30%) than the TNBC which is similar to Dent et al., that showed an increased risk of distant recurrence following diagnosis was noted among patients with TNBC tumors compared with other subtypes[22]. Clinically, HR-positive breast cancer is associated with a higher incidence of bone, soft tissue, and gonadal metastases, whereas HR-negative breast cancer tends to metastases to the brain and liver [7]. That was different from our study where the Liver was reported as the most common site for first metastasis location (in both groups) followed by bone and lung, keeping in mind that 78% of total patients in our study were IDC. This is supported by Timbres et al., results where Liver metastases were more commonly reported in IDC patients compared to the ILC group, as were lung metastases [21]. May this reflect the importance of comparing IDC and ILC in further studies. Differently, in Alzahrani et al. study, they found that bone metastasis occurred in 67% of the TPBC, which is like a study that showed that TPBC mostly metastasized to the bone while TNBC tumors metastasized to multiple visceral sites[13,23]. Our study showed that the prevalence of LVI was statistically higher in TPBC than in TNBC, 12% in TNBC compared to 44% in TPBC. However, after applying multivariable linear regression analysis to study the impact of LVI on disease progression among each group separately, it was found that TNBC - with an absence of LVI has a higher survival time of 2.6 years than TNBC - with the presence of LVI. In contrast to TPBC where there was no significant effect of LVI on survival time among TPBC. In summary, LVI has a prognostic value among TNBC with no significant effect on disease progression among TPBC. Despite the statistically significant difference between the two groups where Extra-nodal extension (ENE) is 28% positive in TNBC compared to 52% in TPBC and no patient has Peri-neural invasion (PNI) in TNBC compared to 20% of TPBC is positive, none of them was found to have a significant impact on DFS. In Pruessmann et al., study, risk factors for poor survival such as advanced infiltration of regional lymph nodes, LVI, and triple-negative subtype proved to be independent risk factors for the progression of disease while age had no further additional statistical significance. However, only LVI remained as a statistically significant predictor for conditional overall survival, while the analysis for disease-free survival identified lymph node involvement as well as LVI as significant predictors[24]. Regarding survival analysis for disease progression, the 3-year cumulative disease-free survival (DFS) was 73.5% and 77.5% of patients with TNBC and TPBC, and after 7 years, the DFS was higher in patients with TNBC (60.5%) than in patients with TPBC (45%). However, there was no statistically significant difference between both groups. The statistically insufficient power in long-term follow-up may be related to the decrease in sample size with time. In addition, the low DFS among TPBC may return to the pathological pathways of ER and HER2. As mentioned, ER and HER2 pathways are the main mechanisms involved in the pathogenesis of breast

cancer growth and are most targeted by the current treatments. Although very effective in selected groups of patients, there is still a high burden of patients that develop resistance to treatment and are difficult to manage with subsequent agents[7,25]. In another Brazilian cohort, TNBC women without lymph node involvement had a survival rate of 69% in 5 years and 61.6% in 10 years. Among non-TNBC patients, the survival was 82.2% and 70.1% in 5 and 10 years, respectively[26]. May further follow up till 10-year DFS can pick up a significant difference between two groups in favor of better DFS in TNBC than TPBC.

Conclusion

In the light of the present study, it has been proven that about two-thirds of patients were ≤50 years old, diabetes and hypertension were the most reported comorbidities in both groups and there is significance between the two groups regarding IDC, ENE, LVI, and PNI. Though there was no significant difference between both groups regarding the net disease progression, multiple independent factors were found to have a significant impact on this progression in each group separately as LVI.

Limitations and Recommendations

The main limitations of the study were the absence of a date of death in the medical records, which limited the calculation of the OS, and the incomplete data in patients' files records that could have influenced the analysis like the absence of ki67, which is important as a predictive and prognostic indicator for prognosis in breast cancer patients. However, the standardized method of data collection and the use of stratified multivariate models resulted in less likely bias. Our data strongly adds an important layer of information in concordance with the literature that TPBC and TNBC have a poor prognosis. However, larger, and longer studies are needed to validate the data and complete 10-year survival as it would add additional information regarding two groups.

Declaration

The protocol was reviewed and approved by the Ethics Committee of the Faculty of Medicine, Suez Canal University. The datasets used and analyzed in this study are available from the corresponding author upon reasonable request. This study had no funding from any resource.

Authors' contributions

F.M suggested the research idea and made a significant contribution to study design, methodology, manuscript preparation, and revision. Data collection, statistical analysis and results writing were done by M.M. S.A supervised the study and minimized the obstacles to the team of work. M.A made a significant contribution to manuscript revision and preparation.

Competing interests

The authors declare that they have no competing interests.

References

1. Gewaifel GI, Bahnasy MM, Kharboush I, et al. Geospatial Analysis of Breast Cancer in Alexandria: Application of a Novel Public Health Tool. Egy J Community Med. 2019;37(2):27–36.
2. Kulkarni A, Kelkar DA, Parikh N, et al. Meta-Analysis of Prevalence of Triple-Negative Breast Cancer and Its Clinical Features at Incidence in Indian Patients With Breast Cancer. JCO Glob Oncol. 2020;(6):1052–62.
3. Howlader N, Cronin KA, Kurian AW, et al. Differences in breast cancer survival by molecular subtypes in the United States. Cancer Epidemiology Biomark-

ers and Prevention. 2018 Jun 1;27(6):619–26.
4. Gonçalves H, Guerra MR, Duarte Cintra JR, et al. Survival Study of Triple-Negative and Non–Triple-Negative Breast Cancer in a Brazilian Cohort. Clin Med Insights Oncol. 2018;12(1):1–10.
5. Vici P, Pizzuti L, Natoli C, et al. Triple positive breast cancer: A distinct subtype? Cancer Treat Rev. 2015;41(2):69–79.
6. Chen B, Tang H, Chen X, et al. Transcriptomic analyses identify key differentially expressed genes and clinical outcomes between triple-negative and non-triple-negative breast cancer. Cancer Manag Res. 2019; 11:179–90.
7. Baeg S, Park I, Kim J, et al. Comparative Study for Clinical Outcomes of Triple-Positive and Triple-Negative Breast Cancer: Long-term Results in 161 Patients Followed in a Single Center. J Breast Dis. 2020;8(1):78–84.
8. Ades F, Zardavas D, Bozovic-Spasojevic I, et al. Luminal B breast cancer: Molecular characterization, clinical management, and future perspectives [Internet]. Vol. 32, Journal of Clinical Oncology. Am Soc Clin Oncol; 2014 [cited 2021 Apr 23]. p. 2794–803.
9. Charan J, Biswas T. How to calculate sample size for different study designs in medical research? Vol. 35, Indian J Psychological Med. Indian Psychiatric Society South Zonal Branch; 2013. p. 121–6.
10. Diana A, Franzese E, Centonze S, et al. Triple-Negative Breast Cancers: Systematic Review of the Literature on Molecular and Clinical Features with a Focus on Treatment with Innovative Drugs. Vol. 20, Current Oncology Reports. Current Medicine Group LLC 1; 2018.
11. Sajid M, Ahmed M, Azhar M, Mustafa Q, … ISJCPS, 2014 undefined. Age-related frequency of triple-negative breast cancer in women. jcpsp.pk. 2014.
12. Mouh FZ, Slaoui M, Razine R, et al. Clinicopathological, Treatment and Event-Free Survival Characteristics in a Moroccan Population of Triple-Negative Breast Cancer. Breast Cancer (Auckl). 2020;14.
13. Alzahrani W, Althoubaity F, Alsobhi D, et al. Clinicopathological Features and Metastatic Pattern of Triple-positive Breast Cancer Among Female Patients at a Tertiary Care Hospital. Cureus. 2019 Dec 24;11(12).
14. Sharma N, Narayan S, Sharma R, et al. Association of comorbidities with breast cancer: an observational study. scholar.harvard.edu. 2016.
15. Qiu JD, Xue XY, Li R, et al. Clinicopathological features and prognosis of triple-negative breast cancer: a comparison between younger (Eur J Cancer Care (Engl). 2016 Nov 1;25(6):1065–75.
16. Derkaoui T, Bakkach J, Mansouri M, et al. Triple-negative breast cancer in North of Morocco: clinicopathologic and prognostic features. BMC Womens Health. 2016 Oct 22;16(1).
17. Sayed S, Moloo Z, Wasike R, et al. Is breast cancer from Sub-Saharan Africa truly receptor-poor? Prevalence of ER/PR/HER2 in breast cancer from Kenya. Breast. 2014 Oct 1;23(5):591–6.
18. Sturtz LA, Melley J, Mamula K, et al. Outcome disparities in African American women with triple-negative breast cancer: a comparison of epidemiological and molecular factors between African American and Caucasian women with triple-negative breast cancer. BMC Cancer. 2014 Feb 4;14(1):62.
19. Fourati A, Boussen H, el May M v., et al. Descriptive analysis of molecular subtypes in Tunisian breast cancer. Asia Pac J Clin Oncol. 2014;10(2).
20. Mathew A, Rajagopal PS, Villgran V, et al. Distinct Pattern of Metastases in Patients with Invasive Lobular Carcinoma of the Breast. Geburtshilfe Frauenheilkd. 2017 Jun 1;77(6):660.
21. Timbres J, Moss C, Mera A, et al. Survival outcomes in invasive lobular carcinoma compared to estrogen receptor-positive invasive ductal carcinoma. Cancers (Basel). 2021 Jun 2;13(12).

22. Negi P, Kingsley PA, Jain K, et al. Survival of Triple Negative versus Triple Positive Breast Cancers: Comparison and Contrast. Asian Pac J Cancer Prev. 2016;17(8):3911–6.
23. Vona-Davis L, Rose DP, Gadiyaram V, et al. Breast Cancer Pathology, Receptor Status, and Patterns of Metastasis in a Rural Appalachian Population. J Cancer Epidemiol. 2014;2014.
24. Pruessmann J, Pursche T, Hammersen F, et al. Conditional disease-free and overall survival of 1,858 young women with non-metastatic breast cancer and with participation in a post-therapeutic rehab program according to clinical subtypes. Breast Care. 2021 Apr 1;16(2):163–72.
25. Iancu G, Vasile D, Claudia Iancu R, et al. "Triple positive" breast cancer-a novel category? Rom J Morphol Embryol. 2017;2017(1):21–6.
26. Eisenberg A. Triple-Negative Breast Cancer in Brazilian Women without Metastasis to Axillary Lymph Nodes: Ten-Year Survival and Prognostic Factors. Br J Med Res. 2013 Jan 10;3(4):880–96.