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Prognostic factors in triple-negative breast cancer: a retrospective cohort

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SUMMARY

OBJECTIVE: Triple-negative breast cancer (TNBC) is characterized by lack of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (HER2) expression and accounts for 15–20% of all breast cancers. This study aims to analyze prognostic factors related to a reduction in overall survival (OS), disease-free survival (DFS), and risk of mortality and recurrence in TNBC.

METHODS: This is a retrospective observational cohort study. Medical records of 532 patients with breast cancer diagnosed from 2007 to 2020 were analyzed. Of these patients, 93 (17%) were women with TNBC. Ten medical records were excluded, and the final sample was composed of 83 women with TNBC. OS and DFS were estimated by the Kaplan-Meier model. Univariate analysis (log-rank test) and multivariate analysis (Cox regression) were used to examine prognostic factors related to a statistically significant reduction ($p<0.05$) in OS and DFS and increased risk of mortality and tumor recurrence.

RESULTS: Smoking, advanced clinical stage, larger tumor size, angiolymphatic invasion, positive sentinel lymph node, axillary node involvement, higher cancer burden, surgical treatment with mastectomy, and recurrence were related to a significant decrease in OS and/or DFS and increased risk of mortality and/or recurrence in TNBC. The 10-year OS and DFS was around 61 and 65%, respectively.

CONCLUSIONS: Advanced clinical stage, positive sentinel lymph node, axillary node involvement, surgical treatment with mastectomy, and higher residual cancer burden were related to a significant reduction in OS and DFS and increased risk of mortality and recurrence in TNBC.

KEYWORDS: Survival analysis. Prognosis. Medical records. Pathological conditions. Anatomical. Triple-negative breast neoplasms.

INTRODUCTION

Breast cancer is a heterogeneous disease involving multiple genetic alterations[1]. It is classified into molecular subtypes, based on the lack of protein expression of estrogen receptor (ER) and progesterone receptor (PR) and the absence of overexpression of human epidermal growth factor 2 receptor (HER2). Triple-negative (TN) subtype is defined as a breast cancer with negative expression of estrogen/progesterone (ER/PR) hormone receptors and human epidermal growth factor receptor-2 (HER2) (either by immunohistochemistry [IHC; 0–1] or by fluorescent in situ hybridization [FISH negative if 2+ on IHC])[2]. TN cancer tends to be more aggressive than other types of breast cancer. It is also associated with a poor prognosis due to its clinical behavior and lack of molecular targets for cancer therapy. Therefore, chemotherapy remains

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the primary treatment of choice for patients diagnosed at early or late stages[3].

In Brazil, the National Cancer Institute estimated that 66,280 new breast cancer cases occurred in women in 2020. Breast cancer was the leading cause of death from cancer among this population[4]. On the other hand, triple-negative breast cancer (TNBC) accounts for around 15–20% of all breast cancers[5]. This molecular subtype of cancer is most commonly observed in young black and Hispanic women. In addition, it is associated with a higher prevalence of BCRA gene mutations (particularly BRCA1)[6].

In comparison to other subtypes of breast cancer, survival is shorter and mortality rate is 40% in patients with TNBC within the first 5 years of diagnosis, as shown by epidemiological data. TNBC is a highly invasive tumor, and approximately 46% of patients with TNBC develop distant metastasis. Median survival time after metastasis is only 13.3 months, and the recurrence rate after surgery achieves 25%. Brain and visceral metastases frequently occur. The mortality rate of patients with TNBC within 3 months of recurrence is up to 75%[7].

In the literature, diverse prognostic factors have been associated with TNBC, including recurrence, lymphovascular invasion, tumor size, lymph node involvement, and Ki-67 expression, among others[8,9]. The prognostic value of Ki-67 in TNBC remains controversial, partly due to the lack of agreement on the cutoff point, which is estimated at 10–61%[9].

Recent studies have also evaluated other prognostic factors. Oshi et al. correlated a high CD8 T-cell score with increased survival rates in patients with TNBC. O'Conor et al. reported that $CD44^{+}/CD24^{-}$ and $ALDH1^{+}$ stem cells are indicators of a poor prognosis, contributing to chemotherapy resistance and metastatic tumors. Furthermore, some ongoing trials currently investigate specific genes or microRNA[10-12].

The current study aimed to analyze prognostic factors related to a reduction in overall survival (OS), disease-free survival (DFS), and risk of mortality and recurrence in TNBC.

METHODS

This is a retrospective observational cohort study. Medical records of 532 patients diagnosed with breast cancer were analyzed. Patients were seen from 2007 to 2020 in a private oncology health care facility in the city of Teresina (PI), Brazil. Of these patients, 93 (17%) were women with TNBC. Ten medical records were excluded: four of patients who had not completed treatment by the end of the follow-up (December 2020) and six with incomplete or missing data. The final sample was composed of 83 women with TNBC.

Data were tabulated using the Microsoft Excel 2010® program. Statistical analysis was conducted in the Stata 14® program. The absolute (n) and relative (%) frequencies of each variable of the study were calculated. OS and DFS were estimated by the Kaplan-Meier method. Univariate (log-rank test) and multivariate (Cox regression) analysis investigated which prognostic factors were related to a statistically significant reduction ($p<0.05$) in OS and/or DFS and a higher risk of mortality and/or recurrence. To perform Cox regression, the hazard ratios along with their respective 95% confidence intervals (95% CI) were estimated.

In the OS and DFS curves presented, follow-up had occurred between the time of TNBC diagnosis and the time of patient death or tumor recurrence, respectively. The maximum follow-up period was 157 months.

The study complied with all Brazilian principles for ethical research (National Health Council Resolution no. 466/12) and was approved by the Research Ethics Committee of the State University of Piauí, Teresina (PI), Brazil (CAAE: 30154720.0.0000.5209).

RESULTS

Prognostic factors (variables) related to the risk of mortality and/or recurrence and impact on the decrease in OS and/or DFS analyzed by univariate and multivariate analysis in this study were age, number of pregnancies, smoking, alcohol dependence, comorbid conditions (hypertension and diabetes), family history (of breast cancer and other cancers), clinical stage, degree of differentiation, tumor size, angiolymphatic invasion, sentinel lymph node, axillary node involvement, Ki-67, residual cancer burden, surgical treatment, and tumor recurrence.

Smoking, advanced clinical stage, larger tumor size, angiolymphatic invasion, positive sentinel lymph node, axillary node involvement, higher residual cancer burden, surgical treatment with mastectomy, and recurrence were regarded as significant risks ($p<0.05$) of mortality in TNBC and are associated with decreased OS (Table 1).

In contrast, advanced clinical stage, positive sentinel lymph node, axillary node involvement, higher residual tumor burden, and surgical treatment with mastectomy were also related to a significant risk ($p<0.05$) of tumor recurrence in TNBC, presenting a reduction in DFS (Table 2).

Survival curves (Figure 1) showed 10-year OS and DFS of around 61% and 65%, respectively.

Table 1. Prognostic factors, deaths, and overall survival (157 m onths of follow-up).

Variables	n (%)	Death(s) n (%)	Univariate analysis		Multivariate analysis	
			Overall survival n (95%CI)	Log-rank test p-value	RR (95%CI)	Wald's test p-value
Age at diagnosis						
≤59 years	50 (60.2)	7 (14.0)	86.0 (73.2–94.2)	0.930	1.0	0.931
≥60 years	33 (39.8)	5 (15.2)	84.8 (68.1–94.9)		1.05 (0.33–3.33)	
Number of pregnancies						
None	17 (20.5)	2 (11.8)	88.2 (63.6–98.5)	0.358	1.0	
1	13 (15.7)	2 (15.4)	84.6 (54.6–98.1)		1.02 (0.14–7.28)	0.987
2	22 (26.5)	5 (22.7)	77.3 (54.6–92.2)		2.19 (0.42–11.41)	0.352
3	19 (22.9)	1 (5.3)	94.7 (74.0–99.9)		0.32 (0.03–3.53)	0.349
4 and more	12 (14.5)	2 (16.7)	83.3 (51.6–97.9)		1.05 (0.14–7.71)	0.964
Smoking						
No	79 (95.2)	10 (12.7)	87.3 (78.0–93.8)	0.004	1.0	0.015
Yes	4 (4.8)	2 (50.0)	50.0 (6.8–93.2)		7.28 (1.48–35.80)	
Alcohol dependence						
No	78 (94.0)	10 (12.8)	87.2 (77.7–93.7)	0.094	1.0	0.118
Yes	5 (6.0)	2 (40.0)	60.0 (14.7–94.7)		3.47 (0.73–16.46)	
Hypertension						
No	60 (72.3)	7 (11.7)	88.3 (77.4–95.2)	0.517	1.0	0.520
Yes	23 (27.7)	5 (21.7)	78.3 (56.3–92.5)		1.46 (0.46–4.70)	
Diabetes						
No	73 (88.0)	10 (13.7)	86.3 (76.2–93.2)	0.328	1.0	0.341
Yes	10 (12.0)	2 (20.0)	80.0 (44.4–97.5)		2.11 (0.45–9.81)	
Family history (breast cancer)						
No	57 (68.7)	10 (17.5)	82.5 (70.0–91.2)	0.459	1.0	0.467
Yes	26 (31.3)	2 (7.7)	92.3 (74.9–99.0)		0.56 (0.12–2.62)	
Family history (cancers)						
No	42 (50.6)	6 (14.3)	85.7 (71.5–94.6)	0.824	1.0	0.825
Yes	41 (49.4)	6 (14.6)	85.4 (70.8–94.4)		1.14 (0.36–3.54)	
Clinical stage						
IB	25 (30.1)	1 (4.0)	96.0 (79.6–99.9)	0.019	1.0	
IIB	24 (28.9)	2 (8.3)	91.7 (73.0–99.0)		1.74 (0.16–19.49)	0.651
IIIB	23 (27.7)	5 (21.7)	78.3 (56.3–92.5)		6.63 (0.77–57.31)	0.085
IIIC and IV	11 (13.3)	4 (36.4)	63.6 (30.8–89.1)		10.67 (1.19–95.66)	0.034

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Table 1. Continuation.

Variables	n (%)	Death(s) n (%)	Univariate analysis		Multivariate analysis	
			Overall survival n (95%CI)	Log-rank test p-value	RR (95%CI)	Wald's test p-value
Grade						
G2	45 (54.2)	6 (13.3)	86.7 (73.2–94.9)	0.932	1.0	0.933
G3	38 (45.8)	6 (15.8)	84.2 (68.7–94.0)		0.95 (0.30–2.98)	
Tumor size (cm)						
0–2.5	48 (57.8)	4 (8.3)	91.7 (68.7–94.0)	0.025	1.0	0.036
>2.5	35 (42.2)	8 (22.9)	77.1 (59.9–89.6)		3.73 (1.09–12.74)	
Lymphatic invasion						
No	63 (75.9)	3 (4.8)	95.2 (86.7–99.0)	<0.001	1.0	<0.001
Yes	20 (24.1)	9 (45.0)	55.0 (31.5–76.9)		17.48 (3.72–82.17)	
Vascular invasion						
No	67 (80.7)	5 (7.5)	92.5 (83.4–97.5)	<0.001	1.0	0.001
Yes	16 (19.3)	7 (47.8)	56.2 (29.9–80.2)		7.59 (2.20–26.18)	
Sentinel lymph node						
Negative	63 (75.9)	6 (9.5)	90.5 (80.4–96.4)	0.009	1.0	0.017
Positive	20 (24.1)	6 (30.0)	70.0 (45.7–88.1)		4.23 (1.29–13.88)	
Axillary involvement						
No	45 (54.2)	3 (6.7)	93.3 (81.7–98.6)	0.025	1.0	0.039
Yes	38 (45.8)	9 (23.7)	76.3 (59.8–88.6)		3.98 (1.07–14.76)	
Ki-67 (%)						
≤60	34 (47.0)	4 (10.3)	89.7 (75.8–97.1)	0.232	1.0	0.243
>60	44 (53.0)	8 (18.2)	81.8 (67.3–91.8)		2.05 (0.61–6.87)	
Residual cancer burden						
pCR	42 (50.6)	2 (4.8)	95.2 (83.8–99.4)	<0.001	1.0	
RCB-I and RCB-II	29 (34.9)	2 (6.9)	93.1 (77.2–99.1)		1.99 (0.26–15.08)	0.505
RCB-III	12 (14.5)	8 (66.7)	33.3 (9.9–65.1)		27.80 (4.74–162.9)	<0.001
Surgical treatment						
Conservative	61 (73.5)	6 (9.8)	90.2 (79.8–96.3)	0.012	1.0	0.020
Mastectomy	22 (26.5)	6 (27.3)	72.7 (49.8–89.3)		3.93 (1.24–12.4)	
Recurrence						
No	65 (78.3)	3 (4.6)	95.4 (87.1–99.0)	<0.001	1.0	0.001
Yes	18 (21.7)	9 (50.0)	50.0 (26.0–74.0)		15.38 (3.26–72.53)	

RR: relative risk; 95%CI: 95% confidence interval; pCR: pathological complete response; RCB-I: minimal burden (residual disease); RCB-II: moderate burden (residual disease); RCB-III: extensive burden (residual disease). The values highlighted in bold are intended to draw the reader's attention to statistically significant variables

Table 2. Prognostic factors, tumor recurrence, and disease-free survival (157 months of follow-up).

Variables	n (%)	Recurrence(s) n (%)	Univariate analysis		Multivariate analysis	
			Disease-free survival n (95%CI)	Log-rank test p-value	RR (95%CI)	Wald's test p-value
Age at diagnosis (year)						
Up to 59	50 (60.2)	12 (24.0)	76.0 (61.8–86.9)	0.529	1.0	0.533
60 or above	33 (39.8)	6 (18.2)	81.8 (64.5–93.0)		0.73 (0.33–3.33)	
Number of pregnancies						
None	17 (20.5)	2 (11.8)	88.2 (63.6–98.5)	0.001	1.0	
1	13 (15.7)	5 (38.5)	61.5 (31.6–86.1)		3.44 (0.66–17.77)	0.140
2	22 (26.5)	9 (40.9)	59.1 (36.4–79.3)		4.88 (1.05–22.67)	0.043
3 or more	31 (37.3)	2 (6.4)	93.6 (78.6–99.2)		0.47 (0.07–3.34)	0.451
Smoking						
No	79 (95.2)	12 (20.2)	79.8 (69.2–88.0)	0.041	1.0	0.062
Yes	4 (4.8)	2 (50.0)	50.0 (6.8–93.2)		4.20 (0.93–18.91)	
Alcohol dependence						
No	78 (94.0)	16 (20.5)	79.5 (68.8–87.8)	0.350	1.0	0.362
Yes	5 (6.0)	2 (40.0)	60.0 (14.7–94.7)		1.99 (0.45–8.73)	
Hypertension						
No	60 (72.3)	14 (23.3)	76.7 (64.0–86.6)	0.471	1.0	0.476
Yes	23 (27.7)	4 (17.4)	82.6 (61.2–95.0)		0.67 (0.22–2.03)	
Diabetes						
No	73 (88.0)	16 (21.9)	78.1 (66.9–86.9)	0.791	1.0	0.793
Yes	10 (12.0)	2 (20.0)	80.0 (44.4–97.5)		1.22 (0.28–5.36)	
Family history (breast cancer)						
No	57 (68.7)	13 (22.8)	77.2 (64.2–87.3)	0.897	1.0	0.898
Yes	26 (31.3)	5 (19.2)	80.8 (60.6–93.4)		0.93 (0.33–2.63)	
Family history (cancers)						
No	42 (50.6)	9 (21.4)	78.6 (63.2–89.7)	0.930	1.0	0.930
Yes	41 (49.4)	9 (22.0)	78.0 (62.4–89.4)		1.04 (0.41–2.63)	
Clinical stage						
IB	25 (30.1)	1 (4.0)	96.0 (79.6–99.9)	0.017	1.0	
IIB	24 (28.9)	6 (25.0)	75.0 (53.3–90.2)		5.04 (0.61–41.9)	0.134
IIIB	23 (27.7)	6 (26.1)	73.9 (51.6–89.8)		7.33 (0.88–61.06)	0.065
IIIC and IV	11 (13.3)	5 (45.4)	54.6 (23.4–83.2)		15.25 (1.78–130.70)	0.013
Grade						
G2	45 (54.2)	10 (22.2)	77.8 (62.9–88.8)	0.633	1.0	0.635
G3	38 (45.8)	8 (21.0)	79.0 (62.7–90.4)		0.80 (0.31–2.03)	
Tumor size (cm)						
0–2.5	48 (57.8)	8 (16.7)	83.3 (69.8–92.5)	0.144	1.0	0.154
>2.5	35 (42.2)	10 (28.6)	71.4 (53.7–85.4)		1.97 (0.78–5.02)	
Lymphatic invasion						
No	63 (75.9)	11 (17.5)	82.5 (70.9–90.9)	0.072	1.0	0.082
Yes	20 (24.1)	7 (35.0)	65.0 (15.4–59.2)		2.34 (0.90–6.10)	

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Table 2. Continuation.

Variables	n (%)	Recurrence(s) n (%)	Univariate analysis		Multivariate analysis	
			Disease-free survival n (95%CI)	Log-rank test p-value	RR (95%CI)	Wald's test p-value
Vascular invasion						
No	67 (80.7)	13 (19.4)	80.6 (69.1–89.2)	0.336	1.0	0.343
Yes	16 (19.3)	5 (31.2)	68.8 (41.3–89.0)		1.65 (0.58–4.66)	
Sentinel lymph node						
Negative	63 (75.9)	10 (15.9)	84.1 (72.7–92.1)	0.008	1.0	0.017
Positive	20 (24.1)	8 (40.0)	60.0 (36.0–80.9)		3.23 (1.27–8.22)	
Axillary involvement						
No	45 (54.2)	5 (11.1)	88.9 (75.9–96.3)	0.009	1.0	0.016
Yes	38 (45.8)	13 (34.2)	65.8 (48.6–80.4)		3.57 (1.27–10.02)	
Ki-67 (%)						
≤60	34 (47.0)	5 (12.8)	87.2 (72.6–95.7)	0.066	1.0	0.077
>60	44 (53.0)	13 (29.6)	70.4 (54.8–83.2)		2.53 (0.90–7.11)	
Residual cancer burden						
pCR	42 (50.6)	1 (2.4)	97.6 (87.4–99.9)	<0.001	1.0	
RCB-I	8 (9.6)	1 (12.5)	87.5 (47.3–99.7)		4.34 (0.27–69.60)	0.300
RCB-II	21 (25.3)	5 (23.8)	76.2 (52.8–91.8)		15.22 (1.77–130.82)	0.013
RCB-III	12 (14.5)	11 (91.7)	8.3 (0.2–38.5)		74.10 (9.39–584.45)	<0.001
Surgical treatment						
Conservative	61 (73.5)	11 (18.0)	82.0 (70.0–90.6)	0.025	1.0	0.033
Mastectomy	22 (26.5)	7 (31.8)	68.2 (45.1–86.1)		2.83 (1.09–7.37)	

RR: relative risk; 95%CI: 95% confidence interval; CR: pathological complete response; RCB-I: minimal burden (residual disease); RCB-II: moderate burden (residual disease); RCB-III: extensive burden (residual disease). The values highlighted in bold are intended to draw the reader's attention to statistically significant variables.

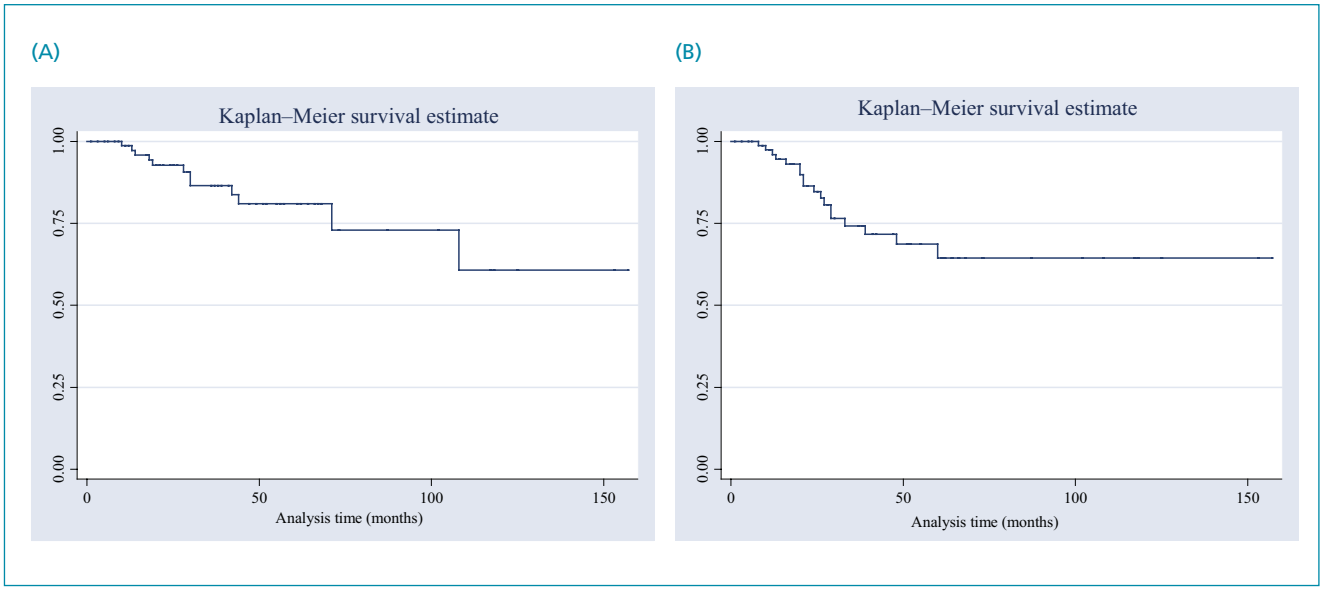

Figure 1. Overall survival (A) and disease-free survival (B) curves (157 months of follow-up).

DISCUSSION

Variables such as age, number of pregnancies, alcohol dependence, hypertension, diabetes, family history of breast cancer and other cancers, degree of differentiation, and Ki-67 did not show any significant reduction in OS and/or DFS in this study. Furthermore, these variables did not present an increased risk of mortality and/or recurrence.

In this study, 60.2% of the patients were diagnosed before the age of 59 years and 79.5% had a history of previous pregnancies. In a study investigating 841 patients with TNBC diagnosed from 1994 to 2015 in four large oncology centers, Urru et al.[13] also described that TNBC predominated in young patients with previous pregnancies.

Alcohol dependence is a well-established risk factor for the development of breast cancer. However, the literature indicates that there is no relationship between alcohol dependence and increased risk of TNBC[14]. Alcohol dependence is also associated with a worse chemotherapy response (first-line treatment for TNBC), worsening survival in these cases[15]. Alcohol-dependent patients in this study did not show a worse OS and/or DFS and an increased risk of mortality and/or recurrence.

Studies have associated hypertension, diabetes, and tumor grade with increased mortality in TNBC[16,17]. However, in this study, there was also no significant reduction in OS and/or DFS and increased risk in mortality and/or recurrence, in relation to these variables.

Ki-67 and family history of breast cancer and other cancers are considered useful in the prognosis of TNBC[18]. Nevertheless, the literature indicates that there is controversy surrounding the methods used for analysis of these prognostic factors[9,18]. In this study, Ki-67 (with a cutoff point stipulated at 60%) and a family history of breast cancer and other cancers were not implicated in a significant decrease in OS and/or DFS and increased risk of mortality and/or recurrence.

Smoking, advanced clinical stage, larger tumor size, angiolymphatic invasion, positive sentinel lymph node, axillary node involvement, higher residual tumor burden, surgical treatment with mastectomy, and recurrence were prognostic factors significantly related to a decreased OS and/or DFS, representing an increased risk of mortality and/or recurrence in TNBC, respectively. These results are based on previous literature data[19-23].

In a study of 583 patients, Mousavi et al.[24] demonstrated that lymph node involvement was the only prognostic factor related to decreased DFS in TNBC. However, other studies have demonstrated that a larger tumor size and residual tumor burden correlate with a higher recurrence risk and lower DFS in TNBC[25]. Data in this study also demonstrated a higher recurrence risk and a lower DFS in relation to all these prognostic factors.

More recent analyses have indicated that breast-conserving surgery shows higher OS and DFS and lower risk of tumor recurrence, compared to mastectomy in TNBC, particularly at early stages[23]. In this study, data also show a higher OS and DFS, along with a decreased risk of mortality and recurrence in patients with TNBC undergoing breast-conserving surgery.

Survival analysis in cancer is influenced by diverse variables inherent in each sample (tumor size, prevalence of tumor stage, and nature of prognostic factors, among others)[26]. Fayaz et al.[27] conducted a study on the 10-year OS and DFS of 359 women diagnosed with TNBC from 1999 to 2009, indicating values of 66% for OS and 59% for DFS. These results were quite similar to findings in this study, showing that 10-year OS and DFS were 61 and 65%, respectively.

Limitations of this study were sample size, the retrospective nature of the study, and its performance in a single center.

CONCLUSION

Advanced clinical stage, positive sentinel lymph node, axillary node involvement, surgical treatment with mastectomy, and higher residual cancer burden were prognostic factors related to a statistically significant reduction in OS and DFS and an increased risk of mortality and recurrence in TNBC.

AUTHORS' CONTRIBUTIONS

REARC: Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Writing – original draft, Writing – review & editing. **FTRO:** Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Writing – original draft. **ALNA:** Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Writing – review & editing. **SCV:** Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Writing – review & editing. All authors have read and approved the final draft.

REFERENCES

1. Perou CM, Sørlie T, Eisen MB, van de Rijn M, Jeffrey SS, Rees CA, et al. Molecular portraits of human breast tumours. Nature. 2000;406(6797):747-52. https://doi.org/10.1038/35021093

2. Kumar P, Aggarwal R. An overview of triple-negative breast cancer. Arch Gynecol Obstet. 2016;293(2):247-69. https://doi.org/10.1007/s00404-015-3859-y

3. Bianchini G, Balko JM, Mayer IA, Sanders ME, Gianni L. Triple-negative breast cancer: challenges and opportunities of a heterogeneous disease. Nat Rev Clin Oncol. 2016;13(11):674-90. https://doi.org/10.1038/nrclinonc.2016.66
4. Instituto Nacional de Câncer José Alencar Gomes da Silva. Estimativa 2020: incidência de câncer no Brasil. Rio de Janeiro: Instituto Nacional de Câncer José Alencar Gomes da Silva; 2019. [cited on 2021 May 30, Internet]. Available from: https://inca.gov.br/publicacoes/livros/estimativa-2020-incidencia-de-cancer-no-brasil
5. Hurvitz S, Mead M. Triple-negative breast cancer: advancements in characterization and treatment approach. Curr Opin Obstet Gynecol. 2016;28(1):59-69. https://doi.org/10.1097/GCO.0000000000000239
6. Sharma P. Biology and management of patients with triple-negative breast cancer. Oncologist. 2016;21(9):1050-62. https://doi.org/10.1634/theoncologist.2016-0067
7. Yin L, Duan JJ, Bian XW, Yu SC. Triple-negative breast cancer molecular subtyping and treatment progress. Breast Cancer Res. 2020;22(1):61. https://doi.org/10.1186/s13058-020-01296-5
8. Rakha EA, El-Sayed ME, Green AR, Lee AHS, Robertson JF, Ellis IO. Prognostic markers in triple-negative breast cancer. Cancer. 2007;109(1):25-32. https://doi.org/10.1002/cncr.22381
9. Zenzola V, Cabezas-Quintario MA, Arguelles M, Pérez-Fernández E, Izarzugaza Y, Correa A, et al. Prognostic value of Ki-67 according to age in patients with triple-negative breast cancer. Clin Transl Oncol. 2018;20(11):1448-54. https://doi.org/10.1007/s12094-018-1877-5
10. Oshi M, Asaoka M, Tokumaru Y, Yan L, Matsuyama R, Ishikawa T, et al. CD8 T cell score as a prognostic biomarker for triple negative breast cancer. Int J Mol Sci. 2020;21(18):6968. https://doi.org/10.3390/ijms21186968
11. O'Conor CJ, Chen T, González I, Cao D, Peng Y. Cancer stem cells in triple-negative breast cancer: a potential target and prognostic marker. Biomark Med. 2018;12(7):813-20. https://doi.org/10.2217/bmm-2017-0398
12. Ding L, Gu H, Xiong X, Ao H, Cao J, Lin W, et al. MicroRNAs involved in carcinogenesis, prognosis, therapeutic resistance, and applications in human triple-negative breast cancer. Cells. 2019;8(12):1492. https://doi.org/10.3390/cells8121492
13. Urru SAM, Gallus S, Bosetti C, Moi T, Medda R, Sollai E, et al. Clinical and pathological factors influencing survival in a large cohort of triple-negative breast cancer patients. BMC Cancer. 2018;18(1):56. https://doi.org/10.1186/s12885-017-3969-y
14. Baglia ML, Cook LS, Mei-Tzu C, Wiggins C, Hill D, Porter P, et al. Alcohol, smoking, and risk of Her2-overexpressing and triple-negative breast cancer relative to estrogen receptor-positive breast cancer. Int J Cancer. 2018;143(8):1849-57. https://doi.org/10.1002/ijc.31575
15. Silva JL, Paula BHR, Small IA, Thuler LCS, Melo AC. Sociodemographic, clinical, and pathological factors influencing outcomes in locally advanced triple negative breast cancer: a Brazilian cohort. Breast Cancer (Auckl). 2020;14:1178223420962488. https://doi.org/10.1177/1178223420962488
16. Swede H, Sarwar A, Magge A, Braithwaite D, Cook LS, Gregorio DI, et al. Mortality risk from comorbidities independent of triple-negative breast cancer status: NCI-SEER-based cohort analysis. Cancer Causes Control. 2016;27(5):627-36. https://doi.org/10.1007/s10552-016-0736-3
17. Bauer KR, Brown M, Cress RD, Parise CA, Caggiano V. Descriptive analysis of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype: a population-based study from the California cancer Registry. Cancer. 2007;109(9):1721-8. https://doi.org/10.1002/cncr.22618
18. Pan Y, Yuan Y, Liu G, Wei Y. P53 and Ki-67 as prognostic markers in triple-negative breast cancer patients. PLoS One. 2017;12(2):e0172324. https://doi.org/10.1371/journal.pone.0172324
19. Lopes CM, Montemor Netto MR, Mansani FP, Stival RSM, Cassapula MR, Oliveira TFB. Clinical, histomorphological, and therapeutic prognostic factors in patients with triple-negative invasive breast cancer. J Bras Patol Med Lab. 2015;51(6):397-406. https://doi.org/10.5935/1676-2444.20150062
20. Seibold P, Vrieling A, Heinz J, Obi N, Sinn HP, Flesch-Janys D, et al. Pre-diagnostic smoking behaviour and poorer prognosis in a German breast cancer patient cohort – differential effects by tumour subtype, NAT2 status, BMI and alcohol intake. Cancer Epidemiol. 2014;38(4):419-26. https://doi.org/10.1016/j.canep.2014.05.006
21. Qiu J, Xue X, Hu C, Xu H, Kou D, Li R, et al. Comparison of clinicopathological features and prognosis in triple-negative and non-triple negative breast cancer. J Cancer. 2016;7(2):167-73. https://doi.org/10.7150/jca.10944
22. Luen SJ, Salgado R, Dieci MV, Vingiani A, Curigliano G, Gould RE, et al. Prognostic implications of residual disease tumor-infiltrating lymphocytes and residual cancer burden in triple-negative breast cancer patients after neoadjuvant chemotherapy. Ann Oncol. 2019;30(2):236-42. https://doi.org/10.1093/annonc/mdy547
23. Macfie R, Aks C, Panwala K, Johnson N, Garreau J. Breast conservation therapy confers survival and distant recurrence advantage over mastectomy for stage II triple negative breast cancer. Am J Surg. 2021;221(4):809-12. https://doi.org/10.1016/j.amjsurg.2020.04.016
24. Mousavi SA, Kasaeian A, Pourkasmaee M, Ghavamzadeh A, Alimoghaddam K, Vaezi M, et al. Assessing the prognostic factors, survival, and recurrence incidence of triple negative breast cancer patients, a single center study in Iran. PLoS One. 2019;14(1):e0208701. https://doi.org/10.1371/journal.pone.0208701
25. Pogoda K, Niwińska A, Murawska M, Pieńkowski T. Analysis of pattern, time and risk factors influencing recurrence in triple-negative breast cancer patients. Med Oncol. 2013;30(1):388. https://doi.org/10.1007/s12032-012-0388-4
26. Bustamante-Teixeira MT, Faerstein E, Latorre MR. Survival analysis techniques. Cad Saude Publica. 2002;18(3):579-94. PMID: 12048585
27. Fayaz S, Demian GA, El-Sherify M, Eissa H, Aziz M, Abuzallouf S. Triple negative breast cancer: 10-year survival update of the applied treatment strategy in Kuwait. Gulf J Oncolog. 2019;1(29):53-9. PMID: 30957764