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Investigation of survival and prognostic factors in triple negative molecular subtype male breast cancer patients: A population-based study

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Abstract

In this study, it was aimed to investigate the survival rate and prognostic factors affecting survival in triple negative male breast cancer patients. Data were obtained from SEER (Surveillance Epidemiology and End Results). Triple-negative male breast cancer patients between 2010 and 2019 were included in the study. Demographic, clinical, and oncology data were evaluated. Among 4930 male breast cancer patients, 92 (1.87%) patients with triple negative molecular subtypes were included in the study. The median age of the patients was 67 (IQR: 58.25-73.5). The majority of the patients were white (68.5%). The rate of being married was 62%. It was on both sides; the most common tumor localization was upper outer quadrant and central, respectively. The most common grades were III-IV (66.3%). The most common stages were T2 (44.6%) in the T stage and N0 (54%) in the N stage. The most common stage was IV (28.3%). Mean follow-up time was 25.76±25.02, and overall survival was 50.5% and cancer specific survival was 59.6%. Grade, metastasis status, and surgical status were found to be independent risk factors for survival. The majority of triple negative male breast cancer patients were in advanced stages, and survival rates were low. It is encouraging that triple negative molecular subtype breast cancer, which is an aggressive tumor, is less common in men.

Keywords: Breast cancer, male breast cancer, survival, triple negative breast cancer

Introduction

Male breast cancer (MBC) is a rare disease that accounts for less than 1 percent of all breast cancer cases. Nonetheless, the prevalence of MBC has been rising recently, and in 2021, there will likely be about 2,650 new cases diagnosed in the US [1]. MBC typically has a later diagnosis than female breast cancer(FBC), which has worse results [2,3]. An aggressive tumor that is negative for the human epidermal growth factor receptor-2 (HER2), progesterone receptor (PR), and estrogen receptor (ER) is known as a triple negative (TN) molecular subtype of breast cancer [4]. TN breast cancer is more common in young women, African and American women, and women with BRCA1 mutations. On the other hand, relatively little is understood regarding the survival rates, clinicopathological characteristics, and epidemiology of TN MBC [5]. The prognosis for MBC is typically poorer than that of female breast cancer, and a number of variables, such as age, stage, grade, hormone receptor status, and treatment, might impact an individual's chance of survival [6-8]. Prognostic variables for TN MBC are unclear, nevertheless.

This study used information from the SEER (Surveillance Epidemiology and End Results) database to examine the prognostic variables and survival rate in patients with TN MBC.

Material and Methods

Data Source and Patient Selection

The SEER Research Plus 17 Registries database, which includes information on about 28% of US citizens, provided the data that we used. Data on cancer incidence, treatment, and survival, as well as patient demographics and clinical features, are available from the SEER database. Between 2010 and 2019, we identified male patients who received a breast cancer diagnosis. Age, race, laterality, grade, T and N stages, tumor localization, surgery status, chemotherapy, radiotherapy, cause of death, survival duration, and malignancies with molecular subtypes other than TN were not

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included in the patient pool. Additionally excluded were patients with non-invasive breast cancer.

This study utilized de-identified data from the SEER database, which is publicly available and maintains patient anonymity; ethical approval and informed consent were not required.

Definitions and Variables

The following factors were taken into account in the analysis: surgical status (operated or not), age at diagnosis, marital status, race, year of diagnosis, tumor localization, side (right or left), grade (I, II, III, IV), T stage (T0, T1, T2, T3, T4), and N stage (N0, N1, N2, N3). The definition of TN status for ER, PR, and HER2 was negative. The period of time from diagnosis to death from any cause was called overall survival (OS). The period of time from breast cancer diagnosis to death was called cancer-specific survival (CSS).

Statistical Analysis

The features of male breast cancer patients who tested negative for triple negative were compiled using descriptive statistics. The categorical data were shown as percentage and frequency, and the continuous variables as median and interquartile range (IQR). Survival curves were constructed using the Kaplan-Meier method, and the log-rank test was used to compare survival curves. Univariate and multivariate Cox proportional hazard regression models were used to determine the prognostic factors affecting OS and CSS. 95% confidence intervals (CIs) and danger ratios (HRs) were computed. At $p<0.05$, statistical significance was established. Version 25 of the SPSS program was used for all statistical analyses.

Results

Of the 628254 patients diagnosed with breast cancer between 2010-2019, 0.78% (4930) were male patients. When male breast cancer patients were analyzed according to molecular subtypes, 86.25% were luminal A and B types, 1.87% (92) were TN, 0.65% (32) were Her2 enrich subtypes. 554 (11.2%) patients had no data on molecular subtype.

The median age of the 92 patients included in the study was 67 years (IQR: 58.25-73.5). The majority of the patients were white race (68.5%). The rate of being married was 62% (Table 1). Laterality rates were similar. The most common tumor localisations on both sides were upper outer quadrant and central, respectively (Figure 1). The most common grade was III-IV (66.3%). The most common T stage was T2 (44.6%) and N stage was N0 (54%). According to TNM staging, the most common stage was the metastatic stage (28.3%) (Table 2). The mean follow-up period was 25.76±25.02, overall survival was 50.5%, and cancer-specific survival was 59.6% (Figures 2, 3). In univariate analysis, grade, metastasis status and surgical status were found to be independent risk factors for survival. In multivariate analysis, only metastasis status was determined as a risk factor. For overall survival, metastasis was found to increase the risk of death 10-fold (HR: 10.094 [95% CI 4.039-25.227]) and cancer-specific survival 15.8-fold (HR: 15.813 [95% CI 5.389-46.402]) (Table 2).

Table 1. Clinical and oncological outcomes of patients

		All patients (n=92)	
		N	%
Age at diagnosis	**Median**	67	
	Interval (IQR)	58.25-73.50	
Race	**White**	63	68.5
	Black	18	19.6
	Other	11	12
Marital status	**Married**	57	62
	Other	35	38
Side	**Right**	48	52.2
	Left	39	42.4
	Unknown	5	5.4
Sequence	**Single cancer**	67	72.8
	Multiple different cancers	25	27.2
Grade	**I**	1	1.1
	II	15	16.3
	III-IV	61	66.3
	Unknown	15	16.3
Tumour size	**T0**	5	5.4
	T1	22	23.9
	T2	41	44.6
	T3	4	4.3
	T4	7	7.6
	Tx	13	14.1
N stage	**N0**	54	58.7
	N1	22	23.9
	N2	4	4.3
	N3	4	4.3
	NX	8	8.7
Metastasis	**M0**	66	71.7
	M1	26	28.3
Stage	**IA**	15	16.3
	IB	4	4.3
	IIA	17	18.5
	IIB	8	8.7
	IIIA	5	5.4
	IIIB	5	5.4
	IIIC	4	4.3
	IV	26	28.3
	Unknown	8	8.7
Surgery	**Performed**	62	67.4
	Not performed	30	32.6
Radiotherapy	**Yes**	37	40.2
	No	55	59.8
Chemotherapy	**Yes**	56	60.9
	No	36	39.1
Metastasis	**Bone**	17	18.5
	Brain	4	4.3
	Liver	4	4.3
	Lung	11	12
Life status - cause of death	**Alive**	54	58.7
	Breast cancer	29	31.5
	Other disease	9	9.8

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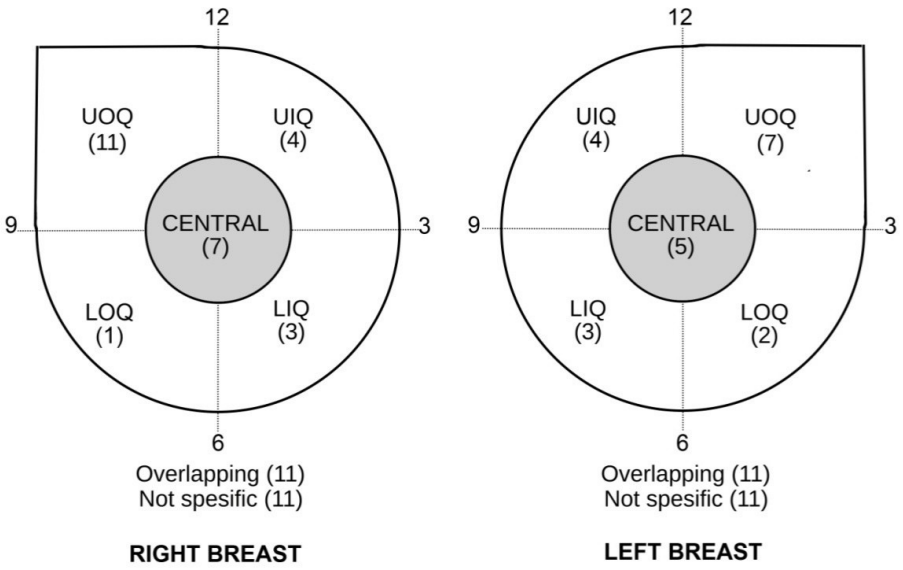

Figure 1. Distribution by side and quadrants

Tablo 2. Cox regression analysis for prognostic factors

	Overall survival				**Cancer-specific survival**			
	Univariate analysis							
	p	**HR**	**95% CI**		**p**	**HR**	**95% CI**	
Marital status	0.822				0.421			
Race	0.838				**0.787**			
Grade 1	Referance				Referance			
Grade 2	**0.006**	0.039	0.004	0.392	**0.002**	0.017	0.001	0.224
Grade 3	**0.018**	0.077	0.009	0.641	**0.009**	0.053	0.006	0.477
T stage	**0.476**				**0.159**			
N stage	**0.822**				**0.898**			
M0	Referance				Referance			
M1	**<0.001**	10.831	5.327	22.023	<0.001	19.138	4.256	86.062
Stage IA	Referance				Referance			
Stage IB	0.987	<0.001	<0.001	-	0.988	<0.001	<0.001	-
Stage IIA	0.983	1.018	0.205	5.052	0.985	1.019	0.143	7.246
Stage IIB	0.289	2.387	0.478	11.907	0.977	<0.001	<0.001	-
Stage IIIA	0.982	<0.001	<0.001	-	0.983	<0.001	<0.001	-
Stage IIIB	0.309	2.532	0.423	15.164	0.182	3.805	0.535	27.047
Stage IIIC	0.208	3.163	0.527	18.987	0.126	4.627	0.650	32.921
Stage IV	**<0.001**	14.998	4.274	52.632	<0.001	19.138	4.256	86.062
Surgery performed	Referance				Referance			
No surgery	**<0.001**	3.383	1.770	6.465	**<0.001**	3.340	1.595	6.991
Radiotherapy	0.095				0.380			
Chemotherapy	0.221				0.506			
	Multivariate analysis							
Grade 1	Referance				Referance			
Grade 2	0.119				**0.041**	0.065	0.005	0.898
Grade 3	0.189				0.097			
M0	Referance				Referance			
M1	**<0.001**	10.094	4.039	25.227	**<0.001**	15.813	5.389	46.402
Surgery	0.903				0.567			

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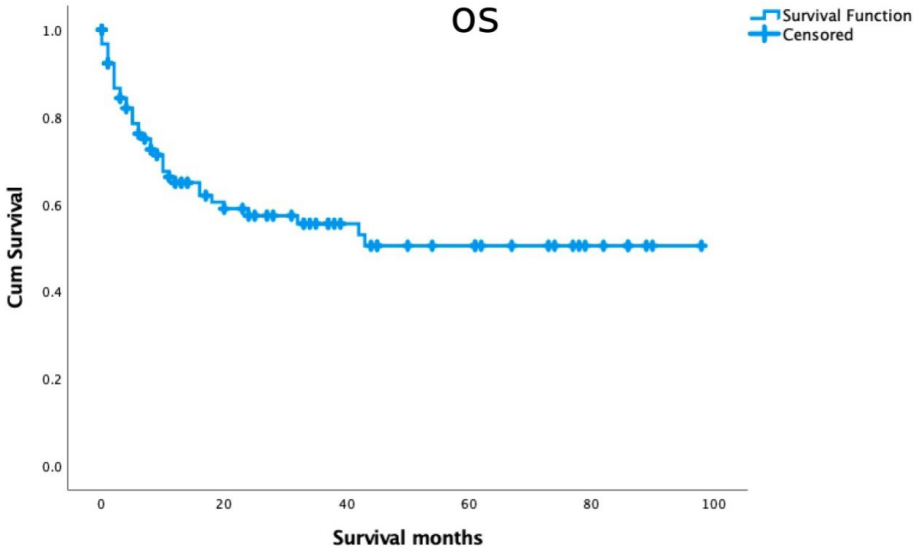

Figure 2. Overall survival graph

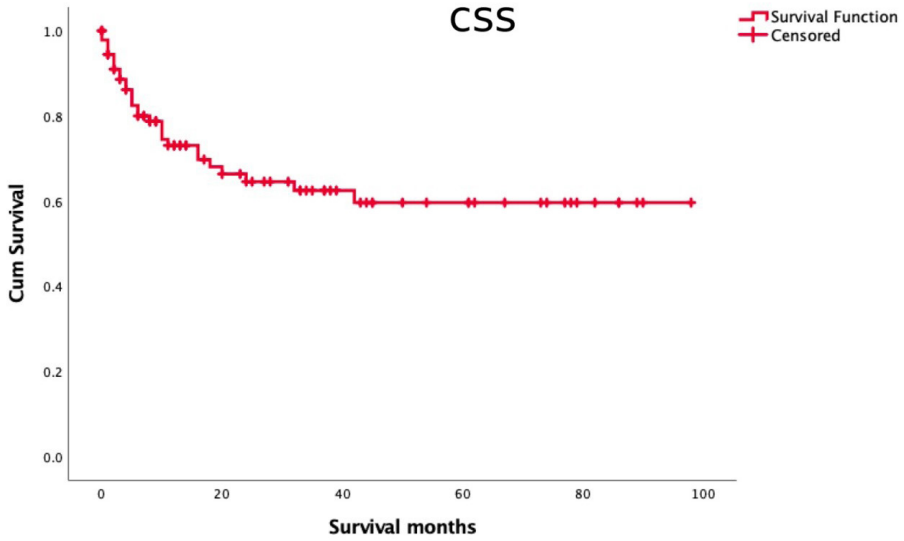

Figure 3. Cancer-specific survival graph

Discussion

MBC is a relatively rare disease, accounting for less than 1% of all breast cancer cases. But it's critical to comprehend the distinct features and prognosis of male breast cancer, particularly when it comes to subcategories like TN breast cancer. Using information from the SEER database, we examined prognostic factors influencing survival and survival in male patients with TN breast cancer in this population-based analysis.

The study included 92 TN MBC patients out of a total of 4930 MBC patients, representing a prevalence of 1.87%. This result is in line with other research showing that men are less likely than women to develop TN breast cancer [9,10].

The majority of male patients with TN breast cancer in our study (86.25%) were assigned to the luminal subtype. Given that TN breast cancer is generally linked to a more aggressive phenotype and a worse prognosis, this finding is noteworthy [11]. Further research is necessary to investigate whether there are any variations in molecular characteristics or treatment responses between triple negative male breast cancer and triple negative female breast cancer, given the prevalence of the luminal subtype in male patients.

Our study's TN MBC patients had a median age of 67 years, which is in line with other research that indicates male breast cancer tends to strike older people than female breast cancer [12,13]. Reflecting the racial distribution of the population included in the SEER database, the majority of patients were white (68.5%). The high prevalence of white patients in our study is consistent with previous reports showing higher male breast cancer incidence rates among white men compared with men of other racial/ethnic backgrounds [14,15].

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An important finding of our study was that the majority of triple negative MBC patients presented with advanced stages of the disease. The most common tumor stage was stage IV (28.3%), indicating a significant proportion of patients with distant metastases at diagnosis. This is consistent with previous studies highlighting advanced stage at diagnosis as a characteristic feature of MBC, which contributes to an overall worse prognosis in male patients [8,16]. The high incidence of advanced disease in triple-negative MBC emphasizes the need for increased awareness, early detection, and improved screening strategies specifically targeting men.

Both the OS and CSS rates that we found in our study were not very high. The OS rate was 50.5%, while the CSS was 59.6%. The median follow-up period was 25.76 months. These results underline the serious difficulties in treating male patients with triple negative breast cancer and the pressing need for better therapeutic strategies for this patient subset. It is important to note that the survival rates reported in our study may be affected by factors such as comorbidities, access to healthcare, and treatment inequalities, which were not specifically evaluated in our analysis. Further studies are needed to investigate these factors and their impact on survival outcomes in TN breast cancer.

In TN MBC patients, our univariate and multivariate analyses identified significant predictive markers for both OS and CSS. In univariate analysis, grade, surgical status, and metastasis status were identified as independent risk factors for survival. Only the status of metastases, however, continued to be significant in the multivariate analysis, indicating that in triple negative male breast cancer patients, the existence of metastatic disease at the time of diagnosis is a strong predictor of a poor prognosis. This result is in line with earlier research showing how metastasis affects survival rates in male breast cancer patients [17,18].

Limitations of our study include the retrospective nature of the analysis and reliance on data from a population-based registry. The SEER database provides valuable information on a large number of cancer cases; however, it may have inherent limitations such as missing data, potential coding errors, and a lack of detailed information.

Conclusion

In conclusion, our study provides valuable information on survival rate and prognostic factors in TN MBC patients. Most triple negative male breast cancer cases are presented at advanced stages, emphasizing the need for improved detection and screening strategies.The relatively low prevalence of triple negative breast cancer in men is encouraging; however, poor survival outcomes require the development of more effective treatment approaches. Future studies should focus on elucidating the molecular features, treatment responses, and underlying factors contributing to luminal subtype predominance in triple-negative male breast cancer. A better understanding of triple negative male breast cancer will pave the way for personalized and targeted interventions and ultimately improve the prognosis and quality of life of affected individuals.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
At this study utilized de-identified data from the SEER database, which is publicly available and maintains patient anonymity, ethical approval and informed consent were not required. His study was performed in line with the principles of the Declaration of Helsinki.

References

1. Arzanova E, Mayrovitz HN. Male breast cancer: treatment trends, reported outcomes, and suggested recommendations. Cureus. 2021;13:e18337.
2. Lee EG, Jung SY, Lim MC, et al. Comparing the characteristics and outcomes of male and female breast cancer patients in Korea: Korea central cancer registry. Cancer Res Treat. 2020;52:739-46.
3. Trogdon JG, Baggett CD, Gogate A, et al. Medical costs associated with metastatic breast cancer in younger, midlife, and older women. Breast Cancer Res Treat. 2020;181:653-65.
4. Chen JQ, Russo J. ERalpha-negative and triple negative breast cancer: molecular features and potential therapeutic approaches. Biochim Biophys Acta. 2009;1796:162-75.
5. Dietze EC, Sistrunk C, Miranda-Carboni G, et al. Triple-negative breast cancer in African-American women: disparities versus biology. Nat Rev Cancer. 2015;15:248-54.
6. Qin W, Qi F, Guo M, et al. Hormone receptor status may impact the survival benefit between medullary breast carcinoma and atypical medullary carcinoma of the breast: a population-based study. Front Oncol. 2021;11:677207.
7. Valachis A, Carlqvist P, Ma Y, et al. Overall survival of patients with metastatic breast cancer in Sweden: a nationwide study. Br J Cancer. 2022;127:720-5.
8. Wang S, Hu J, Zhang Y, et al. Presentation and survival by hormonal receptor status in metaplastic breast cancer: A propensity score-matched analysis. Breast. 2021;60:168-76.
9. Leone JP, Hassett MJ, Leone J, et al. Efficacy of neoadjuvant chemotherapy in male breast cancer compared with female breast cancer. Cancer. 2022;128:3796-803.
10. Wang F, Shu X, Meszoely I, et al. Overall mortality after diagnosis of breast cancer in men vs women. JAMA Oncol. 2019;5:1589-96.
11. Wu Q, Siddharth S, Sharma D. Triple negative breast cancer: a mountain yet to be scaled despite the triumphs. Cancers (Basel). 2021;13:3697.
12. Yao N, Shi W, Liu T, et al. Clinicopathologic characteristics and prognosis for male breast cancer compared to female breast cancer. Scientific Reports. 2022;12:220.
13. Yu XF, Yang HJ, Yu Y, et al. A prognostic analysis of male breast cancer (MBC) compared with post-menopausal female breast cancer (FBC). PLoS One. 2015;10:e0136670.
14. Anderson WF, Jatoi I, Tse J, Rosenberg PS. Male breast cancer: a population-based comparison with female breast cancer. J Clin Oncol. 2010;28:232-9.

DOI: 10.5455/medscience.2024.06.056

15. Chichura A, Attai DJ, Kuchta K, et al. Male breast cancer patient and surgeon experience: the male whysurg study. Ann Surg Oncol. 2022;29:6115-31.

16. Gnerlich JL, Deshpande AD, Jeffe DB, et al. Poorer survival outcomes for male breast cancer compared with female breast cancer may be attributable to in-stage migration. Ann Surg Oncol. 2011;18:1837-44.

17. Rashid NS, Grible JM, Clevenger CV, Harrell JC. Breast cancer liver metastasis: current and future treatment approaches. Clin Exp Metastasis. 2021;38:263-77.

18. Zhang L, Zhang J, Li Z, et al. Comparison of the clinicopathological characteristics and prognosis between Chinese patients with breast cancer with bone-only and non-bone-only metastasis. Oncol Lett. 2020;20:92.