

The association between surgery type and heart-specific mortality in male breast cancer

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Ethics Committee Approval

As 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.

Conflict of Interest

No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Male breast cancer, while less prevalent than female breast cancer, remains a significant health concern for men. Heart-specific mortality presents a significant worry for male breast cancer patients, as treatment and underlying comorbidities may increase their risk for cardiovascular complications. The purpose of this study was to investigate the associations between the type of surgery and heart-specific mortality in male breast cancer patients.

Methods: Data were extracted from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) 17 tumor registry database. The study encompassed a total of 86 male breast cancer patients who succumbed to heart disease. Patients with missing data on key variables were excluded. We divided the patients into two groups based on the type of surgery they received: breast-conserving surgery (BCS) and mastectomy.

Results: The mean age of the BCS group was 78.9 years, while the mean age of the Mastectomy group was 74.7 years. The tumor was most commonly located in the center on both sides. There was no statistically significant difference in the ethnic composition of the groups. All patients in both groups were estrogen receptor (ER) positive. Grade 1 tumors were more prevalent in the BCS group, and Grade 3 tumors were more prevalent in the Mastectomy group. The survival rates did not significantly differ between the two types of surgeries.

Conclusion: This study suggests that the type of surgery (BCS or mastectomy) does not significantly affect heart-specific mortality in male breast cancer patients. For a deeper understanding of any additional factors impacting heart-related outcomes in this cohort, further research is required.

Keywords: male breast cancer, disease of heart, survival

Introduction

When compared to breast cancer in females, male breast cancer is a rare but significant malignancy [1]. Breast-conserving surgery (BCS) and mastectomy are surgical options for treating male breast cancer [2]. Although the main goals of these operations are achieving local control and improving overall survival, it remains unclear how they may influence certain causes of mortality, such as heart-related deaths [3]. To optimize treatment options and enhance patient outcomes, it is essential to understand the relationship between the type of surgery and heart-specific mortality in male breast cancer patients [4].

This study aimed to investigate the relationship between the type of surgery and heart-specific mortality in male breast cancer patients. We aimed to ascertain whether the chosen surgical procedure impacts the risk of heart-related fatalities in this population. We utilized data from the SEER 17 tumor registry database, a comprehensive, population-based compilation of cancer cases across the United States maintained by the National Cancer Institute.

Materials and methods

The data were obtained from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) 17 tumor registry database, updated in November 2021. The information was extracted using the SEER*Stat 8.4.0.1 program. The starting point for SEER was set in 2010, as it began collecting information on HER2 status that year. Male breast cancer patients who died due to heart disease were selected for this study, with a total of 86 patients' data examined based on clinicopathological and oncological outcomes. Patients with unknown age, race, molecular subtype, grade, estrogen receptor (ER), progesterone receptor, Her2 status, stage, and surgery status were excluded from the analysis. Patient groups were determined based on the type of surgery performed: breast-conserving surgery (BCS) or mastectomy.

Statistical analysis

Categorical variables were compared using Pearson's chi-square test, Fisher's exact test, or Fisher Freeman Halton test, as appropriate. The Mann-Whitney U test was used to compare non-normally distributed continuous variables. Survival curves were created using the Kaplan-Meier method. The log-rank test was employed to compare survival outcomes among different patient subgroups. All tests carried out were two-sided, and $P < 0.05$ was deemed statistically significant. Statistical analysis was executed using SPSS for Windows (version 22.0, SPSS Inc., Chicago, IL, USA).

Results

The demographic characteristics of the 86 male breast cancer patients who succumbed to heart disease are summarized in Table 1. The median age at diagnosis was 80 years (range 49–85 years). Nine patients underwent BCS, while 77 patients went through a mastectomy. The majority of patients were 80 years old or older. Notably, a significant decrease in the number of male breast cancer patients dying from heart disease was observed in 2018 and 2019. In terms of laterality, 40 patients had cancer in the right breast, and 46 had it in the left breast. The

tumor was most commonly located centrally on both sides (Figure 1).

Table 1: Patient characteristics.

	n=86	BCS	Mastectomy	P-value
Age, mean (SD)	75.1 (10.11)	78.9 (10.01)	74.7 (10.01)	0.295a
Race				
White	72 (83.7%)	8 (88.9%)	64 (83.1%)	1b
Black	9 (10.5%)	1 (11.1%)	8 (10.4%)	
Other	5 (5.8%)		5 (6.5%)	
ER status				
Positive	86 (100%)	9 (100%)	77 (100%)	
PR status				
Positive	83 (96.5%)	9 (100%)	74 (96.1%)	1c
Negative	3 (3.5%)		3 (3.9%)	
Her2 status				
Positive	9 (10.5%)		9 (11.7%)	0.278d
Negative	77 (89.5%)	9 (100%)	68 (88.3%)	
Grade				
1	10 (11.6%)	3 (33.3%)	7 (9.1%)	0.048b
2	43 (50%)	5 (55.5%)	38 (49.4%)	
3	33 (38.4%)	1 (11.1%)	32 (41.6%)	
Laterality				
Right	40 (46.5%)	3 (33.3%)	37 (48.1%)	0.494c
Left	46 (53.5%)	6 (66.7%)	40 (51.9%)	
Molecular subtype				
Luminal A	77 (89.5%)	9 (100%)	68 (88.3%)	0.278d
Luminal B	9 (10.5)		9 (11.7%)	
Stage				
1A	20 (23.3%)	4 (44.4%)	16 (20.8%)	0.467b
1B	3 (3.5%)	1 (11.1%)	2 (2.6%)	
2A	24 (27.9%)	3 (33.3%)	21 (27.3%)	
2B	18 (20.9%)	1 (11.1%)	17 (22.1%)	
3A	9 (10.5%)		9 (11.7%)	
3B	10 (11.6%)		10 (13%)	
3C	1 (1.2%)		1 (1.3%)	
4	1 (1.2%)		1 (1.3%)	
Survival (month)	35.1 (26.1)	31.8 (31.6)	35.5 (25.6)	0.810e

a: Mann-Whitney U, b: Fisher Freeman Halton, c: Fisher's Exact Test, d: Pearson Chi-Square, e: Kaplan Meier (Long rank)

Figure 1: Patients characteristics. A) year of diagnosis, B) age at diagnosis, C) tumor localization.

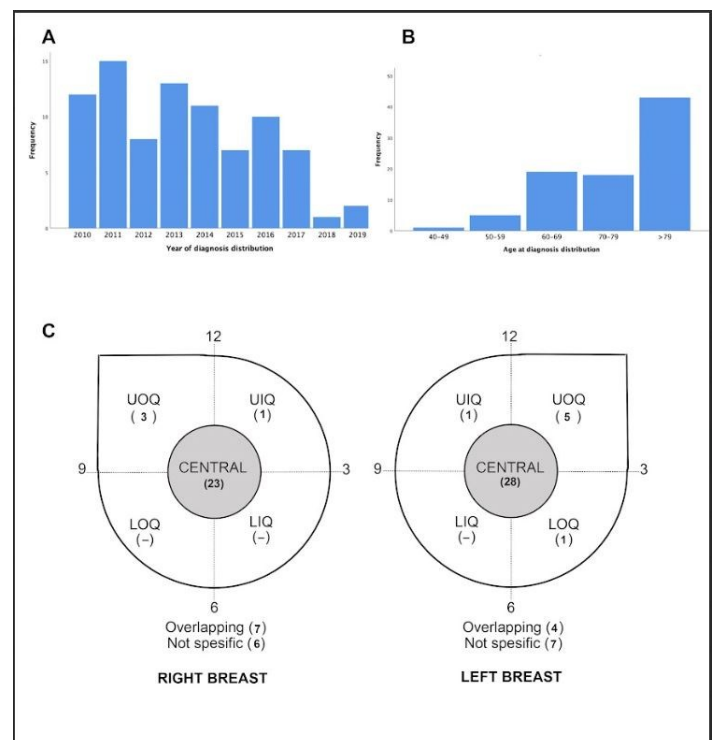


Table 1 outlines the clinicopathologic features of the patients and the results from subgroup tests. The average age was 78.9 (10.01) for the BCS group and 74.7 (10.01) for the Mastectomy group. Most of the patients were of white ethnicity, with whites accounting for 88.9% in the BCS group and 83.1% in the Mastectomy group. However, there was no statistically significant difference in ethnicity between the two groups.

All patients in both groups were ER positive. There were no progesterone receptor (PR) negative patients in the BCS

group, whereas in the Mastectomy group, the PR negativity rate was 3.9%. There were no HER2-positive patients in the BCS group, but 11.7% of patients in the Mastectomy group were HER2-positive.

Grade 1 (33.3% vs. 9.1%) was more common in the BCS group, while Grade 3 (11.1% vs. 41.6%) was more frequent in the Mastectomy group. The rate for Grade 2 was similar in both groups (55.5% vs. 49.4%). There was no significant difference in laterality ($P=0.494$).

Neither group presented with HER2-enriched or triple-negative cancer. In the BCS group, all patients were Luminal A, whereas in the Mastectomy group, 88.3% were Luminal A. All patients who underwent BCS were in the early stage, and 72.8% of patients who underwent mastectomy were also at this stage. However, there was no significant difference in the distribution of stages between these groups.

The average survival time was 35.1 (26.1) months. Notably, there was no significant difference in survival rates across the groups ($P=0.810$). The 5-year survival rate was slightly higher in the BCS group at 22.2% compared to 22.1% in the Mastectomy group (Figure 2).

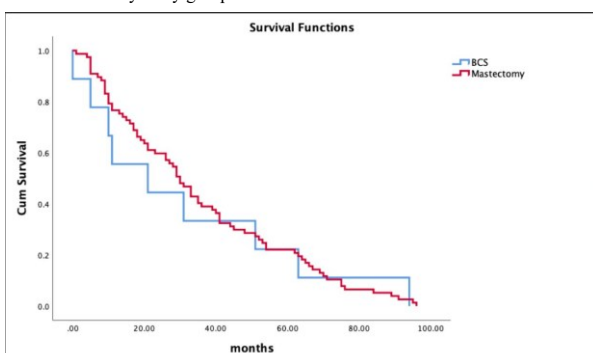
In the univariate regression analysis, race, ER status, PR status, HER2 receptor status, grade, laterality, stage, and molecular subtype were not identified as prognostic factors (Table 2).

Table 2: Cox proportional-hazard models.

	Univariate analysis		
	HR	%95 CI	P-value
Race			
White	Reference		
Black	1.161	0.576-2.430	0.676f
Other	1.856	0.741-4.646	0.187f
PR status			
Positive	Reference		
Negative	1.290	0.405-4.110	0.667f
Her2 status			
Positive	Reference		
Negative	0.748	0.370-1.511	0.418f
Grade			
1	Reference		
2	0.497	0.246-1.007	0.052f
3	0.666	0.325-1.363	0.266f
Laterality			
Right	Reference		
Left	1.316	0.856-2.021	0.211f
Molecular subtype			
Luminal A	Reference		
Luminal B	1.337	0.662-2.702	0.418f
Stage			
1A	Reference		
1B	0.564	0.166-1.920	0.360f
2A	1.162	0.633-2.134	0.627f
2B	1.263	0.662-2.409	0.478f
3A	0.775	0.340-1.768	0.545f
3B	1.308	0.605-2.825	0.495f
3C	0.529	0.070-3.974	0.536f
4	92.407	5.612-1521.487	0.002f

f: Cox-regression analysis

Figure 2: Survival analysis by groups.



Discussion

The present study aimed to investigate the association between surgery type and heart-specific mortality in male breast cancer patients. The findings of our analysis indicate that whether BCS or mastectomy is performed, there is no significant difference in heart-specific mortality in this cohort.

Our results align with earlier research that discovered similar outcomes for overall survival between BCS and mastectomy in male breast cancer patients [5,6]. This suggests that in this patient population, long-term survival may not be primarily influenced by the surgical method. It is crucial to note that our study solely focused on heart-specific mortality and omitted important outcomes such as local recurrence rates and distant metastases.

The mean age at diagnosis in our study was aligned with the older age group that is frequently affected by male breast cancer [7]. The condition primarily affects the elderly, and consequently, the majority of patients in both the BCS and Mastectomy groups were 80 years of age or older [8]. An unexpected finding, which may warrant further investigation, is the reported reduction in the number of male breast cancer patients who died from heart disease in 2018 and 2019. This could be attributed to various factors, including improvements in cardiovascular care, changes in treatment protocols, or enhanced overall cancer management.

The BCS and Mastectomy groups displayed substantial differences, as evidenced by clinicopathological analysis. The BCS group had a higher prevalence of Grade 1 cancers, whereas the Mastectomy group had a higher prevalence of Grade 3 tumors. This suggests potential shifts in tumor biology and aggression between the two groups, which could influence treatment selection and long-term outcomes [9]. Despite these variations, there were no significant differences in survival rates between the BCS and mastectomy procedures.

It was interesting to note that all of the patients in both groups had estrogen receptor (ER) positive breast cancer, demonstrating a high frequency of hormone receptor-positive disease. This finding aligns with previous research [10–13] that highlighted hormone receptor positivity in the majority male breast cancer cases. Additional information about the molecular subtypes of male breast cancer was provided by the absence of PR negativity in the BCS group and some Her2 positivity in a few patients in the mastectomy group [14]. However, in our investigation, there was no significant relationship between the distribution of molecular subtypes and survival outcomes.

The lack of prognostic factors and substantial differences in survival rates among the analyzed variables underscore the necessity to explore new variables that might impact heart disease-related outcomes in male breast cancer patients. These factors might encompass genetic susceptibility, adjuvant treatments, cardiovascular comorbidities, treatment-related cardiotoxicity, lifestyle factors, and cardiovascular comorbidities [15,16]. The management of cardiovascular disease and other potentially influential variables should be carefully considered, in addition to surgical intervention, as part of a comprehensive multidisciplinary approach to patient care [17,18].

Limitations

It is important to acknowledge that our study has several limitations. First, the study's retrospective design, which relies on registry data, has inherent biases and constraints. Second, the slightly small sample size may have impacted our ability to identify minor variations among all types of surgeries. Moreover, the study did not consider additional crucial endpoints, such as local recurrence or distant metastases, focusing solely on heart-specific mortality. To corroborate our findings and gain a more comprehensive understanding of the relationship between the type of surgery and outcomes in male breast cancer patients, further research with larger sample sizes and extended follow-up periods is necessary.

Conclusion

Our research indicates that the type of surgery a male undergoes, whether BCS or mastectomy, has no significant impact on heart-specific mortality. This underscores the need for a comprehensive approach to managing male breast cancer, taking into account many aspects beyond the surgical procedure. To improve survival rates and outcomes for patients with male breast cancer, further studies are required to elucidate the complex relationships between breast cancer, surgical treatments, and cardiovascular outcomes.

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