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Short Communication

Prognostic Factors in Breast Cancer Survival: A Log-Normal Accelerated Failure Time Model Analysis From Western Iran

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Abstract

Introduction: Breast cancer (BC) is the most common malignancy among women worldwide. Thus, this retrospective cohort study aimed to identify prognostic factors for BC-specific survival using parametric accelerated failure time models.

Methods: Data were collected from 820 female patients diagnosed between 2014 and 2020 at Shahid Mostafa Khomeini Hospital in Ilam, Iran, with follow-ups through 2023. Survival time was defined from diagnosis to BC death or censoring. The Kaplan-Meier method, along with log-rank tests, was applied in the model.

Results: Among 798 patients, 72 BC deaths occurred (9.0%). The goodness of fit in the log-normal model was evaluated using the Akaike Information Criterion (AIC = 574.2) and the Bayesian Information Criterion (BIC = 607.0). Moreover, histological type was the only significant independent predictor of survival. Compared with infiltrating ductal carcinoma, lobular carcinoma was associated with shorter survival (time ratio = 0.613; 95% confidence interval: 0.401–0.939; $P = 0.024$). Nonetheless, age, tumor topography, diagnostic method, and tumor grade were not statistically significant predictors.

Conclusion: Histological type is a key prognostic factor for breast cancer survival, with non-ductal tumors indicating poorer outcomes. The log-normal model provides the best statistical fit for this analysis.

Keywords: Breast cancer, Survival analysis, Prognostic factors, Log-Normal model, Cox regression, Iran

Introduction

Breast cancer (BC) is the most common malignancy among women worldwide and remains a major public health challenge.[1] Multiple factors influence the incidence and prognosis of BC, including age, genetic predisposition, tumor characteristics, and timely diagnosis.[2] Despite advances in early detection and treatment that have reduced mortality, the dise[case burden persists, necessitating continued research into prognostic factors and survival outcomes.[2,3]

In cancer epidemiology, survival analysis is essential for evaluating treatment effectiveness, guiding screening programs, and informing health policy.[4] In addition, selecting appropriate statistical models (nonparametric, semiparametric, or parametric) critically impacts the accuracy and interpretability of findings. Parametric accelerated failure time (AFT) models offer advantages over the semiparametric Cox model by incorporating distributional information and enabling direct interpretation of time-to-event outcomes.[5]

Given the high incidence of BC in Ilam Province, this study aims to identify prognostic factors for patient survival using parametric AFT models and compare their performance with nonparametric and semiparametric approaches.

Materials and Methods

Study Design and Population

This retrospective cohort study included 820 female patients with BC who were referred to the Chemotherapy Center of Shahid Mostafa Khomeini Hospital in Ilam Province, Iran, between March 2014 and March 2020. Follow-up data were collected through March 2023.

Data Collection

The required information, including age at diagnosis, tumor grade, diagnostic method, tumor topography, morphology, and death events, was extracted from patients' medical records using a standardized data collection form to ensure accuracy and consistency. The primary outcome was survival time, defined as the interval between the date of diagnosis and the date of death from BC (BC–specific

mortality) or the end of the follow-up period (censoring). Patients were censored if they were alive at last contact or lost to follow up.

Statistical Analysis

Three statistical approaches were applied for data analysis: *Non-Parametric Approach:* Survival curves were estimated using the Kaplan–Meier method.

Parametric Approach: Exponential, Weibull, log-normal, and log-logistic AFT models were fitted to identify prognostic factors associated with survival.

The final model was selected based on the Akaike Information Criterion and Bayesian Information Criterion, with lower values indicating superior model fit. The log-normal model provided the best fit and was selected as the final model. In AFT models, the effect of variables is interpreted using the time ratio (TR), which quantifies the multiplicative change in survival time per unit increase in the predictor.

Moreover, missing data for tumor grade were handled using the multiple imputation technique. All statistical analyses were performed using Stata software (version 15), with a significance level of 0.05 considered for all tests.

Results

Study Population Characteristics

A total of 820 female patients with BC were identified from the Chemotherapy Center at Shahid Mostafa Khomeini Hospital, Ilam, Iran, diagnosed between March 2014 and March 2020, with follow-ups through March 2023. After excluding 22 patients (2.7%) with incomplete follow-up data, 798 patients were included in the survival analysis. During a median follow-up of during a median follow-up (47 months), 72 deaths (9.0%) from BC were recorded months (with an average follow-up of 47 months), 72 deaths (9.0%) from BC were recorded, and the remaining 726 patients (91.0%) were censored.

The mean age at diagnosis was 50.1 years (standard deviation = 13.7; range: 23–87 years after excluding implausible values). In addition, the median survival time for the overall cohort was 5 years (interquartile range: 4–6 years). Table 1 presents the clinical and demographic characteristics of the study population.

Survival Analysis

Univariate Analysis

Kaplan–Meier analysis estimated 5-year and 8-year

Table 1. Clinical and Demographic Characteristics of Breast Cancer Patients (N = 820)

Characteristic		N	%	Mean (SD)	Median (IQR)
Age (years)	-	-	-	50.1 (13.7)	49 (70)
Survival time (months)	-	-	-	5.2 (2.2)	5 (4)
Diagnosis year	2014	93	11.3	-	-
	2015	80	9.8	-	-
	2016	124	15.1	-	-
Diagnostic method	2017	124	15.1	-	-
	2018	101	12.3	-	-
	2019	147	17.9	-	-
	2020	151	18.4	-	-
Tumor topography	Clinical assessment	16	2.0	4.12 (1.02)	4 (0)
	Cytology	8	1.0	8.25 (0.46)	8 (0.5)
	Clinical only	120	14.6	4.11 (2.2)	3 (2)
	Pathology	664	81.0	5.4 (2.1)	5 (3)
	Death certification	12	1.5	2.9 (3.4)	1.5 (6.5)
Histological type	Central portion	37	4.5	5.4 (2.1)	5 (3)
	Upper-outer quadrant	80	9.8	5.7 (2.03)	6 (3)
	Overlapping lesion	32	3.9	6.25 (2.21)	7 (4)
	Mammary gland	671	81.8	5.07 (2.2)	5 (4)
	Neoplasm	48	5.9	4.4 (1.1)	4 (1)
	Carcinoma	30	3.7	4.8 (2.4)	4.5 (4)
	Infiltrating duct carcinoma	316	38.5	5.5 (2.3)	5 (3)
	Lobular carcinoma	399	48.7	5.07 (2.1)	5 (4)
Tumor grade	Infiltrating duct + lobular	27	3.3	5.6 (2.6)	6 (4)
	Grade I	17	2.1	5.3 (1.8)	5 (3)
	Grade II	71	8.7	5.5 (2.2)	5 (3)
	Grade III	61	7.4	5.6 (1.9)	6 (3)
	Undetermined	671	81.8	5.1 (2.2)	5 (4)

Note. IQR: Interquartile range; SD: Standard deviation.

survival probabilities as 0.86 (95% confidence interval [CI]: 0.83–0.89) and 0.80 (95% CI: 0.76–0.84), respectively. Log-rank tests also demonstrated a significant association between histological type and survival ($P=0.046$). Additionally, year of diagnosis approached a significant level ($P=0.049$). Nonetheless, tumor grade ($P=0.079$), diagnostic method ($P=0.178$), and topography ($P=0.723$) were not significant.

Multivariable Analysis

Among all variables, histological type was the only significant independent prognostic factor. Compared to infiltrating ductal carcinoma (reference), lobular carcinoma was associated with a TR of 0.613 (95% CI: 0.401–0.939, $P=0.024$). A TR < 1 indicates shorter survival; thus, after adjusting for age, topography, diagnostic method, and tumor grade, patients with lobular carcinoma had an estimated 38.7% shorter survival time than those with infiltrating ductal carcinoma. However, age (TR = 1.00, $P=0.973$), topography (all $P>0.28$), diagnostic method (pathology showed borderline non-significance, TR = 0.463, $P=0.061$), and tumor grade (all $P>0.62$) did not reach statistical significance (Table 2).

Kaplan–Meier Survival Analysis

In the Kaplan–Meier survival analysis, the overall survival probability decreased from 1.00 at the beginning of the follow-up to 0.76 (95% CI: 0.72–0.80) at the end of the follow-up period (time = 10). The estimated survival probabilities at selected time points at 2, 4, 6, and 8 years were 0.98 (95% CI: 0.97–0.99), 0.92 (95% CI: 0.90–0.94), 0.86 (95% CI: 0.83–0.89), and 0.80 (95% CI: 0.76–0.84), respectively (Figure 1).

Furthermore, the number of patients at risk at the corresponding time points was 798, 786, 614, 366, 142, and 0, respectively.

Discussion

In this retrospective cohort study of 798 BC patients from western Iran, histological type was identified as the only statistically significant independent predictor of BC-specific survival using a log-normal accelerated failure time model. Likewise, patients with histological types other than infiltrating duct carcinoma (specifically lobular carcinoma) experienced a 38.7% reduction in survival time (TR = 0.613; 95% CI: 0.401–0.939; $P=0.024$), indicating a significantly poorer prognosis.

The prognostic value of histological subtype is well established in the literature. Lobular carcinoma, which comprised nearly half of our cases (%48.7), has been associated with distinct biological behavior, including greater multifocality, delayed detection due to subtle clinical presentation, and differential metastatic patterns compared to ductal carcinoma

These characteristics may contribute to the poorer survival observed in our study. However, the predominance of lobular carcinoma in our population diverges from most Iranian studies, where infiltrating duct carcinoma

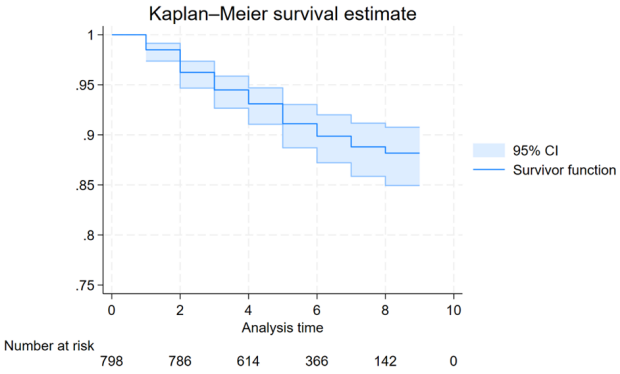

Figure 1. Kaplan-Meier Survival Curve With %95 CIs and Number of Patients at Risk at Selected Time Points
Note. CI: Confidence interval

Table 2. Multivariable Log-Normal AFT Regression Analysis of Breast Cancer-Specific Survival (N = 798, events = 72)

Variable	Category	Time Ratio	95% CI	*P*-Value
Age (per year)	Continuous	0.9997	0.9848–1.0149	0.973
Tumor topography	Central portion of breast	1 (Ref.)	–	–
	Upper-outer quadrant	0.547	0.158–1.896	0.341
	Overlapping lesion	0.938	0.200–4.390	0.935
	Mammary gland	0.541	0.175–1.674	0.287
Histological type	Infiltrating duct carcinoma	1 (Ref.)	–	–
	Neoplasm	1.597	0.400–6.369	0.507
	Lobular carcinoma	0.613	0.401–0.939	0.024
	Infiltrating duct and lobular	0.853	0.275–2.642	0.783
Diagnostic method	Just clinical	1 (Ref.)	–	–
	Clinical assessment	0.325	0.049–2.130	0.241
	Pathology	0.463	0.207–1.036	0.061
Tumor grade	Grade I	1 (Ref.)	–	–
	Grade II	0.718	0.187–2.754	0.629
	Grade III	0.901	0.227–3.578	0.883
	Undetermined	1.171	0.336–4.091	0.805

Note. AFT: Accelerated failure time; CI: Confidence interval.

typically accounts for %70–80 of cases.[6,7] This discrepancy may reflect regional variations in genetic predisposition, environmental exposures, or diagnostic practices, thereby warranting further investigation.[8]

Despite being nonsignificant in univariate analysis, tumor grade demonstrated a borderline association with survival in the multivariable model ($P = 0.066$). This pattern suggests that after adjusting for histological type and other covariates, the effect of grade became more discernible, which is a phenomenon consistent with negative confounding. However, the high proportion of missing grade data (%81.8) and the borderline *P*-value in our study necessitate cautious interpretation. The direction of the effect (TR > 1, suggesting longer survival with higher grade) is counterintuitive and may reflect selection bias, as grading was likely performed preferentially in cases with sufficient pathological material or clearer diagnostic features. Other studies reported similar paradoxical findings when missing data were not randomly distributed.[9,10]

Age at diagnosis was not significantly related to survival in our study, which contradicts the findings of several larger studies that identified older age as an independent risk factor.[11,12] This null finding may be attributable to our relatively young cohort (mean age 50.1 years), limited statistical power due to few events (n = 72), or unmeasured confounding by stage and treatment. Similarly, the diagnostic method and tumor topography failed to predict survival, likely because these variables are proxies for more direct determinants of prognosis such as disease stage and access to care.

Limitations

This study had several limitations. The single-center design limited the generalizability of our findings. Key prognostic variables, including Tumor, Node, Metastasis stage, tumor size, lymph node status, hormone receptor status, and treatment modalities, were unavailable due to incomplete records, thereby introducing potential unmeasured confounding. Moreover, the high proportion of missing grade data (%81.8), despite multiple imputation, may have introduced bias. With only 72 events, the study may be underpowered to detect modest effects, reflected in the width of confidence intervals. Finally, cause of death ascertainment through hospital records may be subject to misclassification. Cautious interpretation is, therefore, warranted.

Conclusion

Histological type was an independent predictor of BC-specific survival in this cohort from western Iran, with non-ductal subtypes associated with significantly shorter survival. In addition, the log-normal accelerated failure time model provided an appropriate fit for these data, demonstrating the utility of parametric approaches in survival analysis. These findings underscore the need for standardized pathology reporting, complete cancer registry data, and strengthened early detection programs in order to improve outcomes for BC patients in Iran.

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Artificial Intelligence Disclosure

During the preparation of this manuscript, the author(s) employed ChatGPT for language editing, grammatical editing, and summarization. Additionally, all content generated with the assistance of these tools was carefully reviewed, validated, and revised by the author(s) in order to ensure accuracy, originality, and scholarly rigor. Moreover, the author(s) assume full responsibility for the integrity and final content of the published articles.

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Competing Interests

The authors declare that they have no conflict of interests.

Ethical Approval

Permission was obtained from the Ethics Committee of Ilam University of Medical Sciences for performing this study (IR.MEDILAM.REC.1402.034).

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