SHORT COMMUNICATION

Five-year Survival Predictors for Breast Cancer in Women: A Retrospective Cohort Study

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Abstract

Objective: To analyze predictors of 5-year survival in women with breast cancer in the state of Sergipe. **Materials and methods:** This is a retrospective cohort study. This study included 100 women aged between 21 and 77 years diagnosed with breast cancer undergoing adjuvant or neoadjuvant chemotherapy in a public tertiary hospital from August 2011 to December 2012. All women were followed up for 5 years or until the date of death. There was no loss in follow-up. Data were collected during the field visit to the specialized health unit and included demographic and socioeconomic variables, tumor staging at diagnosis, patient paths for presentation to health professionals, initial treatment in primary care and treatment. We used a three-stage model: the first ("patient delay"); the second ("delay in diagnosis") and the third ("delay in treatment"). The statistical analysis was performed using the MedCalc version 18 statistical software. The study was approved by the Human Research Ethics Committee of the Federal University of Sergipe (CAAE: 0196.0.107.000-11). Written informed consent was obtained from all participants. **Results:** Tumor staging [risk ratio (HR) = 3.41, p = 0.046] was an independent factor that affected the overall survival curve for women with breast cancer. The overall 5-year survival rates found for women with tumor staging IA-IIB compared to tumor staging IIIA-IV were 88.5% and 59.5%, respectively. Through binary logistic regression with forced entry method, it was evident that age (OR = 2.58, p = 0.050), delay in the first stage (OR = 2.57, p = 0.046) and tumor staging (OR = 3.99, p = 0.042) were predictors of mortality in women with breast cancer. **Conclusions:** Our results highlight the need to strengthen health education actions in primary health care and the implementation of an organized and permanent screening program for the early detection of breast cancer.

Keywords: Breast neoplasm- prognosis- survival analysis- primary health care- delayed diagnosis

Introduction

Breast cancer is the most common non-cutaneous malignancy worldwide and the leading cause of cancer death in women. In Brazil, it is estimated nearly 60,000 new cases of breast cancer and 14 deaths per 100,000 women in 2018 [1]. A recent study showed an increased trend of breast cancer mortality in women in Brazil, especially among young women and in the Northeast and Midwest regions [2].

Differences in survival from breast cancer observed seem to be related to socioeconomic inequities and disparities in access to health services which may lead in delay in diagnosis and treatment of disease [3-4].The delay in attention to breast cancer greater than three months between the identification of symptoms and initiation of treatment is considered an important prognostic factor, decreasing by 12% the survival in five years [5].

In addition actions of screening, diagnosis and treatment should be available to the population independently of their income [6], because the staging profile of women with breast cancer has been characterized by advanced stages of the disease, evidencing the late diagnosis as a national public health issue [7]. We investigated

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predictors of 5-year survival in women with breast cancer in Sergipe state.

Materials and Methods

Design

Little is known about the influence of survival predictors for breast cancer in the Northeast region, Brazil. In this retrospective cohort study, we investigate predictors of 5-year survival in women with breast cancer in Sergipe state, the smallest federal unit in terms of territory extension (21,918 km^2). Sergipe has one of the most incidence rates of breast cancer in Brazil, with 6.34 new cases per 100.000 women [1].

Pacients

This study included 100 women aged 21-77 years (51 ± 10.9 years) diagnosed as having breast cancer submitted to adjuvant or neoadjuvant chemotherapy in a tertiary-level public hospital from August 2011 to December 2012. All women were followed-up for 5 years or to date of death. There was no loss to follow-up. Data were collected during field visit in the specialized health care unit and included demographic and socioeconomic variables, tumor staging at diagnosis [8], patient pathways to presentation to health care professionals, initial management in primary care, and treatment. We used a three-stage model [9] to account for the total time from first noticing a symptom to beginning treatment. The first stage ("patient delay")was defined as the time the patient first noticing a symptom until to seek professional medical care; the second stage ("diagnosis delay") described the time between the first medical consultation and definitive diagnosis of breast cancer; and the third stage ("treatment delay") included the time between diagnosis and the onset of treatment.

Analyses statistics

Statistical analysis was performed using MedCalc Statistical Software version 18 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2018). Survival curves were presented as Kaplan-Meier curves, and significance was classified by the log-rank test. The Cox regression model was used for multivariate prognostic analysis, and a binary logistic regression model was used to analyze the influencing clinical factors. Analyses were performed using cutoffs of 30 (patient and diagnosis delay) and 60 (treatment delay) days [10-11]. Eight potential predictors (age, relationship status, years of schooling, income, residence, tumor staging, delay in first, second and third stages) were included in a multifactor analysis using the Cox multivariate regression model with a forced entry method.

Ethical approval

The study was approved by the Human Research Ethics Committee at the Federal University of Sergipe (CAAE: 0196.0.107.000-11). Informed written consent was obtained from all participants.

Results and Discussion

The results showed that tumor staging [hazard ratio (HR) = 3.41, p = 0.046] was an independent factor affecting the overall survival curve of women with breast cancer (Table 1). The 5-year overall survival rates found for women with tumor staging IA-IIB compared to tumor staging IIIA-IV were 88.5% and 59.5%, respectively (Figure 1). The same eight potential predictors were also analyzed by using a binary logistic regression model with a forced entry method. The results showed that age (OR=2.58, p =0.050), delay in first stage (OR=2.57, p =0.046), and tumor staging (OR=3.99, p = 0.042) were predictors for mortality in women with breast cancer (Table 2).

The advanced stage of breast cancer found in this study seems to be the leading prognostic factor for mortality. The 5-year overall survival rates for women with tumor staging IIIA-IV was similar to the found in earlier studies based on different Brazilian cohorts [12-13]. These findings underline the urgent need for structuring services for early-stage breast cancer detection of women with inclusion criteria for screening. In Brazil, women aged 50-69 years have been encouraged to undergo mammography every 2 years, and to have their breasts examined by a physician from 40 years of age [14]. There is evidence of a 20% relative risk reduction for mortality with mammography at 11 years of follow-up [15]. However, inequalities in health service use in the Northeast Brazil disfavor a regular mammographic screening [16], which may lead in delay in diagnosis of breast cancer.

Despite evidence that young women with breast cancer have a worse prognosis compared to that of middle-aged women even if diagnosed early and receiving intense treatment [17-18], this study showed that age > 50 years was a predictive factor for mortality, which may be related to the delay in diagnosis, advanced-stage tumor, and less-than-standard treatment. In addition, age-related comorbidities may play a role in the survival rate in this
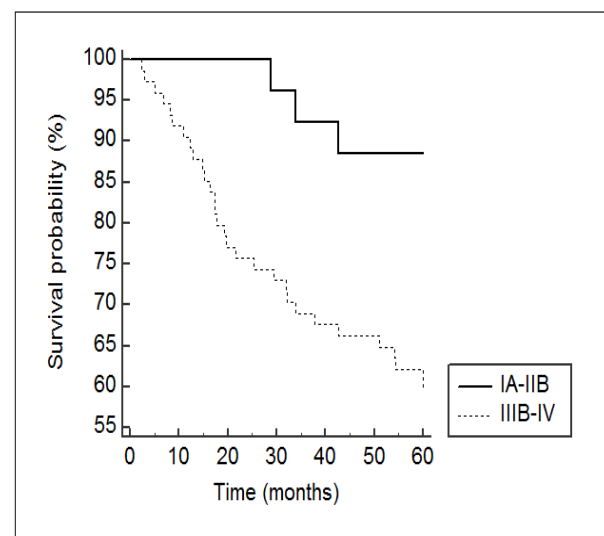

Figure 1. Kaplan-Meir Survival Estimates Based on TNM Stage at the Diagnosis

Table 1. Results of Log-rank Test and Multivariate Cox Regression Analysis of Clinical Factors in Predicting Overall Survival in Breast Cancer

Characteristic	Log-rank HR (95% CI)	p-value	Cox regression HR (95% CI)	p-value
Age (< 50 years vs. ≥ 50 years)	2.10 (1.06-4.16)	0.045	1.93 (0.91-4.07)	0.084
Relationship status (currently single vs. not currently single)	1.03 (0.52-2.06)	0.914		
Years of schooling (< 8 vs. ≥ 8)	1.00 (0.48-2.10)	0.993		
Income (< 2 minimum wages vs. ≥ 2 minimum wages)	1.32 (0.66-2.67)	0.421		
Residence (state city vs. principal city interior)	1.43 (0.71-2.85)	0.331		
TNM stage (IA-IIB vs. IIIB-IV)	4.34 (2.06-9.11)	0.008	3.41 (1.02-11.32)	0.046
Delay in first stage (yes vs. no)	2.18 (1.10-4.32)	0.027	1.87 (0.92-3.85)	0.086
Delay in second stage (yes vs. no)	0.76 (0.38-1.52)	0.44		
Delay in third stage (yes vs. no)	1.09 (0.55-2.17)	0.79		

HR, hazard ratio; CI, confidence interval.

Table 2. Results of Logistic Regression Analysis of Association between Clinical Factors and Death in Breast Cancer.

Characteristic	Univariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value
Age (< 50 years vs. ≥ 50 years)	2.52 (1.04-6.09)	0.041	2.58 (1.00-6.67)	0.05
Relationship status (currently single vs. not currently single)	1.09 (0.47-2.53)	0.837		
Years of schooling (< 8 vs. ≥ 8)	0.98 (0.39-2.43)	0.963		
Income (< 2 minimum wages vs. ≥ 2 minimum wages)	1.40 (0.60-3.26)	0.435		
Residence (state city vs. principal city interior)	1.43 (0.60-3.43)	0.416		
TNM stage (IA-IIB vs. IIIB-IV)	5.23 (1.44-18.98)	0.012	3.99 (1.05-15.13)	0.042
Delay in first stage (yes vs. no)	2.76 (1.16-6.54)	0.021	2.57 (1.02-6.48)	0.046
Delay in second stage (yes vs. no)	0.68 (0.29-1.56)	0.359		
Delay in third stage (yes vs. no)	1.09 (0.48-2.52)	0.832		

OR, odds ratio; CI, confidence interval.

population. Unfortunately, the expression of predictive molecular biological markers for breast cancer prognosis and that are age-dependent were not evaluated and constitute an intrinsic limitation of study design.

Moreover, the present study found an association between the delay in seeking medical attention after self-discovering a potential breast cancer symptom and mortality. Patient delay maybe associated to health behavior, including lack of breast self-examination and general health care utilization, and socioeconomic factors such as old age and ethnicity. In addition, non-attribution of symptoms to cancer, fear of the disease and treatment and low educational level seem to be frequent causes of patient delay [19]. Interestingly, it has been showed that older women are more prone to procrastinate early detection of breast cancer resulting in more advanced disease and fewer a symptomatic cases [20]. Our findings highlight the need to strengthen actions for health education in primary health care and the implementation of an organized and permanent screening program for early detection of breast cancer.

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