

RESEARCH ARTICLE

Delay in Diagnosis and Treatment of Breast Cancer among Women Attending a Reference Service in Brazil

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Abstract

Background: Cancer is a major public health problem. Early diagnosis and treatment are essential for reducing mortality. This study aimed to analyze factors associated with delay in breast cancer diagnosis and treatment among women attending a reference cancer service. **Methods:** This retrospective, cross-sectional study was performed with data collected from medical records and interviews conducted with women diagnosed with breast cancer and treated from October 2013 to October 2014 at a cancer reference hospital in Paraná, Southern Brazil. **Results:** A total of 82 participants were enrolled during the study period; their average age was 58.2 ± 11.5 years. The average time taken for final diagnosis of breast cancer was 102.5 ± 165.5 days. Treatment onset was delayed in the majority of cases, and the average time elapsing from diagnostic biopsy to onset of primary treatment was 72.3 ± 54.0 days. The odds of treatment delay were higher among the women with a low educational level. **Conclusions:** The results underline the need for proposals aimed at early detection, identification of risk factors and timely provision of treatment by health managers that focus on this group.

Keywords: Delay- diagnosis- treatment- breast neoplasms

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Introduction

Cancer is a public health problem due to its epidemiological, social and economic relevance (Barrow and Michels, 2014). Breast cancer is the second most common neoplasm worldwide and is frequent among women in both developed (second most common cause of death) and developing (main cause of death) countries (World Health Organization, 2012). In addition to its high prevalence, breast cancer is the fifth most common cause of death by cancer (World Health Organization, 2012). According to the National Cancer Institute, 57,960 new cases of breast cancer are estimated to occur in Brazil in 2016, with an estimated risk of 56.2 cases per 100,000 women. In the Southern region of Brazil, breast cancer affects 70.98 per 100,000 women (Brasil, 2014).

International studies conducted in areas of Libya, Pakistan, Mexico, Tanzania and Singapore have demonstrated a late presentation of breast cancer among women (Chang et al., 2011; Bright et al., 2011; Mabula et al., 2012; Ermiah et al., 2012; Memon et al., 2013). These cases are often discovered at an advanced stage because of a delay in diagnosis or treatment.

A delay in diagnosis has paramount importance because it may result in advanced stages of the disease. The odds of a cure, improved survival and quality of life are associated with early detection, diagnosis and treatment onset. Studies have shown that a delay in diagnosis and/or treatment favors tumor growth and eventually impairs the odds of a cure among patients (Trufelli et al., 2008; Al-Amri, 2015). These delays are usually associated with a delay on the part of the patient or the healthcare services (Al-Amri, 2015).

The Brazilian Guidelines for the detection of breast cancer aim to reduce the morbidity and mortality associated with later treatment (Brasil, 2013). A recent study (Gonçalves et al., 2014) showed that the greatest barriers in the care trajectory for breast cancer were related to the treatment period.

A retrospective cohort study showed that several factors might be involved in the delay of breast cancer treatment. Moreover, these factors may be different according to the regions in the country (Medeiros et al., 2015).

Although there are several international studies on delay in diagnosis and treatment of breast cancer, to the

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best of our knowledge, few studies have investigated this topic in Brazil.

Early diagnosis and treatment are determinant to reducing mortality. Thus, the present study aimed to analyze factors associated with breast cancer diagnosis and treatment delay among women attending a reference cancer service.

Materials and Methods

This cross-sectional retrospective study was conducted at a philanthropic service supported by the Fight Cancer Association of North Paraná, which is a local and regional reference center for cancer treatment located in the Northern-Central mesoregion of Paraná, Brazil. The hospital services 150 counties in the state of Paraná, and 80% of the cases correspond to patients covered by the Unified Health System.

The sample size was estimated based on the identification of female patients diagnosed with breast cancer during the study period, resulting in a total of 100 participants. Data and primary and secondary information were collected during the study period (October 2013 to October 2014) with interviews using a structured questionnaire designed to collect preclinical data and the review of medical records to extract clinical-pathological information about the participants. Women with mental confusion or who were unable to respond to the questionnaire were excluded from the study, as were those diagnosed with relapse, had started treatment at another institution, and refused to participate in the study (18 women). The inclusion criteria were a confirmed diagnosis of cancer and attending medical consultation and/or receiving treatment at the public reference unit of the hospital within the data collection period. The two aforementioned data collection techniques were used jointly to improve the reliability of the information and complement data missing in the medical records or forgotten by the participants at the time of the interview.

Independent variables collected during the face-to-face interview were: age, marital status, education, race/color, resident's populations and resident's outside the city, resident away from the city, family history of breast cancer; realization of self-examination; clinical examination and routine mammogram.

The independent retrospective information collected from the medical records included date of the last mammogram; date of biopsy; date of results of the biopsy; neoadjuvant or surgical primary treatment and clinic pathological variables such as clinical staging of the tumor based on the assessment of the size of the primary tumor (represented by the letters TNM) and categorized as I, IIA, IIB, IIIA, IIIB, IV and NA (when none of the categories could be applied) (Brazil, 2015) and estrogen and progesterone receptor (positive or negative).

For the analysis of the treatment initiation time, we used the date of the biopsy for the realization of primary treatment (neoadjuvant or surgery). The treatment time was considered a delayed start of treatment when it exceeded 30 days (Fedewa et al. 2011; Mc Gee et al, 2013).

The obtained information was tabulated through

descriptive analysis (mean and standard deviation) and bivariate analysis using the Chi-square test and Fisher's exact test where applicable with the Epi Info 3.5.1 program. In the next stage, we selected the independent variables that were considered important for the outcome analysis (delayed treatment) and studied the independent variables and the outcome variables using multivariate analysis by logistic regression in the program Statistica 7.1 with a level of significance of 5%.

The ignored data were removed and are not shown in the tables.

The present study was authorized by the hospital where it was performed and was approved by the permanent committee of ethics in research with human beings of the State University of Maringá, ruling no. 353,649. All participants signed an informed consent form.

Results

The sample consisted of 82 women (or their medical records) who were diagnosed with breast cancer. The average time for diagnosis was 102.5 ± 165.5 days. Treatment was delayed for 63.4% (52) of the participants. The average time of the treatment delay was 87.3 ± 65.5 days, whereas in the non-delayed cases, treatment was initiated in 19.6 ± 8.8 days ($p < 0.001$).

Of the 82 women interviewed, 54 (65.9%) of them had a partner and 28 (34.1%) did not have a partner. About 69.5% (57) of the participants were less than 8 years of schooling, and the majority (67 / 81.7%), were ethnicity / skin color white. Of the total number of women surveyed, 48 (58.5%) were residents in the city and 62 (75.6%) had no family history for cancer.

Regarding prevention, self-examination was reported by 46 women (56.1%); clinical examination in 40 (48.8%), and routine mammogram, for 51 (62.2%) of them.

The description of the clinical and pathological variables of this study population is provided in Table 1. The time intervals analyzed according to the stages of diagnosis and treatment of breast cancer are shown in Table 2.

In the Table 3 delays, and no delays in diagnosis according to circumstances of breast cancer detection, reason for the delay in seeing a doctor, first symptoms and systemic symptoms were showed.

Factors that influenced the delay in treatment were a low education level (64.9%) ($p = 0.03$) (Table 4).

Analysis of the association between the clinical-pathological variables and the delay in treatment onset did not detect any significant relationships. Older age (≥ 60 years), indefinite tumor stage and tumor stages T2, N1 and M1 were frequent among the women with delayed treatment onset (Table 5).

The logistic regression analysis of the variables included in the model relative to the outcome variable are showed in the Table 6.

Discussion

Delay in diagnosis and treatment of breast cancer affect directly the patient's survival increased morbidity

Table 1. Distribution of Sociodemographic, Clinical and Pathological Variables, Brazil, 2015

Variables	n	%
Marital status (n=82)		
With partner	54	65.9
Without partner	28	34.1
Education levels (years of schooling) (n=82)		
≤ 8	57	69.5
> 8	25	30.5
Ethnicity/skin color (n=82)		
White	67	81.7
Non-white	15	18.3
Resident in the municipality (n=82)		
Yes	48	58.5
No	34	41.5
Family history (n=82)		
Yes	20	24.4
No	62	75.6
Self-exam (n=82)		
Yes	46	56.1
No	36	43.9
Clinical examination (n=82)		
Yes	40	48.8
No	42	51.2
Routine mammogram (n=82)		
Yes	51	62.2
No	31	37.8
Age at diagnosis (years) (n=82)		
≤ 40	6	7.3
41-49	16	19.5
50-59	29	35.4
≥ 60	31	37.8
Tumor staging (n=62)		
I	2	3.2
IIA e IIB	37	59.7
IIIA e IIIB	21	33.9
IV	2	3.2
Estrogen Receptor (n=68)		
Positive	54	79.4
Negative	14	20.6
Progesterone Receptor (n=66)		
Positive	49	74.2
Negative	17	25.8

and mortality (Hansen et al., 2011; Smith et al., 2013).

This current study addresses the delay in diagnosis and treating patients with breast tumors. To the best of our knowledge, this issue is still relatively underexplored in Brazil.

Despite the numerous methods available to detect breast cancer in women, the Brazilian public health system still has difficulties in reducing the time and

Table 2. Average Time, Standard Deviation, and Minimum and Maximum Intervals of the Steps Investigated between the Diagnosis and Treatment of Breast Cancer Brazil, 2015

Intervals	Average (days)	Standard Deviation	Minimum	Maximum
Mammography and biopsy	70.89	72.16	1	318
Biopsy and biopsy results	5.5	3.41	0	30
Biopsy results and surgical	50.06	48.64	2	274
Mammography and first treatment	118.61	81.12	25	422

factors associated with delays in diagnosis and initiating treatment. Notably, there is still concern in advocating the optimum standard time between breast cancer diagnosis and the start of treatment.

The present study revealed that the time to establish the diagnosis of breast cancer in women attended at this Brazilian health service was 102 days, the time delay in initiating treatment following a biopsy was 87.30 ± 65.57 days; treatment onset was delayed (more than 30 days since diagnosis) in 57.3% of the sample.

Azevedo e Silva et al., (2014), emphasized the relevance of early detection of breast cancer within the Unified Health System setting and also highlighted the regional inequalities in the access to early detection and surgery, which are lowest in the Northern and highest in

Table 3. Bivariate Analysis of Delay and No Delay in Diagnosis according to Circumstances of Breast Cancer Detection, Reason for the Delay in Seeing a Doctor, First and Systemic Symptoms Brazil, 2015

Variables	> 30 days n (%)	≤ 30 days n (%)	p
Circumstances of breast cancer detection			0.61
Self-examination	33 (68.75)	15 (31.25)	
Routine mammography	12(57.14)	9(42.86)	
Routine medical examination	2 (50.00)	2 (50.00)	
Ultrasonography	1 (100.00)	0 (0.00)	
Reason for the delay in seeing a doctor			0.002
Lack of knowledge of the severity	9 (100.00)	0 (0.00)	
Fear	0 (0.00)	1 (100.00)	
Lack of time	2 (100.00)	0 (0.00)	
First symptoms			0.27
Breast pain	8 (88.89)	1 (11.11)	
Caked breast	0 (0.00)	1 (100.00)	
Breast lump	22 (68.75)	10 (31.25)	
Itching	1 (100.00)	0 (0.00)	
Nipple retraction	4 (80.00)	1 (20.00)	
Nipple bleeding	0 (0.00)	1 (100.00)	
Redness breasts	1 (100.00)	0 (0.00)	
Systemic Symptoms			0.93
Weight loss	1 (50.00)	1 (50.00)	
Others	3 (60.00)	2(40.00)	
No systemic symptoms	27 (62.79)	16 (37.21)	

Table 4. Bivariate Analysis of Delay and No Delay in Treatment Onset according to Sociodemographic, Reproductive and Maternal Variables Brazil, 2015

Variables	Delay (> 30 days) n (%)	No delay (≤ 30 days) n (%)	P
Age at diagnosis (years) (n=82)			
≤ 40	3 (50.0)	3 (50.0)	0.47
41-49	12 (75.0)	4 (25.0)	
50-59	16 (55.2)	13 (44.8)	
≥ 60	21 (67.7)	10 (32.3)	
Marital status (n=82)			
With partner	30 (55.6)	24 (44.4)	0.04
Without partner	22 (78.6)	6 (21.4)	
Educational levels (years of schooling) (n=82)			
≤ 8	41 (71.9)	16 (28.1)	0.01
> 8	11 (44.0)	14 (56.0)	
Ethnicity/skin color (n=82)			
White	40 (59.7)	27 (40.3)	0.23
Non-white	12 (80.0)	3 (20.0)	
Resides in the municipality (n=82)			
Yes	31 (64.6)	17 (35.4)	0.79
No	21 (61.8)	13 (38.2)	
Distance from the municipality (km) (n=82)			
0	31 (64.6)	17 (35.4)	0.94
1 – 100	12 (63.2)	7 (36.8)	
> 100	9 (60.0)	6 (40.0)	
Family history (n=82)			
Yes	12 (60.0)	8 (40.0)	0.71
No	40 (64.5)	22 (35.5)	
Self-exam (n=82)			
Yes	26 (56.5)	20 (43.5)	0.12
No	26 (72.2)	10 (27.8)	
Clinical examination (n=82)			
Yes	23 (57.5)	17 (42.5)	0.27
No	29 (69.0)	13 (31.0)	
Mammogram (n=82)			
Yes	30 (58.8)	21 (41.2)	0.26
No	22 (71.0)	9 (29.0)	

the Southern region.

In the bivariate analysis, the delay in seeking medical advice (for lack of knowledge of severity, fear or lack of time) was one of the factors associated with delayed diagnosis. The delay in diagnosis is related to more advanced stages of the disease (Trufelli et al., 2008). In integrative literature review, which included 53 studies, no attribution of symptoms to cancer and fear were some of the causes most often cited in the delay for the treatment of breast cancer (Freitas and Weller, 2015). In another study, several factors influence the delay in seeking professional care, such as lack of knowledge, fear of being diagnosed with cancer, not seeing oneself at risk, mental concern and diagnosis wrong by doctors (Rastad et al., 2012). In another study, 38% of patients delayed in seeking medical care for fear of losing the breast (Bourdeanu et al., 2013).

Table 5. Bivariate Analysis of Delay and No Delay in Treatment Onset according to Clinical-Pathological Variables, Brazil, 2015

Variables	Delay (> 30 days) n (%)	No delay (≤ 30 days) n (%)	p
Tumor stage (n=62)			
I	1 (50.0)	1 (50.0)	0.97
IIA and IIB	23 (62.2)	14 (37.8)	
IIIA and IIIB	13 (61.9)	8 (38.1)	
IV	1 (50.0)	1 (50.0)	
Estrogen receptor (n=68)			
Positive	34 (63.0)	20 (37.0)	0.45
Negative	10 (71.4)	4 (28.6)	
Progesterone receptor (n=66)			
Positive	32 (65.3)	17 (34.7)	0.96
Negative	11 (64.7)	6 (35.3)	

Table 6. Logistical Regression Analysis of the Variables Included in the Model Brazil, 2015

Variables	Adjusted OR	Odds ratio (CI)	p
Does not reside in the municipality	1.46	0.30-7.01	0.63
Distance from the municipality 1 – 100 (km)	1.35	0.26-6.96	0.71
Distance from the municipality > 100 (km)	1.49	0.23-7.09	0.72
Without partner	2.55	0.70-9.23	0.15
≤ 8 years of schooling	3.68	1.06-12.69	0.03
Family history	1.66	0.49-5.61	0.41
Age at diagnosis 41-59 years	6.13	0.49-75.92	0.15
Age at diagnosis 50-59 years	1.86	0.18-18.45	0.59
Age at diagnosis ≥60 years	1.79	0.16-19.06	0.62
Does not perform Self-exam	1.67	0.48-5.72	0.41
Clinical examination (no)	0.44	0.10-1.89	0.27
Mammography (no)	2.13	0.61-7.46	0.23

Among the first symptoms identified by the patients in our study, the breast lump was the most frequent (65.3%), both those considered late (> 30 days) and those equal to or less than 30 days, similar to other studies (Rao et al., 2009). This can be explained by accidental identification or by means of breast self-examination (Rao et al., 2009). Although the self-examination is not recognized as a technique for early diagnosis of breast cancer, can be considered as auxiliary because the woman knows the breast itself and can provide information to the doctor about possible changes (Who, 2002). Usually the nodules are palpable in more advanced stages of the disease.

Most of our patients have no systemic symptoms and their occurrence was not associated with delayed diagnosis. The early symptoms of breast cancer are usually not debilitating and can be ignored until worsening symptoms appear (Norsa'adah et al., 2011).

As to the factors possibly associated with delay in

diagnosis, one study suggested some candidates, such as little sensitization to women's health matters, poor information campaigns, and lack of screening programs based on mammograms or other techniques for early diagnosis of breast cancer. Both doctors and patients have to be properly oriented as to the various forms of presentation of the symptoms of breast cancer (Ermiah et al., 2012).

Considering that the National Cancer Institute (Brasil, 2012) recommends that treatment ought to be started within three months from the appearance of signs and symptoms, our results emphasize a serious problem deserving of study to understand the possible causes of such delay, to suggest measures to reduce the time to treatment onset and to promote early disease detection.

In a retrospective study, Trufelli et al., (2008), analyzed the delays in diagnosis and treatment in a sample of 68 women with breast cancer attended at a hospital in the state of São Paulo. The authors concluded that patients attended at public services are exposed to significant delays, particularly during diagnosis. Among the analyzed intervals, the longest delay occurred between the suspicious mammogram and the biopsy. The delay in treatment onset was significantly longer among women with more advanced stages of cancer compared to those in early stages. Trufelli et al., (2008), called attention to the need to reduce the period between mammogram and biopsy of suspicious lesions.

Cancer incidence and its morbidity and mortality are increasing in Brazil due to several barriers, from access to actions aiming at early detection and difficulties in the use of diagnostic resources and indicated treatments. These factors have negative repercussions on society at large, with significant individual, social and political impacts, leading cancer to be considered a public health problem in Brazil and one of the priority targets of the National Policy of Cancer Care (Brasil, 2005; Brasil, 2011).

In a retrospective study, Trufelli et al., (2008) examined delays in the management of breast cancer patients treated at a public hospital and called attention to the gap between suspect mammographies and initial systemic therapy (>180 days). The authors reported that potential micrometastases could become established during this interval, thereby transforming the cancer into a generally incurable metastatic disease.

In a municipality in the South of Brazil, intervals longer than 90 days were observed between breast cancer diagnosis and the start of treatment (Souza et al., 2008). In the state of Pernambuco, Brazil, delays were attributed to the user's difficulty in accessing the various levels of care and health professionals (Paiva and Cesse, 2015).

In contrast, an international study indicated that the average time from diagnosis to the start of primary treatment was 24.69 days; treatment was initiated more than 30 days after the diagnosis in only 30.9% of patients (Mujar et al., 2013). McGee et al., (2013), found that 39.5% of the women they studied had a delay in treatment of more than 30 days.

Other authors highlighted the treatment guidelines in the early stages of breast cancer (Ermiah et al., 2012). In Brazil, there have been increases in the incidence,

morbidity and mortality of cancer due to the persistence of numerous barriers, including access to early detection systems and difficulties in utilizing the diagnostic resources and indicated treatments. These conditions have negative repercussions for society, generate important individual, social and political impacts, and are considered a public health problem. Thus, these conditions are one of the primary goals of the National Policy of Oncology Care (Brasil, 2005; Brasil, 2011).

The Ministry of Health has established a maximum time frame of 60 days for the Unified Health System (Sistema Único de Saúde - SUS) to initiate treatment for a cancer patient (Brasil, 2013).

The delay found in the present study requires immediate action to improve and identify barriers to seeking medical care and breast cancer screening and to improve health outcomes. Both early diagnosis and early treatment are considered effective means of reducing the mortality of this disease (Azevedo e Silva et al., 2014).

Al-Amri (2015), reported that delays in diagnosis and treatment might be patient-dependent (interval between the detection of symptoms and seeking specialized or professional services), physician-dependent (interval between the consultation and referrals), or referral-dependent (initial discovery and the start of care). Azevedo e Silva et al., (2014), noted inequalities in access to surgery that were lower in the North Region and higher in the South Region of Brazil.

Regarding sociodemographic characteristics, women with less education were more likely to experience waits longer than 30 days before starting treatment. Other authors also found that longer delays before the start of treatment were associated with lower levels of education (Sharma et al., 2012).

A study conducted in 12 countries with 6,588 women with breast cancer found that higher levels of education were associated with fewer delays in the start of treatment (Jassem et al., 2015), which could be explained by the fact that people with less education had more difficulty in understanding and completing the cancer prevention process (Oliveira et al., 2011; Melo et al., 2013). Uyeturk et al., (2013), found that patients with low levels of education were diagnosed with stage IV metastatic breast cancer.

The low level of education makes it difficult to acquire important information about the prevention and early detection of diseases and is related to poorer access to healthcare services. The lack of information, beliefs and distorted perceptions about the disease are factors that can lead women to avoid seeking breast exams (Novaes et al., 2006). An analytical study using secondary data examined the association between the variable level of education and the initial clinical staging of malignant breast tumors and found an increased risk of a delayed diagnosis of breast tumors in patients with a lower level of education (Silva et al., 2013).

Among the limitations identified in the present study, the population should have been larger and the collection period longer. Additionally, it should be noted that the use of data reported by women, which are not always consistent with the information verified using medical

records, may introduce possible errors into the physicians' medical records or flaws in the information described by the participants. Another limitation is that the information on the disease signs and symptoms and the demand for specialized services were not verified, although these were important factors that could result in delays in diagnosis and treatment.

In conclusion, the survey's findings identified delays in diagnosis and also in the treatment for women with low levels of education. Greater attention should be paid to breast cancer treatment regardless of any socioeconomic condition, thereby encouraging equity in achieving rapid and adequate therapy. It is worth mentioning again that treatment success is related to how quickly treatment is initiated. However, this study shows that the maximum time interval defined for the diagnosis and early treatment of breast cancer is not being achieved in its entirety.

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