Available online at www.sciencedirect.com

Public Health

journal homepage: www.elsevier.com/puhe

Original Research

Delay in breast cancer diagnosis: a Brazilian cohort study

G.C. Medeiros [a], L.C.S. Thuler [a,b], A. Bergmann [a,*]

[a] Brazilian National Cancer Institute (INCA), Brazil
[b] Rio de Janeiro State Federal University (UNIRIO), Brazil

ARTICLE INFO

Article history:
Received 18 June 2018
Received in revised form
9 October 2018
Accepted 18 October 2018
Available online 12 January 2019

Keywords:
Breast neoplasms
Epidemiology
Delayed diagnosis
Health services accessibility
Healthcare disparities

ABSTRACT

Objectives: To evaluate the delay in breast cancer (BC) diagnosis and its risk factors.
Study design: A cohort study of BC patients referred to treatment at oncological reference hospital, Brazil. Delay in BC diagnosis was defined as a time interval ≥90 days between the first contact with a care provider and a BC diagnosis.
Methods: The association between independent variables and delay was performed by univariate analysis and multiple logistic regression.
Results: Five hundred and twenty-six women were included in the study. Delay was observed in 68.8% and was associated with performing histopathological examination at oncological reference hospital (odds ratio [OR]: 3.96, 95% confidence interval [CI]: 1.91–8.20) or at another public health service (OR: 2.31; 95% CI: 1.50–3.56) and attending gynecological consultations annually (OR: 3.24; 95% CI: 1.97–5.33) or every 2–3 years (OR: 2.86; 95% CI: 1.55–5.28). Patients who presented a lump as the first sign or symptom had a lower chance of delay (OR: 0.43; 95% CI: 0.29–0.65).
Conclusions: Improvements in the structure and access to health services are needed to reduce the time to diagnosis.

Introduction

Breast cancer (BC) is considered a worldwide public health issue. Globally, in 2012, 1,671,701 new BC cases were registered and more than 500,000 deaths occurred because of this disease.[1] In developing countries, most women are diagnosed at an advanced stage.[2] The 5-year survival rate of BC, between 2005 and 2009 standardized by age, was ≥80% in countries such as the United States and Canada; however, in poor countries like Mongolia and South Africa, the survival rates were 57% and 53%, respectively.[3] This reality can be attributed to the lack of financial resources and efficient political strategies.[2]

Mammography (MMG) screening is one of the strategies adopted for the early diagnosis of BC.[4] In countries where organized screening has been implemented, there has been a reduction of about 20% in the relative risk of death in the screened group, although its use is being widely questioned

* *Corresponding author*. Instituto Nacional de Câncer - Centro de Pesquisa Clínica, Rua André Cavalcanti, 37, Anexo - 3o andar - Centro, Rio de Janeiro, 20231-050, RJ, Brazil. Tel.: +55 21 3207 6659; Fax: +55 21 3207 6559.
E-mail address: abergmann@inca.gov.br (A. Bergmann).
https://doi.org/10.1016/j.puhe.2018.10.012
0033-3506/

because of evidence limited benefits and increased damage involving false-positive results and overdiagnosis.[4] The late diagnosis of BC contributes to disease progression, which leads to more aggressive treatments, sequelae, and a worse prognosis.[5–7]

From the start of mammary alterations to a BC diagnosis, women go through different steps. The delay between the first contact with a care provider and a diagnosis of BC is defined as the delay in BC diagnosis[8–11] and is the step that contributed most to a late onset of oncologic treatment.[2,12,13] Currently, there is no established time limit to define a delay in BC diagnosis, ranging from 7 days to 3 months in different studies.[9,14,15] This time interval is influenced by factors associated with the quality and the structure of the healthcare system.[2,6] In this scenario, access to a healthcare system is of significant importance. Among the factors that interfere in this access are the availability of financial resources for investments in the healthcare area, geographic distribution, organization, the type of health service that the patient has access to, and personal characteristics related to perceptions about health and health services.[16]

The increasing incidence of BC and the lack of access to oncologic services in Brazil[17,18] are relevant to a better understanding of the levels of primary and secondary care for this cancer. The identification of women with the greatest chance of delay in BC diagnosis and the barriers to healthcare services will allow the development of strategies to reduce the time until cancer diagnosis. This study aimed to evaluate the time between the first appointment in the healthcare system and the diagnosis of BC and the factors associated with this delay.

Methods

This was a prospective cohort study conducted in patients with BC (International Classification of Diseases - ICD-10: C50) who were treated from October 2, 2014 to October 30, 2015 in the oncological reference hospital, which is located in the city of Rio de Janeiro, Brazil. This hospital offers exclusive BC assistance through the Brazilian free healthcare system called the Unified Public Health System (in Portuguese: *Sistema Único de Saúde - SUS*). We excluded women who were aged younger than 18 years or older than 80 years old, those with a history of a previous neoplastic disease, and those with physical or cognitive conditions who would have difficulty answering the questionnaire. The eligible patients were interviewed at the first consultation at oncological reference hospital.

The variables described below were selected based on the results found in previous studies.[6–15] Variables related to the health service were adapted and classified by authors, according to the specificities of the Brazilian Health System.

The following social demographic variables were collected: age (<60 vs ≥60 years); race/skin color (classified according to the Brazilian Institute of Geography and Statistics [in Portuguese: *Instituto Brasileiro de Geografia e Estatística* :[19] white vs non-white, i.e. brown, black, yellow, or indigenous]; education level (in years of study: ≥8 vs <8); marital status (live with a partner vs do not live with a partner); current employment situation (unemployed vs employed); monthly income per person (the sum of the incomes divided by the number of people in the family, in minimum wage: ≥1 vs <1); children (yes vs no); place of residence (Rio de Janeiro city vs other cities); and family history of BC (yes vs no).

The variables related to health care were as follows: the customarily used health services (public vs private); intervals between the gynecological consultations (≤1 year vs 2–3 years vs >3 years); frequency of clinical breast examination (CBE) (≤1 year vs others: >1 year/once in life/never); frequency of breast self-examination (≤6 months vs others: >6 months, annually, variable, or never); frequency of MMG (≤2 years vs others: >2 years, once in life/variable, or never); previous breast ultrasonography at any moment in life (yes vs no); previous benign breast disease (yes vs no); current use of a hormonal contraceptive (yes vs no); alcohol use in the last 30 days (yes vs no) and current use of tobacco (yes vs no); and body mass index (classified according to the World Health Organization).[20]

The following variables related to the current disease were collected: how the BC was discovered (sign or symptom vs imaging exam or CBE); first sign or symptom (lump vs other signs or symptoms or none); date and location of the first appointment in a healthcare service (public vs private); clinical staging (TNM: <2B vs ≥2B); number of imaging exams performed for the diagnosis (<3 or ≥3); health service where the imaging exams were performed (public and private services vs exclusively private services); date the patient received the histopathological report (for patients who already had the diagnosis confirmed before enrollment at oncological reference hospital—hospital where the research was conducted) or the date of the electronic report release (to patients who received a diagnosis at oncological reference hospital); health service where the breast biopsy was performed (public vs private vs oncological reference hospital); and the perception of the women about the time that had elapsed between the first medical appointment to the diagnosis (the opinion of the women about the delay and its respective related reasons). A delay in BC diagnosis was considered as the time from first contact with a care provider to diagnosis and classified as 'yes' (≥90 days) and 'no' (<90 days).[9–11]

The descriptive analysis of the population data was performed by the measurement of the central tendency (mean and median) and dispersion (interquartile range [IQR]) for continuous variables and by the absolute and relative frequency for the categorical variables. The association between the independent variables and the outcome was performed by a univariate analysis, using crude odds ratios (ORs). The associations with clinical or epidemiologic importance and $P < 0.20$ in the univariate analyses were included in the multiple logistic regression model (stepwise forward). Variables were retained in the model when the *P*-value was <0.05. The Hosmer–Lemeshow test was performed to evaluate model fit. The data were analyzed using the Statistical Package for Social Science for Windows (SPSS), version 21.0.0 (São Paulo, Brazil). This research was approved by the Ethics in Research Committee of the Cancer National Institute according to resolution CNS nº466/12 with the number CAAE 12107913.3.0000.5274 on October 1st, 2014. The study was initiated after signed informed consent was received from each participant.

Results

A total of 662 women were interviewed, of whom 136 were excluded (124 without BC diagnosis, 10 with previous cancer not reported during the interview, and two who received concomitant cancer treatment at another institution). None of the patients eligible for the study died awaiting the diagnosis. Ultimately, this study included 526 women who were diagnosed and treated at an oncological reference hospital during the research period. The mean age was 56 years (IQR: 47–65 years). The median time between first contact with the care provider and the diagnosis of BC was of 5.2 months (IQR: 2.5-10.9 months). A delay in BC diagnosis was observed in 68.8% of cases, with 24.5% between 3 and 6 months. About half of the women reported a per capita income less than one minimum wage (52.5%), lived without a partner (50.2%), and were without actual employment (53.8%). Fewer than 8 years of education was reported by 38.8%. In the univariate analysis we observed that, in relation to sociodemographic variables, only education <8 years was associated with a delay in diagnosis (Table 1).

Most women regularly used the public health system (75.7%), had undergone a gynecological examination with a frequency of ≤1 year (58.2%), and had discovered BC by means of a sign or symptom (73.8%), with a breast lump as most frequent symptom (45.1%). The clinical and healthcare assessment variables associated with a delay in BC diagnosis in the crude analysis are presented in Table 2. The use of public health services, a gynecological examination frequency ≤1 year, and a MMG frequency ≤2 years were associated with delay in diagnosis. Additionally, women in whom BC was discovered by an imaging exam or CBE and those in whom the first sign or symptom were not lump had a high chance of delay.

After the multiple analysis, the independent factors associated with a delay in BC diagnosis were presented in Table 3. A breast lump as the first sign or symptom reduced the chance of delay by 57% when compared to cases who showed other signs or symptoms or those who had no symptoms (OR: 0.43; 95% confidence interval [CI]: 0.29–0.65). With regard to those who received a diagnosis in the private system, the women who underwent a breast biopsy in the public health service had a 2.31 times higher chance of delay in diagnosis (OR: 2.31; 95% CI: 1.50–3.56), and those with a diagnosis from oncological reference hospital had a 3.96 times higher chance (95% CI: 1.91–8.20). Regarding gynecological consultations, women who presented a shorter interval between consultations (more

Table 1 – Descriptive and univariate analysis of sociodemographic factors associated with a delay in the diagnosis of breast cancer.

Characteristics	Total [N (%)][a]	Delay in diagnosis			OR (95%CI)	P-value
		Median [months] (IQR)	Yes [N (%)][a]	No [N (%)][a]		
Age (in years)						
<60	320 (60.8)	4.71 (2.50–10.94)	215 (59.4)	105 (64.0)	1.00	0.31
≥60	206 (39.2)	5.44 (2.62–10.98)	147 (40.6)	59 (36.0)	1.21 (0.83–1.78)	
Race/skin color						
White	178 (33.8)	4.62 (2.19–9.83)	119 (32.9)	59 (36.0)	1.00	0.49
Non-white[b]	348 (66.2)	5.39 (2.64–11.33)	243 (67.1)	105 (64.0)	1.15 (0.78–1.69)	
Education (in years of study)						
≥8	322 (61.2)	4.55 (2.20–9.83)	211 (58.3)	111 (67.7)	1.00	**0.04**
<8	204 (38.8)	6.04 (2.96–12.23)	151 (41.7)	53 (32.3)	1.50 (1.02–2.21)	
Marital status						
Live with partner	262 (49.8)	5.44 (2.55–11.34)	181 (50.0)	81 (49.4)	1.00	0.90
Live without partner	264 (50.2)	4.71 (2.47–9.91)	181 (50.0)	83 (50.6)	0.98 (0.68–1.41)	
Actual employment status						
Unemployed	283 (53.8)	5.55 (2.66–11.14)	203 (56.1)	80 (48.8)	1.00	0.12
Employed	243 (46.2)	4.37 (2.37–10.64)	159 (43.9)	80 (51.2)	0.75 (0.52–1.08)	
Per capita income[c]						
≥one minimum wage	246 (47.5)	4.73 (2.34–10.40)	164 (46.2)	82 (50.3)	1.00	0.39
<one minimum wage	275 (52.5)	5.32 (2.67–11.01)	191 (53.8)	81 (49.7)	1.18 (0.81–1.71)	
Children						
Yes	437 (83.1)	5.26 (2.35–10.97)	298 (82.5)	139 (84.8)	1.00	0.53
No	88 (16.7)	4.14 (2.72–10.90)	63 (17.5)	25 (15.2)	1.18 (0.71–1.95)	
Place of residence						
Other cities	223 (42.4)	5.06 (2.30–11.01)	150 (41.4)	73 (44.5)	1.00	0.51
Rio de Janeiro city	303 (57.6)	5.26 (2.50–10.68)	212 (58.6)	91 (55.5)	1.13 (0.78–1.65)	
Family history of breast cancer						
Yes	139 (26.4)	5.29 (2.66–10.05)	91 (25.1)	48 (29.3)	1.00	0.32
No	387 (73.6)	5.06 (2.37–11.00)	271 (74.9)	116 (70.7)	1.23 (0.81–1.86)	

OR, odds ratio; CI, confidence interval; IQR, interquartile range.
P-values <0.05 are highlighted in bold.
[a] The differences correspond to missing values.
[b] Non-white: brown, black, yellow, or indigenous.
[c] The value of the monthly minimum wage was R$ 724.00 in 2014 and R$ 788.00 in 2015, which is equivalent to about US $300.

Table 2 – Descriptive and univariate analysis of clinical and healthcare assess factors associated with a delay in breast cancer diagnosis.

Characteristics	Total N (%)[a]	Delay in diagnosis			OR (95% CI)	P-value
		Median (months) (IQR)	Yes N (%)[a]	No N (%)[a]		
Health service which customarily uses						
Private	125 (23.8)	3.94 (2.05–9.61)	75 (20.8)	50 (30.7)	1.00	
Public	398 (75.7)	5.39 (2.75–11.38)	285 (79.2)	113 (69.3)	1.68 (1.10–2.56)	0.02
Intervals between the gynecological examination						
>3 years	116 (22.2)	3.15 (1.71–8.81)	59 (16.4)	57 (34.8)	1.00	
2–3 years	101 (19.3)	5.42 (2.63–13.30)	72 (20.1)	29 (17.7)	2.40 (1.36–4.21)	0.002
≤1 year	306 (58.2)	5.83 (2.95–10.98)	228 (63.5)	78 (47.6)	2.82 (1.81–4.41)	<0.001
Frequency of clinical breast examination						
≤1 year	228 (43.3)	5.58 (2.73–10.97)	163 (45.0)	65 (39.6)	1.00	
Others	298 (56.7)	4.71 (2.29–10.96)	199 (55.0)	99 (60.4)	0.80 (0.55–1.18)	0.25
Frequency of breast self-examination						
≤6 months	351 (66.7)	4.76 (2.58–10.79)	240 (67.8)	111 (69.8)	1.00	
Others	162 (30.8)	5.36 (2.48–11.24)	114 (32.2)	48 (30.2)	1.10 (0.73–1.65)	0.65
Frequency of mammography						
≤2 years	227 (43.2)	6.13 (3.18–11.34)	176 (48.8)	51 (31.1)	1.00	
Others	298 (56.7)	4.32 (2.10–9.86)	185 (51.2)	113 (68.9)	0.47 (0.32–0.70)	<0.001
Previous breast ultrasonography						
Yes	460 (87.5)	5.06 (2.36–10.45)	311 (86.1)	149 (90.9)	1.00	
No	65 (12.4)	5.36 (3.23–12.04)	50 (13.9)	15 (9.1)	1.60 (0.87–2.94)	0.13
Previous benign breast disease						
No	336 (63.9)	4.67 (2.51–9.97)	229 (63.4)	107 (65.2)	1.00	
Yes	189 (35.9)	6.06 (2.55–12.34)	132 (36.6)	57 (34.8)	1.08 (0.74–1.59)	0.69
Body mass index in kg/m^2						
<30	302 (57.4)	5.21 (2.26–11.40)	201 (56.8)	101 (64.3)	1.00	
≥30	209 (39.7)	5.19 (2.86–9.82)	153 (43.2)	56 (35.7)	1.37 (0.93–2.20)	0.11
Current use of hormonal contraceptive						
Yes	481 (91.4)	5.06 (2.50–10.18)	327 (90.8)	154 (93.9)	1.00	
No	43 (8.2)	7.31 (4.08–13.33)	33 (9.2)	10 (6.1)	1.55 (0.75–3.24)	0.24
Alcohol use in the last 30 days						
No	368 (70.0)	5.16 (2.60–10.56)	253 (70.3)	115 (70.6)	1.00	
Yes	155 (29.5)	5.32 (2.20–11.63)	107 (29.7)	48 (29.4)	1.01 (0.68–1.52)	0.95
Current use of tobacco						
No	456 (86.7)	5.11 (2.63–10.94)	317 (87.6)	139 (85.3)	1.00	
Yes	69 (13.1)	5.32 (2.02–13.03)	45 (12.4)	24 (14.7)	0.82 (0.48–1.40)	0.47
How the breast cancer was discovered						
Signal or symptom	388 (73.8)	4.40 (2.17–9.65)	245 (67.7)	143 (87.2)	1.00	
Imaging exam or clinical exam	138 (26.2)	7.04 (3.93–12.56)	117 (32.3)	21 (12.8)	3.25 (1.96–5.41)	<0.001
First signal or symptom						
Lump	237 (45.1)	4.34 (2.00–11.63)	143 (39.6)	94 (57.3)	1.00	<0.001
Others[b]	288 (54.8)	5.36 (3.02–10.02)	218 (60.4)	70 (42.7)	2.05 (1.40–2.98)	
Health service of the 1st appointment						
Private	261 (49.6)	4.24 (2.72–11.03)	170 (47.2)	91 (55.5)	1.00	0.08
Public	263 (50.0)	5.78 (2.72–11.04)	190 (52.8)	73 (44.5)	1.39 (0.96–2.02)	
Clinical staging (TNM)						
≥2B	263 (50.0)	5.04 (2.27–11.76)	179 (51.4)	84 (53.2)	1.00	0.72
<2B	243 (46.2)	5.19 (2.56–9.84)	169 (48.6)	74 (46.8)	1.07 (0.74–1.56)	
Number of imaging exams performed for the diagnosis						
<3	415 (78.9)	4.96 (2.30–4.96)	281 (77.6)	134 (81.7)	1.00	0.29
≥3	111 (21.1)	5.51 (2.97–13.33)	81 (22.4)	30 (18.3)	1.29 (0.81–2.05)	
Health service where the imaging exams were performed						
Private	277 (52.7)	4.11 (2.10–9.15)	172 (47.8)	105 (64.8)	1.00	<0.001
Public or public and private	245 (46.6)	6.47 (3.19–12.28)	188 (52.2)	57 (35.2)	2.01 (1.37–2.95)	
Health service where the breast biopsy was performed						
Private	210 (39.9)	3.94 (2.05–9.36)	123 (34.1)	87 (53.0)	1.00	
Public	243 (46.2)	5.26 (2.75–10.97)	177 (49.0)	66 (40.2)	1.90 (1.28–2.81)	**0.001**
HCIII/INCA[c]	72 (13.7)	8.30 (5.21–14.45)	61 (16.9)	11 (6.7)	3.92 (1.95–7.88)	**<0.001**

OR, odds ratio; CI, confidence interval; IQR, interquartile range.
P-values <0.05 are highlighted in bold.
[a] The differences correspond to missing values.
[b] Other signs or symptoms: pain, nipple discharge, hardening, thickening, wounds, and cracking of the skin.
[c] HCIII/INCA: Hospital do Câncer III – the hospital where the study was carried out.

Table 3 – Factors leading to a delay in breast cancer diagnosis as perceived by patients.

Factors for delay	N[a]	%[b]
Delay in receiving the biopsy report	165	58.5
Doctor suspected benign disease/doctor did not give importance to symptoms	113	40.1
Delay in scheduling the biopsy	66	23.3
Delay due to exams, appointments, and delivery of exam reports	51	49.0
Delay in performing the biopsy after scheduling	43	15.2
Own delay	39	16.3
Personal reasons	28	9.9
Need to repeat exams due to poor quality	19	18.3

[a] Regarding the 283 (53.8%) women who reported a delay between the first contact with a care provider and delivery of the histopathological report.
[b] More than one factor may have been mentioned by each patient.

frequently examined) had a higher chance of delayed diagnosis. When compared to the reference group (>3 years), it was observed that patients with interval ≤1 year had a 3.24 times higher chance of delay in diagnosis (OR: 3.24, 95% CI: 1.97–5.33), and those who were examined every 2 or 3 years presented a 2.86 times greater chance (OR: 2.86; 95% CI: 1.55–5.28) (Table 3).

Of the 72 patients who were diagnosed at oncological reference hospital, 30 (41.7%) needed to redo previous complementary examinations that had already been performed at other institutions to confirm the BC diagnosis. This was necessary because of inadequacies in the report (results of neoplasia and benign diagnosis which were not confirmed) and owing to the absence of the tissue slides to confirm the diagnosis (data not shown).

Table 4 describes the factors associated to a delay in BC diagnosis according to the perception of the patients. Most of the women (53.8%) reported the existence of at least one factor that contributed to this delay. The most frequent factor was a delay in receiving the biopsy report (58.5%).

Table 4 – Independent factors associated with a delay in breast cancer diagnosis.

Characteristics	Adjusted OR	95% CI	*P*-value
First signal or symptom			
Other signs or symptoms or absence of signs or symptoms	1.00	–	–
Lump	0.43	0.29–0.65	<0.001
Health service where performed the breast biopsy			
Private	1.00	–	–
Public	2.31	1.50–3.56	<0.001
HCIII/INCA[a]	3.96	1.91–8.20	<0.001
Intervals between the gynecological consultations			
>3 years	1.00	–	–
2–3 years	3.24	1.97–5.33	<0.001
≤1 year	2.86	1.55–5.28	0.001

OR, odds ratio; CI, confidence interval.
Hosmer–Lemeshow test for the model was not significant ($P = 0.31$) indicating good model calibration.
[a] HCIII/INCA: Hospital do Câncer III – the hospital where the study was carried out.

Discussion

Our results show that in 68.8% of the women, there was a delay in BC diagnosis. The women who presented with a breast lump as the first sign or symptom had a lower chance of delay, while those who underwent a breast biopsy in the public health service and those who had a frequency of gynecological examination ≤1 year had a greater chance of delay in diagnosis.

The median time from first contact with the care provider and the BC diagnosis was 5.2 months, which is higher than the figures described by other authors.[9–11] Two other Brazilian studies conducted in the last decade found time intervals greater than 6 months.[13,21] In countries like Lebanon and Malaysia, the time was greater than that observed in this study, with results of 7.5 and 5.5 months, respectively. In these developing countries, which defined a delay in BC diagnosis as a time interval of ≥90 days was observed and a delay in diagnosis occurred in more than 70% of cases, which is similar to the results found in our population.[22,23] In other countries such as Mexico, the United States, and Taiwan, this interval was shorter, varying from 7 days to 4 months.[6,10,15] Although the delay has been assessed in several regions of the world, we should consider regional differences and specificities when comparing developed and developing countries. Regional and population discrepancies may limit such comparisons.

A delay in BC diagnosis, which is also called a delay of referral or a provider delay,[5,8,24] reveals the logistics of the public services and public politics.[2,5] The complexity of confirming a diagnosis has been discussed and represents the main barrier to initiating BC treatment.[12,25,26] The suggested hypothesis is that the greatest delay in this phase is due to the difficulty in the diagnostic evaluation and confirmation, which also represents a lack of structure and quality in health services, barriers to access to health services, interactions among social factors, as well as factors related to the patient and to the doctors.[2,22,25] North American researchers who evaluated the period until surgery attributed the delay to the time needed to execute imaging exams, biopsy methods, medical appointments, and the operational procedures required for a diagnosis.[26]

In this study, women who presented with a breast lump as the first sign or symptom had a lower chance of delay in BC diagnosis when compared to those who presented another sign or symptom or no symptom. This result was also found by other authors.[21–23,27,28] Moroccan women who had a palpable lump were diagnosed about 62 days earlier when they were compared with women who had another symptom.[11] A possible hypothesis is that doctors are better prepared to start an investigation in cases that are more suggestive of cancer.[29] This can be attributed to the existence of structural failures in the health care system, the inferior quality of imaging exams, and the limited professional experience.[22] However, other authors showed

divergent results.[13,30] George et al. observed that women who self-detected the disease showed a greater chance of delay compared with those who were diagnosed by a CBE of the breast or by an MMG (RR = 1.73).[30]

The fact that 73.8% of the women were symptomatic at diagnosis highlights the dire situation of the healthcare system in Brazil. BC has a gradual evolution that requires years to be detected.[31] When used at the right time, MMG screening can change the natural history of the disease, with a greater chance of a cure.[32] This result indicates that there are many failures in the healthcare system, especially regarding access to early diagnosis and health education. In Brazil, there is no organized mammography screening program, and many women cannot access mammography because of its limited availability and costs.[12,13,18] Although the presence of symptoms reduces the chance of a delay in BC diagnosis, a relationship with a poor prognosis is well-established.[5,29] The 5-year survival rate in women who were diagnosed at stage I can reach 92.7%, while for patients with advanced tumors, this rate is around 54%.[33]

In this study, performing the biopsy in the public healthcare system doubled the chance of a delay in BC diagnosis and was almost four times greater for the patients who received a confirmation of diagnosis at an oncological reference hospital. In 2010, data from the SUS showed that the proportion of women with abnormal radiologic findings and who underwent a biopsy in the public healthcare system was lower than the ideal rate. The authors suggested that the healthcare system is unprepared to meet the demand of cases that require specific actions regarding screening and early disease detection.[18]

Patients who were diagnosed at oncological reference hospital where the research was conducted, had a greater chance of delay due to the necessity of redo the biopsy at the institution to confirm the diagnosis. The study performed in 2009 in this same hospital unit suggested that the reason for the delay was the fact that 64.4% of the women had no confirmation of diagnosis at the time of enrollment.[13] We assume that because it is a tertiary hospital specializing in BC treatment, the waiting period for the procedure is greater than that encountered by patients who attended services with less complexity.

In Brazil, there are difficulties in access to public health services before the start of oncologic treatment.[34] SUS users showed advanced staging in relation to patients who used the private healthcare system and, consequently, showed a reduced survival rate.[35,36] Soares et al. observed that, in almost one half of cases, the time interval between suspicion and the confirmation of diagnosis was >6 months and concluded that there was a strong association between this interval and BC staging at diagnosis. In this study, we did not observe an association between the delay and clinical staging of BC.[35]

We observed that women who underwent gynecological examination with a frequency of ≤1 year or every 2–3 years showed a greater chance of delay than those who underwent gynecological examination with a time interval of >3 years. This result may be related to the poor efficiency of the primary health care system. The hypothesis to explain this occurrence is that mammary alterations presented by women who undergo a gynecological exam more frequently is undervalued by health professionals. Another point worth mentioning is that, although 58.0% of the women attended the gynecologist annually, only 26.1% were diagnosed by the imaging exam, indicating the poor quality of assistance offered during gynecological appointments, since breast clinical examination is not routinely performed. On the other hand, Lewis et al. concluded that patients assessed by a gynecologist received more preventive care than those attended by a general practitioner.[37] Moreover, according to the perception of patients, a doctor's suspicion of benign disease or dismissal of complaints or symptoms, plus the substandard quality of exams, reinforce this hypothesis.[22,27,38] The influence of clinical mistakes on the part of health professionals on the delay in diagnosis is difficult to evaluate because there is no objective record, in contrast to a radiologic or histopathological exam.[29] In a North American study, receiving continuous care in a specific health care system before the diagnosis was not associated with earlier detection of BC.[7] Although clinical staging was not associated with the delay, it is important to highlight that more than half of the women showed advanced staging, which is different from what has been observed in developed countries where MMG screening is organized.[28] In developed countries, a delay in diagnosis has been described in some populations corresponding to racial-ethnic and social minorities.[9,14,30] Although other studies have shown that socio-demographic factors are associated with delay,[10,11] we did not observe an influence of these variables in our population.

Among the limitations of this research, we can highlight the retrospective data collection, which can result in biases of information and memory. However, it is important to mention that data collection occurred during an interview with the patients during their first appointment at oncological reference hospital. This strategy was used because of the greater facility to access reports and documents and because the recent memory of the facts occurred during the process of cancer investigation. The use of calendars and the association of the clinical events with commemorative dates and happenings were also tactics used to attenuate possible biases.

Although the questionnaire applied contemplated many important variables related to delay, some factors associated with BC diagnosis were not collected, for example the associated comorbidities. Furthermore, because it is a public hospital, the oncological reference hospital users showed similar demographic characteristics. However, it is not possible to generalize these results to women who have a different sociodemographic profile. Another limitation of this study is that it concerns the evaluation of only one stage of delay, making it impossible to identify the factors associated with delay to start oncologic treatment. We highlight as positive aspects of the study, the number of women included and treated at only one cancer reference center. The homogeneous profile of the patients and the brief period of time required for the recruitment of patients increased the internal validity of the study. The application of a broad and detailed questionnaire created especially for this study enabled the identification of factors that contribute to the delay in BC diagnosis.

Conclusion

In this study, a high percentage of women (68.8%) experienced a delay in BC diagnosis. The women who presented with a lump as the first symptom had a lower chance of delay, while those who underwent a breast biopsy at the hospital where the study was conducted or at another public health service and those who underwent a gynecological examination with a frequency of ≤1 year or every 2–3 years presented a greater chance of delay. This study points to the need for improvements in the structure of and access to the healthcare system to reduce the time to BC diagnosis.

According to our results, we identified two main actions to minimize the delay in diagnosis. Firstly, Training healthcare professionals to enable them to question the existence of the disease even when there are no evidences of the signs or symptoms or when they are non-specific of BC. In addition, qualify the professionals to perform a comprehensive assessment at the time of gynecological examination, prioritizing also the examination of breast. And, secondly, developing medical infrastructure; the disclosure of these results is relevant so that the managers of these health facilities take the necessary measures. One of the main measures to improve the infrastructure is the reorganization of the line of attention to BC in the public health service, especially at secondary level, to avoid the overload of specialized hospitals, with a consequent delay in the diagnosis.

Author statements

Ethical approval

This research was approved by the Ethics in Research Committee of the Cancer National Institute according to resolution CNS nº466/12 with the number CAAE 12107913.3.0000.5274 on October 1st, 2014. The study was initiated after signed informed consent was received from each participant.

Funding

None.

Competing interests

None declared.

REFERENCES

1. Ferlay J, Soerjomataram I, Ervik M, et al. *GLOBOCAN. Cancer incidence and mortality worldwide: IARC cancer base*, vol. 10, 1. International Agency for Research on Cancer; 2012. http://globocan.iarc.fr [Accessed 14 March 2017].
2. Unger-Saldaña K. Challenges to the early diagnosis and treatment of breast cancer in developing countries. *World J Clin Oncol* 2014;**5**:465–77.
3. Allemani C, Weir HK, Carreira H, et al. CONCORD Working Group. Global surveillance of cancer survival 1995-2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). *Lancet* 2015;**385**. 977-10.
4. Marmot M, Altman DG, Cameron DA, et al. Independent UK Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review. *Lancet* 2012;**380**:1778–86.
5. Richards MA, Westcombe AM, Love SB, et al. Influence of delay on survival in patients with breast cancer: a systematic review. *Lancet* 1999;**353**:1119–26.
6. Unger-Saldaña K, Miranda A, Zarco-Espinosa G, et al. Health system delay and its effect on clinical stage of breast cancer: multicenter study. *Cancer* 2015;**121**:2124–6.
7. Mainous AG, Kern D, Hainer B, et al. The relationship between continuity of care and trust with stage of cancer at diagnosis. *Fam Med* 2004;**36**:35–9.
8. Sainsbury R, Johnston C, Haward B. Effect on survival of delays in referral of patients with breast-cancer symptoms: a retrospective analysis. *Lancet* 1999;**353**:1132–5.
9. Gwyn K, Bondy ML, Cohen DS, et al. Racial differences in diagnosis, treatment, and clinical delays in a population-based study of patients with newly diagnosed breast carcinoma. *American Cancer Society* 2004;**100**:1565–604.
10. Ruddy KJ, Gelber S, Tamimi RM, et al. Breast cancer presentation and diagnostic delays in young women. *Cancer* 2014;**120**:20–5.
11. Dianatinasab M, Fararouei M, Mohammadianpanah M, et al. Impact of social and clinical factors on diagnostic delay of breast cancer: a Cross-sectional Study. *Medicine* 2016;**95**, e4704.
12. Trufelli DC, Miranda VdC, Santos MBBd, et al. Análise do atraso no diagnóstico e tratamento do câncer de mama em um hospital público. *Rev Assoc Med Bras* 2008;**54**:72–6.
13. Rezende MCR, Koch HA, Figueiredo JA, et al. Causas do retardo na confirmação diagnóstica de lesões mamárias em mulheres atendidas em um centro de referência do Sistema Único de Saúde no Rio de Janeiro. *Rev Bras Ginecol Obstet* 2009;**31**:75–81.
14. Gorin SS, Heck JE, Cheng B, et al. Delays in breast cancer diagnosis and treatment by racial/ethnic group. *Arch Intern Med* 2006;**166**:2244–52.
15. Shieh SH, Hsieh VC, Liu SH, et al. Delayed time from first medical visit to diagnosis for breast cancer patients in Taiwan. *J Formos Med Assoc* 2014;**113**:696–703.
16. Penchansky R, Thomas JW. The concept of access: definition and relationship to consumer satisfaction. *Med Care* 1981;**19**:127–40.
17. Lee BL, Liedke PE, Barrios CH, et al. Breast cancer in Brazil: present status and future goals. *Lancet Oncol* 2012;**13**:95–102.
18. Azevedo E Silva G, Bustamante-Teixeira MT, Aquino EML, et al. Acesso à detecção precoce do câncer de mama no Sistema Único de Saúde: uma análise a partir dos dados do Sistema de Informações em Saúde. *Cad Saúde Pública* 2014;**30**:1537–50.
19. *Brasil*. Instituto Brasileiro de Geografia e Estatística. Tábuas Completas de Mortalidade; 2010. 2010, http://www.ibge.gov.br/home/estatistica/populacao/tabuadevida/2013/defaulttab_pdf.shtm. [Accessed 1 March 2017].
20. World Health Organization. *Obesity: preventing and managing the global epidemic. Report of a world health organization consultation*, vol. 284. Geneva: World Health Organization. WHO Obesity Technical Report Series; 2000. p. 256. 2000, p.
21. Trufelli DC, Bensi CG, Valada Pane CE, et al. Onde está o atraso?. Avaliação do tempo necessário para o diagnóstico e tratamento do câncer de mama nos serviços de oncologia da Faculdade de Medicina do ABC. *Revista Brasileira de Mastologia* 2007;**17**:14–8.
22. Ermiah E, Abdalla F, Buhmeida A, et al. Diagnosis delay in Libyan female breast cancer. *BMC Res Notes* 2012;**5**:452.

23. Norsa'adah B, Rampal KG, Rahmah MA, et al. Diagnosis delay of breast cancer and its associated factors in Malaysian women. *BMC Canc* 2011;**17**:141.
24. Sharma K, Maben J, Jack RH, et al. A systematic review of barriers to breast cancer care in developing countries resulting in delayed patient presentation. *J Oncology* 2012;**2012**:121873.
25. Hansen RP, Olesen F, Sørensen HT, et al. Socioeconomic patient characteristics predict delay in cancer diagnosis: a Danish cohort study. *BMC Health Serv Res* 2008;**8**:49.
26. Bleicher RJ, Ruth K, Sigurdson ER, et al. Preoperative delays in the US Medicare population with breast cancer. *J Clin Oncol* 2012;**30**:4485–92.
27. Arndt BV, Stürmer T, Stegmaier C, et al. Provider delay among patients with breast cancer in Germany: a Population-Based Study. *J Clin Oncol* 2003;**21**:1440–6.
28. Yuan Y, Li M, Yang J, et al. Factors related to breast cancer detection mode and time to diagnosis in Alberta, Canada: a population-based retrospective cohort study. *BMC Health Serv Res* 2016;**19**:65.
29. Barber MD, Jack W, Dixon JM, et al. Diagnostic delay in breast cancer. *Br J Surg* 2004;**91**:49–53.
30. George P, Chandwani S, Gabel M, et al. Diagnosis and surgical delays in African American and white women with early-stage breast cancer. *J Womens Health (Larchmt)* 2015;**24**:209–17.
31. Kopans DB, Rafferty E, Georgian-Smith D, et al. A simple model of breast carcinoma growth may provide explanations for observations of apparently complex phenomena. *Cancer* 2003;**97**:2951–9.
32. Tan SYGL, van Oortmarssen GJ, de Koning HJ, et al. The MISCAN-fadia continuous tumor growth model for breast cancer. *J Natl Cancer Inst Monogr* 2006;**36**:56–65.
33. Guerra MR, Mendonça GAS, Bustamante-Teixeira MT, et al. Sobrevida de cinco anos e fatores prognósticos em coorte de pacientes com câncer de mama assistidas em Juiz de Fora, Minas Gerais, Brasil. *Cad Saúde Pública* 2009;**25**:2455–66.
34. Medeiros GC, Bergmann A, Aguiar Sd, et al. Determinants of the time between breast cancer diagnosis and initiation of treatment in Brazilian women. *Cad Saúde Pública* 2015;**31**:1269–82.
35. Soares PBM, Quirino Filho S, Souza WPd, et al. Características das mulheres com câncer de mama assistidas em serviços de referência do Norte de Minas Gerais. *Rev bras epidemiol* 2012;**15**:595–604.
36. Liedke PE, Liedke PE, Barrios CH, et al. Outcomes of breast cancer in Brazil related to health care coverage: a retrospective cohort study. *Cancer Epidemiol Biomark Prev* 2014;**23**:126–33.
37. Lewis BG, Halm EA, Marcus SM, et al. Preventive services use among women seen by gynecologists, general medical physicians, or both. *Obstet Gynecol* 2008;**111**. 945-5.
38. Goodson 3rd WH, Moore DH. Causes of physician delay in the diagnosis of breast cancer. *Arch Intern Med* 2002;**162**:1343–8.