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EVALUATION OF DELAYS IN DIAGNOSIS AND TREATMENT OF BREAST CANCER IN A REFERENCE CENTER: A RETROSPECTIVE ANALYSIS

Avaliação do atraso no diagnóstico e tratamento do câncer de mama em um centro de referência: uma análise retrospectiva

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ABSTRACT

Objectives: To evaluate possible causes of delay in the diagnosis and treatment of breast cancer in a population treated exclusively by the Brazilian Unified Health System (SUS) of Brazil. **Methods:** A retrospective analysis of the medical patient charts of 173 patients treated at IMIP, between January 2011 and December 2017. Time intervals (biopsy and treatment intervals) were associated with sociodemographic and clinical variables utilizing statistical analysis. **Results:** The mean age was 56.36 years, 116 (67.1%) were from Recife's metropolitan region and the majority were illiterate or had up to 8 years of schooling. The biopsy interval ranged between 0 and 826 days (41.42; med 12.50) while the treatment interval ranged from 0 and 460 days (94.6; med 69.0). There was no statistically significant association of these intervals with clinical variables such as origin, educational level, age, tumor staging, type of treatment and clinical situation of the patients at the end of the study. **Conclusions:** Although the early diagnosis and treatment of breast cancer are fundamental, the data of this present investigation showed that median delays of 3 months for starting treatment in a public hospital were not associated with worsening of prognosis or survival of the patients.

KEYWORDS: breast cancer; late diagnosis; survival.

RESUMO

Objetivos: Avaliar possíveis causas de atraso no diagnóstico e tratamento do carcinoma mamário em uma população atendida exclusivamente pelo Sistema Único de Saúde (SUS) do Brasil. **Métodos:** Foi realizada uma análise retrospectiva dos prontuários de 173 pacientes tratadas no Instituto Materno Infantil Prof. Fernando Figueira (IMIP), entre janeiro de 2011 e dezembro de 2017. Intervalos de tempo (intervalo de biópsia e de tratamento) foram relacionados com variáveis sociodemográficas e clínicas por meio de análise estatística. **Resultados:** A média de idade foi 56,36 anos, 116 mulheres (67,1%) eram da região metropolitana do Recife e a maioria era analfabeta ou tinha até 8 anos de escolaridade. O intervalo de biópsia variou entre 0 e 826 dias (41,42; med 12,50), enquanto o intervalo de tratamento variou entre 0 e 460 dias (94,6; med 69,0). Não houve associação estatisticamente significante desses intervalos com variáveis clínicas como procedência, nível educacional, idade, estadiamento, tipo de tratamento e situação clínica das pacientes ao final do estudo. **Conclusões:** Embora o diagnóstico e tratamento precoces do câncer de mama sejam fundamentais, os dados da presente investigação mostraram que atrasos medianos de três meses para início do tratamento em hospital público não foram associados com piora do prognóstico ou sobrevida das pacientes.

PALAVRAS-CHAVE: neoplasias da mama; diagnóstico tardio; sobrevida.

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INTRODUCTION

According to the National Cancer Institute (INCA), breast cancer has a high incidence among Brazilian women, with an estimated 57,960 new cases by 2017. Pernambuco in the Northeast of Brazil has the highest incidence of this type of cancer, with an estimated rate of 53.18 new cases of breast cancer per 100,000 women for the biennium 2016/20171.

When detected and treated early, breast cancer has a good prognosis. Despite this, survival in developing countries is 57%, in contrast with 73% in developed countries[2]. The high mortality rate for breast cancer in the less developed nations can be explained mainly by the lack of screening programs and organization, with a large proportion of cases diagnosed at an advanced stage. In addition, the population's lack of knowledge about cancer, fear, prejudice and difficulty accessing health services increases the number of individuals who delay or do not adhere to treatment[3,4].

The literature demonstrates that the effective screening of breast cancer through mammography can detect the disease during the pre-clinical phase, interrupting its natural history and have a favorable impact on the mortality rate[4]. Consequently, delays leading to diagnostic and / or treatment delay allow tumor growth, resulting in more aggressive treatment, higher costs and the potential to reduce the chances of cure for patients.

The definition of the delay in time in cancer care is comprised of three different moments: the first occurs from the onset of symptoms until the first doctor´s consultation; the second, between the first consultation and the first access to the specialized service; and the third, from the first evaluation in the specialized service to the specific treatment[5-7]. A systematic review showed that a delay of more than three months between symptom identification and treatment is associated with a 12% decrease in survival for patients with breast cancer[8]. Access and time for the diagnosis and treatment of breast cancer vary in different regions of Brazil. A preliminary study, conducted at the clinical oncology services of the Faculdade de Medicina do ABC (FMABC), showed that the delay in the diagnosis of breast cancer is mostly related to the time it takes the patient to seek health services from the detection of the first signal or symptom[9].

Systematic review studies have found an association between delayed treatment of breast cancer and the patient's age[10], advanced stage [10-12], tumor size[13] and axillary lymph node involvement[14]. Some of these showed greater delay associated with being black, low educational level, low socioeconomic level and living far away from the treatment location [15].

A study carried out in the United States with women with low incomes showed that one in ten waited for 60 days or more to start treatment after the diagnosis, a time interval associated with a decrease in overall survival of 66% and breast cancer in 85% among patients with advanced stage [16]. Another study evaluated the impact that curative surgery has on survival and concluded that in relation to breast cancer, intervals longer than 12 weeks are associated with increased mortality[17]. However, studies that analyzed only some stages of the journey between the diagnosis and the treatment of breast cancer did not find a relation between the delay with poor prognosis or survival[18,19].

The objective of the present study was to describe the possible stages of delay for patients with breast cancer diagnosis within the oncology department of a public hospital in the state of Pernambuco, in addition to evaluating the possible association of delay at the beginning of treatment with factors such as staging and patient survival.

METHODS

This is a cross-sectional retrospective study with women with breast cancer diagnosed and treated at Instituto Materno Infantil Prof. Fernando Figueira (IMIP), located in the city of Recife, between January 2011 and December 2017.

The patient's medical charts were reviewed and the following variables were analyzed: age, origin, histological subtype, family history of cancer, gestations, smoking, consultation dates, examinations, treatments, type of diagnosis, staging (TNM), type of surgical treatment and need for neoadjuvant and / or adjuvant treatment, in addition to the clinical situation at the end of the study.

All patients with suspected primary breast cancer and who later received a positive diagnosis in the IMIP, having undergone complete treatment within the institution, were initially included in the study. Exclusion criteria were: patients with previous diagnosis of breast cancer who were referred to IMIP for treatment and follow-up, ductal carcinoma in situ and patients with other cancers.

The indication of a quadrantectomy or mastectomy was dependent on the assessment of the institution's mastologist surgeon. Simple mastectomy was characterized by the removal of the entire mammary gland, while in a radical mastectomy, it was associated with axillary lymphadenectomy. In general, locally advanced tumors underwent previous chemotherapy (neoadjuvant chemotherapy) before surgery.

Adjuvant (post-surgery) treatment, with radiotherapy and / or chemotherapy, was dependent on the presence of adverse prognostic factors.

Patient follow-up included consultations and regular examinations every three months in the first two years, every six months in the two subsequent years, and annually from the fifth year. At the end of the follow-up, the patients were classified as living without disease, living with disease, dead due to other causes and dead due to disease.

Two intervals were used to evaluate the treatment time of patient care: the first between the date of the first consultation at IMIP and the histopathological diagnosis, called the biopsy interval; and the second between the biopsy and the start of treatment (with surgery or neoadjuvant chemotherapy), called the treatment interval.

The values obtained by the study of each quantitative variable were organized and described in table form with their respective absolute and relative frequencies. Statistical Package for Social Sciences (SPSS) 13.0 for Windows and Excel 2016 were used for the statistical analysis. To verify the existence of association between categorical variables, the χ^2 test and the Fisher exact test were used. A 95% confidence index (95% CI) was applied to all tests.

The research was approved by the Ethics Committee on Research with Human Beings of the IMIP (CEP-IMIP) (CAAE: 70726017.9.0000.5201), and followed the norms established by Resolution No. 466/2012 of the National Health Council (CNS).

The Informed Consent Form was dismissed considering that the studied patients were no longer receiving treatment in the institution as well as the spaced out follow-up intervals which made contact extremely difficult.

RESULTS

A total of 173 patients were analyzed. The age ranged from 21 to 87 years (mean: 56.36 ± 12.28 years). One hundred and sixteen (67.1%) patients were from the metropolitan area of Recife, while 52 (30.1%) were from the interior of the state. In relation to the schooling level, 15 (8.7%) women were illiterate; 75 (43.4%) had up to 8 years of schooling and 71 (41%), more than 8 years of schooling. The mean number ofgestations was 3.19 ± 3.04. At the start of the study, 75 (43.3%) women had not yet entered menopause. This sociodemographic data are presented in Table 1.

Considering the 155 cases in which information can be retrieved, the majority of women (81; 46.8%) had no family history of breast cancer. In the first evaluation, 19 (11%) women had stage I; 61 (35.3%), stage II; 49 (28.3%), stage III; and 10 (5.8%), stage IV. There was no information on the initial staging in the 34 patient medical records (19.6%).

The main complaints were: breast lumps (91 cases, 52.6%), breast pain (24 cases, 13.9%), skin alterations (17 cases, 9.8%), bulging (6 cases; 3.5%) and abscesses (1 case, 0.6%). Forty-five patients (26%) found the change by routine examination (USG and / or mammography), of which 20 (44.4%) presented BIRADS 4 on mammography, and 6 (13.3%), BIRADS 5.

The most frequent histological type was infiltrating ductal carcinoma, diagnosed in 148 cases (85.5%). The mean tumor size was 4.3 ± 2.86 cm. The main surgical treatment was radical mastectomy, performed in 97 patients (56.1%), followed by quadrantectomy (31 cases, 17.9%) and simple mastectomy (15 cases, 8.7%). Neoadjuvant chemotherapy was used in 46.2% of cases. The aforementioned clinical data are presented in Table 2.

At the end of the study, 110 (63.6%) patients were alive without disease; 28 (16.2%), alive with disease; 2 (1.2%) died from other causes; and 14 (8.1%); from cancer. It was not possible to obtain this information in 19 medical records.

The biopsy interval (time between the first visit and the histopathological diagnosis) ranged from 0 to 826 days (41.42; med 12.50), while the treatment interval (time between histopathological diagnosis and treatment with surgery or chemotherapy) ranged from 0 to 460 days (94.6; med 69.0). There was no statistically significant association of these intervals with clinical variables such as origin, educational level, age, tumor staging, type of treatment and clinical status of patients at the end of the study (Tables 3 and 4).

Table 1. Sociodemographic characteristics of 173 patients with breast cancer. Recife, 2011-2017.

	n	%
Age (years)		
<50	49	28,3
≥50	124	71,7
Race		
White	20	11,6
Black	9	5,2
Brown	96	55,5
Information not given	48	27,7
Schooling level		
Illiterates	15	8,7
Up to 8 years	75	43,4
More than 8 years	61	35,3
Information not given	22	12,6
Smoke		
Yes	52	30,0
No	97	56,1
Information not given	24	13,9
Alcohol use		
Yes	32	18,5
No	116	67,0
Information not given	25	14,5
Breastfeed		
Yes	87	50,3
No	40	23,1
Information not given	46	26,6
Contraceptive use		
Yes	18	10,4
No	67	38,7
Information not given	88	50,9
Menopause		
<40 years	11	6,4
≥40 years	79	45,7
Information not given	8	4,6

DISCUSSION

Aiming to evaluate possible delays in diagnosis and its correlation with clinical factors, the present study analyzed a total of 173 breast cancer patients diagnosed and treated at IMIP, an institution in Pernambuco that exclusively treats patients from the Unified Health System (SUS).

The study population presents comparable socio-demographic and clinical aspects to the majority of specialized researches in the literature. The patients had a mean age of 56 years, the majority self declared as brown and had an schooling level of up to 8 years (8% were illiterate). Regarding the level of schooling, the results are similar to other Brazilian studies, because the sample is predominantly composed of people attended by SUS. In a study by Barros et al.[15], about 53% of the patients were illiterate or had attended school for up to four years.

Table 2. Clinical characteristics of 173 patients with breast cancer. Recife, 2011-2017.

	n	%
Histological type		
IDC	148	85,5
Varied	8	4,7
Information not given	17	9,8
Staging		
Stage I	19	11,0
Stage II	61	35,3
Satge III	49	28,3
Stage IV	10	5,8
Information not given	34	19,6
Type of surgery		
Simple Mastectomy	15	8,7
Radical Mastectomy	97	56,1
Quadrantectomy	31	17,9
Information not given	30	17,3
Neoadjuvance		
CT	76	44,0
RT	8	4,6
CT + RT	4	2,3
None	76	43,9
Information not given	9	5,2
Adjuvance		
CT	38	22,0
RT	45	26,0
CT + RT	47	27,2
None	23	13,3
Information not given	20	11,5
Differentiation grade		
G1	24	13,9
G2	77	44,5
G3	47	27,2
Information not given	25	14,4

IDC: Invasive ductal carcinoma; CT: chemotherapy; RT: radiotherapy.

The main complaint – breast nodule (53% of cases) - and the most common histological subtype - infiltrating ductal carcinoma (85.5% of cases) - are similar to those found in other specialized studies[4,20]. Considering 139 patients who had information on the initial staging, the majority - 110 women - were diagnosed with intermediate stages. Upon analyzing 73 patients in the state of São Paulo, Trufelli et al.[4] reported 17 cases of stage I, 28 cases of stage II, 17 case of stage III and 4 cases of stage IV. In a study by Angeles Llerenas et al.[20], in a Mexican multi-institutional analysis with 854 patients, this distribution was also similar: 88 cases of stage I, 324 cases of stage II, 342 cases of stage III and 62 cases of stage IV.

The most frequent type of surgery in our patients was radical mastectomy (56% of cases) more than likely due to advanced staging. Seventy-six (44%) patients underwent neoadjuvant chemotherapy, reinforcing the late diagnosis in this group of patients. Two other Brazilian studies report neoadjuvant chemotherapy in less than 30% of cases[4,15].

Delay in the diagnosis and treatment of breast cancer is discussed in the literature as having a negative impact on the prognosis of these patients. In a meta-analysis, Richard et al.[8] concluded that the delay in the treatment of breast cancer is associated with more advanced stages and worse survival. On the other hand, in a retrospective analysis that included 36,222 patients, through the Yorkshire Cancer Registry (England), Sainsbury et al.[5], concluded that there was no evidence that treatment delay negatively affected the survival of these women. The fact is that it is difficult to exclude the influence of many other variables, such as tumor aggressiveness, genetic mutations and real onset of symptoms, with the final outcome and evolution of these patients.

Any lesion suspected of breast cancer should be investigated as early as possible, however many detected cancers appear to have existed for a long time in certain individuals, suggesting a less aggressive phenotype or a long tumor duplication, as discussed in the study by Sainsbury et al. al.[5]. On the other hand, some more aggressive cancers metastasize early. In both cases, a slightly earlier detection may not decisively influence overall survival, justifying conflicting literature data.

The analysis of the delay in the diagnosis and treatment of breast cancer is always performed by retrospective studies, [4,20] similar to the present investigation, or by systematic reviews[8]. The ethical impediment for prospective studies is obvious for the subject, since it is not possible to randomize groups and wait for a malignant cancer to evolve.

Another much debated issue in the literature is the time interval analyzed by the various authors. The time between the

detection of symptoms and the first consultation - related to patient problems - or the time between the first consultation and the beginning of treatment - related to problems of the medical service - are the most evaluated intervals. In Brazil, as of 2013, it was determined by the Ministry of Health that all patients with malignant cancer should start treatment within 60 days of diagnosis[21].

The determination of the time between the first symptoms and the diagnosis is susceptible to many interpretation errors. Patients do not remember the onset of symptoms clearly, and confuse the symptoms with those of other diseases.

In studies that evaluate the delay in relation to the time interval from the first symptoms, a high median, often from 7 to 9 months, is almost always observed[15]. An exception is a study by the US National Cancer Institute, finding that approximately 40% of women report a 4-week delay in breast cancer diagnosis from the earliest symptoms; and that about 25% complain of an 8-week delay[22].

In this study, the biopsy - time interval between the first consultation and the histopathological diagnosis – was an average of 41 days, while the treatment - time interval between the histopathological diagnosis and the actual treatment – was 95 days on avergae (approximately three months).

Upon evaluating 250 cases, Barros et al.[15] reported that most of their patients started treatment after 90 days of the first consultation. Another Brazilian study[23], carried out in Vale do Cariri, Ceará, compares this waiting time to start treatment between private and public institutions. The mean time was significantly lower in the private institution (39 days) than in the public institution (71.5 days) (p = 0.031).In a Mexican study [20], the mean treatment interval was 37 days.

The biopsy and treatment intervals of this study were separated in two periods: less than or equal to 60 days and greater than 60 days. We did not observe a statistically significant association between these intervals or variables such as age, educational level, tumor staging, type of treatment and clinical status

Table 3. Association between the biopsy interval and the clinical variables of patients with breast cancer. Recife, 2011-2017.

Variables	Time (days) between the first visit and the biopsy		
	≤60 days n (%)	>60 days n (%)	p
Origin			
RMR	89 (78,1)	25 (21,9)	1,000*
Interior	40 (78,4)	11 (21,6)	
Out of state	2 (100,0)	0 (0,0)	
Age(years)			
<50	39 (83,0)	8 (17,0)	0,412**
≥50	95 (77,2)	28 (22,8)	
Schooling			
Up to 8 years	56 (75,7)	18 (24,3)	0,270**
More than 8 years	59 (83,1)	12 (16,9)	
Staging			
I and II	61 (78,2)	17 (21,8)	0,973**
III and IV	46 (78,0)	13 (22,0)	
Treatment type			
Neoadjuvance	71 (83,5)	14 (16,5)	0,147**
Surgery or surgery + adjuvant	61 (74,4)	21 (25,6)	
Clinical situation at the end of the study			
Alive	81 (75,0)	27 (25,0)	0,205*
Alive with disease	23 (85,2)	4 (14,8)	
Dead due to disease	13 (92,9)	1 (7,1)	
Dead due to other causes	1 (50,0)	1 (50,0)	
Dead			
Yes	14 (87,5)	2 (12,5)	0,525*
No	104 (77,0)	31 (23,0)	

RMR: Metropolitan Region of Recife; *Fisher exact test; **χ^2 test.

of the patients at the end of the study. These data are similar to those of another national author[4], who also did not observe statistical association between the diagnostic-treatment interval with age, type of treatment or patient evolution.

However, in a study by Barros et al.[15], there was a significant association between the level of schooling and the delay in diagnosis and / or treatment. Women with lower educational level had a significant delay in time between the first symptoms and diagnosis (p = 0.04) and between diagnosis and treatment (p = 0.03).

The association of low level of education with delayed treatment seems to be due to the lack of knowledge of these patients about the disease and the means of diagnosis. In addition, there is a tendency for these individuals to consider the disease as incurable.

Our patients over 50 years old or less than 50 years old had a similar distribution in relation to the delay in the biopsy interval (p = 0.616). However, in the study by Sainsbury et al.[5], it was observed that a high proportion of patients aged up to 50 years had a diagnosis delay of 90 days or more (8% of cases), compared to older patients (3% had a delay . Similar results are presented in a Colombian study[24]. It is suggested that this difference may be related to a greater clinical suspicion of cancer in the elderly with consequent fast diagnosis.

The patients in this study were mostly in stages II and III at the first specialist consultation. The distribution of stages in relation to delays in diagnosis and treatment was similar and not significant (Tables 3 and 4). The results of the literature are also discordant. In a study by McLaughlin et al.[25], the time interval between diagnosis and treatment did not affect survival in case with early stages, but it did affect survival in the more advanced stages, especially when the delay was longer than 60 days. Similar results are presented by Pineros et al.[24].

The treatment interval of the patients analyzed in this study was the same among the 14 cases that evolved to death, and there was no significant association between the biopsy intervals and

Table 4. Association between the treatment interval and the clinical variables of patients with breast cancer. Recife, 2011-2017.

Variables	Time (days) between biopsy and general TTO		
	≤60 days n (%)	>60 days n (%)	p
Origin			
RMR	57 (49,1)	59 (50,9)	0,149*
Interior	18 (34,6)	34 (65,4)	
Out of state	1 (50,0)	1 (50,0)	
Age (years)			
<50	23 (46,9)	26 (53,1)	0,616**
≥50	53 (42,7)	71 (57,3)	
Schooling level			
Up to 8 years	33 (44,0)	42 (56,0)	0,764**
More than 8 years	33 (46,5)	38 (53,5)	
Staging			
I and II	30 (37,5)	50 (62,5)	0,704**
III and IV	24 (40,7)	35 (59,3)	
Treatment type			
Neoadjuvance	40 (45,5)	48 (54,5)	0,493**
Surgery or surgery + adjuvant	33 (40,2)	49 (59,8)	
Clinical situation at the end of the study			
Alive	41 (37,3)	69 (62,7)	0,122*
Alive with disease	15 (53,6)	13 (46,4)	
Dead due to disease	7 (50,0)	7 (50,0)	
Dead from other causes	2 (100,0)	0 (0,0)	
Dead			
Yes	9 (56,2)	7 (43,8)	0,230**
No	56 (40,6)	82 (59,4)	

TTO: treatment; RMR: Metropolitan Region of Recife; *Fisher exact test; **χ^{2} test.

the treatment intervals with the clinical evolution. What most likely interfered in this evolution was the stage in which they were in during the first specialist consultation (11 stages III and 3 stages IV).

We chose to seperate the time intervals above and below 60 days, as this is the time recommended by the Brazilian government for cancer treatment to be started. Perhaps this relatively small delay is the reason that there was no significant association of the intervals with the variables mentioned above. In a review by Richards et al.[8] -an analysis of 87 studies with a total of 101,954 patients - only delays of 3 to 6 months are associated with a 12% decrease in patient survival.

As a conclusion, we can infer the extreme importance of an early diagnosis of breast cancer with implication in the reduction of mortality, as demonstrated by several authors[8,9,15,16]. On the other hand, the mean time of three months between diagnosis and treatment did not interfere in the evolution of the patients in this investigation. There is a need to ratify this data by broadening the investigation with more cases and investigating other possible time intervals.

REFERENCES

1. Instituto Nacional de Câncer (INCA). Estimativa 2016: incidência de câncer no Brasil. [Internet]. Rio de Janeiro: Instituto Nacional de Câncer; 2016 [acessado em 12 maio 2017]. Disponível em: https://www.inca.gov.br/campanhas/dia-nacional-de-combate-ao-cancer/2015/estimativa-2016-incidencia-de-cancer-no-brasil
2. Tfayli A, Temraz S, Abou Mrad R, Shamseddine A. Breast cancer in low- and middle-income countries: an emerging and challenging epidemic. J Oncol. 2010;2010:490631. https://doi.org/10.1155/2010/490631
3. Harford J, Azavedo E, Fischietto M. Guideline implementation for breast healthcare in low- and middle-income countries: breast healthcare program resource allocation. Cancer. 2008;113(8 Supl.):2282-96. https://doi.org/10.1002/cncr.23841
4. Trufelli DC, Miranda VC, Santos MBB, Fraile NMP, Pecoroni PG, Gonzaga SFR, et al. Análise do atraso no diagnóstico e tratamento do câncer de mama em um hospital público. Rev Assoc Med Bras. 2008;54(1):72-6. http://dx.doi.org/10.1590/S0104-42302008000100024
5. Sainsbury R, Johnston C, Haward B. Effect on survival of delays in referral of patients with breastcancer symptoms: a retrospective analysis. Lancet. 1999;353(9159):1132-5. https://doi.org/10.1016/s0140-6736(99)02374-0
6. Stiefel F. Understanding why women delay in seeking help for breast cancer symptoms. J Psychosom Res. 2006;60(3):309-10. https://doi.org/10.1016/j.jpsychores.2006.01.005
7. Ezeome ER. Delays in presentation and treatment of breast cancer in Enugu, Nigeria. Niger J Clin Pract. 2010;13(3):311-6.
8. Richards MA, Westcombe AM, Love SB, Littlejohns P, Ramirez AJ. Influence of delay on survival in patients with breast cancer: a systematic review. Lancet. 1999;353(9159):1119-26. https://doi.org/10.1016/s0140-6736(99)02143-1
9. Trufelli DC, Bensi CG, Pane CEV, Ramos E, Otsuda FC, Tannous NG, 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. Rev Bras Mastologia. 2007;17(1):14-7.
10. Sharma K, Costas A, Shulman LN, Meara JG. A systematic review of barriers to breast cancer care in developing countries resulting in delayed patient presentation. J Oncol. 2012;2012:121873. https://doi.org/10.1155/2012/121873
11. Yau TK, Choi CW, Ng E, Yeung R, Soong IS, Lee AW. Delayed presentation of symptomatic breast cancers in Hong Kong: experience in a public cancer centre. Hong Kong Med J. 2010;16(5):373-7.
12. Ukwenya AY, Yusufu LM, Nmadu PT, Garba ES, Ahmed A. Delayed treatment of symptomatic breast cancer: the experience from Kaduna, Nigeria. S Afr J Surg. 2008;46(4):106-10.
13. Brito C, Portela MC, Vasconcellos MT. Sobrevida de mulheres tratadas por câncer de mama no estado do Rio de Janeiro. Rev Saúde Pública. 2009;43(3):481-9. http://dx.doi.org/10.1590/S0034-89102009000300012
14. Ramirez AJ, Westcombe AM, Burgess CC, Sutton S, Littlejonhs P, Richards MA. Factors predicting delayed presentation of symptomatic breast cancer: a systematic review. Lancet. 1999;353(9159):1127-31. https://doi.org/10.1016/s0140-6736(99)02142-x
15. Barros ÂF, Uemura G, Macedo JLS de. Tempo para acesso ao tratamento do câncer de mama no Distrito Federal, Brasil Central. Rev Bras Ginecol Obstet. 2013;35(10):458-63. http://dx.doi.org/10.1590/S0100-72032013001000006
16. McLaughlin JM, Anderson RT, Ferketich AK, Seiber EE, Balkrishnan R, Paskett ED. Effect on survival of longer intervals between confirmed diagnosis and treatment initiation among low-income women with breast cancer. J Clin Oncol. 2012;30(36):4493-500. https://doi.org/10.1200/JCO.2012.39.7695
17. Shin DW, Cho J, Kim SY, Guallar E, Hwang SS, Cho B, et al. Delay to curative surgery greater than 12 weeks is associated with increased mortality in patients with colorectal and breast cancer but not lung or thyroid cancer. Ann Surg Oncol. 2013;20(8):2468-76. https://doi.org/10.1245/s10434-013-2957-y

18. Olivotto IA, Borugian MJ, Kan L, Harris SR, Rousseau EJ, Thorne SE, et al. Improving the time to diagnosis after an abnormal screening mammogram. Can J Public Health. 2001;92(5):366-71.

19. Masood S. Coming together to conquer the fight against breast cancer in countries of limited resources: the challenges and the opportunities. Breast J. 2007;13(3):223-5. https://doi.org/10.1111/j.1524-4741.2007.00413.x

20. Ángeles-Llerenas A, Torres-Mejía G, Lazcano-Ponce E, Uscanga-Sánchez S, Mainero-Ratchelous F, Hernández-Ávila JE, et al. Effect of care-delivery delay on the survival of Mexican women with breast cancer. Salud Publica Mex. 2016;58(2):237-50.

21. Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. [Internet]. 2013 [acessado em 17 maio 2017]. Disponível em: http://bvsms.saude.gov.br/sus/publicacoes/controle-canceres-colo-utero2013.pdf.

22. Coplan LS, Helzlsouer KJ, Shapiro S, Wesley MN, Edwards BK. Reasons for delay in breast cancer diagnosis. Prev Med 1996:25(2):218-24.

23. Ferreira NAS, Carvalho SMF, Valenti VE, Bezerra IMP, Batista HMT, Abreu LC, et al. Treatment delays among women with breast cancer in a low socio-economic status region in Brazil. BMC Womens Health. 2017;17(1):13.

24. Piñeros M, Sánchez R, Cendales R, Perry F, Ocampo R. Patient delay among Colombian women with breast cancer. Salud Publica Mex. 2009;51(5):372-80.

25. McLaughlin JM, Anderson RT, Ferketich AK, Seiber EE, Balkrishnan R, Paskett ED. Effect on survival of longer intervals between confirmed diagnosis and treatment initiation among low-income women with breast cancer. J Clin Oncol. 2012;30(36):4493-500.

Attachment 1. Data collection instrument.

Name: Registration:
Origin: 1 ( ) RMR 2 ( ) State interior 3 ( ) Outside of state
Age:
Race: 1 ( ) white 2 ( ) black 3 ( ) brown Occupation:
Educational level:
( ) Illiterate ; ( ) 1–2 years; ( ) 3–4 years; ( ) 5–6 years; ( ) 7–8 years; ( ) 9–12 years; ( ) More than 12 years;
Smoke: 1 ( ) Yes 2 ( ) No
Drink alcohol: 1 ( ) Yes 2 ( ) No
Age of menarche: Age of menopause:
Parity: Breastfeed: 1 ( ) Yes 2 ( ) No
Contraceptive use: 1 ( ) Yes 2 ( ) No
Family history: 1 ( ) Yes 2 ( ) No
History of benign breast disease 1 ( ) Yes 2 ( ) No
History of other neoplasms: 1 ( ) Yes 2 ( ) No
Date of last mammography:
Date of last clinical breast examination:
Reason for making doctor appointment:
1 ( ) Routine appointment
2 ( ) symptom (palpable nodule, retraction, hyperemia, bulging, abscess, breast pain, abscess, changes in the skin of the breast and axilla)
Date of first medical appointment:
Date of mammography request: Date of mammograpyh result:
Outcome / Result of mammography : BIRADS: Size of nodule: Compromised lymph nodes: 1 ( ) Yes 2 ( ) No
Date of request for breast ultrasound: Date of breast ultrasound result:
Outcome / Results of breast ultrasound : BIRADS: Size of nodule: Compromised lymph nodes: 1 ( ) Yes 2 ( ) No
Date of biopsy: Date of biopsy result:
Histopathological biopsy result:
Did you have any examination in the private service? 1 ( ) yes 1.1 ( ) What? 2 ( ) No
Neoadjuvant treatment: 1 ( ) Yes 1.1 Start date: 2 ( ) No
Date of surgery:
Type of surgery: 1 ( ) Radical mastectomy 2 ( ) Modified radical mastectomy 3 ( ) Simple mastectomy 4 ( ) Quadrantectomy
5 ( ) Setorectomy 6 ( ) Sentinel lymph node
Clinical Tumor Staging:
Tumor size(cm): Histological type:
Histological stage: ( ) I ( ) II ( ) III
Did you do immunohistochemistry? 1 ( ) Yes 2 ( ) No
Immunohistochemistry result:
Chemotherapy: 1 ( ) Yes 1.1 Start date: 2 ( ) No
Radiotherapy: 1 ( ) Yes 1.1 Start date: 2 ( ) No
Hormone Therapy: 1 ( ) Yes 1.1 Start date: 2 ( ) No
Clinical situation at the end of the study: 1 ( ) alive 2 ( ) alive with disease 3 ( ) death due to illness 4 ( ) death from other causes

RMR: Metropolitan Region of Recife.