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RESEARCH ARTICLE

The journey of breast cancer patient from self-perception of breast abnormalities to first cancer treatment- a sectional study in Sul Fluminense region-RJ-Brazil

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ABSTRACT

Breast cancer is the most common female neoplasm in Brazil accounting for 73.610 new cases a year. The organization of public health system is a critical point to provide diagnosis and treatment for these patients, considering that 75% of the population is covered by public health system (Sistema Único de Saúde, SUS). Waiting time for diagnosis procedures and treatment has been used to evaluate accessibility to the health system and can guide governmental strategies to improve them. A retrospective study was conducted by assessing medical records of all patients registered at a High Complexity Oncology Assistance Unit (Unidade de Alta Complexidade em Oncologia, UNACON). The patients registered in the period from October 2021 to September 2022 were included. The medical report was used to collect epidemiological, clinicopathologic data, and main waiting times for diagnosis procedures and treatment. There were registered 143 patients, mean age was 57.6 years (SD±12,6). Symptoms detected cancer was the majority with 112 patients (86,8%). Median waiting times: 1-from breast abnormalities self-perception to first image exam was 60 days; 2-waiting time from the exam to core biopsy was 41,5 days; 3-waiting time from the biopsy to report liberation of biopsy was 11.0 days; 4-waiting time from biopsy report to first visit at oncologic care unit was 31.0 days; 4-waiting time from the oncologic care unit first visit to first treatment was 55.0 days; 5-waiting time from the breast biopsy to treatment beginning was 97.0 days. Our study demonstrates long waiting time from diagnosis to first treatment (above 60 days as established by Brazilian law), long waiting time spending with each step of journey from the breast abnormalities self-detected to treatment beginning. Integration among basic, secondary e high complexity units, and clear strategies to guide patients with self-detected symptoms are points to be target.

Introduction

Breast cancer is the most frequent malignancy with nearly 2.3 million of new cases a year worldwide which account 11.7% of neoplasms, with 686.996 deaths, representing the main cause of cancer-related death among women.1 In Brazil data are consistent with global numbers with 73.610 new cases a year and 18.068 deaths.2 Growing disparities in treatment access and late diagnosis is resulting in huge discrepancy in survival rates in the world3 with 5-year relative survival rate of 66.8% in Malaysian, 88.9% in Japan, and 88.8% in the United States.4-6 In Brazil there is a paucity of prospective data, and we have a 5-years overall survival rate of 75,2% according to National Cancer Institute.7 Prospective data are expected from AMAZONA III study. Therefore, breast cancer is a public health challenge worldwide. Early diagnosis is a worthy strategy to deal with, since that there is no opportunity for primary prevention by this moment. However, there is a high proportion of diagnosis in late stage in low-and-middle-income countries (LMIC). Of note, the distribution by stage at diagnosis for Brazilian patients was stage I (26%), II (42%), III (27%) and IV (5%),8 demonstrating percentage in diagnosis in locally advanced stage III higher than high income countries (HIC) as Sweden, United States, Canada.9 There is many evidence pointing out that getting diagnosis in early stages would be able to save lives.10–12 Optimizing breast cancer patients access offering timely diagnosis in women awareness about their breast abnormalities can downstage invasive cancer13 and utmost improve outcomes. Even in the high-income countries (HIC) with the mature screening programs, less than one-half of breast cancer are screening-detected.10 The Amazona III, a recent prospective epidemiologic trial, demonstrated 34% of diagnosis in breast cancer by screening versus 66% after breast abnormalities self-perception, and analysing only public cohort the percentage of diagnosis by screening was 23.1% versus 76.9% by symptomatic patients highlighting this scenario as a critical point in Brazil where initiatives are desirable.8 Thus there is a clear necessity for suitable strategies to get early diagnosis in symptomatic patients. Also, these strategies are equally important in patients under 40-45 years old who are too young to be appropriate screening candidates.14 The accurate and timely breast cancer diagnosis in symptomatic patients is challenging because at least 80% of clinically detected abnormalities noticed clinical breast examination are benign.15 Adequate training programs targeting health professionals in primary care level to prepare them to recognize breast abnormalities and correctly conduct following tests is in line with World health Organization (WHO) recommendations which has preconized accelerate diagnosis in symptomatic patients as an affordable strategy in countries with scarce resources that can result great impact in outcomes.16,17.

Hence, an important question in Brazil is to provide to the public health system (Sistema Único de Saúde, SUS) assisted population the opportunity to perform fast confirmatory images exams (mammography and ultrasound) in women that noticed breast abnormalities as nodule, skin retraction or colour changing, and after that the fast core

biopsy in case of abnormalities were confirmed. Although SUS has brought significative advances in health access for Brazilian citizens, it has been underfunding since its creation and gaps in the assistance still remains.18 Regarding oncological care, it has been organized since 1980, initially in general hospitals and recently in high complexity services (units or centers).19,20 There are 317 of them distributed around the country, and its localization is based on epidemiologic data.21 However, to be registered in these units or centers patients are required to have the confirmatory cancer biopsy.22 There is a scarcity of data concerning the step before biopsy, which is conducted in the secondary complexity level of assistance. To describe this journey in breast cancer help us to understand barriers to get timely diagnosis.

The length waiting time from the breast abnormalities self-perception up to diagnosis and the first treatment might represent an unmet need in SUS-assisted Brazilian population. Also, there is limited data about waiting times in Brazil since the breast abnormalities self-perception to first treatment at an oncologic care center or unit. We are proposing a unicentric, retrospective study in Sul Fluminense region (Rio de Janeiro state, Brazil) which describes six main waiting times: 1-waiting time between breast abnormalities self-perception up to first image test (mammography or breast ultrasound); 2-waiting time from the image test up to core biopsy; 3-waiting time from biopsy to report of biopsy; 4-waiting time from the biopsy report to first visit at oncologic care unit; 5-waiting time from the oncologic care unit first visit up to first treatment; 6-waiting time from the breast biopsy to first breast cancer treatment. Describing these waiting times, we hope understanding the patient journey and identify points to be worked.

Methods

STUDY DESIGN AND VARIABLES:

A retrospective study was conducted by assessing the medical records of all patients registered at a High Complexity Oncology Assistance Unit (Unidade de Alta Complexidade em Oncologia, UNACON). The patients registered in the period from October 2021 to September 2022 were included and were performed two searches in the medical reports. It was created a questionary with question about epidemiologic and clinical data, and waiting times : 1- waiting time between breast abnormalities self-perception up to first image test (mammography or breast ultrasound); 2-waiting time from the image test up to core biopsy; 3- waiting time from the biopsy to report liberation of biopsy ;4-waiting time from the biopsy to first visit at oncologic care unit; 5-waiting time from the oncologic care unit first visit up to first treatment; 6-waiting time from the breast biopsy to first breast cancer treatment.

In the first search it was fulfil all data as available, and a second search was done after patients' accrual was closed with intent to complete data about time interval from first visit at Unit up to first treatment, and time interval from first image breast exam to first breast cancer treatment.

ETHICAL CONSIDERATIONS:

The study was approved by the Institutional Review Board (IRB) Coeps of Fundação

Oswaldo Aranha CAAE 64290621.8.0000. 5237 There was no patients interview, being dispensable the written informed consent form according to the IRB.

STATISTICAL ANALYSIS

There was no formal sample size calculation for this study due to its descriptive nature. Patients in roll within the period from 06 October 2021 to September 282022 were included to reduce the potential for selection bias. Quantitative variables were described by means and standard deviations and medians and compared with t test. Qualitative variables were described by absolute and relative frequencies and compared with Chi-square test. The p-values were adopted at 5% level of significance in all tests. All analyses were conducted using SPSS version 25.0.

Results

From October 06, 2021, to September 28, 2022, were registered 143 patients with breast cancer diagnosis proven by biopsy in public system health care at High Complexity Oncology Assistance Unit in Volta Redonda (Sul-Fluminense region in Rio de Janeiro State- Brazil). All these patients were included in this study. Patient's characteristics at diagnosis are described in table 1. All of patients were assisted in public health system. Mean age at diagnosis was 57.6 years (SD±12,6). Almost fifty per cent was married N=68 (47.9%), followed by single women N=33 (23.2%), never smoked N=87 (65.4%) and didn't drink alcoholic beverages N=105 (78.9%). Regarding education level 16 (12.5%) was illiterate, 65 (50.8%) complete elementary school, 36 (28.1%) completed high school and 11 (8.6%) had university degree. Out of 143 patients 38 (29.2%) were active workers, 66 (50.8%) inactive workers and 26 (20.0%) were retired. Symptoms detected cancer was the majority with 112 patients (86,8%), and screening detected cancer represented only 17 patients (13.2%). A common characteristic among these patients was that they didn't bring the immunohistochemistry result at UNACON in the first visit (73.43%).

Table 1: Socio-demographic characteristics

Variables		Patients (n)	(%)
Age (Mean/ SD)		57,6 (12,7)	
Civil status	Single	33	23,2
	Married	68	47,9
	Widowed	25	17,6
	Divorced	12	8,5
	Stable Union	4	2,8
Scholarship	Illiterate	16	12,5
	Elementary School	65	50,8
	High School	36	28,1
	University degree	11	8,6
Employment Status	Active worker	26	20,0
	Self-employed	12	9,2
	Inactive worker	6	4,6
	Housekeeper	60	46,2
	Retired	26	20,0
Smoking status	Never	87	65,4
	Current	21	15,8
	Former	22	18,8
CA detection		129	
	After symptoms	112	86,8
	By screening	17	13,2

SD, Standard deviation; CA, cancer

In terms of clinicopathological characteristic at diagnosis (table 2), most patients (N=92, 74.8%) had most common histologic subtype invasive ductal carcinoma, 104 (77.0%) patients were hormonal receptor positive and 24 (17.9%) presented HER 2 positive. Clinical stage breast cancer was in situ N=2 (1.7%), stage I N=19 (16.4%), stage II N=49 (42.2%), stage III N=32 (27.7%), stage IV N=4 (3,4%) and missing N=10 (8.6%).

Table 2: Clinicopathological variables

Variables		N	%
Histologycal tumor type	Ductal	92	74,8
	Lobular	15	12,2
	Tubular	3	2,4
	In situ	8	6,5
	Unknown	3	2,4
	Other	2	1,6
Histologycal grade	I	10	9,3
	II	59	55,1
	III	19	17,8
	Unknown	19	17,8
Clinical stage	In situ	2	1,7
	IA	18	15,5
	IB	1	0,9
	IIA	42	36,2
	IIB	7	6,0
	IIIA	14	12,1
	IIIB	17	14,7
	IIIC	1	0,9
	IV	4	3,4
	Unknown	10	8,6

Regarding waiting times (table 3), the median waiting time between breast abnormalities self-perception up to first image test (mammography or breast ultrasound) was 60 days (range 29.5-120); according to distribution by intervals category, 50 patients (38,8%) took more than 60 days to get the first image test. The median waiting time from the image test up to core biopsy was 41,5 days (range 22,0 to 90,0), with 44 patients (33.6%) taking more than 60 days; the median waiting time from the biopsy to report liberation of biopsy was 11 days (range 7 to 17) with 5 patients (3.8%) taking more than 60 days, the median waiting time from the biopsy liberation to first visit at oncologic care unit was 31 (range 20,0 to 53,5) with 22 (16.1%) patients taking more than 60 days; the median waiting time from the oncologic care unit first visit up to first treatment beginning was 55 days (range 34 to 82); the median waiting time from the breast biopsy to first breast cancer treatment at UNACON was 97.0 days (range to 64-133).

Table 3: Temporal Variables

Variables	N	Mean (SD)	Median	Min-Max
Number of days from the first symptom to first image exam	103	180.95 (455.88)	60 (29,5-120.0)	3-3650
Number of days from the first image exam to biopsy	140	85.79 (198.56)	41.5 (22.0-90.0)	1-2190
Number of days for biopsy release	143	16.51 (16.62)	11 (7-17)	2-130
Number of days from the biopsy release to first consult	143	8.60 (68.91)	31 (20.0-53.5)	6-730
Number of days from the first consult to first treatment at UNACON	129	60.32 (32.91)	55 (34-82)	2-140
Number of days from the biopsy result to first treatment at the service	121	105.73 (75.28)	97 (64-133)	30-778

SD, Standard deviation; IQR, interquartile range (25%-75%)

Variables age, staging, educational level and Laboral activity were analysed with all of 6 waiting times. There was correlation between early stage and waiting time from biopsy to first treatment, being the median 112 days for early stage and 71 days for advanced stage p 0.033. (Table 4).

Table 4: Correlation of number of days from biopsy result to first treatment with clinicopathological and socio-demographic variables

Variables	Number of days from biopsy result to first treatment in the service		*P* value
	Median (P25-P75)	Min – Max	
Scholarship			
Illiterate	96 (73 – 116)	44 – 235	0.151[k]
Elementary School	104 (67 – 142)	30 – 778	
High School	90 (55 – 108)	33 – 154	
University degree	98 (85 – 127)	55 – 183	
Employment status			
Active worker	86 (62 – 103)	43 – 183	0.055[mw]
Inactive worker	105 (66 – 142)	30 – 778	
Stage			
In situ	110 (100 – 116)	64 – 155	0.033[k*]
Early	112 (85 – 142)	42 – 778	
Advanced	71 (58 – 103)	30 – 237	
Age	58 (45 – 64)	31 -84	0.131[r]

K, Kruskal-Wallis Test; Mw, Mann-Whitney Test; R, Pearson Correlation Coefficient; *, Multiple Comparison Advanced x Early, p = 0.002

The first treatment indicated by the physicians in the first visit (surgery, chemotherapy, or endocrine therapy) had relationship with waiting time. The median waiting time for chemotherapy was 40 days (range 28.5 to 54.5) compared to surgery with 69 days (range 48 to 90) p=0.001. (Table 5).

Table 5: Comparison of the time (in days) with the indicated initial treatment.

Variables	Indicated initial treatment Median days (IQR)			*p* value
	Surgical	Chemotherapy	Endocrine Therapy	
Time from first symptom to first imaging exam	n = 58 45 (25.3 – 120)	n = 42 85 (30 – 115)	n = 2 190 (102.5 – 277.5)	0.826[kw]
Time from first imaging exam to biopsy	n = 87 50 (22.5 – 98)	n = 49 35 (21 – 64)	n = 3 35 (27,5 – 77,5)	0.375 [kw]
Time to biopsy release	n = 89 12 (7 – 20)	n = 50 9.5 (6.25 – 16)	n = 3 11 (9 – 20)	0.287[kw]
Time between release of the biopsy and first visit	n = 89 31 (20 – 60)	n = 50 30 (20 – 40.75)	n = 3 31 (27 – 33.5)	0.675[kw]
Time between first visit and first treatment at UNACON	n = 78 69 (48 - 90)	n = 47 40 (28.5 – 54.5)	n = 3 110 (63 – 120)	0.001[kw]

IQR, interquartile range (P25 - P75); kw, Kruskal-Wallis Test; UNACON, High Complexity Oncology Assistance Unit; Multiple comparison by the Mann-Whitney test

Discussion

The breast cancer patients in *Sul Fluminense* region have waited for a long-time interval from the self-perception breast abnormalities to treatment beginning, with median of 97 days as we described in this study only from biopsy to treatment beginning, which is a worrying point. When we analysed the other essential procedures before treatment (mammography and ultrasound, first visit at cancer unit care) there are long lasting waiting time for each one of them.

Our study analysed a cohort with 143 patients that received their treatment into SUS, which reflects the majority of Brazilian population since the 75% of them is covered exclusively by SUS[23]. It also confirms the most of breast cancer being symptomatic at diagnosis (86.8%) instead of screening detected, as well the stage distribution of cancer with high proportion in advanced stages, with 27.7% in stage III which per se represents a challenge. These data are according to demonstrated in AMAZONA III study[8]. Screening strategy was implanted in Brazil in 2004[24], and it has been incentivized by government[25], however the coverage yet is not enough, receiving important efforts by campaigns as pink October, presenting lower rates of screening tests in other months[26–28]. Besides the small proportion of cancer screening detected, this study highlighted other critical points as high number of patients diagnosed in stage III and a long waiting time for procedures after symptoms detected. These points maybe could be explained by the lack of clear approach to receiving and conducting cases of patients known to have self-detected

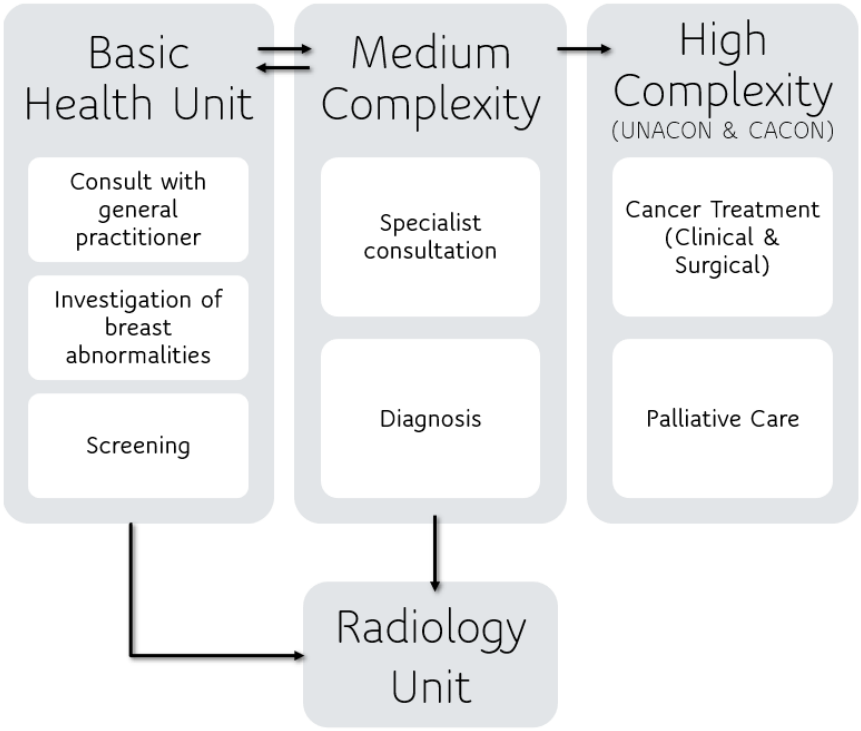
breast abnormalities. The median waiting time from self-abnormalities perception to first image test of 60 days is clearly inadequate. Also, when we analyse the distribution by category of intervals, more than one third (38.8%) took more than 60 days to get the first image exam. Although screening programs and diagnostic procedures for symptomatic patients are different strategies, probably patients in the region requiring a screening mammography have been managed as the same way that patients referring a self-perception breast abnormality when both looking for a primary unit care, explaining the long waiting time for diagnosis procedure. Deepening this question, one important step is clinical breast examination (CBE), which has not been recommended as a primary screening modality due its limitations[29], however there is a difference between its use as primary screening and its use as a first step in the chain of procedures targeting symptomatic patients[30]. There is evidence that previous clinical breast examination (CBE) reduces delays in diagnosis and treatment initiation[31]. Educational programs dedicated to primary care team ensuring history taking and CBE could make short the interval from the self-perception abnormality breast to first image test.[16] The CBE examination by the primary care team would have a confirmatory intention and in case of breast abnormalities are confirmed, such patients would have priority in their following procedures.

The waiting time from breast image exam, (mammography most of times) to biopsy was 41,5 days (range 22,0 to 90,0), with 44 patients (33.6%) taking more than 60 days; with additional 11 days (median) to get biopsy report. One strategy that could shorten these intervals would be adopt cancer diagnosis in one-stop clinic[16]. In Brazil, most of times, the patient is referred from the primary unit care after breast abnormality is confirmed to secondary unit care where the histopathologic diagnosis (biopsy) is required. Once the visit is scheduled at secondary care unit and have the biopsy required, one more time the patients will be referred to another service provider (Radiology Unit), where the biopsy will be done[7]. This migration during confirmatory diagnosis phase contributes to increase delays to diagnosis and consequence treatment beginning.

The printed biopsy report is required for scheduling the first visit at UNACON or CACON (High Complexity Center or Unit for Oncology)[22], with median of 11 days the waiting time to get this result in our region. After getting biopsy result the median waiting time for first visit at UNACON, was 31 days, then ongoing on the journey, the patients are referred to high complexity units or centers. As we can notice, the assistance for women health in Brazil is organized in three steps, the first one is basic attention located at Basic Health Unit (BHU), where women looking for assistance in case of symptoms self-detected or in case of undergoing screening tests. At BHU are done consultants with primary physician care and exams prescription, however these exams will be done in another unit, a radiologic Unit. After return with tests results, in case of tests confirm the suspicious lesions, the patient is referred to a second step, the medium complexity unit, where there are evaluable consultants with breast

surgeon who will require breast biopsy. The biopsy will be done at a local related to a medium complexity (which can be inside this unit or in a service provider in another local). After patients have done the biopsy, they return to the medium complexity unit, and in case of confirmed cancer diagnosis, the breast surgeon will refer them to a third step, the high complexity unit (UNACON) or center (CACON) where the patients will receive the breast cancer treatment (figure 1). Although the procedures are encompassed within a referral and counter-referral system[32], the necessity of transit for several units during pre-diagnosis phase and to a third level after diagnosis, might represent a factor that contributes to delays diagnosis and treatment commencement. The integration of these units as well patient navigation could represent points to be target.

Figure 1: Stages of care for women's health



UNACON, High Complexity Oncology Assistance Unit; CACON, High Complexity Center for Oncology

Inside the UNACON, the first care is done by breast surgeon team. In case of first treatment is surgery, it is required for the same team, in general during the first visit. In case of chemotherapy or endocrine therapy is the first indication, the patients are referred to clinical oncologic department (in the same unit) and after evaluation by oncologist, the treatment is requested. The median waiting time for surgery was 69 days (when surgery is the first performed treatment) and chemotherapy were 40 days (when chemotherapy is the first performed treatment, for instance, neoadjuvant or palliative chemotherapy). These data reflect more accessibility to chemotherapy than surgery, representing one more challenge to be overcome by the local gestor.

In the global analyses, the waiting time from the biopsy report to first treatment is 97.0

days. According to the Brazilian law 12.732/2012 from 2012 the time of 60 days from diagnosis to first treatment is the limit time to beginning the treatment[33]. This time (from diagnosis to first treatment) is used to evaluate the accessibility and quality of health systems[32], however it represents only one waiting time among others that patients need to overcome. When we analyse the waiting time from self-abnormalities to first exam, from first exam to biopsy, from biopsy procedure to biopsy report, from biopsy report to high complexity entrance and high complexity entrance to first treatment, we notice the waiting time from biopsy to first treatment clearly underestimates the total waiting time. Reinforcing that, the waiting time of 97 days, is too long, representing more than one month above that recommended by Brazilian government.

This study doesn't demonstrate correlation between socio-demographic variables (age, educational level and Laboral activity) and waiting-time intervals, which might be explained by the small population sample. There was correlation between early stage and waiting time from the first treatment with more long waiting time for early stage versus advanced stage, representing short waiting time to chemotherapy (first treatment indicated in advanced stage) rather than surgery (first treatment recommended in early stage). This data is confirmed by a correlation between first indicated treatment (chemo versus surgery) and waiting time for them, favouring chemotherapy with small number of days (40 versus 69 days respectively). It also reinforced the clear necessity of a specific National Cancer Control Program, which could plan and execute actions in cancer care, of utmost importance optimizing waiting times mainly regarding early stages breast cancer management. Due to lack of a National Cancer Control Program also there is a scarcity of epidemiological data which becomes difficult to plan cancer care policies resulting in reactive and unplanned approaches health-care provision, with suboptimal resource utilization[34,35].

Hence many variables may contribute to delays in commencement of breast cancer treatment as bureaucracy, overcrowded public health system accounting for long waiting time for scheduling procedures, wasting time with transition among provider services units, issues that need be worked by a Brazilian government, which will certainly improve results in breast cancer care.

Conclusions

Our study demonstrates long waiting time from diagnosis to first treatment (above 60 days as established by Brazilian law), long waiting time spending with each step of journey from the breast abnormalities self-detected to treatment beginning. Integration among basic, secondary, and high complexity units, and clear strategies to guide patients with self-detected symptoms are points to be target in Brazil.

Conflict of Interest Statement:

Heloisa Resende has received research funding from Novartis and Roche, all outside the scope of this manuscript. The other authors have no conflict of interest.

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