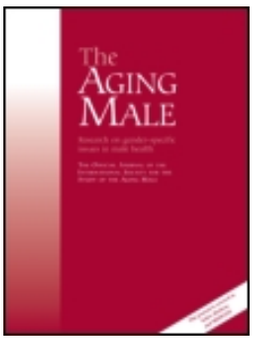

The Aging Male

ISSN: 1368-5538 (Print) 1473-0790 (Online) Journal homepage: https://www.tandfonline.com/loi/itam20

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To cite this article: Luiz Claudio Santos Thuler & Anke Bergmann (2015) Male breast cancer: clinical-epidemiological characteristics of 1189 Brazilian patients, The Aging Male, 18:2, 118-123, DOI: 10.3109/13685538.2014.922532

To link to this article: https://doi.org/10.3109/13685538.2014.922532

The Aging Male

http://informahealthcare.com/tam
ISSN: 1368-5538 (print), 1473-0790 (electronic)

Aging Male, 2015; 18(2): 118–123
 DOI: 10.3109/13685538.2014.922532

informa healthcare

ORIGINAL ARTICLE

Male breast cancer: clinical-epidemiological characteristics of 1189 Brazilian patients

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Abstract

Purpose: To describe the clinical-epidemiological features of male patients with breast cancer in Brazil.

Methods: Data from male patients with breast cancer treated from 2000 through 2009 were obtained from the Brazilian Hospital Cancer Register databases. Descriptive statistics were performed.

Results: A total of 1189 male patients were included. The mean age at diagnosis was 59.6 years (± 13.6). Tumours were categorised as clinical stage I (14.3%), stage II (38.3%), stage III (34.1%) and stage IV (13.3%). The most frequent histological type was invasive ductal carcinoma (83.7%). The first course treatment (alone or combined) consisted of chemotherapy in 53.2%, surgery in 49.2, radiation therapy in 36.8 and hormonal therapy in 21.0%; 3.4% of cases did not receive treatment. Treatment modality varies according to the tumor-node-metastasis (TNM) stage. The inadequate response rate was 15.9%, and 7.4% of patients died after the first course of treatment. Adequate response according to the first-course cancer treatment, after adjusted for clinical stage, was associated with being Caucasian (odds ratio (OR) = 2.50; 95% confidence interval (95% CI): 1.35–4.65) and submitted to chemotherapy (OR = 0.46; 95% CI: 0.28–0.74).

Conclusions: Male breast cancer diagnosis is often made in the advanced stage. Consequently, patients were subjected to more aggressive treatments, with poorer clinical response.

Keywords

Clinical characteristics, male breast cancer, treatment

History

Received 24 March 2014
Revised 6 May 2014
Accepted 6 May 2014
Published online 28 May 2014

Background

Male breast cancer (MBC) is a rare disease accounting for less than 1% of all breast cancers and 1% of all male malignancies [1]. In the United States, MBC deaths represent less than 0.5% of all cancer deaths [2]. By contrast, in some parts of Africa, breast cancer may account for up to 6% of cancers in men [3]. In Brazil, in the past decade (2001 to 2010), data from the Mortality Information System operated by Brazil's Ministry of Health have shown that only 0.97% of 106 425 breast cancer deaths were in men. This percentage varies widely between 0.85 in the first triennium (2001–2003) and 1.12 in the last one (2008–2010), representing a relative increase of 31% [4]. Although incidence data is not available for the entire country, data from the Sao Paulo Cancer Registry concerning different periods of time have shown that adjusted breast cancer incidence rates, per 100 000 males, increased three times in the past two decades: 0.5 (1988), 0.9 (1993) [5], 0.97 (1997–1998) [6], 1.21 (2001–2005) [7] and 1.4 (1997–2008) [8].

These cancers are biologically different from carcinomas of the female breast [9]. However, little is known about its biological and histopathological features, epidemiology, causes, prognosis, ideal management and treatment. Generally, the knowledge is extrapolated from the experience with female patients or a relatively small number of studies in male, mainly case series. In addition, several recent studies show poor survival and suggest that the prognosis is worse than in females as a result of large tumour size, advanced stage, high grade and presence-positive nodes at the time of cancer diagnosis [9,10]. Besides, incidence is rising in the developed world, particularly in the urban US, Canada and UK [11]. This study was carried out to examine the epidemiological and clinical features of male patients with breast cancer diagnosed and treated in Brazil.

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Materials and methods

A retrospective cohort study was accomplished using information from Cancer Hospital Records in Brazil, obtained through the Integrator System (Brazilian National Cancer Institute) and Sao Paulo's Hospital Cancer Registry (Oncocentro Foundation). These bases include information from 239 accredited cancer centres in Brazil involving 25 States and the Federal District. Between 2000 and 2009, it included men with breast cancer (International Classification of Diseases – Oncology – 3rd Edition – ICD-O C50), whose planning, treatment and follow-up were made in a cancer hospital.

Patients were followed up until the end of first course of treatment. The following variables were collected: age at diagnosis (in years), marital status (with partner versus no partner), race/skin colour (white versus non-white), level of education (less than middle school certificate versus middle school certificate or higher), family history of breast cancer (yes versus no), current alcohol consumption (more than three times per week, independent of amount consumed), habitual tobacco use and its derivatives at the time of hospital enrolment (yes versus no) and year of diagnosis and tumour site. TNM stage at diagnosis, histological type, first-course therapy and status at the end of the first course of treatment were classified using surveillance, epidemiology and end results (SEER) definitions [12]. For all cases, the first course of therapy includes all cancer-directed treatment administered to the patient within four months after the initiation of therapy. All modalities of treatment were included regardless of sequence or the degree of completion of any component method. Two or more single agents given at separate times during the first course of cancer-directed therapy were considered a combination regimen.

A descriptive analysis of the study population was performed through measures of central tendency and dispersion to the age variable, and determination of frequency distribution to categorical variables, with intervals of 95% of confidence and *p* values. The crude and adjusted association between adequate response according to the first-course cancer treatment and select variables was estimated by odds ratios (OR) and its 95% confidence interval (95% CI). The statistical program used was SPSS, version 21.0 (São Paulo, Brazil).

This study was approved on 21 October 2011, by the Brazilian National Institute of Cancer (INCA) of Ethics and Research Committee (CAAE – 0104.0.007.000-11).

Results

During the 10-year study period, a total of 85 912 patients with breast cancer were registered, and a total of 1189 (1.38%) were male patients (mean 119 cases per year; minimum 98 – maximum 161).

In male patients with breast cancer, the mean age at diagnosis was 59.6 years (± 13.6); 23.9% were younger than 50 years. A family history of breast cancer was noted in 45.4% of cases. According to the TNM classification, tumours were categorized as stage I (14.3%), stage II (38.3%), stage III (34.1%) and stage IV (13.3%); 30.5% of patients presented with pT4 stage. The most frequent histological type was invasive ductal carcinoma (83.7%) (Table 1).

Table 1. Baseline demographics and clinical characteristics of study population ($n = 1189$).

Demographic characteristics	No. of patients*	Percentage
Age, years		
<50 years	284	23.9
50–69 years	589	49.5
≥70 years	316	26.6
Race		
White	443	65.7
Non-white	231	34.3
Level of education		
Less than middle school certificate	406	55.9
Middle school certificate or higher	320	44.1
Marital status		
No partner	243	37.3
Partner	109	62.7
Family history of breast cancer		
Yes	166	45.4
No	200	54.6
Alcohol drinking		
Yes	96	24.6
No	294	75.4
Tobaco smoking		
Yes	174	40.9
No	251	59.1
Year of diagnosis		
2000-2004	532	45.0
2005-2009	651	55.0
Tumor status		
T0	19	2.3
T1	182	22.1
T2	279	33.9
T3	91	11.1
T4	251	30.5
Axillary lymph node status		
N0	376	45.8
N1	300	36.5
N2	120	14.6
N3	25	3.0
Metastasis		
M0	715	86.9
M1	108	13.1
TNM clinical stage		
I	139	14.3
II	371	38.3
III	330	34.1
IV	129	13.3
Histological type		
Invasive ductal carcinoma	994	83.7
Other	195	16.3
Tumor site		
Bilateral	8	1.1
Right	348	50.9
Left	328	48.0

*Totals here are less than totals due to missing values.

The percentage of advanced stage (stage ≥ 2B) cancers ranged from 54.2 in the year 2005 to 71.1 in 2000. The first-course treatment consisted of chemotherapy (alone or combined) in 53.2%, surgery (alone or combined) in 49.2%, radiation therapy (alone or combined) in 36.8% and hormonal therapy (alone or combined) in 21.0%; 3.4% of cases did not receive treatment (data not shown).

Treatment modality varies according to the TNM stage (Figure 1). At the end of the first treatment, 37.4% of patients had a complete response, 46.7% were in partial remission or had stable disease, 8.5% had progressive disease or relapsed and 7.4% died from breast cancer (data not shown). According to the TNM stage, adequate response was observed

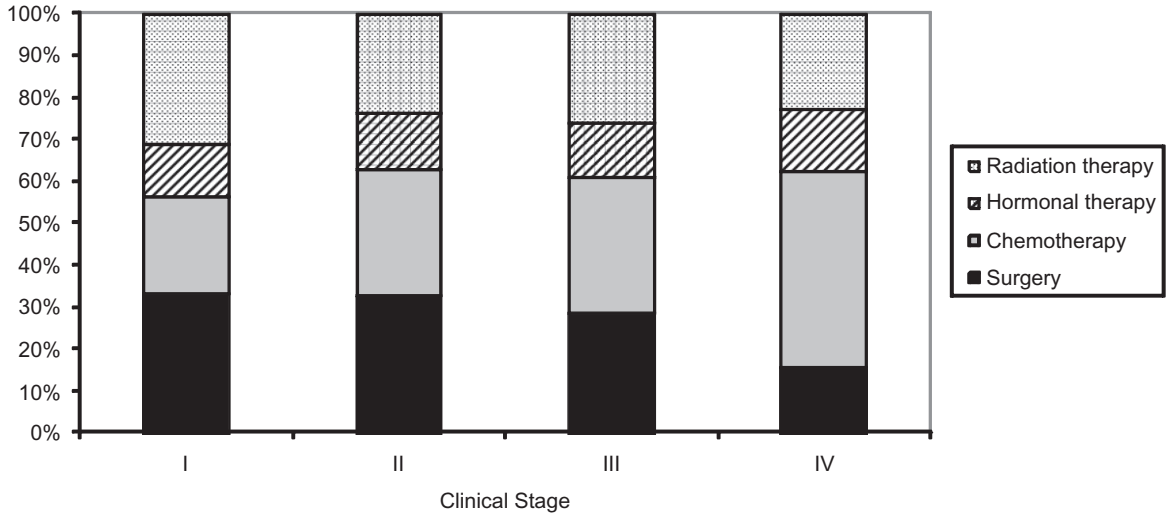

Figure 1. First-course cancer treatment (alone or combined with other treatment), according to clinical stage (TNM).

Table 2. Response classification of male breast cancer according to the first-course cancer treatment ($n = 722$)*.

			Adequate response‡		Inadequate response¶	
Stage	First-course treatment received†	*N*	*N* (%)	95% CI	*N* (%)	95% CI
Stage I ($n = 102$)	Surgery	49	48 (98.0)	89.3–99.6	1 (2.0)	0.4–10.7
	Chemotherapy	34	30 (88.2)	73.4–95.3	4 (11.8)	4.7–26.6
	Hormonal therapy	19	18 (94.7)	75.4–99.1	1 (5.3)	0.9–24.6
	Radiation therapy	46	46 (100.0)	92.3–100.0	0 (0.0)	0–7.7
	Total	102	96 (94.1)	87.8–97.3	6 (5.9)	2.7–12.2
Stage II ($n = 282$)	Surgery	160	155 (96.9)	92.9–98.7	5 (3.1)	1.4–7.1
	Chemotherapy	148	141 (95.3)	90.6–97.7	7 (4.7)	2.3–9.4
	Hormonal therapy	65	62 (95.4)	87.3–98.4	3 (4.6)	1.6–12.7
	Radiotherapy	117	115 (98.3)	94.0–99.5	2 (1.7)	0.5–6.0
	Total	282	272 (96.5)	93.6–98.1	10 (3.5)	1.9–6.4
Stage III ($n = 243$)	Surgery	131	108 (82.4)	75.0–88.0	23 (17.6)	12.0–25.0
	Chemotherapy	151	118 (78.2)	70.0–84.0	33 (21.9)	16.0–29.1
	Hormonal therapy	60	48 (80.0)	68.2–88.2	12 (20.0)	11.8–31.8
	Radiotherapy	122	100 (82.0)	74.2–88.0	22 (18.0)	12.2–25.8
	Total	243	200 (82.3)	77.0–87.0	43 (17.7)	13.4–23.0
Stage IV ($n = 95$)	Surgery	21	10 (47.6)	28.3–67.6	11 (52.4)	32.4–71.7
	Chemotherapy	63	23 (36.5)	25.7–49.0	40 (63.5)	51.2–74.3
	Hormonal therapy	20	8 (40.0)	21.9–61.3	12 (60.0)	38.7–78.1
	Radiotherapy	31	16 (51.6)	34.8–68.0	15 (48.4)	32.0–65.2
	Total	95	41(43.2)	33.7–53.2	54 (56.8)	46.8–66.3
Total ($n = 722$)	Surgery	361	321 (88.9)	85.3–91.8	40 (11.1)	8.2–14.7
	Chemotherapy	396	312 (78.8)	74.5–82.5	84 (21.2)	17.5–26.2
	Hormonal therapy	164	136 (82.9)	76.4–87.9	28 (17.1)	12.1–23.6
	Radiotherapy	316	277 (87.7)	83.6–90.8	39 (12.3)	9.1–16.3
	Total	722	609 (84.4)	81.5–86.8	113 (15.7)	13.2–18.5

*Totals here are less than totals for the other characteristics due to missing values.
†Treatment modalities were considered alone or combined.
‡Adequate response: partial remission, stable disease and complete response.
¶Inadequate response: progressive disease, relapsed disease or death.

in 94.1% (95% CI: 87.8–97.3) of patients in stage I, 96.5% (95% CI: 93.6–98.1) in stage II, 82.3% (95% CI: 77.0–87.0) in stage III and 43.2 (95% CI: 33.7–53.2) in stage IV (Table 2).

The association between adequate response according to the first-course cancer treatment, after adjusted for clinical stage, showed that white men were 2.5 times more likely to have an adequate response (OR = 2.50; 95% CI: 1.35–4.65) and patients submitted to chemotherapy had 54% less chance (OR = 0.46; CI 95%: 0.28–0.74) (Table 3).

Discussion

Male breast carcinoma is similar to breast cancer in women, but there are some distinct features that should be highlighted. During the past few years, there has been an increase in the incidence and mortality in this cancer in Brazil. This can be caused by the coexistence of risk factors such as family history, obesity, low levels of physical activity, environmental exposures and genetic predisposition [13].

Table 3. Association between adequate response of male breast cancer according to the first-course cancer treatment and selected variables.

Variable	*N* (%)	Unadjusted		Adjusted*	
		OR (95% CI)	*p* Value	OR (95% CI)	*p* Value
Age, years					
<65 years	741 (62.3)	1.00 (0.68–1.47)	1.000	1.01 (0.64–1.59)	0.980
≥65 years	448 (37.7)	Reference		Reference	
Race					
White	443 (65.7)	2.42 (1.49–3.94)	0.001	2.50 (1.35–4.65)	0.004
Non-white	231 (34.3)	Reference		Reference	
Level of education					
Less than middle school certificate	406 (55.9)	0.91 (0.56–1.47)	0.714	1.19 (0.66–2.17)	0.561
Middle school certificate or higher	320 (44.1)	Reference		Reference	
Partnership status					
No partner	243 (37.3)	0.74 (0.47–1.20)	0.261	0.88 (0.47–1.63)	0.685
Partner	409 (62.7)	Reference		Reference	
Year of diagnosis					
2000–2004	532 (45.0)	1.14 (0.78–1.66)	0.505	1.02 (0.65–1.60)	0.934
2005–2009	651 (55.0)	Reference		Reference	
Histological type					
Invasive ductal carcinoma	994 (83.7)	1.98 (1.27–3.11)	0.004	1.74 (0.98–3.08)	0.059
Other	194 (16.3)	Reference		Reference	
Surgery					
Yes	585 (49.2)	2.03 (1.39–2.98)	<0.001	1.37 (0.86–2.17)	0.188
No	604 (50.8)	Reference		Reference	
Chemotherapy					
Yes	632 (53.2)	0.36 (0.24–0.55)	<0.001	0.46 (0.28–0.74)	0.002
No	557 (46.8)	Reference		Reference	
Radiation therapy					
Yes	437 (36.8)	1.48 (1.00–2.19)	0.055	1.52 (0.96–2.41)	0.076
No	752 (63.2)	Reference		Reference	
Hormonal therapy					
Yes	250 (21.0)	0.91 (0.58–1.41)	0.649	0.85 (0.51–1.43)	0.854
No	939 (79.0)	Reference		Reference	

*Adjusted for clinical stage.

The mean age of our case series was 59.6 years, confirming that median age of onset of breast cancer in men is approximately 5–10 years later than in women [14–16]. A series from the same database involving 117 601 women has shown that age was slightly inferior (median: 55.5 years; SD: 13.5) (Author, unpublished data), supporting the conclusion that women are typically diagnosed with breast cancer at a younger age than men. In the United States of America in a study that compared 612 males with 2413 females who had breast cancer, the mean age at diagnosis was 67 years for male patients and 57 years for female patients ($p < 0.005$) [17]. Other studies had lower mean ages, such as 58 years [18] in Turkey, 55 in Africa [19] and 59 years [20] in Nigeria. This early presentation in these countries can be explained by, among other things, the lower life expectancy in those countries.

In women, family history of breast cancer is an important risk factor. In men, the prevalence of a positive family history in a first or second relative degree can range between 13% and 30% [16,21,22]. Family history of cancer was observed in a high percentage (45.4%) of our cases, but it was not possible to know the type of cancer and the degree of kinship of these cases. Part of these results may be attributable to reporting bias, due to differential recall between breast cancer cases. The incidence of breast cancer among black people is approximately 15% less than in whites [16]. Our results showed higher frequency of white patients (65.7%), and this variable was associated with an adequate response after the first course of cancer treatment ($p = 0.004$). Studies observed that black men tend to have poorer prognostic features (advanced-stage disease, tumour sizes, more nodal involvement and higher tumour grade) [12,21]. In Brazil, skin colour has been related to the access to treatment and care [23].

In this study, the frequency of patients in stages III and IV was 47.4%, which was less than the findings of Bourhafour et al. [24] in Morocco (80.3%) and Ahmed et al. [20] in Nigeria (93.0%). On the other hand, in an Australian series, only 20.6% of MBC cases were diagnosed in stages III or IV [25]; in a German study, 23.9% of cases were diagnosed [26]. A significant proportion of advanced clinical stage in our series can be, at least in part, caused by the paucity of knowledge and public awareness regarding the existence of MBC, no recommendations for male breast care and difficult access to health care services [27,28].

Invasive ductal carcinoma was the predominant histological type (83.7%). This results confirms other studies, which have shown values ranging from 77.8 [24] to 96.0% [24]. This can be explained by the fact that the male breast does not have lobular elements [29].

Due to the low incidence of MBC, few clinical trials are conducted to assess the effectiveness of cancer treatments in this population [16]. As a general rule, breast cancer in men should be treated similarly to postmenopausal hormone receptor-positive disease in women [21,29]. With no evidence to support female-to-male data extrapolation, epidemiological comparisons become an alternative source of information [27].

The primary therapy in man is modified radical mastectomy or simple mastectomy, with no differences in survival

between these techniques [16]. There is a little evidence that hormonal therapy and chemotherapy is as effective as in women in male patients with primary breast cancer [29,30]. In this study, patients in clinical stages I and II were predominantly treated with surgery (alone or combined) and those in stages III and IV with chemotherapy (alone or combined). After removing the effect of clinical staging, patients receiving chemotherapy had a poorer response in the first course of treatment ($p = 0.002$). According to Korde et al. [21], it is difficult to detect a chemotherapy advantage in MBC because, in general, benefits are more apparent in endocrine non-responsive breast cancer, in high-risk groups and in younger patients. In males, most of the tumours are hormone receptor-positive in older patients and have multiple comorbidities.

A few patients' at all clinical stages underwent hormonal therapy. However, it was not possible to identify the status of oestrogen and progesterone receptor. Others studies have shown that MBC was more likely to be hormone-receptor positive (oestrogen and progesterone) than female breast cancer [16,21,31] and that breast cancer is biologically different between genders [9]. Apart from hormonal status, the use of hormonal therapy in men appears to be less common due to low treatment adherence and an increased frequency of side effects [28,30,32,33].

Adjuvant radiotherapy has been show to decrease local recurrence in large tumours with lymph node and muscle involvement [16]. This involvement is more frequent in men, subsequent to the small breast size and the proximity of the tumour to these structures [29]. In our study, 36.8% of patients received radiotherapy, and it was not associated with an adequate response to the first-course cancer treatment. Other studies have shown similar frequency of radiotherapy in male patients with breast cancer with no impact on overall survival [29].

A number of limitations must be considered to interpret our findings. First of all, studies based on population registries should be less susceptible to selection bias than hospital-based studies. The data used in this study come from 239 cancer hospitals, located in 25 states of Brazil, and were collected over 10 years. This may have caused a loss of quality of information and constraints on adherence to the protocols of the Brazilian Hospital Cancer Registry platforms. Over the years, INCA has promoted trainings of cancer registrars and has published several manuals in order to reduce these biases. Conversely, this is the first study in the country to consider such a large number of MBC cases. In addition, in this series, it was not possible to assess Oestrogen Receptor, Progesterone Receptor and Human Epidermal Growth Factor Receptor 2 expression. However, our findings may have implications for cancer control programs. Although treatment response is associated with earlier detection and the recommendation of more appropriate therapy, these two factors alone do not account for the entire prognosis of men with breast cancer. The quality and promptness of the services provided are critical to patients' recovery.

In conclusion, MBC diagnosis is often made at advanced stages. Consequently, patients were submitted to more aggressive treatments, with poorer clinical responses.

Declaration of interest

The authors declare that they have no conflict of interest.

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