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BREAST CANCER SURVIVAL IN A BRAZILIAN CANCER CENTER: A COHORT STUDY OF 5,095 PATIENTS

Sobrevida do câncer de mama em um centro de câncer brasileiro: um estudo de coorte de 5.095 pacientes

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ABSTRACT

Objectives: To describe the age group, clinical stage at diagnosis, treatment, and survival rates of breast cancer patients treated in a Brazilian specialized Cancer Center. **Method:** A hospital-based retrospective cohort study is presented herein, on women with breast cancer diagnosed between January 1, 2000 and December 31, 2012. Data were extracted from the Hospital Cancer Registry of the A.C.Camargo Cancer Center. Data on age group, histology of the tumor, TNM classification, clinical stage and treatments were described in absolute and relative frequencies for three periods. Survival curves were estimated with the Kaplan-Meier estimator. Hazard ratio (HR) and 95% confidence interval (95%CI) were calculated for all variables. **Results:** A total of 5,095 female breast cancer patients were identified, with most stages classified as I and II (60%). The overall survival was 82.7% for the period of 2000–2004, and 89.9% for 2010–2012 (p<0.001). Patients with invasive ductal carcinoma, who were treated with surgery and hormonal therapy, showed a reduction in the risk of death in the most recent period HR_{adj}=0.42 (95%CI 0.34–0.53) (2010–2012). **Conclusions:** Early stage diagnosis and combined treatment (including HT) are predictive prognostic factors for high survival rates in patients with invasive breast cancer. Specialized cancer centers can provide valuable indications regarding cancer control policies, evaluating overall survival for breast cancer and its associated prognosis.

KEYWORDS: breast cancer; survival; cancer staging; cancer hospital; Brazil; South America.

RESUMO

Objetivos: Descrever as faixas etárias, estadiamento clínico ao diagnóstico, tratamento e sobrevida global das pacientes com câncer de mama tratadas em um centro de câncer brasileiro. **Método:** Estudo de uma coorte retrospectiva de base hospitalar, com mulheres diagnosticadas de câncer de mama entre 1º de janeiro de 2000 e 31 de dezembro de 2012. Os dados foram extraídos do Registro Hospitalar de Câncer do A. C. Camargo Cancer Center. Faixa etária, tipo histológico, classificação TNM, estadiamento clínico e tratamento foram descritos em frequência absoluta e relativa estratificados em três períodos. As curvas de sobrevida global foram estimadas pelo método de Kaplan-Meier. A *Hazard ratio* (HR) com intervalo de confiança de 95% foram calculados para todas as variáveis. **Resultados:** O total de 5.095 pacientes mulheres com câncer de mama foi identificado, a maioria era estágio inicial 60% (I e II). A sobrevida global foi de 82,7% para o período de 2000–2004 e 89,9% para 2010–2012 (p<0,001). Pacientes com carcinoma ductal invasivo que foram tratadas com cirurgia e hormonioterapia, mostraram redução do risco de morte no período mais recente HRaj=0,42 (0,34–0,53 em 2010–2012). **Conclusões:** Diagnóstico precoce e tratamento combinado (incluindo hormonioterapia) são fatores prognósticos preditivos para altas taxas de sobrevida em pacientes com câncer de mama invasivo. Centros especializados em câncer podem prover informações valiosas sobre as políticas de controle do câncer, avaliando a sobrevida global do câncer de mama e fatores associados ao prognóstico.

PALAVRAS-CHAVE: câncer de mama; sobrevida; estadiamento de neoplasias; institutos de câncer; Brasil; América do Sul.

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INTRODUCTION

Breast cancer is the most common cancer diagnosed in women. It is estimated that 1.67 million new cases were diagnosed worldwide in 2012. The highest breast cancer incidence rates were reported in North America, Australia, New Zealand, Europe, and Japan. Conversely, the lowest rates for breast cancer were found in Africa, Eastern Asia, and Latin America. In 2012, 52,000 deaths were attributed to breast cancer, making it the fifth most frequent cancer-related cause of death worldwide[1]. In Latin America, the incidence of breast cancer ranges from 25 to 78 per 100,000 women[2], and the highest Latin American mortality rates were observed in Argentina between 2000 and 2012[3].

In Brazil, breast cancer is the most common type of cancer in women and it is estimated that there will be 59,700 new cases in 2018, with an associated mortality rate of 14%[4]. Breast cancer mortality rates have remained stable in Brazil between 2000 and 2015[5,6], and the highest incidence rates are located in São Paulo (Southeast Brazil)[2].

Screening mammography and adjuvant therapy (treatment) contributed almost equally to the reduction in breast cancer mortality[7]. A recent study by Plevritis et al.[8] predicted that breast cancer mortality in the USA trends for women in the age group of 30–79 years, and revealed that advances in treatment, compared with screening advances, were associated with more pronounced reductions in overall breast cancer mortality between 2000 and 2012. Moreover, early staging (ES) and multidisciplinary treatment have been identified as predictive factors for better survival in invasive breast cancer patients[9-13].

Breast cancer survival has continued to increase in most countries worldwide. When considering population-based survival rates in North America and Oceania, in the period of 2010–2014, the 5-year survival rate was approximately 90%, whereas in Brazil it was 75% for the same time period[14]. However, Brazilian results were based on seven regional population-based cancer registries, and therefore the results for breast cancer survival in Brazil could have underestimated the actual survival rates.

Hospital Cancer Registries (HCR) are administrative databases at specialized cancer centers that evaluate sociodemographics, clinical staging at diagnosis, and overall and cancer-specific survival. A study conducted by the Oncocenter Foundation (FOSP), a foundation that aggregates all HCR data from the state of Sao Paulo (Southeast Brazil), analyzed the survival probabilities of 27,023 breast cancer cases from 2000 to 2005. Approximately 15.6% patients were stage IIb with 82% 5-year survival; 27% were stage III with 60% 5-year survival, and 8.5% patients were IV (metastatic disease) with 30% 5-year survival. The results reported by FOSP[15] and Tiezzi[16] reinforce that early stage at diagnosis is a strong predictor of screening actions, for the improvement of survival rates and verification of the cancer control policies' effects on the population.

The A. C. Camargo Cancer Center is a specialized cancer center with 65 years of experience in cancer care. There are few studies evaluating survival rates and clinical staging in patients with invasive breast cancer, who were treated in specialized cancer centers in Brazil or South America. Survival studies published with cancer center data could provide valuable information regarding early stage at diagnosis, treatments and survival probability of patients with invasive breast cancer. Moreover, these studies could evaluate cancer control policies based on the profile of the patients treated at these specialized cancer centers.

The objective of this study was to describe the age group, stage at diagnosis, prognostic factors, treatments performed, and overall survival of patients with breast cancer treated at the A.C.Camargo Cancer Center throughout a 13-year period (2000–2012).

METHOD

A retrospective cohort study is presented herein, encompassing women with breast cancer admitted from January 1, 2000 to December 31, 2012. The cases were extracted from the HCR at the A. C. Camargo Cancer Center.

Breast cancer characteristics were analyzed according to diagnosis data and classified into three periods: 2000–2004, 2005–2009, and 2010–2012. The variables analyzed were age group (<50 years, 50–59 years, 60–69 years, and ≥70 years), histology (ICD-O-3), Tumor, Node, Metastasis (TNM) classification, and clinical staging. Treatments were grouped into surgery, chemotherapy, radiotherapy or any treatment combination without hormonal therapy (all NoHT); surgery/chemotherapy/radiotherapy with hormonal therapy (all with HT); and only surgery and hormonal therapy (SUR+HT).

Ethical approval

This study complies with Brazil law, has received ethical approval by the Fundação Antonio Prudente — A. C. Camargo Cancer Center, reference number 2462/17. For this type of study, formal consent is not required.

Statistical analyses

Data on age group, TNM characteristics, clinical staging and treatments were described in absolute and relative frequencies for the three periods studied herein. The 5-year and 10-year overall survival rates included cases of invasive ductal carcinoma that were diagnosed between January 1, 2000 and December 31, 2012. These survival rates were calculated considering the dates of diagnosis and death or latest patient information contained in medical records. For 10-year overall survival rates, all ductal invasive cases were included between 2000 and 2006, with all patients monitored until December 31, 2017.

Five-year survival analyses were applied to the following variables: age group, tumor size (T), number of lymph nodes (N), metastasis (M), clinical stage (CS), and treatment groups. Ten-year survival analysis was carried out to verify interaction between clinical stages and treatment.

Survival curves were estimated with the Kaplan-Meier estimator, also known as the product limit estimator. The log-rank test was applied to compare the survival curves regarding each variable as well as the curves for the periods 2000–2004, 2005–2009, 2000–2004 and 2010–2012. The Cox semiparametric proportional hazards model was used to describe the differences between ductal and lobular invasive carcinoma according to age, TNM, clinical stage, treatment and period. Hazard ratio (HR) and 95% confidence interval (95%CI) were calculated for all variables. The assumption of proportional hazards was based on the Schoenfeld residuals. The significance level of the tests was fixed at 0.05. All statistical analyses were carried out with the Statistical Package for Social Science (SPSS) version 23 (IBM Corp., Armonk, NY, USA) and R software version 3.5 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Of all, 5,095 females with breast cancer were treated the A. C. Camargo Center between 2000 and 2012. Most of the patients were over the age of 50 (60%; n=3,056). The most common histology was invasive ductal carcinoma (67%). The frequency of T1 cases was 31.6% for 2000–2004 *versus* 39.4% for 2010–2012. Regarding staging, 64–70% of cases were N0, with approximately 5% of cases presenting metastatic disease at diagnosis. Non-Invasive breast cancer (CS0) ranged between 15 and 18%; stage I/II accounted for 60% of the cases treated in the period. The most frequent treatment was "all with HT" (56%) (Table 1).

Five-year overall survival rates increased significantly in the three time periods regarding age, TNM classification, clinical stage and treatment. Higher rates were obtained for the most recent period, 2010–2012. The survival rate associated with tumor size ranged from 89.7% (2000–2004) to 95% (2010–2012), for T1/T2 tumors. The most pronounced increase in survival rates was associated with T3/T4 tumors, with a survival probability of 59.5% for 2000–2004 and 76.2% for 2010–2012. Regarding regional disease (N2/N3), a significant increase in survival probability (from 56.4 to 76.0%) was observed in 2010–2012. Clinical stage III and IV patients also presented increased survival, from 69% for 2000–2004 to 86.2% for 2010–2012, and from 20.7% (2000–2004) to 40.8% (2010–2012), respectively. Combined treatments (SUR, RXT, CHR) with HT were applied to most patients, increasing 5-year survival in all periods, from 88.1% (2000–2004) to 93.6% (2010–2012) (Table 2).

Ten-year overall survival increased for all time periods but it was higher in the 2010–2012 one (Figure 1A). Patients with combined treatment associated with hormonal therapy presented higher 10-year overall survival rates, independently of their clinical stage (Figures 1B and 1C).

When analyzing the prognostic factors for all invasive breast cancer cases, the adjusted model showed an increase for risk regarding age, clinical stage and histological type. A reduction in risk was observed for treatment type and period of diagnosis (supplementary Table 1). Based on these initial overall results, the prognostic factors were stratified by histological group into ductal and lobular invasive. Increased risk was obtained for both histological groups for age and clinical stage, and a reduction in risk was obtained for the combined treatment with hormonal therapy (all with HT and SUR+HT) (Table 3).

DISCUSSION

At the A.C.Camargo Cancer Center, in the 2000–2012 period, 5-year survival rates for ductal carcinoma breast cancer were approximately 90%, 60% of patients were post-menopausal women (>50 years old), 40% of patients were classified as T1 and 64.3% as N0. Clinical stage I/II accounted for 60.8% of the cases identified in the 2010–2012 period. Throughout the 13-year study period, the 5-year overall survival rates increased for all three time periods studied herein, from 82.7 to 89.9%. The independent prognostic factors were treatment combination including hormonal therapy, clinical stage, age, histology and period.

The profile of this cancer center reflects early diagnoses with efficient treatment in an older population. This means that the policies adopted by the Brazilian government could have influenced to improve early staging at diagnosis and better treatment outcome, hence improving survival rates. Approximately 75% of health coverage in Brazil is public (the remainder is associated with private health plans), and breast cancer has been recognized as a health priority[17]. Data related to early diagnosis in the publicly-funded Brazilian healthcare system highlighted striking regional inequalities in access to early detection and surgery, with the lowest access rates in the North Region and the highest in the South Region[18]. In the study herein presented, the cancer center treated public and private patients indistinctively, and it was not possible to classify patients regarding type of coverage.

Aging is one of the main risk factors for breast cancer. The demographic changes experienced by Latin America were expected to cause epidemiological shifts and increase breast cancer incidence[10]. At the A. C. Camargo Cancer Center, 60% of patients were older than 50 at the time of diagnosis. This is the age profile for breast cancer incidence in Latin America[1], where older women are biologically having more favorable tumors[19] and therefore better survival prognosis. In a study conducted in the South of Brazil, Schneider and d'Orsi[20] reported that older patients presented higher survival rates then young women.

Table 1. Characteristics of 5,095 female breast cancer patients treated at the A. C. Camargo Cancer Center between 2000 and 2012.

Variables	Diagnosis Period			
	2000–2004 (n=1,499) N (%)	2005–2009 (n=1,853) N (%)	2010–2012 (n=1,743) N (%)	Total (n=5,095) N
Age group (years)				
<50	624 (41.6)	750 (40.5)	665 (38.2)	2,039 (40.0)
50–59	365 (24.3)	504 (27.2)	513 (29.4)	1,382 (27.1)
60–69	273 (18.2)	331 (17.8)	339 (19.4)	943 (18.5)
≥70	237 (15.8)	268 (14.5)	226 (13.0)	731 (14.3)
Histology				
In situ (non-invasive)	229 (15.3)	338 (18.2)	283 (16.2)	850 (16.7)
Invasive ductal	1,078 (71.9)	1,207 (65.1)	1,147 (65.8)	3,432 (67.4)
Invasive lobular	77 (5.1)	160 (8.6)	175 (10.0)	412 (8.1)
Other histological types	115 (7.7)	148 (8.0)	138 (7.9)	401 (7.9)
Tumor size (T)				
Is	229 (15.3)	338 (18.2)	283 (16.2)	850 (16.7)
1	473 (31.6)	672 (36.3)	687 (39.4)	1,832 (36.0)
2	446 (29.8)	507 (27.4)	453 (26.0)	1,406 (27.6)
3	59 (3.9)	71 (3.8)	114 (6.5)	244 (4.8)
4	224 (14.9)	210 (11.3)	166 (9.5)	600 (11.8)
No data available	68 (4.5)	55 (3.0)	40 (2.3)	163 (3.2)
No. lymph nodes (N)				
0	966 (64.4)	1,300 (70.2)	1,120 (64.3)	3,386 (66.5)
1	302 (20.2)	304 (16.4)	417 (23.9)	1,023 (20.1)
2	158 (10.6)	147 (7.9)	111 (6.4)	416 (8.2)
3	14 (0.9)	46 (2.5)	57 (3.3)	117 (2.3)
No data available	59 (3.9)	56 (3.0)	38 (2.2)	153 (3.0)
Metastasis (M)				
0	1,424 (95.0)	1,761 (95.0)	1,641 (94.1)	4,826 (94.7)
1	75 (5.0)	92 (5.0)	102 (5.9)	269 (5.3)
Clinical Stage				
0	229 (15.3)	338 (18.2)	283 (16.2)	850 (16.7)
I	412 (27.5)	569 (30.7)	548 (31.4)	1,529 (30.0)
II	472 (31.5)	556 (30.0)	513 (29.4)	1,541 (30.2)
III	262 (17.5)	262 (14.1)	285 (16.4)	809 (15.9)
IV	75 (5.0)	92 (5.0)	102 (5.9)	269 (5.3)
No data available	49 (3.2)	36 (1.9)	12 (0.7)	97 (1.9)
Treatment				
All No HT	470 (31.4)	553 (30.3)	543 (31.3)	1,566 (30.8)
All with HT	857 (57.2)	1,013 (55.4)	966 (55.7)	2,836 (56.1)
SUR+HT	172 (11.5)	262 (14.3)	224 (12.9)	658 (13.1)

HT: hormonal therapy; SUR: surgery.
Source: Hospital Cancer Registry, 2017.

However, Guerra et al.[21] did not find differences in survival rates regarding different age groups in Southeastern Brazil (Juiz de Fora, Minas Gerais).

Ductal invasive carcinoma was responsible for 72–67% of the cases identified; other Brazilian studies have reported that ductal invasive carcinoma rates were 81.7% in Curitiba[22] and 63.9% in Santa Maria[23]. Invasive lobular carcinoma was observed in 14% of the patients over the age of 70, which is higher than the observed in Curitiba (4%)[22].

Herein, 60.8% of cases were diagnosed at early clinical stages (CS I/II), similarly to Florianopolis (64.3%)[20] and Santa Maria (77.4%)[23], and higher than those reported for other cancer institutions in Curitiba (47.4%)[22] and Rio de Janeiro (48.3%)[13]. This difference could be related to the profile of these institutions, as those in Curitiba and Rio de Janeiro treat more patients from the public healthcare system. Regarding clinical staging in Minas Gerais (1998–2000), 74% of early diagnosis were associated with private patients, while this percentage was 63% for public patients[6].

The frequency of clinical stage III/ IV was 19–22% for the time period studied herein (2000–2012), which was lower than the reports of other Brazilian cancer centers (30–44%)[13,20,21]. The A. C. Camargo Cancer Center has diagnosed a high proportion of women with early stage breast cancer, and this profile can be a result of government policies directed to mammography

Table 2. Five-year overall survival (OS) for patients with invasive breast ductal carcinoma at the A. C. Camargo Cancer Center between 2000 and 2012 (n=3,432) according to age, tumor size (T), number of lymph nodes (N), metastasis (M), clinical stage, and treatment by period.

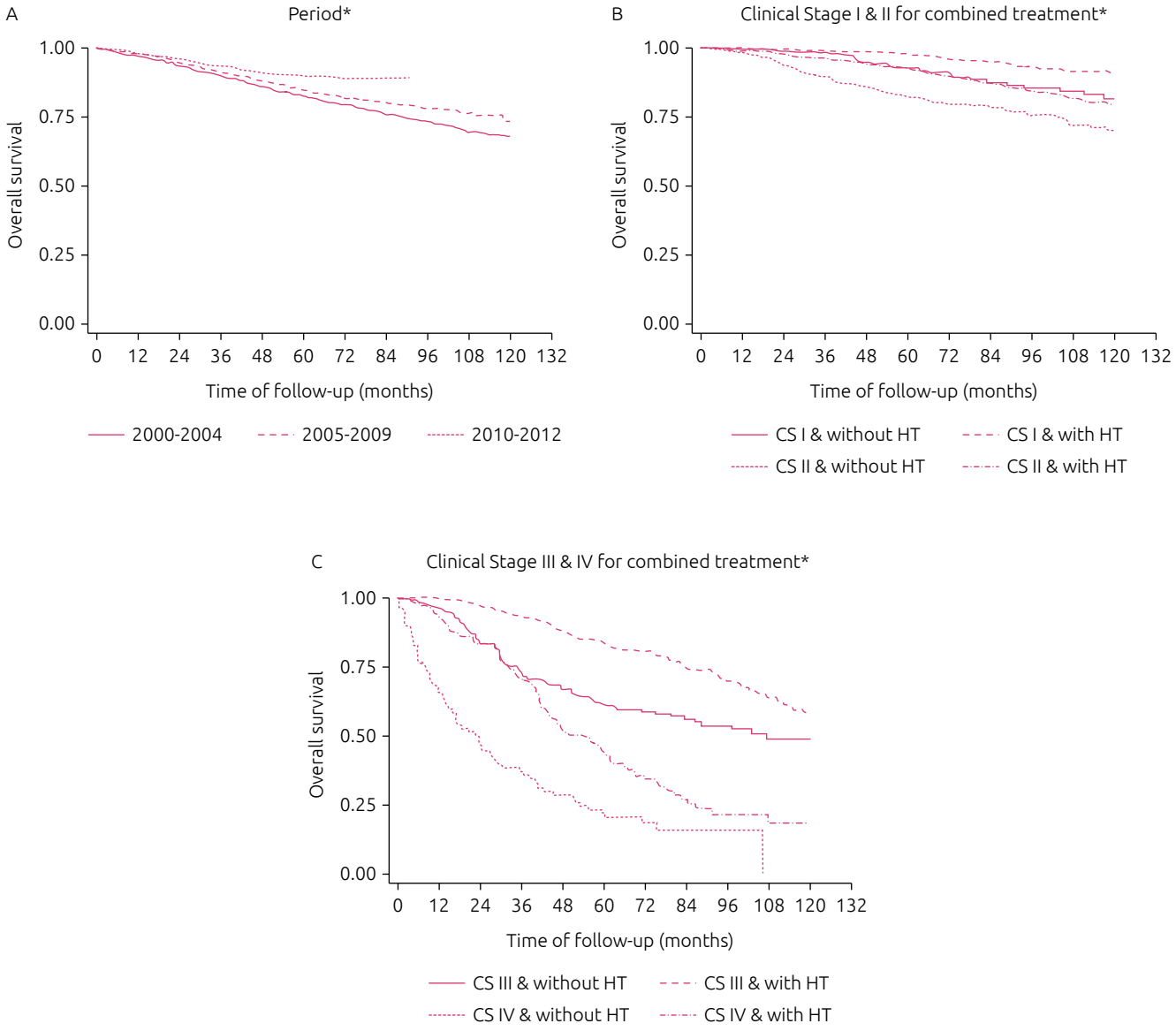
Variables	2000–2004		2005–2009		2010–2012	
	Cases (Events)	5-year OS¶	Cases (Events)	5-year OS¶	Cases (Events)	5-year OS¶
General	1,078 (187)	82.7	1,207 (181)	84.9	1,147 (108)	89.9
Age group (years)						
<50	445 (65)	85.4	505 (62)	87.6	460 (38)	91.3
50–59	263 (36)	86.3	329 (36)	89.0	335 (28)	91.1
60–69	206 (45)	78.2	219 (32)	85.3	201 (18)	90.1
>70	164 (41)	75.0	154 (51)	65.8	151 (24)	82.2
T						
T1/T2	783 (81)	89.7	949 (82)	91.3	896 (42)	95.0
T3/T4	242 (98)	59.5	224 (84)	62.3	224 (50)	76.2
N						
N0	605 (59)	90.2	768 (61)	92.0	646 (25)	95.8
N1	278 (56)	79.9	253 (44)	82.3	339 (37)	88.2
N2/N3	149 (65)	56.4	152 (60)	60.2	137 (31)	76.0
M						
M0	1,020 (141)	86.2	1,138 (135)	88.0	1,069 (64)	93.5
M1	58 (46)	20.7	69 (46)	33.3	78 (44)	40.8
Clinical Stage						
I	335 (13)	96.1	456 (19)	95.8	420 (5)	98.7
II	416 (55)	86.8	446 (50)	88.7	415 (26)	93.3
III	229 (71)	69.0	215 (60)	71.8	225 (29)	86.2
IV	58 (46)	20.7	69 (46)	33.3	78 (44)	40.8
Treatment						
All NoHT	328 (93)	71.6	333 (91)	72.3	351 (61)	80.2
All with HT	670 (80)	88.1	742 (70)	90.5	697 (43)	93.6
SUR + HT	75 (12)	84.0	117 (9)	92.2	93 (1)	98.9

HT: hormonal therapy; SUR: surgery; p<0.05.

screening[8]. However, it is limited and has heterogeneous coverage throughout Brazil[16,24].

At the A. C. Camargo Cancer Center, the 5-year overall survival rates for breast invasive ductal carcinoma stage I were 96.1% for the 2000–2004 period, increasing to 98.7% for 2010–2012. The highest increase in survival rates occurred for stage IV breast cancer, which doubled from 20.7 to 40.8% in the period of 2010–2012. Such improvement in the most recent period could be due to changes in therapeutic procedures, such as the inclusion of new, targeted therapies[8]. The Brazilian Study Group on Breast Cancer (better known by its acronym in Portuguese, GBECAM) reported that women treated in public institutions presented more advanced staging at diagnosis, difficulties in accessing modern therapies, and worse overall survival than patients treated at private institutions[25]. Factors such as delays in diagnosis, due to low levels of awareness regarding cancer, slow implementation of mammography screening, limited quality of surgery treatment and restricted access to radiotherapy and modern systemic therapies could be responsible for disparities in the survival rates for breast cancer[26].

Treatment with HT was the best prognosis indicator for breast cancer survival and early clinical stage at the A. C. Camargo



*p<0.001

Figure 1. Overall 10-year survival rates for patients with invasive breast ductal adenocarcinoma by period (A) and treatment versus clinical stage (B, C) at the A. C. Camargo Cancer Center, 2000–2012.

Cancer Center. In developed countries, widespread population screening and treatment improvements are factors that have influenced reductions in breast cancer mortality[27]. In Brazil, screening for breast cancer has been recommended but has not been fully organized or implemented throughout the country[28]. However, breast cancer mortality rates have remained stable across all Brazilian regions[5,6].

Data regarding hormonal receptors (*e.g.*, estrogen and progesterone), human epidermal growth factor receptor 2 (HER2) and other factors such as histological grade were not analyzed in this work and could limit its conclusions.

An important aspect of this study is the encompassment of a cohort of more than 5,000 women, who were treated for breast cancer at a single institution. In addition, prognostic factors, such as 10- and 5-year overall survival data, were examined throughout a 13-year period, with follow-up losses under 6.5%. This study contributes with a further comprehension of the epidemiological profile of breast cancer cases treated within specialized cancer centers. Herein, it was observed that the A. C. Camargo Cancer Center presented better overall survival rates for older women and for advanced stages of invasive breast cancer over 13-year period. Nevertheless, the combination of treatment including

Table 3. Prognostic factors associated with invasive breast cancer according to histological type data from the Hospital Cancer Registry, 2017, of the A. C. Camargo Cancer Center, 2000–2012.

Characteristics	Ductal		Lobular	
	HR unadjusted	HR adjusted	HR unadjusted	HR adjusted
Age group (years)				
<50	1	1	1	1
50–59	0.90 (0.73–1.11)	1.10 (0.89–1.36)	2.12 (1.17–3.85)*	2.03 (1.09–3.79)*
60–69	1.35 (1.10–1.67)*	1.49 (1.20–1.86)**	1.46 (0.73–2.90)	1.65 (0.80–3.42)
≥70	2.71 (2.23–3.29)**	2.66 (2.16–3.26)**	3.41 (1.86–6.23)**	3.65 (1.91–6.98)**
Tumor size (T)				
T1	1		1	
T2	2.68 (2.14–3.36)**		1.39 (0.78–2.50)	
T3	3.72 (2.64–5.22)**		2.94 (1.46–5.92)*	
T4	9.13 (7.31–11.40)**		5.90 (3.33–10.47)**	
Lymph node (N)				
N0	1		1	
N+	2.97 (2.53–3.48)**		2.65 (1.70–4.16)**	
Clinical Stage				
I	1	1	1	1
II	2.56 (1.98–3.30)**	2.40 (1.86–3.10)**	1.20 (0.62–2.32)	1.22 (0.63–2.39)
III	5.87 (4.56–7.56)**	5.71 (4.41–7.39)**	4.38 (2.39–8.02)**	4.04 (2.17–7.53)**
IV	24.47 (18.70–32.00)**	24.72 (18.76–32.58)**	15.40 (8.11–29.23)**	15.93 (7.98–31.80)**
Treatment				
All No HT	1	1	1	1
All with HT	0.44 (0.38–0.52)**	0.44 (0.37–0.51)**	0.39 (0.24–0.62)**	0.48 (0.29–0.80)*
SUR + HT	0.42 (0.30–0.58)**	0.60 (0.42–0.85)*	0.17 (0.07–0.42)**	0.32 (0.13–0.80)*
Period				
2000–2004	1	1	1	1
2005–2009	0.79 (0.67–0.94)*	0.81 (0.68–0.96)*	0.94 (0.57–1.55)	1.16 (0.67–1.98)
2010–2012	0.50 (0.40–0.62)**	0.42 (0.34–0.53)**	0.70 (0.38–1.31)	0.57 (0.29–1.13)

HR: hazard ratio; HT: hormonal therapy; SUR: surgery; *p<0.05; **p<0.001.

hormonal therapy was the best predictive prognostic factor for survival in patients with invasive ductal breast cancer.

AUTHORS' CONTRIBUTION

Makdissi FB reviewed manuscript. Leite FPM wrote the manuscript. Peres SV analyzed the data, interpreted the results and wrote the manuscript. Silva DRM interpreted the results and wrote the manuscript. Oliveira MM reviewed the manuscript. Lopez RVM analyzed and discussed the data. Sanches SM reviewed the manuscript. Gondim GR reviewed the manuscript. Iyeyasu H discussed and reviewed the manuscript. Calsavara VF analyzed data and interpreted the results. Curado MP designed and supervised the research, interpreted and discussed the data. All authors approved the final version of the manuscript to be published.

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-86. http://doi.org/10.1002/ijc.29210
2. Forman D, Bray F, Brewster DH, Mbalawa CG, Kohler B, Piñeros M et al., eds. Cancer Incidence in Five Continents. Lyon: International Agency for Research on Cancer; 2014;10(164).
3. World Health Organization. WHO Databank. Health statistics and information systems [Internet]. Geneva, Switzerland: World Health Organization; 2018 [cited on Apr 30, 2018]. Available at: https://www.who.int/healthinfo/mortality_data/en/
4. Brasil. Ministério da Saúde. Instituto Nacional do Câncer José Alencar Gomes da Silva. Estimativa 2018 [Internet]. Brazil: Ministério da Saúde; 2018 [cited on Apr 24, 2018]. Available at: http://www1.inca.gov.br/estimativa/2018/
5. Kluthcovsky AC, Faria TN, Carneiro FH, Strona R. Female breast cancer mortality in Brazil and its regions. Rev Assoc Med Bras. 2014;60(4):387-393. http://dx.doi.org/10.1590/1806-9282.60.04.019
6. Guerra MR, Bustamante-Teixeira MT, Corrêa CSL, Abreu DMX, Curado MP, Mooney M, et al. Magnitude and variation of the burden of cancer mortality in Brazil and Federation Units, 1990 and 2015. Rev Bras Epidemiol. 2017;20(Suppl. 1):102-15. http://dx.doi.org/10.1590/1980-5497201700050009
7. Berry DA, Cronin KA, Plevritis SK, Fryback DG, Clarke L, Zelen M, et al. Cancer Intervention and Surveillance Modeling Network (CISNET) Collaborators. Effect of screening and adjuvant therapy on mortality from breast cancer. N Engl J Med. 2005;353(17):1784-92. https://doi.org/10.1056/NEJMoa050518
8. Plevritis SK, Munoz D, Kurian AW, Stout NK, Alagoz O, Near AM, et al. Association of Screening and Treatment with Breast Cancer Mortality by Molecular Subtype in US Women, 2000-2012. JAMA. 2018;319(2):154-64. https://doi.org/10.1001/jama.2017.19130
9. Torre LA, Islami F, Siegel RL, Ward EM, Jemal A. Global Cancer in Women: Burden and Trends. Cancer Epidemiol Biomarkers Prev. 2017;26(4):444-57. https://doi.org/10.1158/1055-9965.EPI-16-0858
10. Justo N, Wilking N, Jönsson B, Luciani S, Cazap E. A review of breast cancer care and outcomes in Latin America. Oncologist. 2013;18(3):248-56. https://doi.org/10.1634/theoncologist.2012-0373
11. Fayer VA, Guerra MR, Cintra JRD, Bustamante-Teixeira MT. Ten-year survival and prognostic factors for breast cancer in the southeast region of Brazil. Rev Bras Epidemiol. 2016;19(4):766-78. https://doi.org/10.1590/1980-5497201600040007
12. Goss PE, Lee BL, Badovinac-Crnjevic T, Strasser-Weippl K, Chavarri-Guerra Y, St Louis J, et al. Planning cancer control in Latin America and the Caribbean. Lancet Oncol. 2013;14(5):391-436. https://doi.org/10.1016/S1470-2045(13)70048-2
13. Brito C, Portela MC, Vasconcellos MT. Survival of breast cancer women in the state of Rio de Janeiro, Southeastern Brazil. Rev Saúde Pública. 2009;43(3):481-9. http://dx.doi.org/10.1590/S0034-89102009000300012
14. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Niksic M, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet. 2018;391(10125):1023-75. https://doi.org/10.1016/S0140-6736(17)33326-3
15. São Paulo. Secretaria de Estado da Saúde de São Paulo. Fundação Oncocentro de São Paulo. Banco de dados RHC [Internet]. São Paulo: Fundação Oncocentro de São Paulo; 2018 [cited on Apr 20, 2018]. Available at: http://200.144.1.68/cgi-bin/dh?rhc/rhc-geral.def
16. Tiezzi DG. Breast cancer screening in Brazil: there is still time to rethink. Rev Bras Ginecol Obstet. 2013;35(9):385-7. http://dx.doi.org/10.1590/S0100-72032013000900001
17. Nigenda G, Gonzalez-Robledo MC, Gonzalez-Robledo LM, Bejarano-Arias RM. Breast cancer policy in Latin America: account of achievements and challenges in five countries. Global Health. 2016;12(1):39. http://dx.doi.org/10.1186/s12992-016-0177-5
18. Azevedo e Silva G, Bustamante-Teixeira MT, Aquino EM, Tomazelli JG, Dos-Santos-Silva I. Access to early breast cancer diagnosis in the Brazilian Unified National Health System: an analysis of data from the Health Information System. Cad Saúde Pública. 2014;30(7):1537-50. http://dx.doi.org/10.1590/0102-311X00156513
19. Gennari R, Curigliano G, Rotmensz N, Robertson C, Colleoni M, Zurrida S, et al. Breast carcinoma in elderly women: features of disease presentation, choice of local and systemic treatments compared with younger postmenopausal patients. Cancer. 2004;101(6):1302-10. https://doi.org/10.1002/cncr.20535

20. Schneider IJC, d'Orsi E. Sobrevida em cinco anos e fatores prognósticos em mulheres com câncer de mama em Santa Catarina, Brasil. Cad Saúde Pública. 2009;25(6):1285-96. http://dx.doi.org/10.1590/S0102-311X2009000600011

21. Guerra MR, Mendonça GA, Bustamante-Teixeira MT, Cintra JR, Carvalho LM, Magalhães LM. Five-year survival and prognostic factors in a cohort of breast cancer patients treated in Juiz de Fora, Minas Gerais State, Brazil). Cad Saúde Pública. 2009;25(11):2455-66. http://dx.doi.org/10.1590/S0102-311X2009001100015

22. Medeiros JMD, Linhares JC, Hatschbach SBB, Hubie DP, Rahman SA, Orlandi D, et al. Perfil epidemiológico e estudo de sobrevida dos pacientes com câncer de mama atendidos no Hospital Erasto Gaertner em Curitiba, PR. Rev Bras Mastologia. 2016;26(3):107-12. http://dx.doi.org/10.5327/Z2016000300005RBM

23. de Moraes AB, Zanini RR, Turchiello MS, Riboldi J, de Medeiros LR. Survival study of breast cancer patients treated at the hospital of the Federal University in Santa Maria, Rio Grande do Sul, Brazil. Cad Saúde Pública. 2006;22(10):2219-28. http://dx.doi.org/10.1590/S0102-311X2006001000028

24 Freitas-Junior R, Rodrigues DC, Corrêa RD, Peixoto JE, de Oliveira HV, Rahal RM. Contribution of the Unified Health Care System to mammography screening in Brazil, 2013. Radiol Bras. 2016;49(5):305-10. http://dx.doi.org/10.1590/0100-3984.2014.0129

25. Simon SD, Bines J, Barrios CH, Nunes J, Gomes E, Pacheco F, et al. Clinical characteristics and outcome of treatment of Brazilian women with breast cancer treated at public and private institutions—the AMAZONE project of the Brazilian breast cancer study group (GBECAM). San Antonio Breast Cancer Symposium 2009; San Antonio, TX, USA; Dec 11, 2009. Abstr 3082. http://dx.doi.org/10.1158/0008-5472.SABCS-09-3082

26. Lee BL, Liedke PE, Barrios CH, Simon SD, Finkelstein DM, Goss PE. Breast cancer in Brazil: present status and future goals. Lancet Oncol. 2012;13(3):e95-e102. http://dx.doi.org/10.1016/S1470-2045(11)70323-0

27. Autier P, Boniol M, Gavin A, Vatten LJ. Breast cancer mortality in neighbouring European countries with different levels of screening but similar access to treatment: trend analysis of WHO mortality database. BMJ. 2011;343:d4411. http://dx.doi.org/10.1136/bmj.d4411

28. Migowski A, Silva GA, Dias MBK, Diz MPE, Sant'Ana DR, Nadanovsky P. Guidelines for early detection of breast cancer in Brazil. II - New national recommendations, main evidence, and controversies. Cad Saúde Pública. 2018;34(6):e00074817. https://dx.doi.org/10.1590/0102-311x00074817

Supplementary Table 1. Prognostic factors associated with invasive breast cancer survival Hospital Cancer Registry (HCR), A. C. Camargo Cancer Center, 2000–2012.

Characteristics	HR unadjusted	HR adjusted
Age group (years)		
<50	1	1
50–59	0.99 (0.82–1.21)	1.18 (0.97–1.44)
60–69	1.36 (1.11–1.66)*	1.50 (1.22–1.85)**
≥70	2.77 (2.30–3.32)**	2.74 (2.26–3.33)**
Tumor size (T)		
T1	1	
T2	2.47 (2.00–3.04)**	
T3	3.66 (2.70–4.97)**	
T4	8.55 (6.96–10.50)**	
Lymph node (N)		
N0	1	
N+	2.93 (2.52–3.40)**	
Clinical stage		
I	1	1
II	2.33 (1.84–2.95)**	2.21 (1.74–2.80)**
III	5.59 (4.43–7.05)**	5.47 (4.32–6.94)**
IV	22.95 (17.92–29.38)**	23.39 (18.13–30.17)**
Histology		
Ductal	1	1
Lobular	1.19 (0.95–1.49)	1.36 (1.08–1.71)*
Treatment		
All No HT	1	1
All with HT	0.45 (0.39–0.52)**	0.44 (0.38–0.51)**
SUR + HT	0.38 (0.28–0.52)**	0.54 (0.39–0.75)**
Period		
2000–2004	1	1
2005–2009	0.81 (0.69–0.95)*	0.82 (0.70–0.97)*
2010–2012	0.52 (0.43–0.64)**	0.43 (0.35–0.54)**

HR: hazard ratio; HT: hormonal therapy; SUR: surgery; *p<0.05; **p<0.001.