Research Article

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Outcomes of Breast Cancer in Brazil Related to Health Care Coverage: A Retrospective Cohort Study

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Abstract

Background: Breast cancer is the most common malignancy in women in Brazil. Differences between patients with public versus private healthcare coverage about general characteristics, disease presentation, treatment of primary tumors, and clinical outcomes have not been fully investigated.

Methods: A national, retrospective cohort of 3,142 patients drawn from a representative sample of Brazilian medical centers was selected. Clinical and demographic data and type of healthcare coverage were retrieved by chart review. Groups were compared using the χ^2 test. The log-rank test was used for comparison of disease-free survival (DFS), postrelapse, and overall survival (OS). Multivariate Cox regression modeling with adjustment for patient characteristics and stage at diagnosis was performed. All P values are two sided.

Results: Patients with public health coverage presented with more advanced disease at diagnosis ($P < 0.001$). DFS and OS for patients presenting with stage 0–II disease did not differ according to the type of healthcare coverage, whereas a significant difference in outcomes was seen for stage III–IV patients ($P = 0.002$ and $P = 0.008$, respectively). In a Cox multivariate analysis, no association was found for the type of health coverage with either DFS or OS, but there was an association for postrelapse survival ($P < 0.001$).

Conclusion: In Brazil, patients with breast cancer with public health coverage present with more advanced disease, and this possibly explains worse DFS and OS when compared with those with private coverage.

Impact: Earlier diagnosis and treatment of breast cancer could improve outcomes of women with public health coverage in Brazil. *Cancer Epidemiol Biomarkers Prev; 23(1); 126–33. ©2013 AACR.*

Introduction

Over 52,000 women in Brazil are diagnosed annually with breast cancer and mortality has risen steadily (1, 2). These trends parallel the aging of the population and the growth of noncommunicable diseases in general (3, 4). Currently, there are few data on the clinical characteristics of patients with breast cancer and their clinical outcomes (5). It has been estimated that screening for breast cancer through the public health system of Brazil is low, with annual rates of less than 10% of the target population (5). Although national data on screening through the private sector are not available, one study has estimated that in the Brazilian State of Goiás, 48% of all exams were done through the private sector in the year of 2008 (6). The 5-year breast cancer survival rates in Brazil have been estimated to be 58%, which are low when compared with the United States (84%; ref. 5). The Brazilian breast cancer mortality-to-incidence ratio is also higher when compared with the United States (0.291 vs. 0.193, respectively; ref. 5).

The Amazona Project is a retrospective observational cohort study of 4,912 women with breast cancer from centers representing all different geographical regions of Brazil (7). The project was planned and conducted by The Brazilian Breast Cancer Study Group (GBECAM) and analyzed in collaboration with the MGH-AVON International Breast Cancer Program. The objective of this study was to assess differences in outcomes according to type of healthcare coverage, public or private. Our secondary objective was to determine whether there are differences in access to specific cancer therapies between these two groups.

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Materials and Methods

Data collection

Data were collected from 28 centers in 11 states through a systematic chart review of women diagnosed with breast cancer between July 2008 and January 2009. Patients were included if their medical chart was accessible, they were 18 years of age or more, had pathologic confirmation of breast cancer, and were registered at the participating centers between January 1st and December 31st of 2001 or January 1st and December 31st of 2006. Information collected included: the patient's age, race, menstrual and gestational history, family history of cancer, date of diagnosis, clinical and pathologic characteristics of breast cancer, institution where the patient received care, date and type of primary local and systemic treatments received, date of recurrences, type of recurrences, date and type of first-line treatment received for recurrences, survival, and date and cause of death. Ethnicity was categorized according to the Brazilian National Institute of Geography and Statistics (4). Patients registered in 2001 were staged clinically according to AJCC/UICC TNM 5th edition, whereas those from 2006 were staged with AJCC/UICC TNM 6th edition (8, 9). For those patients who did not have a clinical stage determined but had available information on tumor, lymph nodes, and metastasis, clinical stage was determined according to AJCC/UICC TNM 6th edition. Participating centers were of three types: public, which attend almost exclusively to public healthcare patients; private, which attend to private healthcare patients; and philanthropic, which have a mixed population of public and private healthcare patients. For the purpose of this analysis, patients from public and private centers were considered to have public and private health coverage, respectively. Individual data on type of health insurance was retrieved for patients from philanthropic institutions. Initial chart review included 4,912 patients, 4,905 of which had valid survival data. Seven hundred and twenty-five patients were originally from private and 1,068 patients from public institutions. Of the 3,112 patients from philanthropic institutions, we were able to categorize by further chart review 262 as privately insured and 1,087 as publicly insured, for a total of 3,142 patients included in this analysis. For hormone receptor data, we considered positive those patients that had positivity stated in records or that received hormonal therapy; patients who had neither were considered as hormone receptor negative. Ethics committees of all participating centers approved the study and the study was conducted according to the Declaration of Helsinki.

Statistical analysis

Comparisons of demographics, disease characteristics, and treatment regimens between those with public and private coverage were analyzed using the χ^2 test. Overall survival (OS) was calculated from the time of diagnosis until death from any cause. Disease-free survival (DFS) was calculated as the time from initial diagnosis to the earlier of either breast cancer recurrence or death. Date of breast cancer recurrence was available for stage 0–III patients, but only date of death was available for stage IV patients. Postrelapse survival (PRS) was calculated from the time of first recurrence of breast cancer to death. OS, DFS, and PRS plots according to type of health coverage and stage at diagnosis were calculated using Kaplan–Meier methodology. Comparisons were made using the log-rank test. Effect of insurance type on DFS and OS were analyzed using Cox regression models with adjustment for patient characteristics (age and race) and stage at presentation (tumor size and nodal status). For PRS, the Cox regression model was adjusted for age, race, type of relapse (locoregional vs. distant), and type of health coverage. All P values are two sided and considered significant when $P < 0.05$. All analyses were performed using SAS version 9.2.

Role of funding sources

Funding sources had no role in study design, data collection, analysis, and interpretation, writing of the report, and decision to submit to publication.

Results

Of the 3,142 patients included in this analysis, 2,155 (69%) had public healthcare coverage and 987 (31%) had private coverage (Table 1). At a median follow-up time of 28 months from diagnosis, 439 patients had progressed and 141 had died. Of these deaths, 128 were attributed to breast cancer, 1 to treatment toxicity, 9 to nondisease-related causes but with evidence of breast cancer, and 3 due to nondisease related causes without evidence of disease.

Patient characteristics

Table 1 provides the characteristics of all subjects shown by type of healthcare coverage. Median age at diagnosis was 53 years (range 15–94) for all patients and not significantly different between the groups ($P = 0.09$). The majority of women were postmenopausal (62%). Overall, the majority of subjects were Caucasian (60%). Ethnicity was significantly different according to the type of healthcare coverage ($P < 0.001$), with public healthcare having more patients of mixed ethnicity and those with private coverage more frequently being Caucasians; however, there were a substantial number of subjects with unknown ethnicity in both groups. Ninety-three percent of patients had invasive breast cancer and 83% of these were ductal. Clinical stage at diagnosis was different according to the type of healthcare ($P < 0.001$): only 15% of patients with public coverage had stage 0–I disease compared with 33% of those with private coverage, whereas 33% of the public patients had stage III compared with only 16% of private patients (Table 1). Sixty-two percent of patients had hormone receptor-positive disease and distribution was similar between the groups ($P = 0.75$). HER2 testing was only analyzed in patients who were diagnosed in 2006 because it was not routinely tested in 2001. Of 1,797 patients, only 1,063 (59%) were tested

Table 1. Patient characteristics for all patients and according to type of insurance

	All, $N = 3,142$	Public, $N = 2,155$ (69%)	Private, $N = 987$ (31%)	
	n (%)	*n* (%)	*n* (%)	P^a
Ethnicity				<0.001
Caucasian	1,450 (60)	986 (55)	464 (75)	
African descendent	84 (4)	61 (3)	23 (4)	
Asian	7 (0)	5 (0)	2 (0)	
Mixed (parda)	885 (37)	753 (42)	132 (21)	
Unknown	716 (23)	350 (16)	366 (37)	<0.001
Menopause status				0.614
Postmenopausal	1,685 (62)	1,242 (63)	443 (61)	
Premenopausal	1,023 (38)	745 (38)	278 (39)	
Unknown	434 (14)	168 (8)	266 (27)	<0.001
Cancer type				<0.001
Invasive ductal	1,899 (83)	1,459 (86)	440 (77)	
Invasive lobular	139 (6)	87 (5)	52 (9)	
Other invasive	74 (3)	57 (3)	17 (3)	
DCIS	161 (7)	100 (6)	61 (11)	
LCIS	4 (0)	2 (0)	2 (0)	
Clinical stage at diagnosis				<0.001
0–I	504 (20)	261 (15)	243 (33)	
IIA	722 (29)	509 (29)	213 (29)	
IIB	466 (19)	331 (19)	135 (18)	
III	702 (28)	588 (33)	114 (16)	
IV	131 (5)	100 (6)	31 (4)	
Unknown	617 (20)	366 (17)	251 (25)	<0.001
Grade				<0.001
G1	138 (10)	97 (10)	41 (11)	
G2	760 (57)	558 (58)	202 (53)	
G3	379 (28)	279 (29)	100 (26)	
GX	65 (5)	29 (3)	36 (10)	
Unknown	1,800 (57)	1,192 (55)	608 (62)	<0.001
Hormone receptor (ER and/or PR)				0.751
Positive	1,945 (62)	1,330 (62)	615 (62)	
Negative	1,197 (38)	825 (38)	372 (38)	
HER2[b]	1,797 (57)	1,159 (54)	638 (65)	
Positive[c]	224 (13)	117 (10)	107 (17)	0.905
Negative[c]	839 (47)	442 (38)	397 (62)	
Unknown/not performed[c]	734 (41)	600 (52)	134 (21)	<0.001

Abbreviations: DCIS, ductal carcinoma *in situ*; LCIS, lobular carcinoma *in situ*; ER, estrogen receptor; PR, progesterone receptor.

[a]*P* values in each category are calculated for comparisons between known variables within each group and separately for the unknown from each group.

[b]Only patients included from 2006 are shown here, because HER2 testing was not routine in 2001.

[c]Percentages were calculated as the number of patients in each cell related to the total number of patients available for HER2 testing in each group. Percentages do not sum 1 due to rounding.

(Table 1) and there was no difference in tumor HER2 expression according to insurance type ($P = 0.91$).

Therapy

Type of therapy received after diagnosis is shown in Table 2. Overall, the proportion of patients undergoing any breast surgery was slightly higher among private patients ($P = 0.003$). The majority of public patients had a mastectomy (68%), whereas mastectomy and lumpectomy were equally distributed among the private patients. Mastectomy was more common in public healthcare patients in all local clinical disease stages when compared with private patients ($P = 0.012$ for stage 0–I; $P < 0.001$ for stage II; $P = 0.008$ for stage III; Supplementary Table S1). Sentinel lymph node biopsy was less frequent in public patients than among private patients (15% vs. 26%,

Table 2. Primary locoregional and systemic treatment received by all patients according to insurance type by stage

	All patients, *n* (%)	Public, *n* (%)	Private, *n* (%)	
	***N* = 3,142**	***N* = 2,155**	***N* = 987**	***P***
Breast surgery (any)	2,551 (85)	1,728 (84)	823 (86)	0.035
Mastectomy[a]	1,582 (62)	1,170 (68)	412 (50)	<0.001[g]
Lumpectomy[a]	956 (38)	550 (32)	406 (49)	
Type unknown[a]	13 (1)	8 (1)	5 (1)	
Sentinel lymph node biopsy[b]	478 (19)	267 (15)	211 (26)	<0.001
Complete axillary dissection[b]	2,014 (79)	1,449 (84)	565 (69)	<0.001
Postoperative radiotherapy	1,912 (61)	1,304 (61)	608 (62)	0.582
Chemotherapy[c,d]	2,163 (69)	1,513 (70)	650 (66)	0.015
Endocrine therapy[d,e]	1,077 (86)	684 (87)	393 (86)	0.521
Trastuzumab[d,f]	67 (30)	10 (9)	57 (53)	<0.001

NOTE: *P* values are for comparison of public and private.

[a]Percentages are calculated by the number of patients in each cell relative to the number of patients that have undergone any surgery.

[b]Percentages use number of patients with any surgery as the denominator.

[c]Percentages are calculated by the number of patients in each cell relative to the total number of patients in each group.

[d]Chemotherapy, endocrine therapy, and trastuzumab include adjuvant therapy for stages 0–III or first-line therapy for stage IV.

[e]Percentages are calculated by the number of patients in each cell relative to the number of hormone receptor–positive patients of each group shown in Table 1 ($n = 1{,}945$ for all patients, $n = 1{,}330$ for public patients, and $n = 615$ for private patients).

[f]Percentages are calculated by the number of patients in each cell relative to the number of HER2-positive patients shown for each group in Table 1 ($n = 224$ for all patients, $n = 117$ for public patients, $n = 107$ for private patients).

[g]*P* value for comparison between number of mastectomies and lumpectomies in each group.

respectively; $P < 0.001$). When analyzed according to stage, this difference was only significant among patients with stage 0–I disease ($P = 0.003$; Supplementary Table S1). Overall adjuvant radiotherapy was given at similar rates in both insurance types ($P = 0.582$), but when analyzed by stage, private patients with stage 0–I disease tended to have more adjuvant radiotherapy ($P = 0.003$; Supplementary Table S1).

More public patients received chemotherapy than private patients (70% vs. 66%, respectively; $P = 0.015$). Among patients receiving chemotherapy, most received anthracycline-based regimens (66.2% of public and 56.3% of private). Taxanes were routinely available only for patients diagnosed in 2006 and overall use of these agents was generally low and not significantly different between patients of the two types of health coverage when analyzed by stage (Supplementary Table S1). Analysis of trastuzumab use included HER2-positive patients from 2006 only and, of these, 9% of public patients compared with 53% of private patients received this drug ($P < 0.001$; Table 2). There was a marginally significant difference between groups in the use of endocrine therapy for patients with hormone receptor-positive tumors ($P < 0.052$), and tamoxifen was the most frequently used drug in both groups and for all the stages. Use of adjuvant aromatase inhibitors alone or in sequence after tamoxifen was analyzed only for patients diagnosed in 2006 because in 2001, this adjuvant therapy was not in routine use. Private patients received more adjuvant aromatase inhibitors than public patients (40% vs. 12%, respectively; $P < 0.001$) and within all early stages of disease (Supplementary Table S1).

Time to therapy

Among patients who received any treatment, the time from diagnosis to first treatment was significantly longer for public patients (public median 1 month vs. private median <1 month; $P < 0.001$). Similarly the time from diagnosis to surgery (public median 2 months vs. private median <1 month; $P < 0.001$) and time from diagnosis to chemotherapy (public median 2 months vs. private median 1 month; $P < 0.001$) were significantly shorter for private patients. There was a marginally significant difference in time from surgery to postoperative radiation therapy among patients who underwent both surgery and radiation therapy ($P = 0.0962$) in favor of private patients.

Insurance type and disease-free survival

Overall, public patients had a shorter DFS compared with private patients ($P < 0.001$; Fig. 1A). When DFS was analyzed by clinical stage, there was no difference between private and publicly insured patients with stage 0–II ($P = 0.89$; Fig. 1B), but public patients with stage III–IV disease had significantly shorter DFS ($P = 0.002$; Fig. 1C).

Insurance type and overall survival

Public patients had worse OS than private patients ($P < 0.001$; Fig. 2A). When analyzed by clinical stage, patients

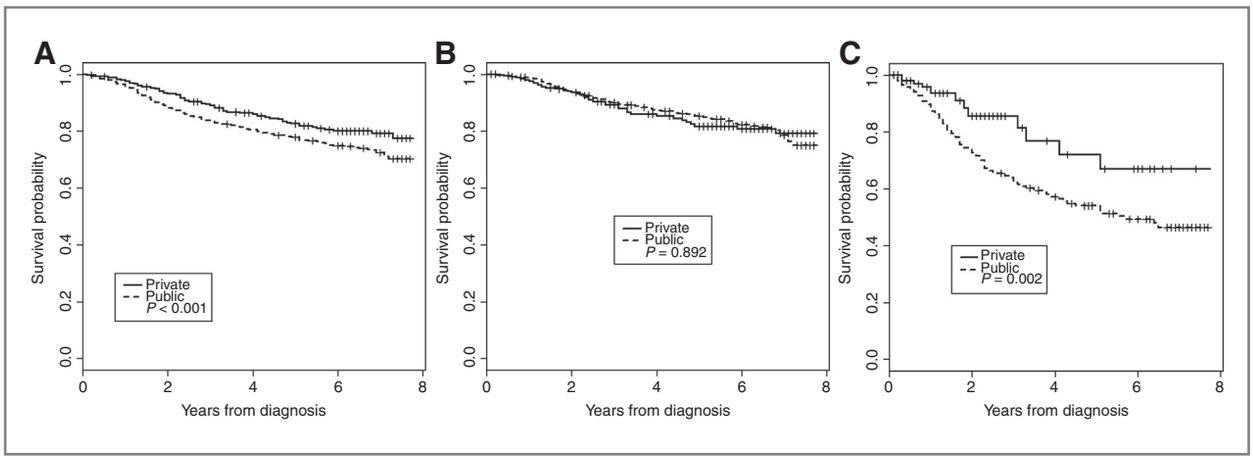

Figure 1. Kaplan–Meier curves for DFS and log-rank analysis for (A) all patients, (B) stage 0–II patients, and (C) stage III–IV patients

with stage 0–II disease did not have significantly different survival outcomes ($P = 0.176$; Fig. 2B), but those with stage III–IV disease with public coverage experienced significantly shorter survival ($P = 0.008$) than those in the private sector (Fig. 2C).

Healthcare coverage and postrelapse survival

When analyzing survival after any relapse (locoregional or distant), patients with private coverage had significantly longer PRS than public patients ($P < 0.001$; Fig. 3). At 3 years, more than 80% of private patients were alive as compared with less than 60% of those with public healthcare.

Multivariate analyses

In a minimally adjusted multivariate model (Supplementary Table S2), adjusting for insurance, age, and race, we found that private insurance was associated with an improved DFS [HR 0.72; 95% confidence interval (CI), 0.55–0.94; $P = 0.017$] and OS (HR 0.39; 95% CI, 0.21–0.73; $P = 0.003$). When expanding the multivariate Cox regression model to include data on clinical stage at diagnosis insurance was not independently associated with improved DFS (HR 0.87; $P = 0.332$; Table 3). In this expanded model, the association between insurance type and OS was marginally significant (HR 0.53; $P = 0.052$). Insurance type, however, was independently associated with PRS, before (HR 0.38; 95% CI, 0.20–0.73; $P = 0.004$) and after adjustment for stage at diagnosis and patients with private coverage had 45% lower risk of death after relapse than those in the public sector in the expanded model (HR 0.55; $P < 0.001$; Table 3).

Discussion

To our knowledge, this is the first large, multicenter retrospective analysis of the impact of medical health coverage on outcomes of patients with breast cancer in Brazil. Many factors such as screening, pathologic characteristics of tumors, and access to medical care can influence outcomes of patients with breast cancer (10–14). Of

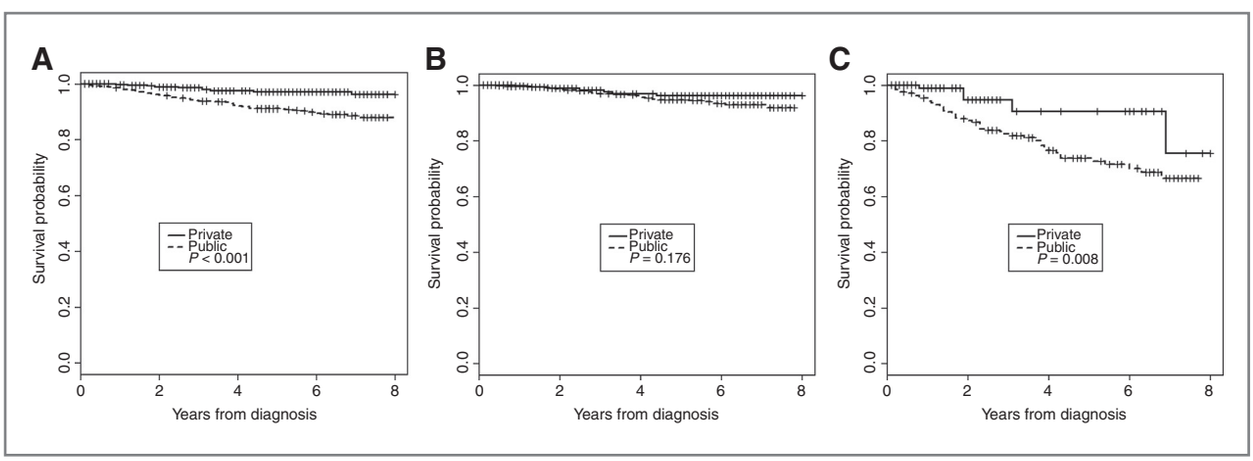

Figure 2. Kaplan–Meier curves for OS from diagnosis and log-rank analysis by insurance type for (A) all patients, (B) stage 0–II patients, and (C) stage III–IV patients.

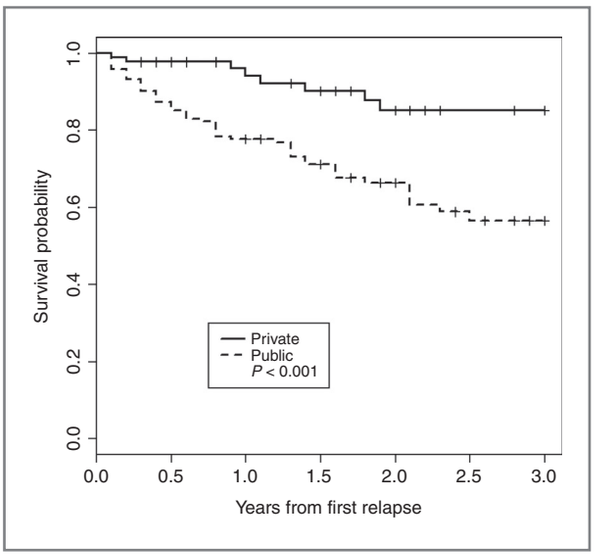

Figure 3. Kaplan–Meier curves for PRS and log-rank analysis for all patients according to type of insurance.

these, socioeconomic factors, specifically health coverage type, have been associated with stage at diagnosis and survival from breast cancer (15–19).

Our results have demonstrated important differences in clinical stage at diagnosis in patients from the public versus private centers. Patients with public healthcare had about half the proportion of stage 0–I breast cancer but were diagnosed with stage III breast cancer about twice as often as patients with private coverage. It is important to note that availability of imaging at diagnosis is probably different between public and private patients, and stage IV disease might be underestimated. Because there was no difference in other characteristics that might suggest a difference in tumor subtypes, these data strongly suggest that dependence on public coverage is an important factor leading to more advanced disease at diagnosis. Ethnicity has been a factor associated with stage of disease presentation (19). In our cohort, there were more patients with mixed ethnicity in the public healthcare group, whereas the privately covered patients were predominantly Caucasians. Unfortunately, the proportion of patients recorded as "unknown ethnicity" was high in both groups, and thus did not allow us to draw any firm conclusions. A possible explanation for the differences in disease stage at diagnosis might be access to healthcare. Although we did not have information on access to screening mammography and time from breast cancer suspicion to diagnosis in this cohort, a previous publication by our group has shown that access to screening and delays to diagnosis are major issues in public healthcare sector patients in Brazil (5). Other factors such as public awareness and education might also contribute to delays in diagnosis (5).

The slightly higher rates of breast surgery seen in privately covered patients were not unexpected because of more advanced stage of public patients, potentially precluding them from having curative surgery. Higher rates of mastectomy in public patients were seen in all stages and the reasons for this should be studied further. Publicly insured patients also had lower rates of sentinel lymph node biopsy, although the precise reasons for this are not clear from our study. There were no clinically significant differences in access to radiotherapy between insurance types, and the higher rates of adjuvant radiotherapy for stage 0–I patients with private coverage are not surprising given more frequent conservative surgery.

Chemotherapy was given slightly more frequently to public patients and again this might reflect more advanced stage at diagnosis. Type of chemotherapy regimen was different between the groups with the use of taxanes being more common in those with private coverage, although overall use was uncommon for both groups in this cohort. Although the type of adjuvant chemotherapy has been shown to influence recurrence and survival, we did not have enough events in this cohort to see a difference (20). There was no difference in use of endocrine therapy for hormone receptor-positive tumors between the groups. Aromatase inhibitors were prescribed more frequently for private patients, but again we had very few events to be able to analyze differences in outcome due to this therapy.

Table 3. Multivariate Cox regression analyses for DFS, OS, and PRS

	Disease-free survival HR (95% CI); *P*	Overall survival HR (95% CI); *P*	Postrelapse survival HR (95% CI); *P*
Private insurance	0.87 (0.65–1.16); 0.332	0.53 (0.28–1.01); 0.052	0.55 (0.41–0.75); <0.001
Age (y scaled by 0.1)	0.94 (0.86–1.03); 0.185	1.14 (0.97–1.34); 0.116	1.08 (0.99–1.17); 0.080
Race: black or mixed	0.82 (0.65–1.04); 0.104	0.92 (0.61–1.39); 0.699	0.88 (0.70–1.10); 0.253
Hormone receptor positivity	0.42 (0.34–0.53); <0.001	0.21 (0.13–0.33); <0.001	0.63 (0.50–0.78); <0.001
T-stage IV at diagnosis	2.46 (1.88–3.21); <0.001	3.04 (1.96–4.72); <0.001	NA
N-stage 0 at diagnosis	0.45 (0.35–0.58); <0.001	0.29 (0.17–0.48); <0.001	NA
Locoregional recurrence	NA	NA	0.74 (0.58–0.94); 0.014

Abbreviation: NA, not applicable to the specified analysis.

Although HER2 testing was performed in only about one third of all patients, there was a clear difference between trastuzumab use and type of health coverage, with less than 10% of those publicly insured receiving this therapy. Median times from diagnosis to any therapy in both groups were within the 12-week period generally considered ideal (21), and although there was a statistically significant difference in this time in favor of the privately covered patients, this difference was not likely of clinical relevance.

Univariate analysis showed that DFS of patients treated through the public system was generally worse than those with private coverage. In the minimally adjusted multivariate analysis insurance maintained association with improved DFS, which was not shown after adjusting for T and N stage. This strongly suggests that stage at presentation is what is driving the difference seen in univariate analysis.

OS was also worse for public healthcare patients in univariate analysis, and this difference can be attributed to death from breast cancer because this was the most common cause of death in the cohort. Again, the minimally adjusted multivariate analysis initially showed association with insurance type and OS, which disappeared when including the stage at diagnosis. This again suggests that later stage at diagnosis is what is related to the higher mortality rates seen in publicly insured patients.

Interestingly, PRS showed a large difference between those with public versus private coverage, with the first group doing considerably worse. This difference persisted even after adjusting for demographic and clinical factors. Reasons for this are not clear. One possible explanation is that privately insured patients might have earlier diagnosis of recurrent disease due to easier access to clinical consultation and imaging. This might cause a lead-time bias, where those privately insured have an apparent longer survival after diagnosis of recurrence. We cannot, on the other hand, exclude that differences in postrelapse therapy might in some way influence these findings.

A potential pitfall of this study is that more than 1,800 patients from the original dataset were excluded because of lack of information on healthcare coverage. Although we still maintained statistical power for our main analysis, subgroup analyses might have been underpowered. In addition, there could be a chance that our cohort was not representative of the population as a whole. We also had relatively short follow-up and a longer observation period with more events might impact these results. Another issue is that for some prognostic variables, there was a high percentage of missing information. It is, however, our assumption that "missingness" occurred randomly, and thus we assumed it did not impact significantly on our results. Despite these caveats, we found no differences between groups in distribution of several other characteristics and prognostic factors known to influence prognosis of breast cancer and even with short follow-up, we were able to detect differences in outcomes.

An important consideration when interpreting these results is that all participating centers attending to publicly covered patients are national centers of excellence and several are academic institutions. Access to treatment, resources, and outcomes at these centers is probably better than for the breast cancer population treated through the general public healthcare system. It is possible that the actual difference in outcomes between publicly and privately insured might be greater than we report.

In conclusion, Brazilian patients with breast cancer with public health coverage present with more advanced stage breast cancer, and in this cohort differences in DFS and OS seem to be mostly related to this factor. The difference in risk of death from breast cancer after recurrence between the groups needs further investigation. Although we have identified disparities in access to therapies such as conservative breast surgery, sentinel lymph node biopsy procedures, and use of taxanes, aromatase inhibitors, and trastuzumab, in this cohort we could not determine with certainty that this was responsible for differences in clinical outcomes. Access to therapy among public and private patients should be an issue for further investigation. Government and society should make efforts to diagnose publicly insured patients earlier and to improve their access to what is currently considered standard therapy for early breast cancer. Avoidance of stage III–IV disease with clinical downstaging would allow for significant decrease in suffering and save the costs associated with end-of-life care.

Disclosure of Potential Conflicts of Interest

C.H. Barrios has commercial research support from Roche and GSK, has honoraria from speakers' bureau from Roche, and is a consultant/advisory board member of Roche. No potential conflicts of interest were disclosed by the other authors.

Authors' Contributions

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Development of methodology: P.E.R. Liedke, D.M. Finkelstein, C.H. Barrios, J. Bines, S.D. Simon, P.E. Goss
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): C.H. Barrios, J. Bines, S.D. Simon
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): P.E.R. Liedke, D.M. Finkelstein, J. Szymonifka, C.H. Barrios, Y. Chavarri-Guerra, J. Bines, S.D. Simon, P.E. Goss
Writing, review, and/or revision of the manuscript: P.E.R. Liedke, D.M. Finkelstein, J. Szymonifka, C.H. Barrios, Y. Chavarri-Guerra, J. Bines, C. Vasconcelos, S.D. Simon, P.E. Goss
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): D.M. Finkelstein
Study supervision: C.H. Barrios, J. Bines, S.D. Simon, P.E. Goss

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References

1. Instituto Nacional de Câncer José Alencar Gomes da Silva. Coordenação Geral de Ações Estratégicas. Coordenação de Prevenção e Vigilância. Estimativa 2012: incidência de câncer no Brasil. Inca, Rio de Janeiro; 2011 [Acessed 2012 May 8]. Available from: http://www.inca.gov.br/estimativa/2012/.
2. Brasil, Ministério da Saúde, Instituto Nacional de Câncer. Atlas de mortalidade por cancer [Accessed on May 8th, 2012]. Available from: http://www1.inca.gov.br/vigilancia/mortalidade.html.
3. Schmidt MI, Duncan BB, Silva GA, Menezes AM, Monteiro CA, Barreto SM, et al. Chronic non-communicable diseases in Brazil: burden and current challenges. Lancet 2011;377:1949–61.
4. Instituto Brasileiro de Geografia e Estatística (IBGE). Sinopse do censo demográfico 2010. Rio de Janeiro, Brazil; 2011 [Accessed April 5th, 2013]. Available from: http://www.ibge.gov.br/english/estatistica/populacao/censo2010/default.shtm.
5. Lee BL, Liedke PER, Barrios CH, Simon SD, Finkelstein DM, Goss PE. Breast cancer in Brazil: present status and future goals. Lancet Oncol 2012;13:e95–102.
6. Correa RS, Freitas-Junior R, Peixoto JE, Rodrigues DCN, Lemos MEFL, Martins LAP, et al. Estimated mammogram coverage in Goiás State, Brazil. Cad Saúde Pública, Rio de Janeiro 2011;27:1757–67.
7. Simon SD, Bines J, Barrios CH, Nunes JS, Gomes EF, Pacheco FC, 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). Cancer Res 2010;69:3082.
8. Sobin LH, Wittekind Ch, editors. Breast tumors (ICD-O C50). In: Sobin LH, Wittekind Ch, editors. International union against cancer (UICC). TNM classification of malignant tumors. 5th ed. New York: John Wiley & Sons, Inc; 1997. p. 123–34.
9. Brasil, Ministério da Saude. Tumores de Mama (CID-O C50). In: Brasil, Ministerio da Saude. Secretaria de Atencao a Saude. Instituto Nacional do Cancer. TNM: classificacao de tumores malignos/traduzido por Ana Lucia Amaral Eisenberg. 6 ed. Rio de Janeiro: INCA; 2004. p. 137–48.
10. Tabar L, Yen M, Vitak B, Chen HT, Smith RA, Duffy SW. Mammography service screening and mortality in breast cancer patients: 20-year follow-up before and after introduction of screening. Lancet 2003;361:1405–10.
11. Gorin SS, Heck JE, Cheng B, Smith SJ. Delays in breast cancer diagnosis and treatment by racial/ethnic group. Arch Intern Med 2006;166:2244–52.
12. Carey LA, Perou CM, Livasy CA, Dressler LG, Cowan D, Conway K, et al. Race, breast cancer subtypes, and survival in the Carolina breast cancer study. JAMA 2006;295:2492–502.
13. Clarke M, Collins R, Darby S, Davies C, Elphinstone P, Evans E, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;366:2087–106.
14. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;365:1687–717.
15. Clegg LX, Reichman ME, Miller BA, Hankey BF, Singh GK, Lin YD, et al. Impact of socioeconomic status on cancer incidence and stage at diagnosis: selected findings from the surveillance, epidemiology, and end results: National longitudinal mortality study. Cancer Causes Control 2009;20:417–35.
16. Ali R, Mathew A, Rajan B. Effects of socio-economic and demographic factors in delayed reporting and late-stage presentation among patients with breast cancer in a major cancer hospital in south India. Asian Pac J Cancer Prev 2008;9:703–7.
17. Arndt V, Sturmer T, Stegmaier C, Ziegler H, Dhom G, Brenner H. Socio-demographic factors, health behavior and late-stage diagnosis of breast cancer in Germany: a population-based study. J Clin Epidemiol 2001;54:719–27.
18. Ayanian JZ, Kohler BA, Abe T, Epstein AM. The relation between health insurance coverage and clinical outcomes among women with breast cancer. N Engl J Med 1993;329:326–31.
19. Halpern MT, Ward EM, Pavluck AL, Schrag NM, Bian J, Chen AY. Association of insurance status and ethnicity with cancer stage at diagnosis for 12 cancer sites: a retrospective analysis. Lancet Oncol 2008;9:222–31.
20. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials. Lancet 2012;379:432–44.
21. 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;353:1119–26.

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