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Health care factors associated with survival among women with breast cancer on hormone therapy in Rio de Janeiro, Brazil, 2004 – 2010

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ABSTRACT

Objectives. *To better understand the role that health care plays in breast cancer survival by investigating the effects that hormone therapy adherence and other select health care variables, adjusted for clinical and sociodemographic factors, had among a population of women in Rio de Janeiro, Brazil.*

Methods. *This was a longitudinal study based on secondary data of 5 861 women treated with hormone therapy (tamoxifen or aromatase inhibitors) at the National Cancer Institute of Brazil (INCA), from 1 January 2004 – 29 October 2010. Four different sources of data were integrated for analysis: INCA Pharmacy Sector Dispensation System; Hospital-based Cancer Registry; Integrated Hospital System and INCA Absolute System; and Mortality Information System. Analyses explored the effects of adherence to hormone therapy, disease care aspects, and sociodemographic, behavioral, and clinical variables, on the time of survival, using Kaplan-Meier and Cox proportional hazards models.*

Results. *The general survival rate was 94% in the first year after initiation of hormone therapy, and 71% in the fifth year. The Cox model indicated a higher hazard of death among women smokers, with more hospitalizations, more exams, and, among those who used, who used only aromatase inhibitors, as hormone therapy modality. The hazard was lower among women with a partner (stable relationship), a high school or college education a family history of cancer, and those who were treated by a mastologist, oncologist, and/or psychotherapist, who underwent surgery, and who adhered to hormone therapy.*

Conclusions. *The study indicated more vulnerable sub-groups and the aspects of care that provide best results, bringing new knowledge to improve assistance to this group of women.*

Keywords Breast neoplasms; survival analysis; patient compliance; antineoplastic therapy; hormones, therapeutic uses; quality of health care; women's health; Brazil.

Breast cancer is the most frequent tumor among women in Brazil (1). Though this is the case in most developed countries (2), the challenges it raises in each context are quite distinct. Developed countries have shown a decreasing trend of breast cancer incidence and mortality (3) and an emergence of new treatment approaches focused on long-term health care for patients with long survivals (4), plus emotional support for women recovering from a cancer diagnosis (5). Brazil, however, is coping with high breast cancer incidence and mortality rates that continue rising (1), a high occurrence of late diagnoses and the resulting poor prognoses, and problems with health care access and quality (6).

Survival studies for the disease may fulfill an important role in subsidizing policies and improving health care delivery (7). General survival estimates for a population with breast cancer reflect

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several factors: stage of the disease at the time of diagnosis, (reflecting the efficiency of early detection programs), access to health care, and effectiveness of the treatment adopted (7). According to the World Health Organization (WHO), countries should structure multidisciplinary health care programs with efficient, sustainable, and equitable practices, adapted to current scientific evidence and capable of facilitating early detection.

In the early 1990s, some authors (8) attributed the pronounced fall in breast cancer mortality rates in developed countries to the introduction of mammographic screening (8), while others (9) gave credit to early detection by palpation and the addition of tamoxifen to breast cancer treatment (mammography playing only a minor role). Recently, faced with an excess of diagnoses and unnecessary and possibly harmful treatments, the scientific community has again raised questions regarding the benefits of mammographic screening (10). In fact, since mammography's benefits are lower than supposed, rethinking of breast cancer early detection programs is imperative, as is identification of other health care aspects that can impact prognosis and survival.

In the available literature, few studies on breast cancer survival examine or account for the characteristics of health services or health care organization, and still fewer involve Brazilian women cohorts (6). In developing countries, the lowest rates of breast cancer survival are attributed to late diagnosis, inadequate treatment, and especially, to the challenges with providing the adjuvant hormone therapy (11).

At this point there is consensus that early diagnosis increases the probability of longer survival among breast cancer patients, and that endocrine therapy contributes to decreased recurrence and metastases, lower mortality rates, and increased disease-free survival among eligible women (7, 9).

Breast cancer hormone treatment is characterized by the use of hormone-inhibiting or similar substances to restrain neoplasias that are dependent on hormonal action. It is only indicated when there is a positive response of the tumor to the hormonal receptors of estrogen and progesterone. Despite its recognized good outcomes, hormone therapy is a long-term treatment and is associated with side effects that may induce its abandon. Some health care factors may exacerbate non-adherence to the treatment (12), and it is worth noting that these factors can adversely affect breast cancer survival.

The objective of this study was to better understand the role that health care plays in breast cancer survival by investigating the effects that hormone therapy adherence and other select health care variables, adjusted for clinical and sociodemographic factors, had among a population of women in Rio de Janeiro, Brazil.

MATERIALS AND METHODS

A retrospective, longitudinal study was performed on a hospital-based population using secondary data for women with breast cancer treated with hormone therapy at the National Cancer Institute (INCA) of Brazil in Rio de Janeiro city. INCA, the Ministry of Health's reference center for cancer policies and care in the country, integrates the public health system and provides all modalities of inpatient and outpatient oncologic treatment free of charge. It is also the largest service provider of breast cancer care in Rio de Janeiro, the state with the nation's highest incidence rate—an estimated 57 960 new cases in 2016 (1).

The study included all of the women recorded with breast cancer in the Hospital-based Cancer Registry (HCR) in 2002 – 2008 and who, according to data from the INCA Pharmacy Sector Dispensation System, began hormonal treatment with tamoxifen (TMX) and/or aromatase inhibitors (AIs; letrozole or anastrozole) and had medication dispensed at least twice from 1 January 2004 – 29 October 2010. Since they received hormone therapy, it follows that these women had hormone receptor-positive cancer.

Four sources of data were integrated for analysis:

1. INCA Pharmacy Sector Dispensation System – dispensation data for medications, including dispensation date, type of medication (tamoxifen and/or AIs), and quantity. Only patients who started hormone therapy after 1 January 2004 were considered since the database was established in October 2003 with patients already in treatment. The last dispensing date considered was 10 October 2010.
2. The HCR – a hospital-based database including sociodemographic, clinical, and death variables related to cancer. The inclusion criteria considered patients registered with breast tumors in 2002 – 2008. The HCR, according to the recommendations of the International Agency for Research on Cancer (IARC), is set "per tumor," which allows for a patient with more than one primary malignant tumor (excluding relapse or metastasis) to be registered more than once. For patients with more than one breast cancer tumor recorded, the study preferentially used either (a) the most complete observation; (b) the observation related to the later stage, if diagnosis dates were the same; or (c) the first observation, if diagnosis dates were different.
3. Integrated Hospital System (IHS) and INCA Absolute System – source of data on the health care procedures provided to patients. The IHS was used by INCA from 1998 – 2004, and was replaced by the Absolute System as of that date. The study took into account data from 1 January 2002 – 29 October 2010. Because the Absolute System involves higher disaggregation of variables into categories than does the IHS, actions to make them compatible were necessary.
4. Mortality Information System – used to confirm patient death data available from the HCR.

After merging the databases, the difference between the dates of each woman's breast cancer diagnosis and initial hormone therapy was calculated. There were 198 cases with negative values, mostly due to typographical errors. Data were corrected according to the following process: (a) When the initial hormone treatment date was up to 3 months earlier than the diagnosis, the diagnosis and the initiation of hormone treatment were assumed to coincide; (b) When the negative difference between the start of hormone therapy and the diagnosis was greater than 3 months, and the second medication dispensing date was consistent with the diagnosis date, the first dispensing date was ignored and replaced with the second date, and the quantity of pills dispensed on the discarded date was deducted from the total. With this process, it was possible to retain 185 cases for analysis; 13 cases were eliminated due to a complete lack of data consistency.

Data related to 5 861 women remained in the integrated database for analysis. Note that it is very unlikely that any exclusions motivated by operational issues have introduced bias into the study; there were no systematic associations regarding the variables of interest.

As the survival measure, the study considered the time from the date of the initial hormone therapy to the date of death by breast cancer (failure) or the date of the last dispensation of medication (censored).

With regard to the independent variables, the study was mainly focused on health care-related aspects. It takes into account the use of medical resources (type of hormone therapy, surgery, chemotherapy, radiotherapy, exams, and inpatient care), the way health care was provided (cancer specialists involved and multiprofessional supportive care), and time to the initiation of and adherence to hormone treatment, which itself may reflect health care organization and provision.

As control variables, the study considered these factors among the women follow-up sociodemographics, i.e., age at the time of diagnosis, educational level, marital status; behavior, i.e., tobacco and alcohol use; and clinical conditions, i.e., histological type of the tumor, curable stages (0, I, and II) and non-curable stages (III and IV), laterality, and family history of cancer.

Assuming the recommendation of a daily dose of tamoxifen or aromatase inhibitor for 5 years, adherence to hormone therapy (HT) was determined by the medication possession ratio (MPR) (13). Any patient with MPR ≥ 80% was considered adherent to the treatment, a reference that is widely applied in the literature (14):

$$\text{MPR} = \frac{\begin{array}{c}\text{Total pills dispensed}\\ \text{to the patient}\end{array}}{\begin{array}{c}\text{Last date (LD) of dispensation}\\ \text{of HT - HT start date}\\ \text{+ supply delivered}\\ \text{at the LD}\end{array}} \times 100$$

The analyses of factors associated with breast cancer hazard of death from initiation of hormone therapy were performed through Kaplan-Meier technique and the multivariable Cox proportional hazards model (15). The Kaplan-Meier analyses sought to identify differences in survival curves over time, related to the strata of the variables. The Wilcoxon and log-rank tests were employed to test differences among the curves, guiding the inclusion of variables in the multivariable model. The multivariable model, in turn, was used to identify the independent effects of the explanatory variables. The hazard proportionality assumption was tested through the inclusion in the model of interaction terms of the independent variables and time, maintaining those statistically significant for correcting the assumption violations (15).

Right censoring in the analyses was related to interruption in the follow-up due to treatment abandonment or patient transference, the occurrence of death due to other causes (excluding breast cancer), the end of treatment, or the end of the observation period.

The analyses were performed with the SAS® statistic software, version 9.2 (SPSS Inc., an IBM company, Chicago, Illinois, United States)

The study was approved by the Research Ethics Committee of INCA (protocol nº84/2010) and procedures were used to guarantee patient anonymity.

RESULTS

The mean, standard deviation median, and interquartile range follow-up periods were 1 224, 630, 1 208, and 1 064 days, respectively, and the total number of deaths observed was 1 319 (22.5%). Age of the study population at the time of breast cancer diagnosis ranged from 21 – 103 years, with a mean of 57.5 years and a standard deviation of 13.6. The median age was 56.6 years and interquartile range was 21.1 years. Approximately 50% of the women were 40 – 59 years of age, and only a minority was younger than 40.

Half the women in the cohort presented low levels of education (illiterate or incomplete elementary school); 10% had a college education. Of the total, 55.5% had a family history of cancer; 46.5% had a partner at the diagnosis; 27.4% were alcohol users; 34.7% were smokers; and 40.5% were diagnosed in the later stages (stages III and IV).

Regarding breast cancer treatment, 57.6% of women used tamoxifen and an aromatase inhibitor; 42.4% used, exclusively, either tamoxifen or an aromatase inhibitor; 59.4% underwent a breast cancer surgical procedure; 60.2% were treated with chemotherapy; and 47.3% received radiotherapy. Moreover, 76.3% adhered to the hormone therapy.

Survival analysis

Based on the Kaplan-Meier analysis, the general survival rate of women who began hormone therapy for breast cancer at INCA was 94% at 1 year, 87% at 2 years, 81% at 3 years, 76% at 4 years, and 71% at 5 years. As expected, the differences in survival probabilities were statistically significant ($P < 0.05$), when comparing strata of the variables *age*, *education level, marital status, family cancer history, histological type of the primary tumor,* and *disease stage* (Tables 1 and 2). Additionally, differences in survival were associated with *type* and *adherence to hormone therapy; use of surgery, chemotherapy, radiotherapy, inpatient care and exams; visits to mastologist*, *clinical oncologist*, and *other physicians*; use of *psychotherapy* and *multiprofessional supportive care* (Table 3). Survival was lower for those that used aromatase inhibitors, did not undergo surgery, had treatment with chemotherapy, received radiotherapy, and had more hospitalizations. Survival was also lower among women with no or few visits to mastologists, with at least 13 visits to clinical oncologists, with less than 10 consultations with other physicians, who did not use psychotherapy or other supportive services, and who had more exams (Table 3).

The results obtained with the Cox model (Table 4) indicated that the hazard of death was 0.6% higher for each additional month between diagnosis and initiation of the hormone therapy. The hazard of death was also 26.1% higher for each additional hospitalization, 0.9% higher for each unit increase in the number of exams performed, and 45.3% higher among those that used only aromatase inhibitors compared to those that used only tamoxifen. In addition, it was 26.6% higher among women that were at least 70 years of age and 12.9% higher among smokers.

Table 4 also shows a gradual effect of disease stage on the hazard of death at the moment the hormone therapy initiation—145.5% higher among women at stage II, 1 839.6% higher among women at stage III, and 2 379.0% higher among women at stage IV, compared to stages 0 and I. Over time, the effect of stage II is sustained. However, interacting effects of stages III and IV with time

TABLE 1. Kaplan-Meier analysis of survival rates among 5 681 women with breast cancer treated with hormone therapy, according to sociodemographic variables, Rio de Janeiro, Brazil, 2004–2010.

Sociodemographic variables	Probability of survival[a]		Log-rank	Wilcoxon
	n	%	*P*	*P*
Age			< 0.0001	< 0.0001
< 35 years	185	67.6		
35 – 74 years	4 972	78.5		
≥ 75 years	704	73.0		
Education			< 0.0001	< 0.0001
Illiterate/incomplete primary school	2 943	75.0		
Primary school	1 032	77.4		
Secondary school or college	1 839	81.4		
No information	47	85.1		
Marital status			< 0.0001	< 0.0001
With a partner	2 725	79.9		
Without a partner	3 098	75.4		
No information	38	76.3		

***Source*:** Produced by the authors from the study data.
[a] Survival by the end of the observation period, which was defined as….

TABLE 2. Kaplan-Meier analysis of survival rates among 5 681 women with breast cancer treated with hormone therapy (HT), according to clinical and behavioral variables, Rio de Janeiro, Brazil, 2004–2010.

Clinical and behavioral variables	Probability of survival[a]		Log-rank	Wilcoxon
	n	%	*P*	*P*
Family history of cancer			0.0176	0.0100
Yes	3 251	78.9		
No	2 426	78.3		
No information	184	77.7		
Alcohol use			0.7949	0.5883
Yes	1 605	78.6		
No	4 088	77.2		
No information	168	75.6		
Tobacco use			0.0959	0.061
Yes	2 033	76.7		
No	3 734	78.2		
No information	94	66.0		
Tumor type			0.0002	0.0003
Ductal carcinoma	4 678	76.5		
Other tumors	1 183	81.6		
Laterality			0.0546	0.0832
Unilateral	5 618	77.7		
Bilateral	236	72.5		
No information	7	100.0		
Stage			< 0.0001	< 0.0001
Curable	3 286	91.8		
Non-curable	2 371	56.5		
No information	204	98.2		

Source: Produced by the authors from the study data.
[a] From date of the initial hormone therapy to the date of death by breast cancer (failure) or the date of the last dispensation of medication (censored).

reduce hazard by 2.32% and 1.23%, respectively, per month.

In the reverse direction, denoting protective effects, the hazard of death was 72.0% lower among those that consulted mastologists, 2.9% lower for each unit increase in psychotherapy consultations, and 40% lower among women adherent to hormone therapy. Furthermore, hazard of death was 9.9% lower among women with partners, 25.1% lower among women with a college education, and 7.0% lower among women with a family history of cancer (Table 4).

It is worth emphasizing that the results presented here remained very similar when the Cox model was applied with the pseudo-likelihood estimation method, considering the diagnosis date as the time counting start. In order to be consistent with the Kaplan-Meier results, the choice was made to present the results obtained using initiation of hormonal therapy as reference.

DISCUSSION

According to WHO (7), the prognosis for breast cancer is relatively good, with early diagnosis and adequate treatment resulting in a 5-year survival rate in 75% of the cases. In the European community, the average survival probability for 5 years is 79%, with the lowest estimate in the area, 73.9%, observed in Eastern Europe (16). In the United States of America, 84.0% of breast cancer patients survive for at least 5 years post-diagnosis (17).

The probability of survival in 5 years among this study's cohort was slightly lower than that indicated by WHO, and quite lower than what has been confirmed in Europe and the United States. This study's survival rates were more similar those of Eastern Europe. It is important to recognize the limitations of the comparisons that use estimations based on the beginning of the hormone treatment rather than the diagnosis date as the start time of follow-up. Actually, a lower survival rate was expected. On the other hand, survival among the study cohort was higher than that observed by a previous study in Rio de Janeiro (18) that showed a survival probability of only 66% at 3 years after treatment initiation.

The profile of patients with breast cancer in this study's cohort was similar to that of others with regard to age (6, 19, 20) and tumor type (19, 20). On the other hand, it differs from the profile of European and North American women who are more likely to be diagnosed in a curable disease stage (19, 21).

Most of the women in this study underwent breast cancer surgery, radiotherapy, and chemotherapy. Taking into account national and international protocols and the disease stage distribution of the population studied, the high prevalence of these procedures was expected.

TABLE 3. Kaplan-Meier analysis of survival rates among 5 681 women with breast cancer treated with hormone therapy (HT), according to health care and treatment variables, Rio de Janeiro, Brazil, 2004–2010.

Health care and treatment variables	Probability of survival[a]		Log-rank	Wilcoxon
	n	%	*P*	*P*
HT type			< 0.0001	< 0.0001
Tamoxifen only	3 776	86.0		
Aromatase inhibitors only	339	61.1		
Both	1 746	62.4		
Surgery			< 0.0001	< 0.0001
Yes	3 495	81.3		
No	2 366	71.9		
Chemotherapy (CT; except for HT)			< 0.0001	< 0.0001
Yes	3 531	72.4		
No	2 330	85.2		
Radiotherapy (RT)			0.0004	0.0215
Yes	2 772	74.0		
No	3 089	80.6		
Therapeutic combination			< 0.0001	< 0.0001
HT only	552	78.6		
HT and surgery	899	88.3		
HT and CT	579	65.3		
HT and RT	503	86.3		
HT, CT, and surgery	1 059	83.6		
HT, RT, and surgery	376	85.6		
HT, CT, and RT	732	62.2		
HT, CT, RT, and surgery	1 161	72.4		
CT frequency (except HT; by number of procedures)			< 0.0001	< 0.0001
0	2 330	85.2		
1 – 3	690	83.6		
4 – 6	1 777	84.7		
≥ 7	1 064	45.8		
Hospitalization frequency (number of admissions)			< 0.0001	< 0.0001
0	961	84.4		
1	2 794	87.8		
2	1 182	73.3		
≥ 3	924	44.7		
Mastology (consultation)			< 0.0001	< 0.0001
0	617	37.6		
1 – 4	1 001	71.1		
5 – 13	2 971	86.5		
≥ 14	1 272	80.9		
Clinical oncology consultation			< 0.0001	< 0.0001
0	1 257	85.4		
1 – 4	1 674	81.4		
5 – 12	1 510	76.6		
≥ 13	1 420	66.8		
Other physicians (consultation)			< 0.0001	< 0.0001
≤ 9	604	69.5		
10 – 22	2 158	80.4		
23 – 34	1 635	80.0		
≥ 35	1 464	73.6		
Psychotherapy consultation			< 0.0001	< 0.0001
0	3 331	71.6		
1 – 3	1 971	84.6		
≥ 4	559	87.3		
Therapeutic support (consultation)			< 0.0001	< 0.0001
0	1 404	69.9		
1 – 3	2 010	78.6		
4 – 7	1 130	78.1		
≥ 8	1 317	83.4		

(*Continued*)

Regarding the control variables of this study, the survival probabilities were similar to those of other studies for age (14), disease stage (14), educational level (22), marital status (14, 23), and tobacco use (24).

In relation to health care provided to the patients, findings of higher survival rates among women who underwent surgery and had more visits to a mastologist are also ratified by guidelines (7, 20) and other studies (6, 14). The importance of emotional support during the course of breast cancer treatment should also be highlighted (7) and is reflected in this study by the association between psychotherapy and higher survival rates. On the other hand, lower probabilities for survival among patients with more hospitalizations and more exams seem to be explained by the plausibility of these patients presenting more comorbidities (14).

Many randomized clinical trials (25 – 27) and systematic reviews (28) have been performed to verify the benefit of AIs over tamoxifen. While these clinical trials show a higher disease-free survival rate related to AIs, they do not demonstrate an advantage to the general survival. Goldhirsch and colleagues (29) point out that the benefit of AIs may be specific to women with a higher risk of relapse. For women with a very low relapse risk, there seems to be little benefit of AIs over tamoxifen in the first 5 years. Besides that, the isolated use of AIs is not ratified by consensus (29, 30). Although the present study's analysis did not account for comorbidities and polypharmacy—more likely to occur in postmenopausal women eligible for AIs—the worst survival rate verified for isolated use of AIs seems consistent with the considerations raised above.

Since neither approach seems to be superior to the other, regarding general survival, the conclusions of studies fall back on the importance of treatment adherence (25–27). Studies that evaluated the impact of hormone therapy adherence on breast cancer mortality concluded that higher duration of tamoxifen use and adherence over 80% are associated with higher survival rates (21); and also, that incomplete hormone therapy is associated with a lower survival rate (14, 31). The results obtained here, therefore, concur with the importance of treatment adherence for improved probability of

TABLE 3. (*Continued*). Kaplan-Meier analysis of survival rates among 5 681 women with breast cancer treated with hormone therapy (HT), according to health care and treatment variables, Rio de Janeiro, Brazil, 2004–2010.

Health care and treatment variables	Probability of survival[a]		Log-rank	Wilcoxon
	n	%	*P*	*P*
DATS[b] (exams)			< 0.0001	< 0.0001
0	1 112	84.1		
1	2 007	79.9		
2 – 3	1 816	76.2		
≥ 4	926	65.8		
Adherence to HT			< 0.0001	< 0.0001
Yes	4 469	82.2		
No	1 392	46.5		

Source: Produced by the authors from the study data.
[a] From date of the initial hormone therapy to the date of death by breast cancer (failure) or the date of the last dispensation of medication (censored).
[b] Diagnostic and therapeutic support services.

TABLE 4. Cox regression model for analysis of survival rates among 5 681 women with breast cancer treated with hormone therapy (HT), as of the treatment initiation date, Rio de Janeiro, Brazil, 2004–2010.

Variable	Coefficient	Standard deviation	Hazard ratio	95% Confidence Interval
Time from diagnosis to HT initiation (in months)	0.00607	0.00140	1.006	1.003 – 1.009
Age ≥ 70 years	0.23584	0.07223	1.266	1.099 – 1.458
With a partner	–0.10408	0.05776	0.901	0.805 – 1.009
College education	–0.28836	0.11342	0.749	0.600 – 0.936
Disease stage				
stage II	0.89817	0.15721	2.455	1.804 – 3.341
stage III	2.96505	0.19212	19.396	13.310 – 28.264
stage IV	3.21046	0.20402	24.790	16.620 – 36.978
Tobacco use	0.12135	0.05845	1.129	1.007 – 1.266
Surgery	–0.85491	0.11587	0.425	0.339 – 0.534
Hospitalizations	0.23186	0.01662	1.261	1.221 – 1.303
DATS[a]	0.00876	0.00237	1.009	1.004 – 1.013
Family history of cancer	–0.07230	0.01975	0.930	0.895 – 0.967
Mastology	–1.27219	0.07193	0.280	0.243 – 0.323
Clinical oncology	–1.29190	0.14932	0.275	0.205 – 0.368
Psychotherapy	–0.02970	0.01224	0.971	0.948 – 0.994
Aromatase inhibitors only	0.37338	0.09708	1.453	1.201 – 1.757
Adherence to HT	–0.51014	0.06062	0.600	0.533 – 0.676
Interaction – stage III	–0.02343	0.00401	0.977	0.969 – 0.985
Interaction – stage IV	–0.01237	0.00482	0.988	0.978 – 0.997
Surgery interaction	0.01105	0.00366	1.011	1.004 – 1.018
Clinical oncology interaction	0.03684	0.00724	1.038	1.023 – 1.052

Source: Produced by the authors from the study data.
[a] Diagnostic and therapeutic support services.

survival. There is, however, a counterpoint by Weaver and colleagues (32) who did not find a significant association between these variables.

According to the clinical guidelines applied by the Ministry of Health of Brazil during the study period, hormone therapy duration was 5 years. Some controversy about the extended, 10-year hormone therapy still remains and the Brazilian Unified Health System has not incorporated it widely (33). It is now possible to indicate individually extended treatment with tamoxifen to women with high risk of cancer recurrence (33).

The finding that showed higher survival rates among women with shorter delays between breast cancer diagnosis and initiation of hormonal therapy is strongly supported by the literature (7, 20). It can be explained by the intervention timeliness against the disease, the greater effectiveness of the treatment at earlier disease stages (7, 19), and the indication of post-surgery hormone therapy to avoid micrometastases (29).

Limitations

This study relied on the data of only one hospital; however, the large number of patients was a counterpoint, as was the hospital's universal access, which makes it reasonable to presume that the study population was representative of the general population in terms of most sociodemographic and clinical aspects. On the other hand, since INCA is a high complexity reference hospital, one could presume that the hospital case-mix tends to be more severe than that observed more generally, and that patients have better access to treatment options.

The use of secondary data always implies some limits, and the unavailability of data on comorbidities and medication side-effects are noteworthy. Some detected inconsistencies were carefully corrected to avoid losses that could affect results.

Despite limitations, this work plays a role in filling the gap in breast cancer survival studies among cohorts of patients using hormone therapy in Brazil.

Conclusions

These study results show that, in addition to certain sociodemographic and clinical characteristics, the health care organization and therapy adherence can change survival estimates for those with breast cancer. There have not been enough studies dedicated to understanding precisely how the organization of health care impacts disease outcomes for patients with chronic diseases, especially disease that require aggressive treatment and have severe collateral effects such as cancer does. Studies have mostly focused on specific clinical variables, contributing to the development of clinical guidelines and protocols, but not to health policy nor to the management and planning for health systems and services. The results provided here may help formulate a more

comprehensive perspective of health care as it relates to increasing hormone therapy adherence, avoiding overuse of tests, and improving access to psychotherapy and multiprofessional supportive care, and ultimately, to extending survival among women with breast cancer in Brazil.

Conflict of interests. None declared.

Disclaimer. Authors hold sole responsibility for the views expressed in the manuscript, which may not necessarily reflect the opinion or policy of the RPSP/PAJPH and/or PAHO.

REFERENCES

1. Ministério da Saúde, Instituto Nacional de Câncer. Estimativa 2016: Incidência de câncer no Brasil. Rio de Janeiro: INCA/MS; 2011. Available from: www.inca.gov.br/wcm/dncc/2015/por-tipos.asp Accessed on 13 January 2016.
2. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. Cancer incidence and mortality worldwide. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr Accessed on 11 January 2016.
3. Bosetti C, Bertuccio P, Levi F, Chatenoud L, Negri E, La Vecchia C. The decline in breast cancer mortality in Europe: An update (to 2009). The Breast. 2012;21(1):77–82.
4. Wheelock A, Mihalis E, Hamolsky D, Ernest ML, Lopez NS, Hwang J, et al. Survivorship clinic group educational sessions: adoption, acceptance, and attendance. J Cancer Educ. 2013;28(1):79-83. doi:10.1007/s13187-013-0452-6.
5. Kantsiper M, McDonald EL, Geller G, Shockney L, Snyder C, Wolff AC. Transitioning to breast cancer survivorship: perspectives of patients, cancer specialists, and primary care providers. J Gen Intern Med. 2009;24(2):S459-66. doi: 10.1007/s11606-009-1000-2.
6. Brito C, Portela MC, Vasconcellos MTL. Sobrevida de mulheres tratadas por câncer de mama no estado do Rio de Janeiro. Rev Saúde Pública. 2009;43:481-9.
7. World Health Organization. National cancer control programmes: policies and managerial guidelines. 2nd ed. Geneva: WHO; 2002. Available from: www.who.int/cancer/media/en/408.pdf Accessed on 20 January 2016.
8. Blanks RG, Moss SM, McGahan CE, Quinn MJ, Babb PJ. Effect of NHS breast screening programme on mortality from breast cancer in England and Wales, 1990–1998: comparison of observed with predicted mortality. BMJ. 2000;321:665-9.
9. Jatoi I, Miller AB. Why is breast-cancer mortality declining? Lancet Oncol. 2003;4(4):251-4.
10. Marmot MG, Altman DG, Cameron DA, Dewar JA, Thompson SG, Wilcox M. Independent UK Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review. Lancet. 2012;380:1778-86.
11. Swaminathan R, Black RJ, Sankaranarayanan R. Database on cancer survival from developing countries. IARC Sci Publ. 1998;145:19-25.
12. Brito C, Portela MC, Vasconcellos MTL. Adherence to hormone therapy among women with breast cancer. BMC Cancer. 2014;14:397. doi:10.1186/1471-2407-14-397
13. Cramer JA, Roy A, Burrell A, Fairchild CJ, Fuldeore MJ, Ollendorf DA, et al. Medication compliance and persistence: terminology and definitions. Value Health. 2008;11:44-7.
14. Hershman DL, Shao T, Kushi LH, Buono D, Tsai WY, Fehrenbacher L, et al. Early discontinuation and non-adherence to adjuvant hormonal therapy are associated with increased mortality in women with breast cancer. Breast Cancer Res Treat. 2011;126(2):529-37.
15. Allison PD. Survival analysis using the SAS system: a practical guide. Cary, NC: SAS Publishing; 1995. Pp. 161-5.
16. Verdecchia A, Francisci S, Brenner H, Gata G, Micheli A, Mangone L, et al. Recent cancer survival in Europe: 2000-02 period analysis of EUROCARE 4. Lancet Oncol. 2007;8(9):784-96.
17. Allemani C, Sant M, Weir HK, Richardson LC, Baili P, Storm H, et al. Breast cancer survival in the US and Europe: a CONCORD high-resolution study. Int J Cancer. 2013;132(5):1170-81. doi: 10.1002/ijc.27725
18. Brito, Cláudia. Avaliação do Tratamento à Paciente com Câncer de Mama nas Unidades Oncológicas do Sistema Único de Saúde no Estado do Rio de Janeiro. Master's thesis. Escola Nacional de Saúde Pública Sergio Arouca, Rio de Janeiro, 2004. Available from: http://teses.icict.fiocruz.br/pdf/britocm.pdf Accessed on 15 May 2016.
19. American Cancer Society. Breast Cancer. 2010. Available from: www.cancer.org/acs/groups/cid/documents/webcontent/003090-pdf.pdf Accessed on 15 January 2016.
20. Institute of Medicine, Commission on Life Sciences, National Research Council. Ensuring quality to cancer care. Hewitt M, Simone JV, eds. National Cancer Policy Board. Washington, DC: National Academy Press; 1999. Pp. 1-226.
21. McCowan C, Shearer J, Donnan PT, Dewar JA, Crilly M, Thompson AM, et al. Cohort study examining tamoxifen adherence and its relationship to mortality in women with breast cancer. Br J Cancer. 2008;99:1763-8.
22. Mendonça GAS, Silva AM, Caula WM. Características tumorais e sobrevida de cinco anos em pacientes com câncer de mama admitidas no Instituto Nacional de Câncer, Rio de Janeiro, Brasil. Cad. Saúde Pública. 2004;20(5):1232-9.
23. Kroenke CH, Kubzansky LD, Schernhammer ES, Holmes MD, Kawachi I. Social networks, social support, and survival after breast cancer diagnosis. J Clinic Oncol. 2006;24(7):1105-11.
24. Calle EE, Miracle-McMahill HL, Thun MJ, Heath Jr CW. Cigarette smoking and risk of fatal breast cancer. Am J Epidemiol. 1994;139:1001-7.
25. Breast International Group 1-98 Collaborative Group, Thürlimann B, Keshaviah A, Coates AS, Mouridsen H, Mauriac L, et al. A comparison of letrozole and tamoxifen in postmenopausal women with early breast cancer. N Engl J Med. 2005;353:2747-57.
26. Arimidex, Tamoxifen, Alone or in Combination Trialists' Group, Forbes JF, Cuzick J, Buzdar A, Howell A, Tobias JS, et al. Effect of anastrozole and tamoxifen as adjuvant treatment for early stage breast cancer: 100-month analysis of the ATAC trial. Lancet Oncol. 2008; 9:45-53.
27. Coombes RC, Kilburn LS, Snowdon CF, Paridaens R, Coleman RE, Jones SE, et al. Survival and safety of exemestane versus tamoxifen after 2-3 years' tamoxifen treatment (Intergroup Exemestane Study) a randomised controlled trial. Lancet. 2007;369:559–70.
28. John-Baptiste AA, Wu W, Rochon P, Anderson GM, Bell CMA. Systematic review and methodological evaluation of published cost-effectiveness analyses of aromatase inhibitors versus tamoxifen in early stage breast cancer. PLoS One. 2013;8(5):e62614. doi: 10.1371/journal.pone.0062614
29. Goldhirsch A, Ingle JN, Gelber RD, Coates AS, Thürlimann B, Senn H-J, et al. Expert on the primary therapy of early breast cancer. Ann Oncol. 2009;20:1319-29.
30. Goldhirsch A, Wood WC, Gelber RD, Coates AS, Thürlimann B, Senn HJ. Progress and promise: highlights of the international expert consensus on the primary therapy of early breast cancer 2007. Oxford J Med Annals Oncol. 2007;18(7):1133-44.
31. Makubate B, Donnan PT, Dewar JA, Thompson AM, McCowan C. Cohort study of adherence to adjuvant endocrine therapy, breast cancer recurrence and mortality. Br J Cancer. 2013;108(7):1515-24. doi: 10.1038/bjc.2013.116
32. Weaver KE, Camacho F, Hwang W, Anderson R, Kimmick G. Adherence to adjuvant hormonal therapy and its relationship to breast cancer recurrence and survival among low-income women. Am J Clin Oncol. 2013;36(2):181-7. doi: 10.1097/COC.0b013e3182436ec1
33. Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Portaria nº 1.008, de 30 de setembro de 2015. Aprova as diretrizes diagnósticas e terapêuticas do carcinoma de mama. Diário Oficial da República Federativa do Brasil, Poder Executivo, Brasília, DF, 01 de outubro de 2015. Seção 1, p.101. Available from http://bvsms.saude.gov.br/bvs/saudelegis/sas/2015/prt1008_30_09_2015.html Accessed on 17 January 2016.

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RESUMEN

Factores de la atención de salud asociados con la supervivencia de las mujeres con cáncer de mama que siguen hormonoterapia en Río de Janeiro, Brasil, 2004-2010

Objetivo. Conocer mejor la función que desempeña la atención de salud en la supervivencia del cáncer de mama, investigando los efectos que tienen el cumplimiento de la hormonoterapia y otras variables relativas a la atención de salud, ajustados según los factores clínicos y sociodemográficos, en una población de mujeres de la ciudad brasileña de Río de Janeiro.

Métodos. Estudio longitudinal realizado a partir de los datos secundarios de 5 861 mujeres tratadas con hormonoterapia (tamoxifeno o inhibidores de la aromatasa) en el Instituto Nacional del Cáncer del Brasil (INCA), desde el 1 de enero del 2004 hasta el 29 de octubre del 2010. Se combinaron para el análisis cuatro fuentes de datos: el sistema de dispensación al sector farmacéutico del INCA; el registro oncológico hospitalario; el sistema integrado hospitalario y el sistema absoluto del INCA; y el sistema de información sobre mortalidad. Los análisis exploraron los efectos del cumplimiento terapéutico de la hormonoterapia, de determinados aspectos de la atención a la enfermedad y de las variables sociodemográficas, conductuales y clínicas sobre el tiempo de supervivencia, con la metodología de Kaplan-Meier y los modelos de riesgos instantáneos proporcionales de Cox.

Resultados. La tasa de supervivencia general fue del 94% al año de iniciar la hormonoterapia y del 71% a los cinco años. El modelo de Cox indica que el riesgo de muerte es mayor para las mujeres fumadoras, para las que fueron hospitalizadas más veces, para las que se sometieron a más exploraciones y para las que solo toman un inhibidor de la aromatasa como hormonoterapia. El riesgo es menor para las mujeres con pareja (relación estable), con estudios secundarios o universitarios y con antecedentes familiares de cáncer, así como para las atendidas por un mastólogo, oncólogo o psicoterapeuta, para las intervenidas quirúrgicamente y para las que cumplieron la hormonoterapia.

Conclusiones. El estudio señala los subgrupos más vulnerables y los aspectos de la atención de salud que se corresponden con resultados más favorables, aportando datos nuevos para mejorar la asistencia dispensada a este grupo de mujeres.

Palabras clave Neoplasias de la mama; análisis de supervivencia; cooperación del paciente ; antineoplásicos; hormonas, usos terapéuticos; calidad de la atención de salud; salud de la mujer; Brasil.