

Mammography Coverage and Tumor Stage in the Opportunistic Screening Context

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Abstract

We assessed the effect of mammography screening in the context of opportunistic screening. There was an increase in screening coverage. The proportion of early stages increased during the same period.

Introduction: The increment of breast cancer screening coverage should lead to an increase in the proportion of early tumors diagnosed and the decrease of the cancer-related mortality. However, the effectiveness of opportunistic mammography screening is not well documented for public health systems in middle-income countries. **Patients and Methods:** We conducted an ecologic study to evaluate the association of mammography coverage with trends in breast cancer stage distribution. We used data from a total of 42,850 breast cancer patients, diagnosed between 2000 and 2016, combined with estimated mammography coverage from 3 surveys (2003, 2008, and 2013). **Results:** Biannual mammography coverage increased from 62.4% in 2003 to 73.9% in 2013. From 2000 to 2016, the proportion of in situ tumors increased 6.9%, the proportion of localized tumors increased 3.9%, the proportion of regional tumors decreased 6.9% and the frequency of distant tumors decreased 4% ($P < .00001$). **Conclusion:** Mammography coverage in the context of opportunistic breast cancer screening was associated with the increase of in situ and localized tumors and decrease of regional and distant tumors.

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Introduction

Worldwide, screening mammography is the most accepted strategy to reduce breast cancer mortality. Screening programs aim to detect small tumors and the World Health Organization claims it reduces breast cancer mortality by 25%.¹ However, we should also consider some aspects that limit the efficacy of the screening. Breast cancer treatment evolved after the clinical trials on mammography screening.²⁻⁴ Besides the time of progression, the biology of the tumor is also associated to the size at the time of diagnosis. Small tumors tend to be grade 1 and positive for hormonal receptors, whereas larger tumors tend to be grade 3 and negative for hormonal

receptors.⁵ In some countries, breast cancer screening is on the basis of an opportunistic strategy.⁶

The detection of indolent and subclinical tumors increases the disease incidence.⁷ This scenario is especially problematic in places with insufficient resources for treatment. Women with indolent tumors from more affluent areas overload the health system. However, women with larger and biologically unfavorable tumors have to wait longer for diagnosis and treatment.⁸ The idea of overdiagnosis is challenged by some authors on the basis of the annual percentage of change in breast cancer incidence of 1% to 1.3% per year since 1940.^{9,10}

The Brazilian Ministry of Health recommends biannual screening mammography for women aged 50 to 69 years. There have been several initiatives aiming to increase screening coverage,¹¹ but there is no organized population-based screening program in place. The screening is typically opportunistic. Mammography is ordered when the patient attends a primary care unity. However, the facilities for diagnosis and treatment are insufficient and poorly distributed. The goal of this study was to estimate the effect of mammography coverage on breast cancer stage in the context of opportunistic screening.

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Patients and Methods

Study Design

We performed an ecologic study to evaluate mammography coverage and tumor stage for women aged between 50 and 69 years, in São Paulo state, Brazil. An ecologic study focuses on the comparison of groups, rather than individuals.¹² Mammography coverage and outcomes (tumor stage shifting) were measured in distinct series of cases from the same population and their relation was examined.

Ethics Approval and Consent to Participate

The study was approved and the requirement of written informed consent was waived by the institutional review board of Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo (CAAE: 66233317.5.0000.5440). The study was performed in accordance with the Declaration of Helsinki.

Data Source

Data on mammography coverage were obtained from the Brazilian Geography Institute (IBGE). IBGE collects data on public health variables using surveys every 5 years. There are data sets publicly available for download for the years 2003, 2008, and 2013. The 2013 mammography coverage from the Health National Survey is available at <http://tabnet.datasus.gov.br/cgi/tabcgi.exe?pnspnskb.def>. For 2003 and 2008 there is no consolidated table on mammography coverage, but the information can be extracted from the supplements of National Housing Sample Surveys. The raw data for 2003 can be downloaded from ftp://ftp.ibge.gov.br/Trabalho_e_Rendimento/Pesquisa_Nacional_por_Amostra_de_Domicilios_anual/microdados/reponderacao_2001_2009/PNAD_reponderado_2003.zip, and for 2008 from ftp://ftp.ibge.gov.br/Trabalho_e_Rendimento/Pesquisa_Nacional_por_Amostra_de_Domicilios_anual/microdados/reponderacao_2001_2009/PNAD_reponderado_2008.zip.

Demographic, baseline, and survival data for individual patients were obtained from the Registro Hospitalar de Câncer (RHC)/Fundação Oncocentro de São Paulo (FOSP). In the RHC/FOSP, there are recorded data of cancer patients from São Paulo state since 2000. Currently, the registry receives data from 77 institutions. The data are updated every 3 months.¹³

Mammography Coverage

All 3 surveys conducted by IBGE in 2003, 2008, and 2013 contained specific questions about the last time the women received mammography. For 2003, the options were: less than 1 year, between 1 and 2 years, 3 or more years, or never; for 2008 and 2013, the options were: less than 1 year, between 1 and 2 years, between 2 and 3 years, more than 3 years, or never. To account for the differences among the surveys, the answers were coded as: (1) never had been submitted to mammography; (2) submitted to mammography during the past 2 years before the survey; (3) submitted to mammography more than 2 years before the survey.

For the 2013 survey, the percentage of women aged between 50 and 69 years living in São Paulo state, who were submitted to mammography during the past 2 years and the percentage of those who never had mammography were available from the published summary tables. For 2003 and 2008, because equivalent results

were not available from summary tables, raw data were downloaded, and a script (Supplemental Appendix 1) applied to extract the needed information.

The question in the survey was designed to convey a screening mammography. However, because in São Paulo State the screening is opportunistic, it is not possible to exclude that some women were symptomatic at the time of mammography.

Patient Selection

A file containing the data of patients with breast cancer from São Paulo state was provided by FOSP. The patients were included in the registry from January 2000 to December 2016. For the analysis of trends in the stage, we selected all women with age between 50 and 69 years. We excluded lobular in situ tumors, Paget disease, nonepithelial breast tumors (eg, phyllodes tumor, sarcoma), metastatic carcinomas, and patients with missing stage.

Variables

Terms, definitions, and staging system for cases recorded in the RHC/FOSP varied throughout the years; therefore, the variables were harmonized. The variables selected from the database for the analysis were: date of birth, stage, histology, and date of diagnosis. Age was calculated in years at the date of the patient's first appointment. The stage was provided according to the Tumor, Node, Metastases (TNM) fifth edition from 2000 to 2005, according to the TNM sixth edition from 2006 to 2013, and according to the TNM seventh edition from 2014 to 2016. To maintain the uniformity, the stage of the tumor was coded according to TNM sixth edition for the entire data set. Patients were classified according to the summary stage in 4 groups: in situ, localized (stage I-IIA), regional (stage IIB-IIIC), and distant (stage IV). Patients were also grouped according to histology: in situ, ductal invasive, lobular invasive, mixed ductal, and lobular carcinomas, special type carcinoma, and unclassified carcinoma.

Statistical Analysis

Data manipulation and statistical analysis were carried out using RStudio (Rstudio: Integrated Development for R; RStudio, Inc, Boston, MA [<http://www.rstudio.com>]).

Time series graphical analyses were used to evaluate summary stage trends from 2000 to 2016. First, the total of cases was grouped according to months and the proportion of each summary stage calculated. After a time series object was generated for each stage, the seasonal and random components were extracted, and finally, the trend component was plotted for visual analysis.

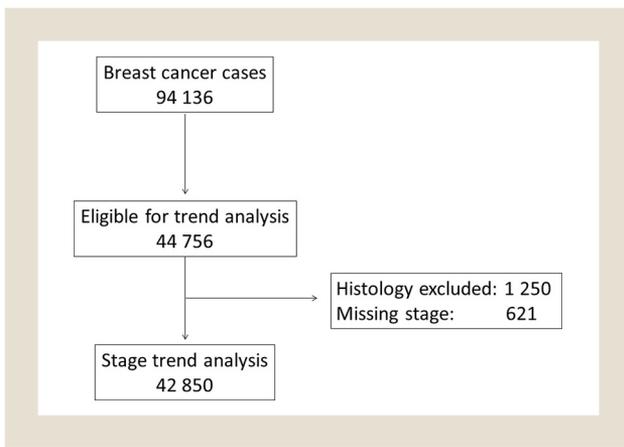
Results

Mammographic Coverage for Women Aged Between 50 and 69 Years

There was a substantial increase in mammography coverage from 2003 to 2013. The proportion of women who responded never had been submitted to mammography were 28% in 2003, 13.4% in 2008, and 9.2% in 2013, a decrease of 18.8% in 10 years. The proportion of women submitted to mammography during the past 2 years before the survey were 62.4% in 2003, 69.1% in 2008, and 73.9% in 2013, an increase of 10.5%. The proportion of women

Mammography Coverage and Breast Cancer Stage

Figure 1 Flow of Patients Through Trends and Survival Analysis



submitted to mammography more than 2 years before the survey were 9.6% in 2003, 17.5% in 2008, and 16.9% in 2013.

Breast Cancer Cases

In Figure 1 the cases selected for the stage shifting are shown. In the data set from FOSP, there were 94,136 cases of female breast cancer. Among them, 44,756 were between 50 and 69 years old at diagnosis. Baseline characteristics of women diagnosed with breast cancer aged between 50 and 69 years are shown in Table 1. From this group 42,850 were included in the stage shifting analysis, 1285 were not eligible on the basis of histology, and 621 because of missing stage.

Stage Distribution and Stage-Specific Frequency

The shift in breast tumor stage from 2000 to 2016 is shown in Figure 2. There was a steady increase in the proportion of in situ tumors during the period, the frequency of localized tumors increased during the first 5 years of the period; however, the frequency of advanced stages presented a less consistent decrease.

There was a significant change in the stage distribution from 2000 to 2016 ($\chi^2 = 61.43$; $P < .00001$). The frequency of women diagnosed with in situ tumors was 4.4% (72/1623) in 2000 and the proportion increased to 11.3% (120/1059) in 2016. The frequency of women with localized tumors was 41.5% (673/1623) in 2000, the proportion increased to 47.6% (1104/2320) in 2006, and in 2016 they were 45.4% (481/1059). The frequency of women with regional tumors was 40.8 in 2000 (662/1623), the proportion decreased to 37.5% in 2006 (862/2320), and in 2016 they were 33.9% (359/1059). The frequency of women with distant tumors was 13.3% in 2000 (216/1623), the proportion decreased to 6.5% in 2004 (150/2312), and in 2016 were 9.3% (99/1059).

Discussion

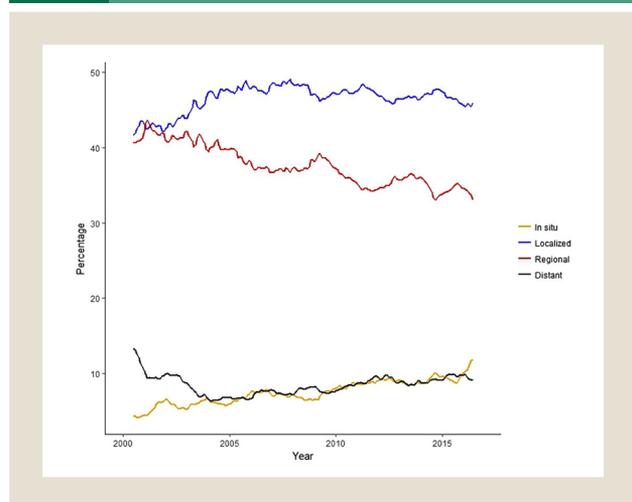
From 2003 to 2013, the biannual mammography coverage increased by 10.5%. From 2000 to 2016, the proportions of in situ and localized tumors increased 6.9% and 3.9%, respectively. During the same period, the proportions of regional tumors and distant tumors decreased by 7.1% and 4%, respectively.

Table 1 Baseline Characteristics of Women Aged Between 50 and 69 Years, Diagnosed With Breast Cancer in São Paulo State From 2000 to 2016

Variable	Overall
Number of Cases	44,746
Mean Age (SD), Years	59.17 (5.66)
Histology, n (%)	
Ductal in situ	3263 (7.3)
Ductal invasive	33,314 (74.5)
Lobular invasive	2537 (5.7)
Mixed invasive	1156 (2.6)
Nonclassified carcinoma	1844 (4.1)
Special type carcinoma	1357 (3.0)
Excluded histology	1275 (2.8)
Stage, n (%)	
Is	3492 (7.8)
I	10,143 (22.7)
IIA	10,270 (23.0)
IIB	5613 (12.5)
IIIA	4884 (10.9)
IIIB	4594 (10.3)
IIIC	1104 (2.5)
IV	3692 (8.3)
Missing	954 (2.1)
Treatment, n (%)	
Surgery	35,771 (79.9)
Radiotherapy	24,629 (55.0)
Hormone therapy	23,708 (53.0)
Chemotherapy	29,629 (66.2)

The estimated mammography coverage in Sao Paulo state in 2013 (74%) is very similar to the rates in Western countries.¹⁴ In Brazil, breast cancer screening is opportunistic. Women are not

Figure 2 Trends in Breast Cancer Stages According to Year of Diagnosis in São Paulo State for Women Aged Between 50 and 69 Years



formally invited to attend a screening program. However, breast cancer awareness campaigns seem to be effective in achieving good mammography coverage. Our study assessed a relatively small difference in screening coverage (11.5%). A difference in compliance of 80%, like that observed in clinical trials,² would be associated with 30% of the decrease in breast cancer deaths (eg, 80%/11.5% × 4.5% = 31.3%). Because of the study design, it is possible that a small proportion of mammography were performed in symptomatic women. However, this proportion is likely to be similar in all 3 surveys. Therefore, our data support the use of mammography screening even in the opportunistic context.

The proportions of regional and distant tumors were very high in our series. Regional and distant tumors comprised 43% of all tumors. Stage III and IV tumors were 17.4% in the Surveillance, Epidemiology, and End Results data,¹⁵ less than half of the proportion observed in our study. Although many other factors related to diagnosis and treatment delay are related to advanced stage and mortality, our data might suggest that opportunistic screening is less effective than organized population screening.

The main strength of our work was the data collected from a large population living in a well defined area. Most of the published data on opportunistic screening are extrapolated data from small regions. Sao Paulo is inhabited by 44 million people, and opportunistic screening is in place all over the state. RHC/FOSP includes women from all regions of Sao Paulo state. Because of the study design, our results cannot be applied at the patient level. This is a typical limitation of ecologic studies.¹⁶

Conclusion

Mammography screening is associated with an increase in the frequency of early stage breast cancer in opportunistic scenarios.

Clinical Practice Points

- The increase of breast cancer screening coverage should lead to an increase in the proportion of early tumors diagnosed and the decrease of cancer-related mortality.
- We conducted an ecologic study to evaluate the association of mammography coverage with trends in breast cancer stage distribution.
- Mammography coverage in a context of opportunistic breast cancer screening was associated with an increase in detection of in situ and localized tumors and decrease in detection of regional and distant tumors.
- Our data might suggest that opportunistic screening is less effective than organized population screening.

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Disclosure

The authors have stated that they have no conflicts of interest.

Supplemental Data

Supplemental appendix accompanying this article can be found in the online version at <https://doi.org/10.1016/j.clbc.2019.04.014>.

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