Original Article Open Access

Archives Of Breast Cancer

DOI: 10.32768/abc.2024112172-182

Evaluation of the Possible Benefits of Breast Cancer Screening in Women Aged 40 to 49 Years in the Steel Valley Region, Brazil

Cátia Cilene Aires Lima[a,b], Carla Daruich de Souza*[b]

[a]*Márcio Cunha Hospital, 41 Kiyoshi Tsunawaki Avenue, Ipatinga, Minas Gerias, Brazil*

[b]*Nuclear and Energy Research Institute, 2242 Prof. Lineu Prestes Avenue, São Paulo, Brazil*

ARTICLE INFO

Received:
15 November 2023
Revised:
3 February 2024
Accepted:
4 February 2024

Keywords:
Mammography, Breast cancer, screening, Prospective studies, Medical records, analysis

ABSTRACT

Background: This study investigates the effectiveness of mammographic screening for women aged 40 to 49 in Brazil's Steel Valley Region. Despite a Ministry of Health recommendation to start screenings at 50, 25% of breast cancer cases occur in the 40-49 age group.

Methods: The retrospective analysis, spanning 2008-2019 at Marcio Cunha Hospital, compared two groups: cancer diagnosed via screening mammography (277) and diagnostic mammography (229).

Results: The results showed delayed diagnoses for non-screened women, with a 4.16 times higher mortality rate. Screening facilitated earlier detection of less malignant cancers (85.9% vs. 43.7%). Women diagnosed through screening were more likely to preserve their breasts (28.9% vs. 55.5% for Radical Breast Surgery and 71.1% vs. 28.9% for Breast-Sparing Surgery), and fewer axillary lymphadenectomies were performed. All statistical tests performed returned a P-value lower than 0.05, showing high statistical significance.

Conclusion: The findings support extending screening mammography access to all women over 40 in the Steel Valley region and underscore the need for broader-scale research in other areas. Recommendations include enhancing public awareness and establishing a breast cancer surveillance service.

INTRODUCTION

The commencement age for breast screening lacks a consensus. Historically, in the United States, most medical societies advocated initiating breast cancer screening at age 40 for women with moderate risk. However, since 2009, controversies have emerged, driven by the U.S. Preventive Services Task Force (USPSTF), which revised its guidelines. The USPSTF now suggests, for women with moderate risk, screening between the ages of 50 and 74, every two years. This recommendation is also endorsed by the American College of Physicians (ACP).[1,2]

***Address for correspondence:**
Carla Daruich de Souza, PhD,
Nuclear and Energy Research Institute, 2242 Prof. Lineu Prestes Avenue, São Paulo, Brazil; ZIP: 05508-000
Tel: +551128105000
Email: cdsouza@ipen.br, carladdsouza@yahoo.com.br

The American College of Obstetricians and Gynecologists (ACOG), American College of Radiologists (ACR), and the US National Comprehensive Cancer Network (NCCN) recommend screening mammography starting at age 40 and at annual intervals. The American Cancer Society recommends starting at age 45 with an annual interval (between 40 and 44 years to discuss risk and benefit). In Europe, the European Society of Breast Imaging (EUSOBI) recommends screening from the age of 50 with a bi-annual interval.[3]

In Brazil, the Ministry of Health, in collaboration with the National Cancer Institute (INCA), advises women with moderate risk to undergo mammography every two years between the ages of 50 and 69. Conversely, the Brazilian Society of Radiologists (SBR), the Brazilian Federation of Gynecologists and

Obstetricians (FEBRASGO), and the Brazilian Society of Mastologists (SBM) recommend that women at moderate risk have an annual mammogram between the ages of 40 and 74. After reaching 74, it is suggested to evaluate the woman's life expectancy, considering underlying health conditions.[4]

The Brazilian AMAZONA III study (GBECAM 0115) was a prospective cohort study developed among 23 Brazilian states including women diagnosed with breast cancer between January 2016 and March 2018. A total of 2950 women were included in the study and the mean age at breast cancer was 53.9 years. They reported that approximately 20% of women had breast cancer under the age of 45, compared with 12% in countries with higher per capita income. The main hypothesis is that the higher prevalence of breast cancer among younger women in Brazil (and other Latin American countries) may be related to a proportionately younger population compared to richer countries. However, this finding may be due to risk factors (incorporation of habits of urban life, lower income parity, sedentary lifestyle, obesity, late age of the first child compared to previous generations) and a higher prevalence of subtypes with a more reserved prognosis.[5] This result can imply that guidelines would be more accurate if derived from local studies and not copied from other nations.

Mammography is a powerful tool in diagnosing breast cancer. According to Berry[6], it is the greatest method to detect breast cancer early on, when it is most treatable. Breast cancer can be found with a mammogram even before symptoms appear even at a non-palpable state. Despite that, the recommendation for increasing the use of radiation in diagnosis is not trivial, since its use in medicine must, according to the principles of radiation protection, be justified. That is, there must be a direct benefit that justifies the possible detriment that radiation can cause[7]. Research that verifies the need to change the screening age is extremely important and can lead to change in public policies.

The aim of the present study is to evaluate the benefits of screening mammography in women aged between 40 and 49 years, in the Steel Valley Region located in the southeast region of Brazil.

METHODS

Study Population

The project was submitted to the Research Ethics Committee of Marcio Cunha Hospital, through the National on-line ethics platform “Plataforma Brasil”, and was approved on January 10, 2020. After approval, a search was performed on medical records (all electronic) of patients diagnosed with breast cancer between 40 and 49 years old, between 2008 and 2019.

Marcio Cunha Hospital is a philanthropic institution that provides services for the Public Unified Health System (SUS), Private Health Care Plans, and individuals in general. It is a hospital located in the Brazilian municipality of Ipatinga, Brazil with 530 beds, serving an average of more than 1 million people annually. It is a reference service for cancer treatment in the Steel Valley region.[8]

The Steel Valley Metropolitan Region (RMVA) is located in the interior of the state of Minas Gerais, in the Southeast Region of Brazil. The region receives its name due to the influence of the steel industry. It is composed by the cities of Coronel Fabriciano, Ipatinga, Santana do Paraíso, Timóteo, and a metropolitan collar consisting of 24 other municipalities. The population is estimated at around 500,000 inhabitants.[9] According to the Brazilian Institute of Geography and Statistics (IBGE- 2023 census), 50.3% of people self-declare as brown (mix in any proportion of indigenous, white, and/or black), 37.4% as white, 12.1% as black and 0,3% as Asian.

Inclusion criteria

In the period 2008 and 2019, Marcio Cunha Hospital treated 2602 women with breast carcinoma. Of these, 603 were aged between 40 and 49 years, that is, 23% of the cases.

All medical records of women diagnosed with breast cancer between 40 and 49 years of age were evaluated. However, 97 of them were excluded due to lack of information or medical records not found (incorrect record number). The limited availability of information in certain medical records resulted from cases where patients exclusively received radiotherapy at the institution and subsequently continued their treatment elsewhere. In such instances, the essential data were not consistently documented. Additionally, some patients initiated their care at Marcio Cunha Hospital but transitioned to another healthcare facility. Moreover, a number of medical records contained incomplete entries related to the specific data of interest in this survey. Consequently, these incomplete records were excluded, resulting in a final cohort of 506 patients.

From the retrospective search of data in electronic medical records and excluding those with insufficient information, 229 patients underwent diagnostic mammography and 277 underwent screening mammography. In all cases, the diagnosis was confirmed from the anatomopathological study (histology).

From the review of medical records, two study groups were established:

- Women between 40 and 49 years old, asymptomatic, diagnosed with breast cancer obtained through mammographic screening. The screening was prescribed by the physician for several reasons such as having previous breast and/or ovary cancer in the family history;
- Women between 40 and 49 years old, symptomatic, diagnosed with breast cancer, without previous screening or with an interval between mammograms greater than 12 months. If interval cancers were found, they would be placed in this group;

Diagnostic procedure

These two groups were evaluated according to the following criteria:

- Disease Staging at Diagnosis:
  - Tumors classification using the eighth edition of the American Joint Commission on Cancer (AJCC) TNM classification.[10]
  - Presence of Stage IV Diagnosis (Systemic Disease);
  - Differences in Early (0-I-II) and Late Stages (III-IV);
- Surgical Approach to the Breast: comparison between breast-conserving vs. surgery and total mastectomy;
- Axillary Surgical Approach: comparison between axillary lymphadenectomy vs. sentinel lymph node biopsy;
- Type of Chemotherapy:
  - Use of Neoadjuvant Chemotherapy: performed before surgery for locally advanced cases (late diagnosis);
  - Use of Palliative Chemotherapy: applied for cases with distant metastasis (late diagnosis);
- Relationship Between Molecular Subtype and TNM Stage: Luminal tumors are categorized into two subtypes, luminal A and luminal B, through an assessment of hormone receptors and Ki-67 levels. In cases where Ki-67 data is unavailable, consideration is given to the histological differentiation of the tumor. Specifically, tumors exhibiting well-differentiated characteristics (histological grade I) with positive hormone receptors are classified as luminal A, while those displaying a lower degree of differentiation (histological grade III) are categorized as luminal B. Moderately differentiated tumors (histological grade II) fall into the luminal subtype as well;
- Percentage of Women Who Died: Comparison of the mortality rate.

Statistical Analysis

We utilized frequency and percentage measures to present findings for qualitative variables, while for normally distributed quantitative variables, we reported the mean along with its standard deviation. In instances where normal distribution was not observed, we employed the median and interquartile range to provide a comprehensive summary. The t-test was employed to assess whether there were statistically significant differences in age based on the presence or absence of screening.

Shapiro–Wilk test was used to check the normal distribution of quantitative variables. The Chi-square test was employed to evaluate the associations between screening and the number of deaths, cancer stage, type of surgery, type of chemotherapy (CT), and the surgical approach to the axilla.

Multivariate analysis technique (MANCOVA) was performed using Pillai's Trace and Wilks's Lambda. The analysis of this work was performed using the SPSS statistical software (Statistical Package for the Social Sciences) version 25. All the analyses were conducted at a significance level of 5%.

RESULTS

From the retrospective search of data in medical records and excluding those with insufficient information, 229 patients underwent diagnostic mammography and 277 underwent screening mammography. The mean general age was 45 years.

In the women submitted to and not submitted to screening, there is a small difference: 44.85 years for screened women and 45.41 years for non-screened women (Table 1). T-test resulted in P=0.037 meaning that the two groups are statistically different.

Table 1. Age distribution in relation to screening with average and deviation.

Screening	N	Age			Deviation
		Min	Max	Average	
No	229	40.0	49.0	44.85	3.20
Yes	277	40.0	49.0	45.41	3.04

Of the 506 patients diagnosed with breast cancer, 6 had bilateral synchronous breast cancer at diagnosis; 3 cases among the unscreened ones and 3 among the screened ones. The remainder had unilateral breast carcinoma at diagnosis. There were 13 cases of interval cancer patients. They were included in the group of screened patients.

Table 2 provides a comprehensive summary of the results obtained in this study. Degree of freedom was equal to 1 for all variables.

Table 2. Evaluating the association between early screening and the treatment approach.

Variable		Screening			Chi-square test result
		No	Yes	Total	
Deaths, N (%)	No	151 (65.9%)	257 (92.8%)	408 (80.6%)	57.8
	Yes	78 (34.1%)	20 (7.2%)	98 (19.4%)	
Stage, N (%)	0-II	100 (43.7%)	238 (85.9%)	338 (66.8%)	100
	III-IV	129 (56.3%)	39 (14.1%)	168 (33.2%)	
Surgical approach to the breast, N (%)	Radical	101 (55.5%)	79 (28.9%)	180 (39.6%)	32.2
	Breast-Sparing	81 (44.5%)	194 (71.1%)	275 (60.4%)	
Surgical approach to the axilla, N (%)	Sentinel Lymph Node Biopsy	41 (23.6%)	130 (55.6%)	171 (41.9%)	41.9
	Axillary Lymphadenectomy	133 (76.4%)	104 (44.4%)	237 (58.1%)	
Neoadjuvant CT, N (%)	No	155 (67.7%)	250 (90.6%)	405 (80.2%)	41.3
	Yes	74 (32.3%)	26 (9.4%)	100 (19.8%)	
Palliative chemotherapy	No	179 (78.2%)	272 (98.2%)	451 (89.1%)	51.9
	Yes	50 (21.8%)	5 (1.8%)	55 (10.9%)	

Among these patients, 102 deaths were recorded. One of the patients was undergoing chemotherapy and had sepsis as the main cause of death. Two others died due to a second primary tumor - anaplastic astrocytoma and gastric carcinoma. Another patient died due to cardiovascular problems. The remaining 98 patients died due to metastases caused by breast cancer. Of these, 20 belonged to the screened group and the other 78 patients belonged to the unscreened group. Among the unscreened patients, 48 had a stage IV diagnosis at the first visit. Among the patients screened, at the first consultation only 4 were diagnosed at the same stage. In contrast, among the screened patients, 49 were diagnosed at stage 0. Among the unscreened patients, only 6 were diagnosed at this stage. There is an association between screening and disease stage at diagnosis (P<0.000). Most patients (85.9%) who underwent screening had an early stage, while those that were not screened, the initial stage was found in only 43.7%.

There is an association between screening and type of surgery (P<0.000). Mastectomy had a higher percentage among those who did not undergo screening, i.e., 55.5%. Among those who underwent screening, only 28.9% underwent complete breast removal. Amid the unscreened patients, in 3 cases there was no description of the surgical approach to the breast, 4 underwent hygienic mastectomy due to an ulcerated and bleeding tumor, and 44 patients did not have their breasts surgically treated due to the presence of metastatic disease and, therefore, without any benefit from surgical treatment. Regarding the patients screened, in 4 cases there was no description of the surgical approach to the breast.

About the surgical approach to the axilla, two groups were divided into screened and unscreened patients: sentinel lymphnode biopsy (less extensive surgery) x axillary lymphadenectomy (more extensive surgery). There is an association between screening and type of surgery (P<0.000). Axillary lymphadenectomy had a higher percentage among those who did not undergo screening, 76.4%. Among those who underwent screening, 44.4% underwent axillary lymphadenectomy and the remainder underwent sentinel lymph node biopsy.

Among the unscreened group, in 48 patients there was no surgical approach to the breast because it was a disease with distant metastasis. In 7 cases, there was no description of the surgical approach to the axilla.

In the screened group, 43 patients had no surgical approach to the axilla due to a ductal carcinoma in situ, whose surgical approach was restricted to breast-conserving surgery (quadrantectomy or segmentectomy).

Regarding systemic treatment, through intravenous chemotherapy, the application of neoadjuvant and palliative chemotherapy was evaluated (at initial diagnosis) between the two groups (screened vs. unscreened). Neoadjuvant chemotherapy is commonly used in patients with advanced stages of the disease, when the tumor is unresectable or is large enough to make the surgical procedure difficult. In addition to the proposed systemic treatment, it also aims at tumor reduction. Palliative chemotherapy is used in stage IV patients with no curative proposal because these are patients with distant metastasis. Therefore, in both cases, neoadjuvant and palliative chemotherapy are used in patients with advanced disease. There is an association between neoadjuvant chemotherapy and screening (P<0.000) as 32.3% of unscreened patients and 9.4% of screened patients underwent neoadjuvant chemotherapy. An association between palliative chemotherapy and screening was also observed (P<0.000). Among unscreened patients, 21.8% underwent palliative chemotherapy at the initial diagnosis, while only 1.8% of screened patients received palliative chemotherapy.

In the elaboration of this work, we sought to answer whether screening mammography is capable of diagnosing invasive breast carcinomas in early stages (I and II), even among the most aggressive molecular subtypes. And it was seen that there is a favorable association between stage and screening for all molecular subtypes except Luminal B/HER-2 positive (P<0.244), as shown in Table 3. As an example, for triple negative tumors (TN) only 30.6% of women who did not undergo screening have an initial stage and, among those who underwent mammography screening, 78.1% of women are diagnosed at an initial stage.

Table 3. Relationship between molecular subtype, stage, and screening.

		Screening			
	Stage	No	Yes	Total	p* value
Luminal A	Initial (I-II)	17 (53.1 %)	63 (94 %)	80 (80.8 %)	0.000
	Late (III-IV)	15 (46.9 %)	4 (6 %)	19 (19.2 %)	
Luminal B	Initial (I-II)	35 (50.7 %)	51 (82.3 %)	86 (65.6 %)	0.000
	Late (III-IV)	34 (49.3 %)	11 (17.7 %)	45 (34.4 %)	
Luminal B/ HER 2 positive	Initial (I-II)	16 (59.3 %)	14 (73.7 %)	30 (65.2 %)	0.244
	Late (III-IV)	11 (40.7 %)	5 (26.3 %)	16 (34.8 %)	
HER 2 positive	Initial (I-II)	1 (7.7 %)	8 (57.1 %)	9 (33.3 %)	0.009
	Late (III-IV)	12 (92.3 %)	6 (42.9 %)	18 (66.7 %)	
TN	Initial (I-II)	11 (30.6 %)	25 (78.1 %)	36 (52.9 %)	0.000
	Late (III-IV)	25 (69.4 %)	7 (21.9 %)	32 (47.1 %)	

*Stage 0 was excluded- carcinoma in situ.

The distribution of invasive tumors, according to molecular subtype, among the patients screened was: 34.5% => luminal A; 32 %=> luminal B; 9.8% =>Luminal B/HER 2 positive; 7.2 %=> HER 2 positive and 16.5 %=> triple negative. Among unscreened patients, the distribution of invasive tumors according to molecular subtype was: 18 % => luminal A; 39 %=> luminal B; 15% =>luminal B/HER 2 positive; 7.3 %=> HER 2 positive and 20 %=> triple negative. Among the screened and unscreened patients, there were, respectively, 34 and 46 cases of patients with invasive tumors and incomplete immunohistochemistry records.

As of the latest medical update examined, it was found that seven patients who had not undergone screening were diagnosed with distant metastases. Among them, six exhibited bone metastases, while one showed evidence of lung metastasis. Of the patients screened, 7 also had distant metastasis (bone, lung, liver, bone, contralateral axilla). All of these were under palliative control.

During follow-up, twelve patients had a second primary breast tumor and seven had primary cancer at other sites: lung cancer (1), colon cancer (1), acute myeloid leukemia (1), anaplastic astrocytoma (1), ovary (2), stomach (1).

Multivariate analysis resulted in P<0.001 for both Pillai's Trace (0.224 value) and Wilks's Lambda (0.776 value). This confirms that all the variables have strong statistical relationships with the presence of screening. In the correlation matrix, the P-value showed a correlation between:

- Cancer stage and deaths (p<0.001), Cancer stage and both surgical approaches (p<0.002, for breast and axilla), and cancer stage and type of chemotherapy (p<0.002, for palliative and neoadjuvant);
- Type of surgery and deaths (p<0.002, for breast and axilla), and type of surgery and type of chemotherapy (p<0.001, for palliative and neoadjuvant).

DISCUSSION

In our investigation, among the 506 cases of women aged between 40 and 49 with breast cancer, 98 individuals succumbed to the disease, accounting for 19.3% mortality between 2008 and 2019. However, mortality among the unscreened group was 5 times higher compared to the screened group. Among unscreened patients, 34.1% died and among screened patients, the percentage of death during the same period was 7.2%. The Multivariate analysis proved a strong correlation between cancer stage and deaths (P<0.001) and type of surgery and deaths (P<0.002) for both the breast and axilla approaches.

This result is in agreement with a retrospective study carried out in Boston, United States. Women with invasive breast cancer diagnosed between 1990 and 1999 were followed until 2007 or until death. Two groups were compared: women diagnosed by mammographic screening versus diagnostic mammography. A total of 7301 women were followed up and, during this period, there were 609 deaths from invasive breast carcinoma. Overall, 29% of deaths occurred among screened women, while 71% of deaths occurred among unscreened patients.[11]

Our study has limitations because it is a retrospective observational study with insufficient follow-up time to assess the reduction in mortality among the patients screened. Furthermore, it is not possible, based on these data and during this period, to state whether or not there was an increase in the mortality rate from breast cancer. Despite this, the aforementioned finding regarding mortality between the two groups reveals that the lack of access or lack of information related to preventive exams has an important impact on mortality, in a short period of time, and this is due to diagnosis delays among unscreened patients.

In our study, between 2008 and 2019, 23% of breast cancers were diagnosed in women between 40 and 49 years old. Therefore, the incidence of this disease in this age group was higher than that found in developed countries. This finding is in accordance with the Brazilian AMAZONA III study (GBECAM 0115). A total of 2950 women were included in the study and the mean age at breast cancer was 53.9 years. This is approximately 10 years younger than women in the US or other developed countries.[5]

In the elaboration of this work, stages 0, I and II were grouped and considered early and stages III and IV grouped as late. There was an association between screening and disease stage at diagnosis (P<0.000). Most patients (85.9%) who underwent screening were diagnosed at an early stage while among those not screened, the initial stage was found in only 43.7%. Therefore, screening has the benefit of diagnosing breast cancers at earlier stages. There was also a strong correlation between cancer stage and both surgical approaches (P<0.002, for breast and axilla), and cancer stage and type of chemotherapy (P<0.002, for palliative and neoadjuvant) calculated by multivariate statistical analysis.

Our study revealed that the distribution of invasive breast carcinomas, according to molecular subtypes, among the screened patients was: 34.5% for luminal A; 32% for luminal B; 9.8% for luminal B/HER 2 positive; 7.2% for HER 2 positive and 16.5% for triple negative tumors. Among unscreened patients, the distribution of invasive tumors according to molecular subtype was: 18% for luminal A; 39% for luminal B; 15% for luminal B/HER 2 positive; 7.3% for HER 2 positive and 20% for triple negative tumors.

In the AMAZONA study, the prevalence of triple negative tumors was 21%. The incidence was higher in the North and Northeast regions, where there is a higher proportion of Afro-descendants.[12] In our study, the incidence of triple negative tumors was similar to that found in the AMAZONA investigation, especially among the group of unscreened patients.

Among the patients screened in our study, there was a higher incidence of luminal A tumors compared to unscreened patients, 34.5% and 18%, respectively. This is due to the fact that luminal A tumors are less aggressive compared to others, with slower growth, and greater diagnostic opportunity through mammographic screening. However, the incidence of luminal A tumors in both groups is well below the incidence found in developed countries and even below the findings in the AMAZONA study (most common subtype was luminal A, with a prevalence of 49%). In Switzerland, Spitale *et al.* recorded a proportion of 73% for luminal A.[12]

Considering that luminal A tumors have a better prognosis and represented a very small proportion in the two groups analyzed, most patients in our study had tumors of more aggressive molecular subtypes. This is very relevant data, including for public health, as the postponement of breast cancer screening in a population group where there is a predominance of more aggressive subtypes leads to later diagnoses and short prognosis. The study showed that mortality was

5 times higher among unscreened women during the data collection period (2008-2019). This fact was due to the later diagnosis of breast cancer in the unscreened group.

We also aimed to investigate the efficacy of screening mammography in detecting early-stage invasive tumors (Stage I and II), even within the context of the most biologically aggressive molecular subtypes. In this analysis, carcinoma in situ (Stage 0) was excluded. A positive correlation between the screening and the tumor stage was observed across all molecular subtypes, except for Luminal B/HER2 positive (P<0.244). For the remaining molecular subtypes, a significant association was found between women who underwent screening and a higher likelihood of being diagnosed at an early stage (I and II) (P<0.000). A notable example is the triple-negative tumor subtype, where 78.1% of those screened were diagnosed at an early stage, in contrast to 30.6% among unscreened women.

When screening is omitted, even among patients with less aggressive tumors (luminal A), the delay in diagnosis also implies more advanced tumors, as demonstrated in our study. Among patients with luminal A tumors who were not screened, 46% were diagnosed at stage III and IV. Therefore, the absence of screening leads to late diagnoses and, therefore, lower chances of cure in any molecular subtype.

The findings of our study are in accordance with the results of other published studies. Although screening primarily detects slow-growing, hormone receptor positive and HER 2 negative cancers, the findings also indicate that a substantial proportion of HER 2 positive and triple negative breast cancers can be detected by screening. HER 2 positive and triple negative cancers detected at screening were diagnosed at an earlier stage and the prognosis was much better than those detected by symptoms.[13,14]

Among the unscreened patients, 48 had a stage IV diagnosis while among the screened patients, 4 patients were diagnosed at the same stage. Therefore, among the unscreened group, 12 times more women did not have a curative treatment proposal at diagnosis. In contrast, among the screened patients, 49 were diagnosed at stage 0 (ductal carcinoma in situ) and among the unscreened patients, only 6 were diagnosed at this stage. Therefore, there were 8 times more diagnoses of ductal carcinoma in situ among screened patients.

In the 1980s, randomized trials demonstrated that most women with stage I and II breast cancer (absence of multicentricity or diffuse microcalcifications and adequate tumor/breast ratio) are eligible for breast-sparing surgery. In the south-east region of the Netherlands, between 1990-1998, 4788 women were diagnosed with invasive breast tumors, with 2341 cases occurring between 50-69 years. In this age group, 68% of the patients had their breasts preserved compared to 54% among unscreened women.[15] An analysis of six cancer registries made it possible to compare data before and after the introduction of the national screening program in Bavaria in 2006. Cancers were detected at an earlier stage after the introduction of mammography screening, resulting in a lower rate of total mastectomies (32.6% in 2000 vs 19.6% in 2008), a higher rate of radiotherapy (59.7% vs 66.6%) in parallel with an increase in conservative surgeries and a lower rate of chemotherapy (20.4% vs 13.1 %) [16, 17] Using the Multidisciplinary Breast Service Database at Royal Perth Hospital, Australia, the medical records of women treated for breast cancer between January 2000 and August 2002 were reviewed. Of all patients undergoing surgery for breast cancer, 58 % in the screening group and 36% in the non-screening group had breast-conserving surgery (P<0.0001).[18]

One of the disadvantages for screening mammography is overdiagnosis, mainly related to the diagnosis of ductal carcinoma in situ. It was observed that among screened women much more diagnoses of ductal carcinoma in situ were made compared to the group of unscreened women. However, science is unable to differentiate lesions that can remain indolent from those that can progress and cause harm to the patient.[19]

Screening is likely to be associated with the detection of some cancers that might not become apparent during a woman's lifetime. However, the absence of screening is associated with excess mortality. Given the uncertainty about the overdiagnosis estimate, probably less than 10%, the American College of Radiology considers screening to be beneficial.[20]

In addition, overdiagnosis is more likely to affect older women because of differences in life expectancy. Finally, neither early initiation of screening nor annual versus biannual screening will increase the frequency of overdiagnosis because the cancer would simply be detected at the next routine screening test.[19,21] Our results showed that screening increases the possibility of diagnoses at earlier stages, even among tumors with a more aggressive biological behavior. And this leads to other benefits such as less crippling and costly treatments.

Our study revealed a significant association between screening and the type of breast surgery performed (P<0.000). Mastectomy had a higher percentage among those who did not undergo screening, 55.5%. Among those who underwent screening, only 28.9% underwent complete breast removal. Regarding the axillary approach, there is also an association between screening and type of

surgery (P<0.000). Axillary lymphadenectomy had a higher percentage among those who did not undergo screening, i.e., 76.4%. Among those who underwent screening, 44.4% underwent axillary lymphadenectomy and the remainder underwent sentinel lymph node biopsy.

Women who undergo breast-conserving surgery have a better body image than those who have a total mastectomy, as well as better physical fitness. Axillary lymphadenectomy, proposed in cases of axillary metastasis, can result in pain, lymphedema and restriction of movement, which can also impact women's quality of life.[17]

A cohort study described reduced muscle strength in 28% of the study population undergoing axillary lymphadenectomy. Regarding sentinel lymphnode biopsy, reduced muscle strength was reported in 17%–19% of patients after sentinel lymph node biopsy and in 11% in the long term. In another study, in relation to axillary lymphadenectomy x sentinel lymph node biopsy, muscle weakness was reported in 48% vs. 16% of patients.[22]

Our study demonstrated that mammographic screening is associated with an increased likelihood of breast-conserving surgeries and less extensive axillary procedures, often involving sentinel lymph node biopsy. This correlation translates into reduced morbidity, improved self-image, and an enhanced quality of life for individuals undergoing such interventions.

Regarding systemic treatment, through intravenous chemotherapy, the application of neoadjuvant and palliative chemotherapy was evaluated (at initial diagnosis) between the two groups (screened vs. unscreened). There is an association between neoadjuvant chemotherapy and screening (P<0.000). Overall, 32.3% of unscreened patients and 9.4% of screened patients underwent neoadjuvant chemotherapy. There is also an association between palliative CT and screening (P<0.000). Also, 21.8% of unscreened patients underwent palliative chemotherapy at initial diagnosis, and only 1.8% of unscreened patients underwent palliative chemotherapy. These findings portray the fact that there was a greater number of advanced stage disease among unscreened patients. However, when also considering patients who underwent adjuvant chemotherapy (after surgery), excluding stage 0 cancers and considering only patients with invasive tumors, most women underwent chemotherapy, regardless of whether they were screened or not. As already explained, within the population sample studied, most patients had tumors with a more aggressive biological behavior and, as they were younger women, many of them underwent adjuvant chemotherapy due to a higher risk of recurrence.

Epidemiological data show that the proportion of invasive breast cancer in developing countries has increased rapidly in recent decades. In Latin America, breast cancer mortality has increased in the last 20 years, with a 20% lower survival rate compared to the United States and Western Europe. The lower proportion of screening, more advanced clinical stages and lack of access to adequate treatment are the main causes for many of the unfavorable outcomes.[5]

It is known that lifestyle is directly linked to the incidence of cancer. Howell *et al.* showed that the fraction of breast cancer cases attributable to lifestyle and environmental factors in the UK was estimated to be 26.8% in 2010.[23] A report by the International Agency for Research on Cancer estimated that about a quarter to a third of cancer cases are associated with high body weight and inadequate physical activity.[24]

In addition to risk factors related to comorbidities, lifestyle, reproductive history, breast cancer does not affect all racial and ethnic groups equally. White women are more likely to be diagnosed with breast cancer compared to black women. However, the incidence of breast cancer before age 45 is higher in black women than in white women. Between the ages of 60 and 84, breast cancer incidence rates are notably higher in white women than in black women. But black women are more likely to die of breast cancer at all ages.[24] In the medical records used in our work, there was no record of the patients' race/color. A growing body of evidence also suggests that there are notable demographic differences between the molecular subtypes of breast cancer. Triple negative breast cancer has been shown to be more likely to occur among younger women and black women.[25] One of the first studies to associate Afro-descendant patients and triple negative tumors was carried out in North Carolina, United States. This study evaluated that triple negative breast cancer has a higher incidence in Afro-descendant women, predominantly in pre-menopause. (24, 26)

According to the estimate of the Brazilian Institute of Geography and Statistics (IBGE) for 2021, the Steel Valley population was 778,983. The 2010 (the latest official IBGE survey) age pyramid stated that women represented 51.3% of the population. Of these, 7.4% were in the 40-49 age group (~30 thousand). In Brazil, in 2021, the incidence of new cases of breast cancer was 61.61 women/100,000. From this consideration, 479 women should be diagnosed with cancer and 33.53 should be in the 40-49 age group. In our study, an average of 56 women aged between 40-49 years are diagnosed with breast cancer/year, implying that the incidence is 67% higher than the national average. It is possible to

conclude that this region needs extra attention, with more funding diverted to awareness campaigns.

It was not possible to make a parallel with other Brazilian regions, as there are no other similar studies. There is access to information that demonstrates the incidence of breast cancer in different regions of the country and mortality rates. This information can be consulted through the records released by INCA. However, there are no data relating to age, socioeconomical status, molecular subtypes, disease stage at diagnosis, lifestyle habits, BMI, race/ethnicity, among others. In our study, information such as parity, duration of breastfeeding, age at first delivery, use of hormones, sociological factors (socioeconomic, education, and marital status), and physical activity were not recorded in the medical records and, therefore, could not be added to the results. The lack of overall information poses a significant challenge, preventing the formulation of effective strategies for both primary and secondary prevention. Brazil, being a diverse and mixed-race nation, has derived its breast cancer screening recommendations from studies conducted on population groups with varying racial, cultural, and social characteristics, starting from the age of 50. Furthermore, Brazil appears to experience a higher incidence of breast cancer among younger patients when compared to developed countries. This discrepancy is likely attributed to a broader age demographic profile in comparison to developed nations, as well as various biological, environmental, and behavioral risk factors. Expanding studies of this nature to encompass diverse regions within the country would enable the development of a more tailored and effective breast cancer screening strategy aligned with our population's unique profile.

Brazil does not have a central medical records system and each hospital has their own methodology. It would be of significance to install a nation-wide comprehensive system accessible to all physicians containing the patient’s history, sociological factors (socioeconomic, education, and marital status), clinical and histological characteristics, gene expression, molecular patterns, prognosis, survival, and risk factors.

It is noteworthy to acknowledge additional bottlenecks in the diagnosis of breast cancer. Prolonged intervals between the request and execution of a mammogram can lead to delays in the diagnostic evaluation of symptomatic women, potentially impeding adherence to screening. Furthermore, the time elapsed between the examination and the release of reports may compromise the investigative process for suspected cases. Therefore, the regulation of mammography services should prioritize scheduling for symptomatic cases, and the procurement of services should consider expeditious report issuance as a crucial factor.[27] In 2019, the North and Southeast regions of Brazil were the least efficient in prioritizing the timely release of diagnostic mammography reports within a 30-day timeframe. Specifically, for the state of Minas Gerais, which encompasses the Steel Valley, only 38.9% of diagnostic mammograms had their reports released within the recommended 30-day period, as reported by the INCA bulletin in 2021.[27]

The mammography report quality indicator reinforces the need for control actions to ensure the appropriate technical level of this exam. The early detection of breast cancer requires a technical standard that allows the correct identification of lesions, with minimal exposure to risks. Finally, the need for continuous monitoring of actions to identify problems that can be corrected is reiterated.[27]

The search for indicators within international standards is important to reduce false positives, false negatives, unnecessary biopsies, minimize exposure to X-rays, optimize the service, and reduce unnecessary expenses. Therefore, performing quality mammography exams is as necessary as accessing the exam and optimizing the delivery of results, especially when it comes to diagnostic mammography.

CONCLUSION

There are controversies about breast cancer screening in women aged 40-49 years, mainly due to the lower impact on the mortality rate. This study showed that mortality among unscreened women was 5 times higher within the data collection period, and this is due to later diagnoses. It was also shown that screening provided a higher percentage of initial diagnoses, even among biologically more aggressive tumors, and less extensive surgeries. Therefore, in view of the results found, it is suggested that breast cancer screening, among women at moderate risk in Steel Valley, be started from the age of 40.

It is also suggested that the medical records should present as much information as possible, and that a more complete national cancer information system be established, with adhesion of all the states of the country. Recording information on race/ethnicity, physical inactivity, BMI, reproductive history, alcohol consumption, smoking, and molecular subtypes will make it possible to carry out epidemiological studies that contribute information to more effective primary and secondary prevention measures at the national and regional levels.

ETHICAL CONSIDERATIONS

The project was submitted to the Research Ethics Committee of Marcio Cunha Hospital, through the

National on-line ethics platform "*Plataforma Brasil*", and was approved on January 10, 2020.

ACKNOWLEDGEMENTS

The authors express their gratitude to the staff of Marcio Cunha Hospital for their valuable assistance.

CONFLICTS OF INTEREST

The authors affirm the absence of any conflicts of interest, including both financial and personal relationships with individuals or organizations that could potentially exert undue influence on their work.

FUNDING

None.

REFERENCES

1. Federação Brasileira das Associações de Ginecologia e Obstetrícia. Manual de Orientação Mastologia. Available from: https://www.febrasgo.org.br/pt/component/zoo/category/mastologia; 2010.
2. American College of Physicians. ACP issues guidance statement for breast cancer screening of average-risk women with no symptoms. Available from: https://www.acponline.org/acp-newsroom/acp-issues-guidance-statement-for-breast-cancer-screening-of-average-risk-women-with-no-symptoms2022
3. World Heath Organization. Breast cancer now most common form of cancer: WHO taking action. Available from: https://www.who.int/news/item/03-02-2021-breast-cancer-now-most-common-form-of-cancer-who-taking-action2021
4. MINISTÉRIO DA SAÚDE - INSTITUTO NACIONAL DO CÂNCER. Controle do câncer de mama/ conceito e magnitude. Available from: https://www.inca.gov.br/controle-do-cancer-de-mama/conceito-e-magnitude2022
5. Rosa DD, Bines J, Werutsky G, Barrios CH, Cronemberger E, Queiroz GS, et al. The impact of sociodemographic factors and health insurance coverage in the diagnosis and clinicopathological characteristics of breast cancer in Brazil: AMAZONA III study (GBECAM 0115). Breast Cancer Res Treat. 2020;183(3):749-57. doi: 10.1007/s10549-020-05831-y.
6. Berry DA. Benefits and Risks of Screening Mammography for Women in Their Forties: a Statistical Appraisal. JNCI. 1998;90(19):1431-9. doi: 10.1093/jnci/90.19.1431.
7. International Commission on Radiological Protection. ICRP 60: Occupational radiological protection in interventional procedures. Available from: https://www.icrp.org/publication.asp?id=icrp%20publication%2060: International Commission on Radiological Protection. ICRP Publication 21; 1991.
8. Hospital Márcio Cunha. Sobre nós. Available from: https://www.anahp.com.br/associado/hospital-marcio-cunha/2022
9. Estado de Minas Gerais - Região Metropolitana do Vale do Aço. Conheça os municípios. Available from: https://www.agenciarmva.mg.gov.br/conheca-os-municipios/2022
10. National Cancer Institute. AJCC staging system. Available from: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/ajcc-staging-system2022
11. Webb ML, Cady B, Michaelson JS, Bush DM, Calvillo KZ, Kopans DB, et al. A failure analysis of invasive breast cancer: most deaths from disease occur in women not regularly screened. Cancer. 2014;120(18):2839-46. doi: 10.1002/cncr.28199.
12. Simon SD, Bines J, Werutsky G, Nunes JS, Pacheco FC, Segalla JG, et al. Characteristics and prognosis of stage I-III breast cancer subtypes in Brazil: The AMAZONA retrospective cohort study. Breast. 2019;44:113-9. doi: 10.1016/j.breast.2019.01.008.
13. Alanko J, Tanner M, Vanninen R, Auvinen A, Isola J. Triple-negative and HER2-positive breast cancers found by mammography screening show excellent prognosis. Breast Cancer Res Treat. 2021;187(1):267-74. doi: 10.1007/s10549-020-06060-z.
14. Moss SM, Wale C, Smith R, Evans A, Cuckle H, Duffy SW. Effect of mammographic screening from age 40 years on breast cancer mortality in the UK Age trial at 17 years' follow-up: a randomised controlled trial. Lancet Oncol. 2015;16(9):1123-32. doi: 10.1016/S1470-2045(15)00128-X.
15. Ernst MF, Voogd AC, Coebergh JW, Repelaer van Driel OJ, Roukema JA. The introduction of mammographical screening has had little effect on the trend in breast-conserving surgery: a population-based study in Southeast Netherlands. Eur J Cancer. 2001;37(18):2435-40. doi: 10.1016/s0959-8049(01)00316-1.
16. Paci E, Duffy SW, Giorgi D, Zappa M, Crocetti E, Vezzosi V, et al. Are breast cancer screening programmes increasing rates of mastectomy? Observational study. BMJ. 2002;325(7361):418. doi: 10.1136/bmj.325.7361.418.
17. Lefeuvre D, Catajar N, Le Bihan Benjamin C, Ifrah N, De Bels F, Viguier J, et al. Breast cancer screening: Impact on care pathways. Cancer Med. 2019;8(8):4070-8. doi: 10.1002/cam4.2283.
18. Samnakay N, Tinning J, Ives A, Willsher P, Archer S, Wylie E, et al. Rates for mastectomy are

lower in women attending a breast-screening programme. ANZ J Surg. 2005;75(11):936-9. doi: 10.1111/j.1445-2197.2005.03584.x.
19. Destounis S, Santacroce A. Age to Begin and Intervals for Breast Cancer Screening: Balancing Benefits and Harms. AJR Am J Roentgenol. 2018;210(2):279-84. doi: 10.2214/AJR.17.18730.
20. Monticciolo DL, Newell MS, Hendrick RE, Helvie MA, Moy L, Monsees B, et al. Breast Cancer Screening for Average-Risk Women: Recommendations From the ACR Commission on Breast Imaging. J Am Coll Radiol. 2017;14(9):1137-43. doi: 10.1016/j.jacr.2017.06.001.
21. Ray KM, Joe BN, Freimanis RI, Sickles EA, Hendrick RE. Screening Mammography in Women 40-49 Years Old: Current Evidence. AJR Am J Roentgenol. 2018;210(2):264-70. doi: 10.2214/AJR.17.18707.
22. Hidding JT, Beurskens CH, van der Wees PJ, van Laarhoven HW, Nijhuis-van der Sanden MW. Treatment related impairments in arm and shoulder in patients with breast cancer: a systematic review. PLoS One. 2014;9(5):e96748. doi: 10.1371/journal.pone.0096748.
23. Howell A, Anderson AS, Clarke RB, Duffy SW, Evans DG, Garcia-Closas M, et al. Risk determination and prevention of breast cancer. Breast Cancer Res. 2014;16(5):446. doi: 10.1186/s13058-014-0446-2.
24. Yedjou CG, Sims JN, Miele L, Noubissi F, Lowe L, Fonseca DD, et al. Health and Racial Disparity in Breast Cancer. Adv Exp Med Biol. 2019;1152:31-49. doi: 10.1007/978-3-030-20301-6_3.
25. Howlader N, Altekruse SF, Li CI, Chen VW, Clarke CA, Ries LA, et al. US incidence of breast cancer subtypes defined by joint hormone receptor and HER2 status. J Natl Cancer Inst. 2014;106(5). doi: 10.1093/jnci/dju055.
26. Corrêa PB, Toralles MBP, Abe-Sandes K, Machado TMB, Bonfim TF, Meyer L, et al. Câncer de mama triplo negativo e sua associação com ancestralidade africana. Revista de Ciências Médicas e Biológicas. 2010;9(1):3-7. doi: 10.9771/cmbio.v9i1.4631.
27. INSTITUTO NACIONAL DE CÂNCER. Monitoramento das ações de controle dos cânceres de mama. https://www.inca.gov.br/publicacoes/informativos/informativo-deteccao-precoce-no-2-2021; 2021. Contract No.: Boletim ano 12, no 2.

How to Cite This Article

Aires Lima CC, de Souza CD. Evaluation of the Possible Benefits of Breast Cancer Screening in Women Aged 40 to 49 Years in the Steel Valley Region, Brazil. Arch Breast Cancer. 2024; 11(2):172-182.
Available from: https://www.archbreastcancer.com/index.php/abc/article/view/842