

EFFICIENCY OF MAMMOGRAPHY FOR BREAST CANCER SCREENING

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Abstract: The present study is an integrative literature review, which aims to evaluate the efficiency of mammography in reducing mortality from breast cancer and regarding a possible excess of cancer diagnosis, a phenomenon that will henceforth be called by the established term “overdiagnosis”. In addition, it will assess which women in the general population must undergo screening mammography, as well as how often this exam must be performed. The central research questions are: given the numbers of mammography overdiagnosis, which subgroup of women in the general population must undergo screening mammography and how often? Is mammography effective for early detection of breast cancer? Health descriptors were selected for article research using the PICO technique. Subsequently, the inclusion and exclusion criteria were selected and the articles to be analyzed were selected. The results indicate that there is no consensus in the national and international literature, but that mammography still appears as one of the main tests for early detection of breast cancer and its performance is essential for the adequate treatment of the disease.

Keywords: screening mammography; breast cancer; overdiagnosis.

INTRODUCTION

The industrial and technological revolution led to an increase in life expectancy, a decrease in mortality and, consequently, the aging of the population. Technological advances in medicine are reflected in the change in morbidity and mortality, where infectious diseases become supporting factors in the face of the increasing presence of neoplasms, cardiovascular and degenerative diseases (Santos; Chubaci, 2011). In Brazil, the third leading cause of death in the elderly is neoplasms and, among these, breast cancer stands out. According to Ancelle (2006),

60% of breast cancer cases are detected late and occur more frequently as age advances. In this scenario, early diagnosis improves treatment and reduces mortality (Araújo et. al., 2006). Among the most common methodologies for diagnosing breast cancer are breast self-examination, clinical exams and mammography, the latter being the most effective (Santos; Chubaci, 2011).

Mammography consists of a radiological examination that uses a device (mammograph) that provides an image that covers the entire breast tissue, showing cellular changes that can detect early diseases (Espadaro et. al., 2019). This exam was created in 1913 by the German Albert Salomon, when he performed breast x-rays and, later, a mastectomy, finding some microcalcifications (Kalaf, 2014). Then, in 1930, the first mammogram was performed on a patient in New York, carried out by radiologist Stafford Warren. From this, several advances were achieved, of which we highlight: the HIP study (Health Insurance Plan, New York), which showed that mammography reduces breast cancer mortality in women; the work of Charles Gross, from 1965, who differentiated parenchyma, fat and microcalcifications in mammography images; and the work of László Tabár, from 1985, when he published a study carried out through mammographic monitoring of 134,867 women between 40 and 79 years old, whose results pointed to a 30% reduction in mortality (Kalaf, 2014; Loberg et. al., 2015).

Today, mammography is used to screen for neoplasia in breast tissue, in addition to being useful in identifying suspicious areas for subsequent biopsy. It is a quick, sensitive and decisive exam that, with just four images (two of each breast), presents sufficient results to draw different conclusions about the patients' health status (Espadaro et. al., 2019). However, some studies are against the use of mammography to screen for neoplasms, on the grounds that

tumors grow slowly, do not produce symptoms and, supposedly, would never be discovered without the exam. Such conditions end up generating false-positive results, contributing to patients' anxiety and anguish, as well as unnecessary treatments (Loberg et. al., 2015; Niel et. al., 2017; Lannin, 2018).

Given this scenario, an integrative literature review is pertinent to verify whether radiological breast examinations are still effective for screening and preventing breast cancer and, if so, how frequently they must be performed. The relevance of this investigation is justified because, despite the excellence of mammography for screening breast tumors, up to 30% of them may not be detected due to the density of the breast tissue or due to poor exam conduct (Majid et. al., 2003). Furthermore, there are studies that suggest that mammography is responsible for many cases of overdiagnosis, that is, slow-growing tumors that are treated unnecessarily. Therefore, a systematic review of the literature can help professionals make the best choice about when to perform the exam and how often it must be recommended to patients, to avoid cases of overdiagnosis and the rate of unnecessary treatments.

THEORETICAL FOUNDATION

The breast is made up of lobules, alveoli and acini, and the mammary gland is made up of the lobular and ductal systems. One of them is made up of 20 to 40 lobes and each lobe has 10 to 100 alveoli (acini). The lobules are the morphofunctional units of the breast, while the alveoli are the resting secretory units and the acini are the secretory units developed during pregnancy and lactation. It is worth noting that the breast undergoes different changes at different ages in a woman's life. In young patients, there is a predominance of supporting and glandular tissue. As age advances, the liposubstitution process begins,

which involves atrophy of the gland and an increase in adipose and connective tissue (Fonseca; Sá, 2018).

The liposubstitution process is associated with genetic factors that may favor the appearance of breast disorders, such as breast tissue neoplasms. Factors such as family history, age over 40 years, white race, mutations in genes such as BRCA 1 and 2, Cowden disease, environmental factors, menstrual history (early menarche and late menopause), obstetric history (nullity and elderly primiparity), consumption of alcoholic beverages, use of oral contraceptives, hormone therapy, among others, may be associated with these processes (Alves, 2011; Rocha et. al., 2013).

Breast cancer itself is a neoplasm that involves some genes and countless other factors. There is a possible genetic factor, which is expressed when the disease starts from a mutation in the ductolobular unit, in which there is more susceptibility to DNA damage and more repairs. Other multifactorial phenomena may result from the interaction of endocrine, environmental and nutritional mechanisms. In breast cancer there is an uncontrollable proliferation of abnormal cells in the breast tissue that can involve both the lobules and the ducts. This carcinoma may have a high potential for morbidity and mortality and therefore early detection increases the survival rate and generates a better prognosis (Silveira et. al., 2012).

Regarding mammographic screening, mammography is a radiological examination performed on the breasts, which can be conventional (MC) or digital (MD) directly or indirectly. It was found that, in women under 50 years of age, the performance of digital mammography is considered better compared to conventional mammography due to breast density (Espadaro et. al., 2019). We currently have numerous advances in

the visualization of mammographic images, such as, for example, contrast mammography, tomosynthesis and Positron Emission Tomography (PET). Contrast allows vascular changes to be visualized more clearly. Tomosynthesis increases and improves the detection of cancer diagnosis in women with radiodense and/or fibrocystic breasts, allowing the obtaining of various planes of the breast and, thus, improving the visualization of suspicious or hidden structures due to the overlap of denser tissues. PET, on the other hand, uses the labeling of glucose molecules with a radioactive isotope of fluorine to monitor and record its uptake by cells. Furthermore, it evaluates accumulation rates (Warburg effect), making it an important biological tumor marker. Another marker that shows great promise in PET/PEM is FLT (18-fluoro-L-thymidine), whose uptake is less sensitive to areas of inflammation or recent damage, such as biopsies (Kalaf, 2014).

A mammogram is the first exam performed on the patient to begin screening for breast cancer and the most effective for this purpose, becoming a gold standard exam for early detection (ACR, 2016). In a global context, there is a certain similarity between recommendations for breast cancer screening. When studying recommendations in countries such as the United States, Luxembourg, Switzerland, Norway, the Netherlands, Germany, Sweden, Ireland, Austria, Denmark, Belgium, Canada, Australia, France, Japan, Iceland, the United Kingdom, Finland, New Zealand, Italy and Spain, Khrouf et. al. (2020) identified that most countries recommend starting screening between 50 and 69 years of age, with exams being carried out every two years. In this list, only Japan does not specify the age range and the United Kingdom recommends a longer screening period, every three years.

In Brazil, breast cancer screening, as well as

its recommendation, entered the field of public policies in 2004 (Migowski et. al., 2018). The publication Guidelines for the Early Detection of Breast Cancer in Brazil indicates that screening must be offered to women between 50 and 69 years old, once every two years, following international guidelines. However, technical associations, such as the Brazilian Society of Mastology and the Brazilian Society of Gynecology and Obstetrics, understand that screening must start at the age of 40 and that it must be carried out annually. In the case of women with a prevalent family history of breast cancer in first-degree relatives, associations recommend starting screening at age 35 (Migowski et. al., 2018; INCA, 2019).

Regardless of the recommendation, we understand that it is essential that mammograms are performed by women and that it is the role of public authorities and professionals in the field to raise awareness in society about the importance of screening, as this condition brings a series of damages to physical and emotional health. of women, in addition to increasing public spending. Women must be informed about the risks and benefits of having a mammogram, and its performance must be a shared decision between the health professional and the patient. Migowski et. al. (2018) emphasize that this screening must be carried out even in women without suspected signs or symptoms of breast cancer.

The World Health Organization (WHO) recommends that screening be carried out in several spheres, involving communication, planning, monitoring and evaluation. To this end, screening, as a public prevention and treatment policy, must involve everything from raising awareness and inviting women in the established age group, to diagnostic investigation, treatment and care for women with altered exams. In all these stages, an active and capable multidisciplinary team is

essential, as well as sufficient and appropriate resources and materials to carry out the entire process (INCA, 2019).

In Brazil, the Ministry of Health developed parameters for breast cancer screening (Brazil, 2009) that help the best conduct to be carried out by professionals after the mammographic report. For this, there is the BI-RADS classification, stratified from 0 to 5, with category 0 indicating an incomplete or inconclusive result and category 5 indicating a highly suspicious result. We organize, in Table 1, the description of the recommendations of the BI-RADS classification.

Category	Features and recommendation
BI-RADS 0	Inconclusive exam. Need for additional evaluation in other mammography incidences, maneuvers and ultrasound assistance. A comparison of exams carried out in the last 3 years can also be used. After reevaluation, another classification will be given in place of category 0.
BI-RADS 1	There are no mammographic findings. It is recommended that the screening routine be followed.
BI-RADS 2	There are benign mammographic findings. As in category 1, it is recommended that the screening routine be followed
BI-RADS 3	There are probably benign findings. In this category, it is recommended that radiological control be carried out for three years, as follows: every six months in the first year and annually in the second and third years. When the suspected lesion is stable, you can return to your usual screening routine. Eventually, it is decided to perform a biopsy.
BI-RADS 4	There are findings highly suspicious of malignancy. The procedure to be performed is biopsy and histopathology.
BI-RADS 5	There are findings highly suspicious of malignancy. As in category 4, perform biopsy and histopathology.

Table 1: BI-RADS classification

Source: organized by the authors, from Brasil (2009) and ACR/CBR (2016)

Given this information, it is clear that screening mammography has many benefits as it has the potential to detect small lesions and prevent the spread of the disease. Consequently, mortality and treatment intensity decrease

(less chemotherapy, less aggressive surgery, etc.). The HIP Trial (Health Insurance Plan) study, carried out in the 1960s, carried out randomized clinical trials and demonstrated a reduction in breast cancer mortality through screening, with a 20% mortality reduction rate (Niel et. al, 2017).

One of the negative points of mammography is related to being an exam that uses radiation, which can bring risks and consequences in the long term, in addition to being an operator-dependent exam. Furthermore, false positive results may occur, with up to 15% of reports requiring additional tests to confirm benignity. It is also worth noting that this exam does not make the final diagnosis of breast cancer, as it requires medical interpretation and biopsy (Moynihan et. al., 2012).

In addition to these factors, it is worth highlighting the problem of overdiagnosis, a discussion that is gaining more and more space in the academic and professional field on the topic. Overdiagnosis is a theoretical concept that involves the possibility that some asymptomatic women who undergo screening mammography may be diagnosed with cancer that, ultimately, would never cause symptoms or premature death. In addition to considerably increasing courses for the health system, overdiagnosis can lead to unnecessary exams, treatments and even surgery (Duffy; Parmar, 2013).

Cases of overdiagnosis could be invasive cancers or, mainly, in situ cancers. Theoretically, these cases would have the potential to regress or disappear spontaneously, and if they had not been found in routine mammographic screening, they would never have become a problem in the lives of the women diagnosed. Studies on this topic differ in opinions, especially in the case of carcinoma in situ, which, although it can, theoretically, regress, all cases undergo treatment, as until now medicine is unable to know, exactly, which cancers are

present. *situ* detected will evolve into invasive cases and which may regress or disappear spontaneously (Duffy; Parmar, 2013).

Given these limitations in knowledge on the topic, isolated observational studies on overdiagnosis must be interpreted carefully and judiciously, taking into account the particularity of each case and the differences of each patient. In the understanding of Moynihan et. al. (2012), these studies must not be taken as an absolute truth, as they may unfairly stigmatize mammographic screening.

Mammography is still the most used method worldwide for the early diagnosis of breast cancer. However, it is not so well regarded by some scholars, who understand that it can treat a carcinoma that would take a long time to become invasive or cause harm to the patient. This way, patients would be treated and subjected to stress and emotional exhaustion without real need. As an example, overdiagnosis occurs mainly in ductal carcinoma *in situ*, which accounts for less than 30% of all cancers diagnosed in the United States of America. This carcinoma increased its incidence rate after the advent of mammography, as it appears in a calcified form and becomes more visible in this exam. According to scholars who oppose mammography, as ductal carcinoma *in situ* progresses in rare cases to invasive carcinoma, it subjects the patient to unnecessary aggressive treatments, as the treatment of this tumor is through surgery, radiotherapy and chemotherapy, which, if the carcinoma did not develop, it would not need to be treated (Moynihan et. al., 2012).

In view of the above, the debate between different medical societies about the benefits and harms of screening mammography for breast cancer is growing. There is no consensus among scholars, as while some authors affirm its importance for early detection and reduction of mortality, others

reinforce the problem of excessive diagnoses and unnecessary treatments in patients.

METHODOLOGICAL PROCEDURES

This study is characterized by an integrative literature review regarding the role of mammography for breast cancer screening. The methodology used is qualitative, as the review was carried out by consulting articles and books. The methodological organization was carried out as follows: (a) determination of the research question, through identification of the problem; (b) review of articles that integrate the guiding question and definition of inclusion and exclusion criteria for data collection; (c) data collection using keywords in search engines; (d) critical analysis of included studies; and (e) presentation of the integrative review and discussion of the results.

For the data collection stage, we used the crossing of terms in the DeCS system (Descriptors in Health Sciences – a single language standard for indexing scientific works in the area), with the following combinations: (1) mammography AND breast cancer AND screening; (2) mammography AND overdiagnosis; (3) mammography AND screening AND breast cancer AND overdiagnosis; and (4) screening mammography AND efficiency. The source of data used was the Pubmed and LILACS platforms.

The investigation was carried out between August and September 2019. The inclusion criteria took into account the date of publication (articles from the last 5 years), the language (English, Spanish or Portuguese), the target audience (articles that dealt with mammography screening in women who had no signs or symptoms and no family history) and the structure of the study (preference for studies with a systematic review on the efficiency of mammography), discarding

articles that dealt with breast cancer itself or its metastases. The exclusion criteria were: studies with women who already had symptoms, breast lumps or a family history of breast cancer; articles published before 2015 or on paid access platforms.

In Table 2, we present a quantitative summary of the number of references obtained by crossing keywords on both platforms, the number of abstracts analyzed, the number of references selected for prior analysis and the final number of works selected for review literature.

RESULTS AND DISCUSSION

The World Health Organization (W.H.O.) defines criteria for carrying out adequate screening for a given pathology. This screening is universal and very important to make a better diagnosis and develop an appropriate treatment. Breast cancer, due to its importance and need for care, meets the ten WHO criteria for organized screening, presented in Table 3.

1	It is a public health problem, as it is the main cause of death from cancer in women worldwide.
2	There is a proven effective treatment for this pathology.
3	The means of diagnosis (biopsies) and treatment (surgery, chemotherapy, radiotherapy, hormonal therapy, targeted therapies) are available to patients.
4	There is a latency phase for breast cancer, even before the patient presents symptoms, where the pathology is detectable through increasingly improved mammography techniques.
5	There is an excellent test for breast cancer screening: mammography.
6	This exam is generally well accepted by the population.
7	The course of the pathology is known.
8	The choice of patients who must undergo surgical treatment is in accordance with pre-established criteria and recommendations from scientific societies.
9	The cost of research, including diagnosis and treatment of patients, is not disproportionate to the overall cost of drug treatment, even though it is very expensive.
10	The discovery of cancer cases is an ongoing process as it is carried out annually.

Table 3: World Health Organization screening criteria for breast cancer

Source: organized by the authors, from Khrouf *et. al.* (2020)

For the study, we read 33 articles that included everything from breast cancer in general, anatomy and physiology of the breast, how breast cancer screening is carried out and discussions about overdiagnosis. Among these, 15 articles address breast cancer screening, with the majority still defending mammography as the main method for this screening.

In screening, overdiagnosis is not a precise phenomenon, but it is a hypothesis that can explain the discrepancy between the increase in the incidence of cancer after the start of screening, compared to the mortality rate, which changed little. In a Canadian study published in 2014 (Kalaf, 2014), where cases were analyzed over 25 years, it was noted that the increase in the incidence of breast cancer did not reduce the mortality rate and, according to the study, the hypothesis is that cancer would not lead to death. In this sense, overdiagnosis could be an explanation for this data, that is, the increase in incidence without the increase in mortality.

When cancer is detected in mammographic screening, the literature points to three theoretical possibilities about the meaning and outcome of the exam: (1) it is an important cancer that has a chance of being cured if diagnosed early; (2) it is an extremely aggressive cancer that will not be cured, even if treated early; and (3) it is an overdiagnosed cancer (Duffy; Parmar, 2013). For Lichtenfeld (2011), the biggest problem is recognizing this excess of diagnoses, since its identification is only possible if the patient refuses treatment, does not present symptoms and dies from other causes, facts that practically do not occur or are difficult to identify.

Another problem is that there are still no studies that accurately determine which in situ cancers will evolve into invasive cases. Also, there is no evidence that invasive cancers can or cannot regress or disappear

Database	Crosswords	Number of references obtained	Abstracts analyzed	References selected for analysis	Selected for review
Pubmed	<i>mammography AND breast cancer AND screening</i>	17	14	8	8
	<i>mammography AND overdiagnosis</i>	18	5	3	1
	<i>mammography AND screening AND breast cancer AND overdiagnosis</i>	73	12	6	4
	<i>screening mammography AND efficiency</i>	21	4	2	2
LILACS	<i>breast cancer AND overdiagnosis</i>	13	9	7	7
	<i>mammography AND overdiagnosis</i>	11	5	4	3
	Benefits of mammography/ breast cancer screening	25	12	12	8

Table 2: summary of the works found

Source: organized by the authors (2021)

spontaneously (Arleo et. al., 2017). On the other hand, there are studies that do not show overdiagnosis: Siu and the U.S. Preventive Services Task Force (2016) promoted a randomized controlled study in the United Kingdom and Sweden and concluded that overdiagnosis rates are very low with longer follow-up. Other recent studies also highlight the benefits of mammographic screening due to the number of cases diagnosed at early stages of the disease, which reduced mortality compared to women who did not undergo routine screening (Duffy; Parmar, 2013; Buseman et. al., 2003).

According to studies pro and against mammography, in the 2010s government agencies in Brazil, the United States and Canada reduced the age and frequency indication for mammography, being recommended for women over 50 years old and with a biannual frequency. The justifications point to the need for complementary ultrasound, the high rate of false positives (positive mammogram with negative biopsy), false negatives (negative mammogram and presence of cancer), overdiagnosis and the large financial cost.

However, some medical societies, such as the Brazilian Society of Mastology and the Brazilian Society of Gynecology and Obstetrics, maintained the recommendation

for annual mammography from the age of 40 onwards. The arguments used by these organizations are the results of 6 of the 7 large randomized controlled studies that investigated this topic and pointed to a proven reduction in mortality in the United States and other developed countries after the introduction of routine mammography.

FINAL CONSIDERATIONS

Throughout our literature review, we found that there is no consensus on the minimum age and frequency of mammography exams in the literature, despite everyone recognizing its importance in diagnosis. While some studies highlight high rates of overdiagnosis, which result in treatment costs for government agencies and frustration and anxiety among patients, other studies indicate that these rates are very low among the list of early diagnoses that can identify diseases in their early stages., increasing the chances of successful treatments.

In our interpretation, we consider that, until we have more efficient methodologies for accurate diagnosis and with less margin for error, mammography is still an essential resource for the prevention and treatment of breast cancer. In summary, it is necessary to carry out a cautious interpretation of data

obtained in very heterogeneous populations, so that overdiagnosis results are not replicated as absolute truths, which would end up stigmatizing mammographic screening and reducing consideration of its benefits.

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