CONSENSUS MEETING
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BREAST CANCER SCREENING: UPDATED RECOMMENDATIONS OF THE BRAZILIAN COLLEGE OF RADIOLOGY AND DIAGNOSTIC IMAGING, BRAZILIAN BREAST DISEASE SOCIETY, AND BRAZILIAN FEDERATION OF GYNECOLOGICAL AND OBSTETRICAL ASSOCIATIONS

Recomendações do Colégio Brasileiro de Radiologia e Diagnóstico por Imagem, da Sociedade Brasileira de Mastologia e da Federação Brasileira das Associações de Ginecologia e Obstetrícia para o rastreamento do câncer de mama*

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ABSTRACT

Objective: To present the current breast cancer screening guidelines in Brazil, as devised by the Brazilian College of Radiology and Diagnostic Imaging (CBR), the Brazilian Society for Breast Disease (SBM) and the Brazilian Federation of Gynecological and Obstetrical Associations (FEBRASGO). **Methods:** We analyzed scientific studies available in Medline and Lilacs databases. In the absence of evidence, the guidelines reflected the consensus opinion of an expert panel. **Guidelines:** Annual mammography screening is recommended for women aged 40–74 years. Among women aged 75 years or older, annual mammography screening should be reserved for those with an expected survival of 7 years or more. Complementary ultrasound should be considered for women with dense breasts. Complementary magnetic resonance imaging is recommended for women at high risk. When available, an advanced form of mammography known as tomosynthesis can be considered as a means of screening for breast cancer.

KEYWORDS: Breast Neoplasms; Breast cancer screening; Mammography; Ultrasonography, mammary; Magnetic resonance imaging.

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RESUMO

Objetivo: Apresentar as recomendações do Colégio Brasileiro de Radiologia e Diagnóstico por Imagem (CBR), da Sociedade Brasileira de Mastologia (SBM) e da Federação Brasileira das Associações de Ginecologia e Obstetrícia (FEBRASGO) para o rastreamento por imagem do câncer de mama no Brasil. **Métodos:** Foram analisados os estudos disponíveis nas bases científicas Medline e Lilacs. Na ausência de dados probatórios, as recomendações refletiram o consenso da comissão de especialistas. **Recomendações:** O rastreamento mamográfico anual é recomendado para as mulheres entre 40 e 74 anos. Acima de 75 anos deve ser reservado para as mulheres que tenham expectativa de vida maior que 7 anos. O rastreamento complementar com ultrassonografia deve ser considerado para as mulheres com mamas densas. O rastreamento complementar com ressonância magnética é recomendado para as mulheres com alto risco. A tomossíntese é uma forma de mamografia que pode ser considerada para o rastreamento do câncer de mama, quando disponível.

DESCRITORES: Câncer de mama; Rastreamento; Mamografia; Ultrassonografia mamária; Imagem por ressonância magnética.

INTRODUCTION

Organized screening programs have led to a reduction in breast cancer mortality in several countries.[1,2] In Brazil, despite all efforts, an increase in both breast cancer incidence and mortality rates has been noticed.[3-5] One peculiarity of breast cancer in Brazil and in other developing countries is that its incidence among women aged 40-50 years is proportionally higher than that reported in developed countries.[6-8]

Programs that aim at standardizing breast cancer screening guidelines – as well as educating the population regarding the importance of such tests – should be promoted. In 2012, the Brazilian College of Radiology and Diagnostic Imaging (CBR), the Brazilian Society for Breast Disease (SBM) and the Brazilian Federation of Gynecological and Obstetrical Associations (FEBRASGO), via the Brazilian National Mammography Commission, published their joint recommendations for breast cancer screening in Brazil.[9]

The purpose of this article is to present an update of those recommendations, based on the most recent and relevant scientific data on the subject.

METHODS

We analyzed studies available in Medline and Lilacs databases to answer the following clinical question: "What impact do mammography, ultrasonography, magnetic resonance and tomosynthesis have on breast cancer screening according to age bracket and personal and family risk?" Our assessment was based on the levels of scientific evidence established by the Oxford Centre for Evidence-based Medicine[10] and on the criteria employed by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.[11] In the absence of evidence, the recommendations reflected the consensus of an expert committee composed of CBR, SBM and FEBRASGO members.

The recommendations were classified in four categories, according to the degree of scientific evidence and the consensus of th e expert committee, as follows:

- Category A – Recommendation based on strong scientific evidence, with a consistent consensus among CBR, SBM and FEBRASGO members that this recommendation should be strongly supported.
- Category B – Recommendation based on reasonable scientific evidence, with a clear consensus among CBR, SBM and FEBRASGO members that this recommendation should be strongly supported.
- Category C – Recommendation based on little scientific evidence, but with a consensus among CBR, SBM and FEBRASGO members that this recommendation should be strongly supported.
- Category D – Recommendation based on a consensus among CBR, SBM and FEBRASGO members that this recommendation should be supported.

These recommendations will be reviewed every three years.

Recommendations on breast cancer screening in average-risk women

Mammography

- Annual screening with mammography – preferably digital mammography – is recommended for women aged 40-74 years (category A).
- After the age of 75, annual screening with mammography – preferably digital mammography – is recommended for women with an expected survival rate of more than 7 years according to comorbidities (category D).

Ultrasound

- There are no data to support the use of ultrasound scan for breast cancer screening for all average-risk women.

- Ultrasound should be considered as an adjuvant therapy to mammography among women with dense breasts (category B).

Magnetic resonance imaging

- There are no data to support the use of magnetic resonance imaging for breast cancer screening for average-risk women.

Tomosynthesis

- It is recommended that tomosynthesis – when available – be considered in association with digital mammography (combo or synthesized mode) for breast cancer screening (category B).

Breast cancer screening in women at high risk

Mammography

- Women who have a BRCA1 or BRCA2 gene mutation or women who have first-degree relatives with a proven mutation should undergo annual screening mammography for the detection of breast cancer from age 30 onward (category B).
- Women with a projected ≥ 20% lifetime risk – as calculated with one of the mathematical models based on family history – should undergo annual screening mammography starting 10 years before the age at diagnosis of the youngest relative (but not before the age of 30) (category B).
- Women between 10 and 30 years of age with a history of chest irradiation should undergo annual screening mammography from the 8th year after radiotherapy treatment (but not before the age of 30) (category C).
- Women diagnosed with genetic syndromes that increase breast cancer risk (such as Li-Fraumeni syndrome and Cowden syndrome) or women who have first-degree relatives who have been affected should undergo annual screening mammography from diagnosis onward (but not before the age of 30) (category D).
- Women with a history of atypical lobular hyperplasia, lobular carcinoma in situ, atypical ductal hyperplasia, ductal carcinoma in situ or invasive breast carcinoma should undergo annual screening mammography from diagnosis onward (category C).

Magnetic resonance imaging

- Women who have a BRCA1 or BRCA2 gene mutation or women who have first-degree relatives with a proven mutation should undergo annual breast magnetic resonance imaging screening from age 25 onward (category A).
- Women with a projected ≥ 20% lifetime risk – as calculated with one of the mathematical models based on family history – should undergo annual breast magnetic resonance imaging screening starting 10 years before the age at diagnosis of the youngest relative (but not before the age of 25) (category A).
- Women between 10 and 30 years of age with a history of chest irradiation should undergo annual breast magnetic resonance imaging screening from the 8th year after radiotherapy treatment (but not before the age of 25) (category C).
- Women diagnosed with genetic syndromes that increase breast cancer risk (such as Li-Fraumeni syndrome and Cowden syndrome) or women who have first-degree relatives that have been affected should undergo should undergo annual breast magnetic resonance imaging screening from diagnosis onward (but not before the age of 25) (category D).
- Women with a history of atypical lobular hyperplasia, lobular carcinoma in situ, atypical ductal hyperplasia, ductal carcinoma in situ or invasive breast carcinoma could undergo annual breast magnetic resonance imaging screening from diagnosis onward (category C).

Ultrasound

- Ultrasound should be used as a substitute for magnetic resonance imaging in women who, for some reason, cannot undergo the test (category B).

Tomosynthesis

- It is recommended that tomosynthesis – when available – be considered in association with digital mammography (combo or synthesized mode) for breast cancer screening (category B).

Justification

The main benefit of breast cancer screening is the reduction of breast cancer mortality in women over aged more than 40 years. To evaluate the effect of mammography screening on mortality rate, 11 prospective controlled randomized trials have been conducted.[1,2] Except for 2 studies conducted in Canada (Canadian National Breast Screening Study – CNBSS 1 and 2),[12] – which had a strong selection bias for having included a disproportionate number of patients with palpable nodules – all studies showed that the relative risk of death from breast cancer was lower among women who underwent mammography screening than among those who did not.[1,2] The study that showed the largest mortality reduction associated with mammography screening was the Swedish Two-County Trial, which reported a 31% reduction in the mammography screening group after 29 years of follow-up.[13] Several meta-analyses were performed from these studies. In a meta-analysis conducted by the Independent UK Panel, the reduction in breast cancer mortality was estimated at 20%,[14] compared to the 19% reduction reported in another meta-analysis, conducted by a Cochrane center.[15]

On the other hand, the magnitude of the reduction in breast cancer mortality reported in the studies has been questioned by some researchers. Practically, these authors give more consideration to the Canadian studies cited (CNBSS), without considering their flaws. They also argued that most studies were

conducted in the 1960s, 1970s and 1980s, and their results do not express the therapeutic advances that have occurred since then. They speculated that some women who were not screened and died of breast cancer would have survived if they had been treated under the current protocols. They also speculated that therapeutic advances have made the early detection of breast cancer with mammography screening less relevant.[16] However, there is little scientific evidence to support these speculations. It is noteworthy to mention that estimates from studies conducted in the 1970s, 1980s and 1990s also failed to reflect the technological advances in mammography and the potential detection of more curable cancers than in the past.[17,18]

Breast cancer screening for women aged 40-49 years

Major debate occurs in relation to mammographic screening in women aged between 40 and 49. Some studies evaluated the specific impact of mammography screening for breast cancer in this age group. The UK Age Trial, a prospective controlled randomized study, showed a 25% reduction in the relative risk of death in the first 10 years of breast cancer screening in women aged 39-49 years.[19] Hellquist et al. observed – after 16 years of follow-up – a 29% reduction in mortality associated with breast cancer screening for women aged 40-49 years, whereas the reduction reported was of 18% in the subgroup of women aged 40-44 years, and 32% in the subgroup of women aged 45-49 years.[20] In an observational study conducted in Sweden, Jonsson et al. reported that the rate of reduction in mortality associated with breast cancer screening was 38% in women aged 40-49 years.[21] In addition, as previously mentioned, the incidence of breast cancer among women aged 40-50 years in Brazil and other developing countries is proportionally higher than that reported in developed countries.[3,5] Therefore, the CBR, SBM and FEBRASGO recommend that this group of women be included in breast cancer screening protocols in Brazil.

Screening for women aged 74 years and older

The prospective controlled randomized trials failed to include women aged 74 years and older, explaining the lack of direct data on screening for this age group. However, life expectancy for women has increased, with a consequent increase in the incidence of breast cancer among women older than 75 years. Currently, approximately 26% of breast cancer deaths occur in women diagnosed after the age of 74. Another factor that supports the use of mammography screening for this age group is the high sensitivity and specificity of the method.[22,23] Taking into account all these factors, many medical organizations recommend that the decision be made on a case-by-case basis after consulting with the patient. Therefore, the CBR, SBM and FEBRASGO recommend that this group of women with an expected survival rate of more than 7 years be included in breast cancer screening protocols in Brazil.

Breast cancer screening for high-risk patients

When a woman is considered at high risk, breast cancer screening is intensified, which includes two changes compared to screening for the general population. The first change consists of earlier screening, since breast tumors tend to develop sooner among these women. The second change is the incorporation of complementary methods such as magnetic resonance imaging or ultrasound, given the limitations of mammography, which are greater in this group.

Breast cancer screening for patients at high genetic risks

The use of supplemental screening with ultrasound or magnetic resonance imaging has been associated with the detection of a higher number of tumors among women with a BRCA1 or BRCA2 gene mutation, with magnetic resonance imaging proving to be superior to ultrasound.[24-26] A systematic review published in 2007 showed that the sensitivity of mammography and ultrasound was 36% and 40%, respectively, when the methods were used separately, and 55% when they were used in combination. In contrast, magnetic resonance imaging showed a sensitivity of 81% when used alone, and 93% when combined with mammography. Therefore, although nearly 50% of the tumors still went unidentified, the use of ultrasound as an ancillary method was found to increase the number of tumors detected.[27] More recent studies have confirmed these findings. In 2015, Riedl et al. reported that mammography and ultrasound both had an overall sensitivity of 38% when used separately, compared with 50% when they were used together.[28] The authors found that magnetic resonance imaging had 90% sensitivity when used alone, and 93% when combined with mammography. However, they observed no significant increase when magnetic resonance imaging was combined with ultrasound.[28] However, these favorable results can only be achieved if the magnetic resonance imaging scans are of high quality and interpreted by qualified physicians. Another key factor is the continued investigation with a biopsy of the lesions detected only by magnetic resonance imaging or the support of a reference center to perform these procedures.[29,30] Therefore, magnetic resonance imaging is the ancillary screening method of choice for women at high genetic risk and ultrasound should only be used if magnetic resonance imaging cannot be performed for some reason.

Other genetic syndromes

Other genetic syndromes that increase the risk of breast cancer are rare with no specific studies on their relationship with screening for breast cancer. Currently, experts recommend breast cancer screening for women with Cowden, Bannayan-Riley-Ruvalcaba or Li-Fraumeni syndrome, as well as for untested women who have a first-degree relative with any of those syndromes.[24] It is suggested that these women follow a similar screening protocol to that recommended for women with a BRCA1 or BRCA2 gene mutation.

Chest wall irradiation

Women submitted to chest wall irradiation show a higher lifetime risk of developing breast cancer comparable to the risk reported for women with a BRCA gene mutation. However, the risk is variable among these women. The lifetime risk of developing breast cancer shows positive linear correlations with the radiation dose, volume of the field irradiated, and patient age at the beginning of the treatment. In this group, mammography and magnetic resonance imaging complement each other in breast cancer screening.[31] Ng et al. reported that, among these patients, the sensitivity of mammography and magnetic resonance imaging, when used separately, is 68% and 67%, respectively. However, when the two methods are used in combination, the sensitivity increases to 94%.[32] Therefore, it is recommended that all patients exposed to chest wall irradiation before the age of 30 follow a similar screening protocol to that recommended for women with a BRCA1 or BRCA2 gene mutation.

Atypical ductal hyperplasia and lobular neoplasia

Atypical ductal hyperplasia and lobular neoplasms (atypical lobular hyperplasia and lobular carcinoma in situ) are not only precursor lesions, but also risk factors for breast cancer. Their diagnosis may increase the relative risk of developing cancer by 4-10 times.[33,34] There is a consensus that breast cancer screening with mammography should start right after the diagnosis of such lesions. The big issue still under debate is the use of magnetic resonance imaging for breast cancer screening in such patients. The updated recommendations for breast cancer screening of the American Cancer Society (ACS) state that there is no evidence to recommend or contraindicate the use of magnetic resonance imaging. Therefore, the decision regarding its use should be made on a case-by-case basis.[35] However, the number of advocates of the use of magnetic resonance imaging in breast cancer screening is growing. Therefore, it is recommended that women with atypical ductal hyperplasia or lobular neoplasia follow a similar screening protocol to that recommended for women with a BRCA1 or BRCA2 gene mutation.

Personal history of breast cancer

Women with a personal history of breast cancer are at higher risk of developing a second tumor in the treated or in the contralateral breast.[36] In a recent study, the lifetime risk for the development of a second tumor was estimated to be at least 20-25%, a threshold considered by the ACS to classify women as being at high risk and to indicate complementary screening with magnetic resonance imaging.[35] Another study investigated the role of magnetic resonance imaging in women undergoing conservative treatment with negative mammography and ultrasound results. The detection rate was 18 neoplasms per 1,000 women, which is comparable to the detection rate observed in women with BRCA gene mutations. The reported sensitivity and specificity of magnetic resonance imaging for detecting breast neoplasms in women with a personal history of breast cancer are 92% and 82%, respectively.[37] Other authors observed similar values.[38] Therefore, it is recommended that women who received conservative treatment for breast cancer undergo screening with a combination of mammography and magnetic resonance imaging.

Considerations regarding breast tomosynthesis

Tomosynthesis represents a recent step in the evolution of digital mammography, allowing a more accurate evaluation of the breast. Several studies have confirmed the efficacy of tomosynthesis in screening for breast cancer for increasing cancer detection rates as well as reducing false-positive and recall rates.[39-41] The Oslo Trial was a prospective study comparing the combination of tomosynthesis and digital mammography with digital mammography alone. The authors observed that, when the combination of tomosynthesis and digital mammography was used, the cancer detection rate was 27% higher and the false-positive rate was 15% lower, with a consequent reduction in the need for invasive procedures.[40] The STORM Trial compared digital mammography with tomosynthesis associated with digital mammography in a sample of 7,292 women.[41] The authors observed a 51% increase in the breast cancer detection rate and a 17% reduction in the false-positive rate with the use of tomosynthesis. Friedewald et al. retrospectively analyzed 454,850 examinations, of which 281,187 were digital mammograms and 173,663 were tomosynthesis images obtained in 13 centers in the United States.[42] The authors found that the use of tomosynthesis resulted in a 41% increase in the rate of detection of breast neoplasms, mainly primary invasive tumors, with a 15% reduction in the false-positive rate, which has the benefit of reducing screening costs. Other studies corroborated these findings.[43,44]

Some points are yet to be discussed regarding the tomosynthesis protocol. The Food and Drug Administration recommends a combined approach (combo mode) to breast cancer screening, in which conventional digital mammography views (mediolateral-oblique and cranial-caudal) are combined with tomosynthesis acquisition in those same two planes. The dose of radiation, which was the main initial concern, has been shown to be lower than the maximum dose (3.0 mGy per view). Recent studies have demonstrated the efficacy of synthesized mammography, which is a new technique for digital mammography reconstruction based on tomosynthesis images. The use of synthesized mammography maintains the benefits of tomosynthesis while reducing the dose of radiation by nearly half.[45] Therefore, on the basis of data in the literature, the CBR, SBM and FEBRASGO state that tomosynthesis (combo or synthetized mode), when accessible and available, may be considered in breast cancer screening protocols. These data will be reviewed in three years.

CONCLUSION

The reduction in breast cancer mortality, initially recorded in the United States and Europe, is the result of decades of investment focused on early diagnosis and access to appropriate treatment. Breast cancer early detection benefits women with less invasive surgical procedures, increased healing potential and reduced treatment costs. These benefits would keep a significant portion of the female population economically active. It is fundamental that policies aimed at increasing the rate of early detection be implemented in Brazil.

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