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ULTRASONOGRAPHY IN ASYMPTOMATIC DENSE BREAST: A SYSTEMATIC REVIEW

Arizal Abdulloh*

**Faculty of Medicine, University of Tanjungpura, Indonesia*

***Corresponding Author:**
arizalbaru@gmail.com

Abstract

Breast cancer is a group of abnormal cells in the breast that continue to grow in multiples. Eventually these cells form a lump in the breast. If the cancerous lump is not controlled, the cancer cells can metastasize to other parts of the body. Metastases can occur in the axillary lymph nodes or above the scapula. In addition, cancer cells can nest in the bones, lungs, liver, skin and under the skin. Ca Mamae is a malignancy of the breast tissue which can originate from the ductal or lobule epithelium. Breast cancer ranks as the second leading cause of mortality in women who have been diagnosed with the disease. According to some studies, screening women for breast cancer once a year beginning at the age of 40 can reduce the risk of dying from the disease by approximately 40 percent. It is well acknowledged that mammography is an effective screening procedure for detecting breast cancer in its early stages; yet, the test is not without its limitations, particularly for women who have dense breasts. The sensitivity of mammography is reduced when performed on people who have dense breast tissue. In addition, women who have dense breast tissue have an increased risk of getting breast cancer, despite the fact that mammography has a lower detection rate for dense breast tissue. Mammographically undetected cancer can sometimes be found in women with dense tissue by the use of ultrasound screening, which can be performed manually or automatically. Studies have shown that ultrasonography makes a significant improvement in the diagnosis of clinically significant tumors that are relatively small, predominantly invasive, and lack lymph nodes. The use of supplemental breast ultrasonography in the population of women who have mammographically dense breast tissue makes it possible to detect tiny breast tumors that would have been occult otherwise. An elevated rate of biopsies is connected with the possibility of unfavorable consequences for the women who fall into this intermediate risk category.

Keyword: *Breast cacer; Dense; Mammographic; Ultrasonography*

INTRODUCTION

Cancer ranks second as the largest cause of death due to Non-Communicable Diseases every year (8.8 million people), with an incidence of 14 million cases in 2012, while cardiovascular disease ranks first (17.7 million people).[1] According to the American Cancer Society, breast cancer is the most common type of cancer in women and is the second leading cause of death from cancer in women after lung cancer. In 2017 in the United States it is estimated that there will be around 252,710 new cases of invasive breast cancer, 63,410 new cases of carcinoma in situ, and around 40,610 women will die from breast cancer.[2,3]

Dense breasts cause low mammographic sensitivity and breast cancer. The US screening population over 40 had 43.3% thick breasts and Korea 54.8%. It rose to 56% and 83.2% for young women in their 40s.[4] Dense breast tissue may reduce mammography sensitivity. According to the Breast Cancer Surveillance Collaboration, mammography sensitivity declined from 85.7–88.8% in patients with breast tissue constituted nearly exclusively of fatty tissue (non-dense breast tissue) to 62.2–68.1% in patients with extremely thick breast tissue.[5,6] Density of the breasts is a risk factor for breast cancers on its own.[7,8]

Dense breasts are in the middle range of risk for breast cancer (15–20% lifetime risk). Women with a breast density of more than 75% were 4–6 times more likely to get breast cancer than women with a breast density of less than 10%. Women with a breast density of 50–74% were 2.9 times more likely to get breast cancer than women with a breast density of less than 10%.[9] Park et al. found that Korean women with more dense breasts were more likely to get breast cancer. Women with extremely dense breasts were five times more likely to get breast cancer than women whose breasts were mostly made of fat. Women with heterogeneously dense breasts were 3.8 times more likely to get breast cancer.[10]

There isn't enough proof that screening in the US makes people live longer, so no recommendations have been made for the screening guidelines. In the United States, however, new laws require doctors to tell women about the density of their breast tissue and tell women with dense breasts to get extra screenings.[11] The American College of Radiology (ACR) says that women with dense breasts can get supplemental ultrasound screening, and women with an intermediate risk of breast cancer who have a history of lobular carcinoma in situ can get supplemental magnetic resonance imaging. The Korean guidelines neither suggest US as a screening method nor say it shouldn't be used.[12–14] This article explores the utility of ultrasonography in the diagnostic process of individuals who present with no symptoms despite having dense breast tissue.

METHODS

Protocol

All data collection, processing, and reporting for this study adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 project's specifications. These factors served as the basis for the development of the implemented regulations.

Eligibility Criteria

The goal of this review of the literature on the utility of ultrasonography in the examination of patients with asymptomatic dense breasts was to assess the existing research on these two topics. These are the primary issues raised by the current study. 1) Articles must always be written in English and highlight the utility of ultrasonography in the examination of patients with asymptomatic dense breasts in order to be considered for publication. 2) Articles published after 2015 but before the period of this systematic review were considered for this evaluation. Editorials, submissions without a DOI, reviews of previously published articles, and entries that are substantially identical to those already published in the journal will not be included in the anthology.

Search Strategy

The search for studies to be included in the systematic review was carried out from March, 5th 2023 using the PubMed and SagePub databases by inputting the words: “ultrasonography” and “asymptomatic dense breasts”. Where *("diagnostic imaging"[MeSH Subheading] OR ("diagnostic"[All Fields] AND "imaging"[All Fields]) OR "diagnostic imaging"[All Fields] OR "ultrasonography"[All Fields] OR "ultrasonography"[MeSH Terms] OR "ultrasonographies"[All Fields]) AND ("asymptomatic"[All Fields] OR "asymptomatically"[All Fields] OR "asymptomatics"[All Fields]) AND ("dense"[All Fields] OR "densely"[All Fields]) AND ("breast"[MeSH Terms] OR "breast"[All Fields] OR "breasts"[All Fields] OR "breast s"[All Fields])* is used as search keywords.

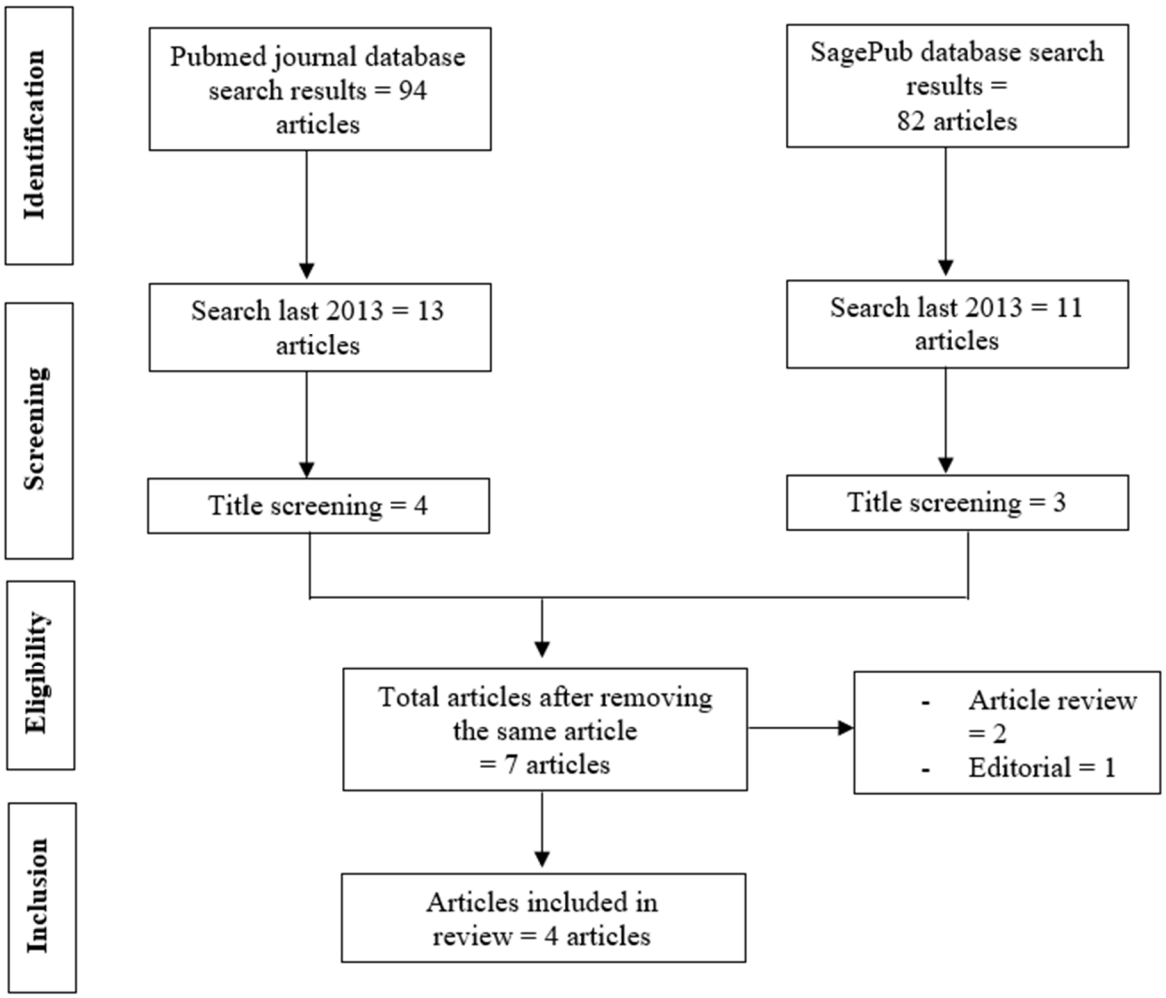

Figure 1. Article search flowchart

Data retrieval

After reading the abstract and title of each study, the authors decided whether or not it met the criteria for inclusion. After that, the authors decided that historical literature would be their main source for this topic. This conclusion was reached after a thorough look at a large number of investigations, all of which pointed in the same clear direction. All submissions must be written in English and can't have been published anywhere else. In the systematic review, only studies that met all of the criteria for inclusion were looked at. This narrows down the search results to only those that match the query.

Our team doesn't look at the results of studies that don't meet our standards. After that, the research will be looked at in a lot of detail. When the analysis for the study was done, the following pieces of information were found: names, authors, publication dates, location, study activities, and parameters. After the search results were put into an EndNote file, the database was then cleaned up by getting rid of duplicate articles. Two different reviewers looked at the titles and abstracts of all the papers to figure out which ones were still relevant to this study.

Quality Assessment and Data Synthesis

Before deciding which papers to dig deeper into, each author looked at the research listed in the title and abstract of the publication on their own. The next step will be for us to look at all of the papers that meet the review's criteria and should be included. When we're done with our research, we'll choose the relevant research papers for the review. Based on this rule, the manuscripts that will be looked at will be chosen. As much as possible, the process of choosing articles for further review should be made as easy as possible. Which earlier studies were done, and what about them made it possible to include them in the review, if any?

RESULT

Ohuchu, et al (2016)[15] showed tat the intervention group was significantly more sensitive than the control group (91.1%, 95.0%). CI 87.2-95.0 versus 77%, 70.3-83.7; p = 0.0004), but specificity was considerably lower (87.7%, 87.3-88.0 vs 91.4%, 91.1-91.7; p <0.0001). More malignancies were diagnosed in the intervention group than in the control group (184 [0.50%] vs 117 [0.32%], p = 0.0003; 144 [71.3%] vs 79 [52.0%]; p = 0.0194); these tumors were more frequently stage 0 and I. 18 (0.05%) interval cancers were found in the intervention group versus 35 (0.10%) in the control group (p = 0.034). Park, et al (2017)[10] study showed that the breast cancer risk for women with extremely dense breasts was five times that of women with almost entirely fatty breasts (adjusted odds ratio [aOR] =5.0; 95% confidence interval [CI =3.7–6.7); however, the risk varied between recalled women (aOR =3.3, 95% CI =2.3–3.6) and women without recalled results (aOR

=12.1, 95% CI =6.3–23.3, P-heterogeneity = 0.001). aORs for BI-RADS categories of breast density were comparable when participants who developed cancer after presenting non-recall findings during initial screening were classified by time to cancer diagnosis (1 and 1 year).

The link between dense breasts and breast cancer was larger in younger women (heterogeneously dense breast: aOR =7.0, 95% CI =2.4–20.3, women in their 40s) than in older women (heterogeneously dense breast: aOR =2.5, 95% CI =1.1–6.0, women in their 70s or older). This study found that an increased risk of breast cancer was associated with larger breast density in Korean women. This association was maintained regardless of the BI-RADS assessment category, the time interval after originally non-recall results, or the presence or absence of menopause.[10]

Table 1. The litelature include in this study

Author	Origin	Method	Sample	Recommendation
Ohuchi, 2016[15]	Japan	Randomised controlled trial	72,998 women enrolled, 36,859 were assigned to the intervention group and 36,139 to the control group	Women who have thick breasts may benefit from ultrasonography because it is a low-cost method that has the potential to boost the sensitivity and detection rates of early malignancies. Long-term monitoring is required in order to determine whether or not the combined method has the potential to lessen the incidence of advanced breast cancers at the time of identification and the death rate associated with breast cancer.
Park, 2017[10]	Republic of Korea	Case–control study	1,561 breast cancer patients and 6,002 matched controls	This study found that an increased risk of breast cancer was associated with larger breast density in Korean women. This association was maintained regardless of the BI-RADS assessment category, the time interval after originally non-recall results, or the presence or absence of menopause.
Korpraphong, 2014[16]	Thailand	Case–control study	14,483 breast cancer screenings in women who had non-fatty breast density, 115 cancers were documented	The use of US as an addition to MX for the detection of breast cancer in asymptomatic women who are not fatty and who have an average risk of developing breast cancer is an interesting and potentially useful diagnostic method. It was shown that women between the ages of 40 and 59, as well as women with a breast density of D4, experienced the greatest benefit from the treatment.
Shoji, 2021[17]	Japan	Randomized clinical trial	76,119 women	Mammography alone exhibited a low level of sensitivity, however adjunct ultrasonography was related with an enhanced level of sensitivity. Our results imply that supplementary ultrasonography may improve the diagnosis of early-stage and invasive breast cancers in dense and nondense breasts. Regardless of breast density, supplemental ultrasonography should be regarded a suitable imaging technique for breast cancer screening in asymptomatic women aged 40 to 49 years.

Other study showed the cancer detection rate (CDR) as a whole was 7.9 per 1000 examinations (95% CI = 6.5–9.5). The CDR for mammography (MX) alone (also known as MX-CDR) was 6.5 per 1000 examinations (95% CI = 5.2–7.9). Adding US has the potential to considerably improve CDR (P <0.001; 95% CI = 0.9–2.2); the US-ICDR was 1.4 per 1000 exams. In terms of age group, the range of 40–59 years was the one that showed the most statistically significant improvement of ICDR (P <0.001). The US-ICDR for D4 breast density was 2.5 per 1000 exams, making it the subtype with the greatest incidence of breast cancer.[16]

Study showed sensitivity was significantly higher in the intervention group than the control group (93.2% [95% CI = 87.4%-99.0%] vs 66.7% [95% CI = 54.4%-78.9%]; P < .001). Similar trends were observed in women with dense breasts (sensitivity in intervention vs control groups, 93.2% [95% CI = 85.7%-100.0%] vs 70.6% [95% CI = 55.3%-85.9%]; P < .001) and nondense breasts (sensitivity in intervention vs control groups, 93.1% [95% CI = 83.9%-102.3%] vs 60.9% [95% CI = 40.9%-80.8%]; P < .001). The rate of interval cancers per 1000 screenings was lower in the intervention group compared with the control group (0.5 cancers [95% CI = 0.1-1.0 cancers] vs 2.0 cancers [95% CI = 1.1-2.9 cancers]; P = .004).[17]

Within the intervention group, the rate of invasive cancers detected by ultrasonography alone was significantly higher than that for mammography alone in both dense (82.4% [95% CI = 56.6%-96.2%] vs 41.7% [95% CI = 15.2%-72.3%]; P = .02) and nondense (85.7% [95% CI = 42.1%-99.6%] vs 25.0% [95% CI = 5.5%-57.2%]; P = .02) breasts. However, sensitivity of mammography or ultrasonography alone did not exceed 80% across all breast densities in the 2 groups. Compared with the control group, specificity was significantly lower in the intervention group (91.8% [95% CI = 91.2%-92.3%] vs 86.8% [95% CI = 86.2%-87.5%]; P < .001).[17]

DISCUSSION

Breast cancer is a group of abnormal cells in the breast that continue to grow in multiples. Eventually these cells form a lump in the breast. If the cancerous lump is not controlled, the cancer cells can metastasize to other parts of the body. Metastases can occur in the axillary lymph nodes or above the scapula. In addition, cancer cells can nest in the bones, lungs, liver, skin and under the skin. Ca Mamae is a malignancy of the breast tissue which can originate from the ductal or lobule epithelium.[18,19]

The second greatest cause of cancer-related deaths among women is breast cancer. Studies estimate an approximate 40% reduction in breast cancer mortality when screening women annually beginning at age 40. Although mammography is widely recognized as an effective screening method for detecting breast cancer in its early stages, it is imperfect, particularly for women with thick breasts. In women with dense breast tissue, mammography's sensitivity is diminished.[6,20]

Moreover, women with thick breasts have a higher risk of developing breast cancer, although mammography has a lesser sensitivity. Ultrasound screening, whether handheld or automated, is helpful for finding mammographically undetectable malignancy in women with dense tissue. According to studies, ultrasonography dramatically improves the diagnosis of clinically relevant, tiny, mainly invasive, node-negative tumors.[21,22]

Mammography is an X-ray imaging of compressed breast tissue. A mammogram is a picture of the results of a mammography. To obtain a good interpretation of imaging results, it is necessary to have two mammogram positions with different projections of 45 degrees (craniocaudal and mediolateral oblique). The goals of mammography are breast cancer screening, breast cancer diagnosis, and follow-up after treatment.[23]

Mammography is performed on women aged over 35 years, but because Indonesians' breasts are denser, the best mammography results are obtained at ages> 40 years. Mammography is done on days 7-10 counting from the first day of menstruation. BIRADS, developed by the American College of Radiology, is used to standardize the assessment and reporting of mammography results. Mammographic features for malignant lesions are divided into primary and secondary signs.[23]

Primary signs include: 1. increased density of the tumor 2. irregular tumor boundaries due to infiltration into the surrounding tissue or unclear boundaries (comet sign) 3. translucent appearance around the tumor 4. stellate appearance 5. presence of microcalcifications according to Egan's criteria 6. clinical size of tumor was larger than radiologic. Secondary signs: 1. skin retraction or skin thickening; 2. increased vascularity; 3. change in nipple position; 4. axillary lymph nodes (+); 5. the state of the tumor area and irregular fibroglandular tissue; and 6. dense threadlike subareolar tissue.[23]

Park, et al. (2017) is the first population-based screening to examine the effect of breast density on breast cancer risk in Asians. Very dense breasts increased breast cancer risk fivefold compared to fatty breasts. Despite masking effects, breast density increased breast cancer risk. Dense breasts increased breast cancer risk regardless of age or menopausal state, but younger and premenopausal women were more at risk.[10]

Handheld and automated screening ultrasound is effective in detecting mammographically occult cancer in women with dense tissue. Ultrasound has been shown in studies to significantly improve detection of clinically significant, small, invasive, node-negative cancers. The goal of this review article is to summarize the literature on screening breast ultrasound (SBU), focusing on differences in cancer detection in high risk and intermediate risk women, and to discuss practical ways to implement screening ultrasound in clinical practice, including automated whole breast ultrasound (ABUS), as a viable solution to the growing need for additional screening.[26]

Breast density is an independent breast cancer risk factor. Dense breasts fall into the group of intermediate risk for breast cancer (15–20% lifetime risk). Women with breast density 75% were 4–6 times more likely to develop breast cancer than women with breast density ≤10%, while women with breast density of 50–74% were 2.9 times more likely to develop breast cancer than women with breast density ≤10%.[5,26] Park et al. found that Korean women with denser breasts had a higher risk for breast cancer. Compared to women with breasts consisting nearly completely of fatty tissue, women with highly dense breasts had a five-fold increased risk of breast cancer, and women with heterogeneously dense breasts had a three-and-a-half-fold increased risk.[10]

Ultrasound detects cystic masses. According to BIRADS, the American College of Radiology has also standardized ultrasound reading and reporting like mammography. Mass shape, borders, orientation, posterior acoustic, lesion boundaries, and echo pattern were characterized. Malignant lumps have uneven surfaces, taller than wider, hyperechoic edges, heterogeneous internal echo, enhanced, irregular vascularization, and 90-degree vascularization into the tumor. Mammography accuracy increases to 7.4% with ultrasound. Ultrasound is not suggested as a screening method due to evidence showing its ineffectiveness.

CONCLUSION

In the group of women with mammographically dense breast tissue, supplemental breast ultrasonography enables the diagnosis of tiny, otherwise undetectable breast tumors. An increase in the number of biopsies performed on women in this intermediate-risk group is associated with potential deleterious effects.

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