

Review Article

The Use of Ultrasound in Breast Cancer Screening of Asymptomatic Women with Dense Breast Tissue: A Narrative Review

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ABSTRACT

Introduction: Mammography is the standard screening modality for breast cancer; however, sensitivity reduces with increasing breast density, resulting in the potential for masking of cancer. Ultrasound is a potential supplemental screening tool, but its routine use is controversial.

Methods: A database search was performed with keywords “ultrasound” and “breast density and screening”, including variations. Articles were included if they assessed the use of hand-held ultrasound as a supplemental screening modality in women with dense breasts.

Discussion: Twelve articles were identified. No high-level evidence articles were identified. Cancer detection rates increased with the addition of ultrasound-to-mammography screening protocols. However, this was associated with increased costs per cancer detected, an increased biopsy rate, and a low positive predictive value. The survival benefit, cost versus benefit, and psychological impact of the addition of ultrasound is unknown.

Conclusions: The addition of ultrasound to a screening program in an asymptomatic population of women with dense breast tissue detects additional cancers compared with mammography alone. Knowledge regarding a survival or cost benefit associated with increased cancer detection, and the psychological impact of the addition of ultrasound is unknown. Further research is needed to assess whether the addition of ultrasound is cost-effective with respect to clinical outcome and survival.

RÉSUMÉ

Introduction : La mammographie est la modalité de dépistage standard pour le cancer du sein; cependant, la sensibilité diminue avec l'augmentation de la densité du tissu mammaire, entraînant une possibilité de masquage du cancer. L'échographie est un outil de dépistage supplémentaire potentiel, mais son utilisation de routine suscite une certaine controverse.

Méthodologie : Une recherche documentaire a été faite à l'aide des mots-clés « ultrasound », « breast density » et « screening », avec leurs variations. Les articles ont été retenus s'ils évaluaient l'utilisation des appareils d'échographie à baguette comme modalité de dépistage supplémentaire pour les femmes présentant une densité élevée du tissu mammaire.

Discussion : Douze articles ont été recensés, mais aucun présentant des données probantes de haut niveau. Les taux de détection du cancer ont augmenté avec l'ajout de l'échographie aux protocoles de dépistage par mammographie. Cette augmentation était cependant associée à une augmentation du coût par cancer détecté, une augmentation du nombre de biopsies et une faible valeur de prédiction positive. L'avantage au plan du taux de survie, le rapport coût-avantage et l'incidence psychologique de l'ajout de l'échographie sont inconnus.

Conclusion : L'ajout de l'échographie à un programme de dépistage au sein d'une population asymptomatique de femmes présentant une densité élevée du tissu mammaire permet de détecter des cancers additionnels par rapport à la mammographie utilisée seule. L'avantage sur le plan du taux de survie ou des coûts associé à un taux de détection plus élevé est inconnu, tout comme l'incidence

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psychologique de l'ajout de l'échographie. Des recherches plus poussées sont nécessaires afin d'évaluer si l'ajout de l'échographie

présente un rapport coût-avantage positif en matière de résultat clinique et de survie.

Keywords: Mammographic density; ultrasound; dense breast; screening; asymptomatic

Introduction

Breast cancer is a leading cause of mortality in women worldwide [1–3]. It is a heterogeneous disease [4] with many identified environmental, reproductive, and genetic risk factors [4–9]. Breast density has been shown to be an independent risk factor for the development of breast cancer [10], with a 4–6 times higher risk of breast cancer for women with dense breasts than for women with fatty breasts [11, 12].

Breast cancer screening programs for asymptomatic women have been introduced in many countries in an effort to improve early diagnosis and reduce mortality associated with breast cancer [13]. Mammography is the screening test of choice and is the only imaging modality shown to improve survival, with reported 10%–63% reduction in breast cancer mortality among women undergoing screening [11, 13–15]. Reported sensitivity of mammography for cancer detection varies from 0.2 to 0.98 and is influenced by the women's age, breast density, and histologic tumor type [11, 16–18].

Mammography sensitivity reduces substantially with greater than 50% breast density [19], with reported sensitivities for women with extreme density being less than 0.48 [13]. This results in the potential masking of cancers [20] with a reported 17.8-fold increase in interval cancer [11], which is associated with a more aggressive cancer [21]. Breast density, due to increased epithelial and stromal, or fibroglandular tissue components in the breast [11, 22] varies with life stage [22]. Younger women typically have increased density (67.9% in women aged 26–49 years compared with 42.3% in women aged 60–92 years [22]), with an average of 47% of women having dense breasts [21].

The most common method currently used to report mammographic breast density is the Breast Imaging Reporting and Data System (BI-RADS). This standardized mammography reporting lexicon was developed by the American College of Radiology (ACR) to improve consistency in reporting of mammogram findings [4]. The BI-RADS system has four categories for breast density, with categories three and four considered to be dense breast tissue (see Table 1 for category details) [11, 23]. Interobserver and intraobserver agreement using BI-RADS lexicon exists within the literature, with moderate-to-substantial agreement reported [24–30]. Winkel et al [30] reported a 13% difference between high-risk and low-risk mammograms based on BI-RADS density. Given this variation, misclassification of a mammogram into dense or nondense categories may influence the recommendation for a need for supplemental imaging [29].

Recent legislation passed in the United States dictates that women undergoing screening mammography must be informed if they have >50% breast density, with the

legislation recommending either a supplemental screening ultrasound or magnetic resonance imaging be performed in these women [31]. Despite this recommendation, actual guidelines in the literature with regard to the best supplemental imaging modality based on costs, sensitivity, and specificity are not clear [2].

Breast ultrasound is a relatively inexpensive, readily available modality that does not use ionizing radiation, can be used for interventional procedures, and is generally well tolerated by women [32]. It has also been reported to diagnose cancers at an earlier stage than mammography [19]. Given the general benefits of ultrasound as an imaging modality, the aim of this work is to review the current knowledge regarding the use of sonography as a supplemental imaging modality for screening of asymptomatic women with dense breast tissue and assess the evidence available for its recommendation as a first-line supplemental modality in screening programs.

Methods

This narrative review was designed to assess the current knowledge surrounding the use of ultrasound in screening of asymptomatic women for breast cancer. A review of the literature was performed using electronic databases including DiscoverIT, PubMed/Medline, CINAHL with full text, and the Cochrane Library databases.

Search keywords included dense breast, breast density, ultrasound, ultrasonography, sonography, screening, breast cancer, and mammographic density.

Articles with full-text access were collated. Abstracts were reviewed for relevance to the topic, and preference was given to English language, peer-reviewed primary research articles. A secondary manual search of reference lists from relevant articles was then performed to further identify any relevant articles. Neither publication date nor location were criteria for exclusion.

Inclusion Criteria

Articles were included if they assessed screening hand-held ultrasound in asymptomatic women with dense breast tissue. All risk-level women were included if they were asymptomatic. Both film and digital mammography studies were included for review. Articles were included if an asymptomatic subgroup of women was analyzed.

Exclusion Criteria

Articles were excluded if the study population included women with palpable abnormalities, pain or mammographic abnormalities, or if automated breast ultrasound was used.

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