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Breast density and breast cancer

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ABSTRACT

Breast density is increasingly recognized as an independent risk factor for the development of breast cancer. It has been shown to be associated with a four- to sixfold increase a woman's risk of malignant breast disease. Increased breast density, as identified on mammography, is known to decrease the diagnostic sensitivity of the examination, which is of great concern to women at increased risk for breast cancer. Dense tissue has generally been associated with younger age and premenopausal status, with the assumption that breast density gradually decreases after menopause. However, the actual proportion of older women with dense breasts is unknown. Unfortunately, mammography is less accurate on dense breast tissue compared to fattier breast tissue. Multiple studies suggest a solution to this by demonstrating the ability of supplemental screening ultrasound to detect additional malignant lesions in women with dense breast tissue but with negative mammography. Improved screening methods for women with dense breasts are needed due to their increased risk of breast cancer and of failed early diagnosis by screening mammography.

Keywords: mammography, breast ultrasound, increased breast density

INTRODUCTION

Breast tissue comprises skin, blood vessels, ductal and stromal elements of the glands, appearing radio-opaque or white on mammography, and fat, which appears radiolucent or black on mammography. The density of breast tissue reflects the relative amount of glandular and connective tissue (parenchyma) as compared to adipose tissue (1). Women with mammographically dense breast tissue, generally defined as dense tissue comprising more than 75% of the breast, have a higher breast cancer risk compared with women of similar age with less or no dense tissue (2). Breast density does not appear to be associated with a specific breast cancer subtype or with higher breast cancer mortality. Although breast density is a largely inherited trait, other factors can influence density, such as age (40-49 years), body mass index and hormonal treatments during menopause (1,3).

SCREENING MAMMOGRAPHY IN PATIENTS WITH INCREASED BREAST DENSITY

Screening mammography has lower sensitivity and specificity for women with increased breast density (4). Mammographic breast density is defined as the relative amount of radio-opaque (white) elements to radiolucent (black) fat on the image. Breast density does not correlate with physical examination findings. Increased breast density may obscure the detection of a benign mass or, more importantly, a breast cancer (5). Reduced sensitivity of mammography in younger women in part is related

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to increased mammographic density due to a higher proportion of breast epithelial and stromal elements in younger breasts. There is much variation in the physical composition of the breast. Differing proportions of fat, connective tissue, and ductal and lobular elements contribute to differences in mammographic breast density (4). Mammographic density is not related to the size or firmness of the breast. Breast density is greater in younger women and also varies with menopausal status, genetic factors, parity, use of estrogen, use of chemoprevention and body habitus (5,6). Breast density can vary during different phases of the menstrual cycle, with slightly increased density in the luteal as compared with the follicular phase (1).

There are several ways to report mammographic breast density. The most commonly used method is the Breast Imaging Reporting and Data System (BI-RADS), in which the determination of breast density is made by the radiologist using visual assessment that is subject to inter-rater variability (7).

BI-RADS is based on a scale that identifies breast tissue density as being in one of four categories, A-D. Type A (almost entirely fatty, the lowest density): around 10% of women who undergo a mammography will have mostly fatty, very low-density breasts; type B (scattered areas of fibro-glandular density): roughly 40% of women who undergo a mammography will have this low level of density; type C (heterogeneously dense): another 40% of women will have this type of mammographic density, which is considered dense and may obscure small masses; type D (extremely dense): around 10% of women undergoing a mammography will have extremely dense breasts, which lowers the sensitivity of mammography (7,8).

For most purposes, the term "dense breasts" refers to either heterogeneously dense or extremely dense breasts (categories C or D BI-RADS) (7).

Digital mammography is more sensitive than film mammography for dense breasts and is preferred, when available. Also, for dense breast patients, regarding efficacy detection, contrast-enhanced digital mammography is superior to synthetic two-dimensional mammography or digital breast tomosynthesis (DBT) (8). DBT compared with digital mammography may decrease the recall rate for women with dense breasts, but may, somehow, increase the radiation exposure rate, depending on the type of tomography available (5). Consensus exists regarding the need for association of another type of imaging technique, breast ultrasound and/or magnetic resonance imaging (MRI).

BREAST ULTRASOUND AND MRI IN PATIENTS WITH INCREASED BREAST DENSITY

Supplemental screening ultrasound may be beneficial to women with dense breast tissue. The addition of ultrasonography to mammography increases sensitivity for small cancers but greatly decreases specificity (4). Two types of ultrasound have been investigated for supplemental screening: screening handheld ultrasound and automated breast ultrasound. Whole-breast ultrasound screening can detect early-stage, mammographically occult breast cancers in women with dense breast tissue, but the additional screening test carries a substantial risk for false-positive results (5). When used as a supplement to mammography, ultrasound can improve the sensitivity of screening at the expense of decreased specificity, with increased need for follow-up imaging, an increased breast biopsy rate and breast biopsies with benign results leading to patient anxiety (9). Furthermore, the usage of machine learning on color Doppler features, develops models for breast cancer diagnosis and offers a higher precision and accuracy in cases of borderline diagnoses (10).

In Figure 1 and Figure 2 we present the ultrasound examination aspect of a 39 years old patient with BI-RADS 3 and ACR-C density, with diagnosed lobular breast carcinoma.

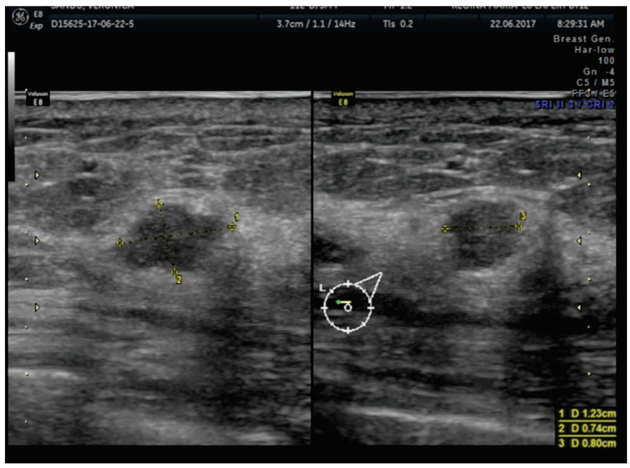

FIGURE 1. Ultrasonographic aspect of a 39 years-old patient with BI-RADS 3, ACR-C density and diagnosis of lobular breast carcinoma

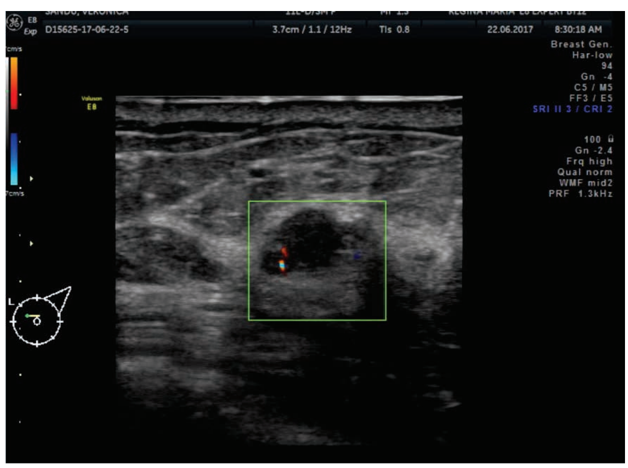

FIGURE 2. 2D color Doppler ultrasound aspect of a 39 years-old patient with BI-RADS 3, ACR-C density and diagnostic of lobular breast carcinoma

Routine supplemental screening breast MRI, as an adjunct to mammography, is recommended for women who have a lifetime risk>20% according to the risk models, regardless of breast density (4). Breast density for such women is not a relevant factor, and ultrasound is unnecessary for women who are undergoing MRI examination. The cancer detection rate of supplemental MRI is greater than supplemental ultrasound. Supplemental ultrasound found additional cancers, beyond those seen on the combination of mammography and MRI in a large multi-institutional trial in high-risk women, but cost-effectiveness should not be neglected (11,12). Women with dense breasts who also have other high-risk factors (such as known deleterious gene mutations, prior mantle radiation exposure, and sufficiently strong family history) should follow the supplemental screening guidelines for high-risk women that may include annual supplemental MRI in addition to annual mammography (4,13). Supplemental MRI screening in women of intermediate risk with BI-RADS class D and extremely dense breast tissue is an option, recognizing that this will find some cancers, but the probability of a false positive result is elevated, with an increase in biopsies, cost, possibly overdiagnosis and, most important, a higher patient's anxiety, with no evidence of a reduction of breast cancer specific or overall mortality (7,14).

The role of digital breast tomosynthesis (DBT) in medical practice has increased continuously over the last decade. A number of early clinical studies has showed a higher accuracy of DBT as compared to standard full-field digital mammography, but the better results are dependent regarding age and breast density category (15). Also, screening with abbreviated breast MRI, compared to DBT, depicted a higher accuracy for invasive breast cancers, but there is need for further research in comparing the screening methods (16). The limitations of DBT include longer interpretation duration, higher costs and increased radiation exposure (17,18).

CONCLUSIONS

Breast density is a normal mammographic finding. Multiple factors contribute to breast density in women, including age, genetics, body habitus, parity, use of estrogen, and phase of the menstrual cycle. The term "dense breasts" refers to either heterogeneously dense or extremely dense breasts (categories C or D of the Breast Imaging Reporting and Data System [BI-RADS]). The presence of dense breast tissue on mammography decreases the sensitivity of mammography and is an independent risk factor for breast cancer, as most cancers develop in the glandular parenchyma. The addition of ultrasonography to mammography increases sensitivity for incipient cancers but greatly decreases specificity. Supplemental screening with MRI is also limited by high false-positives results and costs, limited availability and potential adverse reactions to contrast medium.

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