https://doi.org/10.29289/259453942021V31S2006

CLINICAL SIGNIFICANCE OF BREAST DENSITY: IS THERE ANY NEED FOR SUPPLEMENTAL SCREENING?

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Objectives: Mammographic density (MD) is the amount of fibroglandular breast tissue, which appears relatively radiopaque on mammography when compared with fat that appears radiolucent. It may obscure an underlying breast cancer (BC), thus decreases mammographic sensitivity. MD is also an independent BC risk factor. MD is most commonly classified by the Breast Imaging Reporting and Data System (BI-RADS), fifth edition, 2012, where breast density is determined by radiologists using visual assessment that is subject to inter-rater variability. The term "dense breasts" refers to either heterogeneously dense or extremely dense breasts (category C or D), accounting for approximately 47%–50% of women. Supplemental screening modalities, such as digital breast tomosynthesis (DBT), MRI, and ultrasound, when combined with digital mammography (DM) have shown to be effective in the identification of mammographically occult breast lesions in high breast density patients. In this study, we examined the potential value of available screening modalities and their importance in patients with increased MD. Methodology: We conducted a systematic review of the literature via MEDLINE assessing the clinical importance of MD and its role in supplemental screening protocols. Results: Reduced mammographic sensitivity — Mammographic sensitivity rate is adversely proportional to MD. Breast stromal component and hence stromal stiffening promote an increase in MD. Another important factor is that extracellular matrix stiffness has been found to be tumorigenic and is significantly associated with BC. As a consequence, the combined relative BC risk is increased exponentially in levels A, B, C, and D BI-RADS categories, respectively. Supplemental screening modalities — To overcome the limitations of digital mammography in higher MD categories, the introduction of DBT has significantly improved BC detection and reduced recall rates when added to mammography. Both STORM-1 and STORM-2 trials showed the significant improvement in BC detection rate when DBT was combined with DM. On the other hand, MBTST trial revealed an increase of false-positive rates when BC screening was carried out with DBT alone. In another multicenter study, the ACRIN Protocol 6666 established that the addition of ultrasound (US) to DM in women within BI-RADS C and D groups will identify an additional 1.1–7.2 cancers per 1,000 high-risk women, but substantially increase the number of false positive results. Breast MRI may be offered as supplemental screening modality in women with heterogeneous or extremely dense breast tissue. The combination of MRI with DM and US in screening of heterogeneous or extremely dense breasts with at least one risk factor for BC produces a 100% sensitivity rate. Also, supplemental MRI screening in women with extremely dense breasts can reduce the incidence of undetected interval BC. On the contrary, the addition of MRI possesses low specificity rates and increased cost. **Conclusions**: Increased BD is a common mammographic finding in women. Although very common, its association with reduced mammographic sensitivity and consequently BC detection masking is of high clinical significance. Additionally, BD alone is a risk factor for BC, despite the fact that the exact mechanisms of tumorigenesis associated to it are yet to be fully understood. Supplemental screening modalities, such as DBT, MRI, and US, when combined with DM have been shown to be effective in the identification of mammographically occult BC in high BD patients. The increased number of unnecessary biopsies as a result of increased false positivity rates may increase the physical and psychological patient burden. Since there is no consensus for routine use of DBT or MRI in screening of women with increased BD, the decision for supplemental screening should be personalized.

Keywords: Mammographic Density; Breast Screening; BI-RADS.