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The relationship of obesity, mammographic breast density, and magnetic resonance imaging in patients with breast cancer

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ABSTRACT

Purpose: The purpose was to evaluate the relationship between body mass index (BMI), mammographic breast density, magnetic resonance (MR) background parenchymal enhancement (BPE), and MR fibroglandular tissue (FGT) in women with breast cancer.
Methods: Our institutional database was queried for patients with preoperative mammography and breast MR imaging.
Results: There were 573 women eligible for analysis. Elevated BMI was associated with advanced stage of disease (P=.01), lower mammographic density (P<.0001), lower FGT (P<.0001), higher BPE (P=.005), and nonpalpable lesions (P=.04).
Conclusions: Higher BMI was associated with decreased breast density and FGT. Higher BMI was also associated with advanced stage disease and nonpalpable tumors on clinical exam.

1. Introduction

According to the Centers for Disease Control and Prevention, more than one third of adult women are obese, and the rate of obesity significantly increases with age [1]. As of 2013, the American Medical Association officially recognized obesity as a disease, and it is a modifiable risk factor for type-2 diabetes mellitus and cardiovascular disease. In addition, postmenopausal obese women have a 31% increased risk of developing breast cancer [2]. This would suggest that obese women represent a population that would benefit from regular breast cancer screening.

Screening mammography provides information regarding the presence or absence of suspicious findings and also provides the referring clinician with information regarding the density of the breast tissue. Mammographic breast density is described as the proportion of glandular tissue to fatty tissue. In clinical practice, it is assessed using a four-category score defined in the American College of Radiology's Breast Imaging Reporting and Data System (BI-RADS) [3]. Dense breast tissue on mammography is an independent risk factor for breast cancer which also lowers the sensitivity of the exam [4–7]. According to Boyd et al., extremely dense breast tissue causes a masking effect which increases the odds of detecting breast cancers between screenings [odds ratio (OR)=17.8, comparing ≥75% to <10% dense breast tissue] [4]. Furthermore, the relative risk of breast cancer in women with ≥50% dense breast parenchyma is 2.5–6-fold higher compared to women with predominantly fatty breasts [7]. At present, 21 states require women to be notified if they are found to have dense breast tissue [8] on routine screening mammography, presumably in order to allow for a discussion regarding the advisability of supplemental screening methods. Although elevated body mass index (BMI) is associated with lower breast density, obese women are at increased risk for postmenopausal breast cancer [9–12].

In addition to regular mammography, magnetic resonance imaging (MRI) is increasingly used as part of the recommended screening for women at higher risk for developing breast cancer. Breast tissue characteristics that are assessed on MRI include background parenchymal enhancement (BPE) and fibroglandular tissue (FGT). BPE represents the enhancement of normal breast tissue after administering intravenous contrast and reflects the vascularity of the FGT. FGT is a three-dimensional (3D) representation of fibroglandular tissue on MRI. BPE and, to a lesser extent, FGT are hormonally regulated and decrease with menopause, use of antiestrogen therapies, and history of bilateral salpingo-oophorectomy [13–17].

Despite the association of obesity with an increased risk for breast cancer, higher BMI is associated with decreased breast density on mammography. At present, there is no information regarding the effect of BMI on FGT or BPE as evaluated on MRI. The main purpose of this study was to examine the association between BMI and mammographic breast density, BPE, and FGT in women with breast cancer. Additionally, we examined the association between BMI and clinical characteristics, such as clinical presentation and stage of disease.

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2. Materials and methods

2.1. Study participants

The Breast Cancer Database at our medical center is a longitudinal registry that was established in January 2010. All patients undergoing definitive breast cancer surgery at our institution are eligible to enroll in the Breast Cancer Database. The variables collected include information on personal and family history, screening history, methods of diagnosis, stage at diagnosis, details of treatment, and outcomes. All clinical data were obtained from detailed questionnaires filled out at the time of diagnosis and review of the electronic medical records. This study was approved by the Institutional Review Board and was compliant with the standards of the Health Insurance Portability and Accountability Act.

Patients included in this study were enrolled in the Breast Cancer Database between January 2010 and September 2014 and had both mammography and breast MRI prior to surgery. Each patient contributed a single examination to the study. Men were excluded from this study. Demographic information, indication for the examination, and information including mammographic density and BI-RADS assessment were obtained from the electronic medical record. Reader interpretations of BPE, FGT, and mammographic breast density (below) were sent to a data manager who consolidated this information in an Excel spreadsheet.

2.2. Diagnostic imaging

2.2.1. Mammography imaging technique

All mammograms were performed with digital technique and were acquired using MAMMOMAT Novation DR software (version V8.3, Siemens Healthcare). Based on routine institutional practice, the images were further analyzed by iCAD computer-aided detection software (iCAD, version VA20E; iCAD, Inc., Nashua, NH, USA).

2.2.2. MRI technique

Bilateral dynamic contrast-enhanced breast MRI examinations for premenopausal women are scheduled during the second week (days 8–14) of their menstrual cycle. All breast MRI examinations were performed on commercially available systems at 1.5 T (Avanto, Siemens Medical Solutions) or 3.0 T (TIM Trio, Siemens Medical Solutions) with the patient in prone position using a dedicated surface breast coil (7-channel Breast Biopsy Array, InVivo Research). The standard imaging protocol includes a localizing sequence followed by a sagittal T2-weighted sequence (repetition time/echo time, 7220/84), a sagittal T1-weighted non-fat-suppressed 3D fast spoiled gradient-recalled echo sequence (4.01/1.52; flip angle, 12°; matrix, 384×384; field of view, 270 mm; section thickness, 1 mm), followed by the same sagittal T1-weighted fat-suppressed 3D fast spoiled gradient-recalled echo sequence performed before and four times after a rapid bolus injection of 0.1 mmol/L of gadopentetate dimeglumine (Magnevist, Bayer Healthcare Pharmaceuticals) per kilogram of body weight at an injection rate of 2.0 ml/s via an intravenous catheter. Image acquisition began immediately after administration of the contrast material and saline bolus. The first contrast-enhanced dynamic sequence was obtained at approximately 100 s, followed by four additional consecutive sequences (three sagittal followed by one delayed axial). The delayed axial images were obtained so that subtle asymmetric BPE could be appreciated. Postprocessing included subtraction images and maximum intensity projection images. Images were reviewed on high-resolution picture archiving and communication system monitors.

2.3. Image assessment

Mammographic breast density was categorized according to the American College of Radiology as entirely fatty, scattered fibroglandular, heterogeneously dense, or extremely dense breasts (Table 1 and Fig. 1) [3]. All mammograms were assessed for breast density by two fellowship-trained breast radiologists in consensus.

Table 1
BI-RADS classifications of mammographic breast density, FGT, and BPE

BI-RADS	Mammographic breast density	FGT	BPE
a	Almost entirely fatty	Almost entirely fatty	Minimal
b	Scattered fibroglandular	Scattered fibroglandular tissue	Mild
c	Heterogeneously dense	Heterogeneous fibroglandular tissue	Moderate
d	Extremely dense	Extreme fibroglandular tissue	Marked

All breast MRI examinations were assessed for BPE, in consensus, by two fellowship-trained breast radiologists who had up to 12 years of experience in reading breast MRI. Both readers were blinded to mammographic density, clinical data of the patients, and pathology results. The level of global BPE, rather than the highest BPE in a single quadrant, was assessed using a combination of pre- and the first postcontrast T1-weighted fat-saturated and subtracted images and was recorded on a four-point scale (a: minimal, b: mild, c: moderate, d: marked) in accordance with latest BI-RADS categories (Table 1 and Fig. 1) [3]. The volume and intensity of enhancement were considered in the global assessment of BPE and categorized on the basis of MR BI-RADS criteria as minimal, mild, moderate, or marked. The volume of breast parenchymal enhancement was estimated qualitatively by reviewing the amount of enhancing FGT on multiple contiguous slices. Furthermore, the amount of FGT was evaluated using the following scale based on American College of Radiology BI-RADS criteria: entirely fatty, scattered fibroglandular, heterogeneously fibroglandular, and extreme fibroglandular tissue (Table 1 and Fig. 1) [3]. In cases of asymmetry of the breasts, the higher level of mammographic density, BPE, and FGT was recorded.

2.4. Statistical analyses

Statistical analyses were performed using descriptive statistics, analysis of variance (ANOVA), Pearson's chi-square, and linear and logistic regression. The variables of interest included age, family history of breast cancer, atypical hyperplasia, lobular carcinoma in situ (LCIS), tumor characteristics, palpability, mammographic breast density, BPE, FGT, menopausal status, use of chemoprevention, and screening frequency as defined as the number of mammograms the patients had in the past 6 years. In our analyses, we looked at BMI as a categorical variable: underweight (≤18 kg/m^2), normal weight (18–24 kg/m^2), overweight (25–29 kg/m^2), and obese (≥30 kg/m^2), in accordance with the World Health Organization criteria [18]; as a dichotomous variable (<25 kg/m^2 and ≥25 kg/m^2) in accordance with the increased risk of breast cancer demonstrated in overweight and obese postmenopausal women [2,19,20]; and as a continuous variable. All analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA).

3. Results

Out of a total of 1991 women enrolled in the Breast Cancer Database at the time of the study, 573 (29%) patients had both a mammogram and a breast MRI prior to their breast cancer surgery. Of these women, the median age was 53 years (22–86 years). The majority of women were Caucasian (73%) and postmenopausal (54%) with a median BMI of 24.9 kg/m^2 (range: 16.8–46.3). The majority of women underwent annual screening mammography (52%) prior to their cancer diagnosis. The majority of breast cancers in this group were detected by mammography (53%). The majority of the patients had stage 0 or stage 1 breast cancer, with ductal carcinoma in situ representing 23% of the total. The median invasive tumor size was 1.4 cm (range 0.01–12.5 cm). The majority of patients were estrogen receptor (ER) positive (84%), progesterone receptor positive (71%), and HER2neu negative (86%) (Table 2). Forty-three3 (8%) of the patients had triple-negative breast cancer. Only