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Original Article

The relationship between breast density and bone mineral density after menopause

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Abstract. [Purpose] The purpose of this study was to analyze the relationship between breast density and bone mineral density after menopause. [Subjects and Methods] The subjects were 130 patients who participated in a bone densitometry test and had a mammogram taken between January 1st, 2013 to October 1st, 2014. The mammograms were scored breast imaging-reporting and data system. Grade 1 indicates almost only fat, Grade 2 indicates fibroglandular densities, Grade 3 indicates heterogeneously dense tissue, and Grade 4 indicates an extreme density. Correlation analysis was carried out to investigate the relationship between breast density grades and bone mineral densities by age and body mass index. [Results] Breast density had a close relationship with age (−0.59), Body mass index (−0.39), and T-score (0.29). The results indicate that as age and body mass index increase, the grade of the breast density decreases, and as the T-score increases, the grade increases. [Conclusion] A precise evaluation of the of breast cancer risk associated with breast density should be conducted as a large scale prospective study for women in Korea.

Key words: Breast density, Bone mineral density

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INTRODUCTION

It is not unusual for women to suffer from osteoporosis and breast cancer after menopause[1–4)]. The incidence of these two diseases has been reported to be related to estrogen levels. Since estrogen stimulates the mitosis of breast cells, it can also promote the occurrence and growth of breast cancer. Estrogen levels in urine or blood are related to breast cancer[5)], and osteoporosis is a metabolic bone disease that can manifest as a highly dangerous musculoskeletal disorder when bone mineral density decreases, significantly raising the risk of bone fracture[6)]. In particular, a high bone mineral density has been reported to be the result of overexposure to estrogen[7)], and therefore, the bone mineral density is considered to have a close relationship with breast cancer. Some studies have observed a correlation between breast cancer and bone mineral density. Cauley et al.[8)] performed an epidemiologic investigation of 6,854 people over the age of 65 in a study by the Osteoporotic Fracture Research Group. During shadow tracking, they found 97 patients had breast cancer and compared their bone mineral density levels. When the bone mineral density increased, the risk breast cancer also increased.

Even though prior studies have found a correlation between breast cancer and bone mineral density levels, a study of breast density had never been conducted. Breast density is highly related to breast cancer incidence[9–11)], and it is a higher determinant for risk than family history or menstruation/fecundity[12)]. That is to say, breast density is very relevant to breast cancer, and this is due to bone mineral density. A quantitative analysis of the relationship had not previously been performed; therefore, this study analyzed the relationship between breast density and bone mineral density.

SUBJECTS AND METHODS

The study subjects were 130 patients who were examined by mammography and a bone densitometry test between January 1st, 2013 to October 1st, 2014. Among these patients, women who had undergone menopause were selected, with the exception of patients with conditions that could affect bone mineral density level, such as diabetic patients (fasting glucose ≥ 126 mg/dl, ≥7.0 mmol/L) or those who had been administered hormonal treatments for more than a year. Six diabetic patients, 14 women that had not experienced menopause, and 10 who were administered hormone treatments were excluded from the study on this basis. One hundred people were chosen to be the subjects of the study, and the average age of the subjects was of 57.10±7.45 years. All the subjects signed a written informed

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Table 1. General characteristics of the subjects

Division		Average and frequency
Age (years)		57.1±7.4
Height (cm)		156.8±5.5
Weight (kg)		57.8±8.2
BMI		23.5±2.8
T-score		−1.1±1.1
Breast density	Grade 1	17 (17.0%)
	Grade 2	57 (57.0%)
	Grade 3	24 (24.0%)
	Grade 4	2 (2.0%)

BMI: body mass index

Table 2. Differences in age, BMI, and bone mineral density according to breast density

Division	Classification	N	Average
Age (years)	Grade 1	17.0	64.8±6.1
	Grade 2	57.0	57.4±6.8
	Grade 3	24.0	51.6±3.8
	Grade 4	2.0	48.0±1.4
BMI	Grade 1	17.0	24.6±2.7
	Grade 2	57.0	24.0±2.8
	Grade 3	24.0	21.8±2.2
	Grade 4	2.0	19.75±0.9
T-score	Grade 1	17.0	−1.4±1.1
	Grade 2	57.0	−1.3±1.1
	Grade 3	24.0	−0.5±1.0
	Grade 4	2.0	−0.5±0.7

Grade 1 indicates the tissue is almost entirely fat, Grade 2 indicates the presence of fibroglandular densities, Grade 3 indicates heterogeneously dense tissue, Grade 4 indicates extremely dense tissue

consent form approved by the Institutional Review Board at Soonchunhyang University Hospital. The images were acquired using existing data. Mammograms were captured by a LORAD Elite Trex Mammo (TREX-LORAD, USA) at 26 kVp, 80 mas. The breast imaging-reporting and data system categorizes the density of the parenchyma into 4 grades. Grade 1 indicates the tissue is almost entirely fat, Grade 2 indicates the presence of fibroglandular densities, Grade 3 indicates heterogeneously dense tissue, and Grade 4 indicates extremely dense tissue. The bone mineral density was measured using Dual Energy X-ray Absorptiometry (DXA, hologic, USA) of the lumbar spine, L1–L4, which is a standard measurement in bone mineral test. To improve the accuracy of the test, the average value of bone mineral density from L1 to L4 was used, and the left femur from the test that had a low accuracy was excluded. The height and weight were measured using an automatic height and weight machine. Body mass index (BMI) was caculated by dividing weight (kg) by the square of the height (m^2). Differences in age, BMI, and bone mineral density among the grades of breast density were tested using ANOVA. Then, every factor that showed a correlation with breast density was subjected to multi-variable logistic regression analysis. The statistical analysis was performed using SPSS software (SPSS v. 18.0, USA, Chicago), and significance was accepted for values of $p<0.05$.

RESULTS

The general characteristics of the subjects were an average age of 57.10 ± 7.45 years, BMI of 23.52 ± 2.86, and T-score of −1.17 ± 1.12. A Grade 1 breast density was observed in 17 patients (17.0%), Grade 2 in 57 patients (57.0%), Grade 3 in 24 patients (24.0%), and Grade 4 in 2 patients (2.0%) (Table 1). Differences in age, BMI, and the bone mineral density gap according to breast density are shown in Table 2. Patients with a Grade 1 density had the oldest average age of 64.88 ± 6.15 and Grade 4 patients were the youngest showing an average age of 48.00 ± 1.41. Grade 1 patients had the highest BMI, 24.67 ± 2.73, and Grade 4 had the lowest BMI, 19.75 ± 0.92. Grade 1 had the lowest T-score, −1.47 ± 1.07, and Grade 4 had the highest T-score, −0.50 ± 0.71 ($p<0.05$) (Table 2). The results of the correlation analysis of age, BMI, and bone mineral density gap according to breast density are presented in Table 3. Breast density exhibited a close relationship with age (−0.59), BMI (−0.39), and a T-score (0.29) ($p<0.05$). The results indicate that as age and BMI increase, the grade of the breast density decreases, and as the T-score increases, the grade of the breast density increases. The results of the large-scale logistic regression for differences in age, BMI, bone mineral density according to breast density are presented in Table 4. With Grade 1 as the basis for the logistic regression of age according to breast density, Grade 2 was 0.85 times smaller, Grade 3 was 0.70 times smaller, and Grade 4 was 0.50 times smaller in terms of age. Using Grade 1 as the basis for the logistic regression of BMI according to breast density, Grade 2 was 0.92 times smaller, Grade 3 was 0.64 times smaller, and Grade 4 was 0.38 times smaller in terms of BMI. Using Grade 1 as the basis for the logistic regression of the T-score according to breast density, Grade 2 was 1.09 times bigger, Grade 3 was 2.27 times bigger, and Grade 4 was 2.36 times bigger ($p<0.05$) (Table 4).

DISCUSSION

There are many reasons for the occurrence of breast cancer, but a long-term exposure to estrogen seems to be the most significant factor[13]. As the estrogen level increases, so does the risk of breast cancer[14]. Therefore, recent studies have attempted to find an indicator of the estrogen hormone that has accumulated by examining the bone mineral density of subjects[15, 16].

Several studies have been carried out to investigate the correlation between breast cancer and bone mineral density. Van der Klift et al.[1] found that the risks for breast cancer and bone mineral density are related, and the relative risk was 2.1 times higher (1.1–3.7) was found in the Rotterdam cohort study. This study found a correlation between breast density and bone mineral level that had nothing to do with breast cancer. As a result, the T-score increased, and so did breast density. Breast density has been found to be highly

Table 3. Correlation analysis of age, BMI, and bone mineral density according to breast density

Division		Age	BMI	T-score	Breast density
Age	Pearson correlation coefficients	1.0	0.2	−0.3	−0.6
BMI	Pearson correlation coefficients	0.2	1.0	0.1	−0.4
T-score	Pearson correlation coefficients	−0.3	0.1	1.0	0.3
Breast density	Pearson correlation coefficients	−0.6	−0.4	0.3	1.0

Table 4. Logistic regression of age, BMI, and bone mineral density according to breast density

Division	Breast density	B	SE	Exp (B)	95% CI	
					Lower	Upper
Age	Grade 2	−0.2	0.1	0.9	0.8	0.9
	Grade 3	−0.4	0.1	0.7	0.6	0.8
	Grade 4	−0.7	0.3	0.5	0.3	0.1
BMI	Grade 2	−0.1	0.1	0.9	0.8	1.1
	Grade 3	−0.5	0.1	0.6	0.5	0.8
	Grade 4	−0.9	0.5	0.4	0.2	0.9
T-score	Grade 2	0.1	0.3	1.1	0.7	1.8
	Grade 3	0.8	0.3	2.3	1.2	4.3
	Grade 4	0.9	0.7	2.4	0.6	9.8

B: coefficient, SE: standard error

related to breast cancer, and it has been reported that when breast density increases, the probability of getting breast cancer occurring is higher[17]. Consequently, when the T-score increases, the breast density also increases, and the chances of breast cancer occurring also increase.

The correlation between breast cancer and bone mineral density is influenced by many growth factors, interleukin and estrogen. For example, both insulin-like growth factor type 1 and insulin stimulate the process of bone assimilation and are related to the a risk of breast cancer[18, 19]. Moreover, there is a correlation between insulin-like growth factor and estrogen metabolism. Problems in the metabolism of transforming growth factor β are relevant to tumor genesis in breast cancer as well as the increase of bone mineral density[20]. Breast density is also related to estrogen levels. After menopause, there is a decline in estrogen and progesterone that leads to the involution of breast tissue, and there is more fatty tissue than in the breast parenchyma, lowering the breast density[21]. The present study found that bone mineral density, breast density, and breast cancer are related, and there is a negative correlation between BMI and breast density. A study of western women revealed that breast density is one of the most important factors[22, 23], and that when obesity was low, even after adjusting for age, the breast density was high. In the case of underweight women, 40 years of age or younger, the breast density was 60%, similar to the results of the present study. The limitations of the present study are that only a few subjects were investigated, so it is difficult to suggest the relevancy between breast density and bone mineral density at an objective level. Therefore, there needs to be a precise assessment of breast cancer by conducting a large-scale prospective study for women in Korea.

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