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Original Article

Correlations between female breast density and biochemical markers

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Abstract. [Purpose] The aim of this study was to identify biochemical markers related to breast density. The study was performed with 200 patients who received mammography and biochemical marker testing between March 1, 2014 to October 1, 2014. [Subjects and Methods] Following the American College of Radiology, Breast Imaging Reporting and Data System (ACR BI-RADS), breast parenchymal pattern density from mammography was categorized into four grades: grade 1, almost entirely fat; grade 2, fibroglandular densities; grade 3, heterogeneously dense; and grade 4, extremely dense. Regarding biochemical markers, subjects underwent blood and urine tests after a 12-h fast. We analyzed correlations among breast density, general characteristics, and biochemical markers. [Results] Breast density-related factors were age, height, weight, body mass index (BMI), hematocrit, MCH, RDW, AST, ALT, ALP, uric acid, γGT, triglycerides, total cholesterol, HDL-cholesterol, and LDL-cholesterol. [Conclusion] The results can be used as basic and comparative data for the prevention and early control of breast cancer.
Key words: Breast density, Biochemical marker, Related factors

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INTRODUCTION

It is known that breast density is a risk factor of breast cancer. A woman who has more than 75% breast density is 4–6 times more likely to have breast cancer than a woman who has a breast density of less than 25%[1]. Guidelines for breast cancer screening have been suggested, and women over 50 years old are generally recommended to undergo mammography. One study even says women in their 40s can also increase their lifespan through mammography, recommending they too should undergo mammography[2, 3].

One of the key factors that affects mammography's sensitivity is breast density. Not only does higher breast density mean a higher chance of having breast cancer, but breast density can also cause false negatives and increase re-examination rates by lowering mammography's sensitivity[4, 5]. Breast density is affected by race, age, BMI, and the level of female sex hormones. In particular, body mass index (BMI) is a risk factor for breast cancer in women who are in menopause. It has also been shown in several pilot studies that abdominal obesity and weight increase, even after correcting for BMI, have some connection with the increased rate of breast cancer after menopause[6, 7]. As the amount of body fat grows due to obesity, so does the amount of fatty tissue generally, and eventually the density in mammography decreases.

As mentioned above, some factors related to breast density have been reported, but they are only basic characteristics. Thus, this study examined biochemical markers related to breast density.

SUBJECTS AND METHODS

The study subjects were 230 patients who underwent mammography and biochemical marker tests between March 1 and October 1, 2014, at Soonchunhyang University hospital. All the subjects signed a written informed consent form approved by the Institutional Review Board of Soonchunhyang University Hospital.

Subjects who may have had abnormal bone density levels, such as diabetic patients, fasting glucose ≥ 126 mg/dl, ≥ 7.0 mmol/l, or those who had taken hormone treatment for over a year were excluded, and we chose only post-menopausal women. Six diabetic patients, 14 before menopause, and 10 hormone treatment patients were excluded, leaving 200 subjects whose average age was 48.64±10.92 yrs. To perform mammography, we used a LORAD Elite Trex Mammo (TREX-LORAD, USA) at 26 kVp and 80 mAs.

The American College of Radiology, Breast Imaging Reporting And Data System (ACR BI-RADS, USA) categorizes breast parenchymal pattern density from mammography into four grades: grade 1, almost entire fat; grade 2, fibroglandu-

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lar densities; grade 3, heterogeneously dense; and grade 4, extremely dense (Fig. 1). Height and weight were measured with an automatic height and weight scale, and body mass index (BMI) was computed using the formula weight (kg)/ height squared (m^2).

Subjects fasted for at least 12 h before blood and urine collections for biochemical marker tests. Fifty items were assayed: erythrocyte sedimentation rate (ESR), white blood cell (WBC), red blood cell (RBC), hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet count, red cell distribution width (RDW), platelet distribution width (PDW), mean platelet volume (MPV), neutrophil (%), lymphocyte (%), monocytes (%), eosinophil (%), basophil (%), neutrophil, lymphocyte, monocytes, eosinophil, basophil, HbA1C, protein, albumin, glucose, total bilirubin, direct bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), urea nitrogen, creatinine, uric acid, calcium, phosphrus, gamma-glutamyl transferase (γGT), lactate dyhydrogenase (LDH), amylase, triglyceride, total cholesterol, high-density lipoprotein (HDL-cholesterol), low-density lipoprotein (LDL-Cholesterol), iron (Fe), total iron binding capacity (TIBC), C-reactive protein (CRP), rheumatoid factor (RA factor), HIV Combo, HBsAg, Anti-HBs, α-fetoprotein (AFP), carbohydrate antigen 19-9 (CA 19-9), cancer antigen 125 (CA-125), free thyroxine (Free T4), thyroid-stimulating hormone (TSH), anti-hepatitis-C (Anti HCV). The data were collected as study variables.

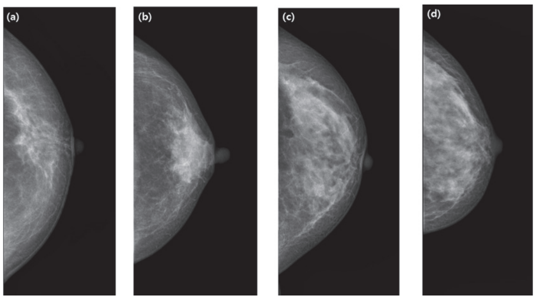

Fig. 1. Mammography
a) represents almost entirely fat, b) represents fibroglandular densities, c) represents heterogeneously dense, and d) represents extremely dense

Simple correlation analysis was performed to investigate correlations among breast density, general characteristic, and biochemical markers. Then, multiple regression analysis was performed to evaluate the factors that showed a significant correlation. SPSS software (ver.18.0, Chicago, USA) with a significance of 0.05 was used.

RESULTS

The simple correlation analysis of breast density, general characteristics, and biochemical markers before and after menopause is shown in Table 1. Items exhibiting significant correlations with breast density were: age, −0.55; height, 0.26; weight, −0.30; BMI, −0.48; hematocrit, −0.15; MCH,

Table 1. Simple correlation analysis of breast density, general characteristics, and biochemical markers

Variable	Breast density	Variable	Breast density	Variable	Breast density	Variable	Breast density
Age	−0.55	Neutrophil %	0.05	AST (GOT)	−0.22	TIBC	0.00
Height	0.28	Lymphocyte %	−0.07	ALT (GPT)	−0.27	CRP	−0.13
Weight	−0.30	Monocytes %	0.06	ALP	−0.28	RA factor	0.03
BMI	−0.48	Eosinophil %	0.04	Urea Nitrogen	−0.07	HIV Combo	−0.04
ESR	−0.07	Basophil %	0.03	Creatinine	−0.10	HBsAg	−0.09
WBC	−0.12	Neutrophil	−0.06	Uric acid	−0.16	AntiHBs	0.06
RBC	0.01	Lymphocyte	−0.04	Calcium	−0.09	AFP	−0.03
Hemoglobin	−0.14	Monocytes	0.05	Phosphorus	−0.06	CA 19-9	0.02
Hematocrit	−0.15	Eosinophil	−0.02	γGT	−0.18	CA 125	0.04
MCV	−0.13	Basophil	−0.08	LDH	−0.05	Free T4	0.11
MCH	−0.19	HbA1C	−0.10	Amylase	0.03	TSH	0.05
MCHC	−0.05	Protein	−0.02	Triglyceride	−0.30	AntiHCV	−0.12
Platelet count	−0.04	Albumin	0.04	Cholesterol, Total	−0.16		
RDW	0.15	Glucose	−0.15	HDL-Cholesterol	0.23		
PDW	−0.10	Bilirubin, Total	0.07	LDL-Cholesterol	−0.29		
MPV	0.07	Bilirubin, Direct	0.09	Iron	0.00		

BMI: body mass index, ESR: erythrocyte sedimentation rate, WBC: white blood cell, RBC: red blood cell, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, RDW: red cell distribution width, PDW: platelet distribution width, MPV: mean platelet volume, AST: aspartate aminotransferase, ALT: alanine aminotransferase, ALP: alkaline phosphatase, γGT: gamma-glutamyl transferase, LDH: lactate dyhydrogenase, HDL-cholesterol: high-density lipoprotein, LDL-cholesterol: low-density lipoprotein, TIBC: total iron binding capacity, CRP: C-reactive protein, RA factor: rheumatoid factor, AFP: α-fetoprotein, CA19-9: carbohydrate antigen 19-9, CA-125: cancer antigen 125, Free T4: free thyroxine, TSH: thyroid-stimulating hormone, Anti HCV: anti-hepatitis-C

−0.19; RDW, 0.15; glucose, −0.15; AST(GOT), −0.22; ALT(GPT), −0.27; ALP, −0.28; uric acid, −0.16; γGT(GGT), −0.18; triglyceride, −0.30; total cholesterol, −0.16; HDL-cholesterol, 0.23; and LDL-cholesterol, −0.29 ($p < 0.05$). The results of multiple regression analysis using breast density-related variables are shown in Table 2. Significant factors were: age, −0.04±0.00, height, 0.04±0.01; weight, −0.03±0.01; BMI, −0.13±0.02; T-score, 0.13±0.05; hematocrit, −0.01±0.00; MCH, −0.06±0.02; RDW, 0.08±0.04; AST(GOT), −0.01±0.00; ALT(GPT), −0.02±0.00; ALP, 0.00±0.00; uric acid, −0.03±0.01; γGT(GTP), −0.01±0.00; triglyceride, 0.00±0.00; total cholesterol, 0.00±0.00; HDL-cholesterol, 0.02±0.00; and LDL-cholesterol, −0.01±0.00 ($p < 0.05$).

DISCUSSION

Of the many risk factors that cause breast cancer, the best known is long-term exposure to female sex hormones[8–12]. It has been reported that as estrogen levels increase, so does the risk of breast cancer[13]. Additionally, breast density has a high correlation with breast cancer; as breast density increases, women are more likely to have breast cancer[8]. Factors that affect breast density include race, age, BMI, and levels of female sex hormones[6, 7]. In this study, the factors related to breast density were age, height, weight, BMI, hematocrit, MCH, RDW, AST, ALT, ALP, uric acid, γGT, triglyceride, total cholesterol, HDL-cholesterol, and LDL-cholesterol.

Breast density, in general, is related to estrogen. After menopause, breast tissue degenerates due to the decline in estrogen and progesterone, and breast density starts to decrease due to an increase in fatty tissue[14]. Bone density level, breast density, and breast cancer are related. In this study, BMI and breast density showed a correlation. Studies of Western women reported BMI as one of the major factors that affecting breast density[15, 16]. According to those studies, when BMI was low, even after correcting for age, it indicated high density breasts. the proportion of dense breast was 60% in low-weight women under age 40, similar to the results of our present study. A limitation of this study was that, because there were a small number of subjects, it was difficult to identify correlations between breast density and biochemical markers objectively. Thus, an effort is needed to make more precise risk evaluations of breast density by conducting a large-scale prospective study of Korean women.

Table 2. Multiple regression analysis of each variable related to breast density

Variable	B	SE
Age	−0.04	0.00
Height	0.04	0.01
Weight	−0.03	0.01
BMI	−0.13	0.02
Hematocrit	−0.01	0.00
MCH	−0.06	0.02
RDW	0.08	0.04
AST	−0.01	0.00
ALT	−0.02	0.00
ALP	0.00	0.00
Uric acid	−0.03	0.01
γGT	−0.01	0.00
Triglyceride	0.00	0.00
Cholesterol, total	0.00	0.00
HDL-cholesterol	0.02	0.00
LDL-cholesterol	−0.01	0.00

BMI: body mass index, MCH: mean corpuscular hemoglobin, RDW: red cell distribution width, AST: aspartate aminotransferase, ALT: alanine aminotransferase, ALP: alkaline phosphatase, γGT: gamma-glutamyl transferase, HDL-cholesterol: high-density lipoprotein, LDL-cholesterol: low-density lipoprotein

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