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Original Article

Association between Mammographic Breast Density and Lifestyle in Japanese Women

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A high mammographic breast density is considered to be a risk factor for breast cancer. However, only a small number of studies on the association between breast density and lifestyle have been performed. A cross-sectional study was performed using a survey with 29 questions on life history and lifestyle. The breast density on mammography was classified into 4 categories following the BI-RADS criteria. The subjects were 522 women with no medical history of breast cancer. The mean age was 53.3 years old. On multivariate analysis, only BMI was a significant factor determining breast density in premenopausal women (parameter estimate, −0.403; *p* value, 0.0005), and the density decreased as BMI rose. In postmenopausal women, BMI (parameter estimate, −0.196; *p* value, 0.0143) and number of deliveries (parameter estimate, −0.388; *p* value, 0.0186) were significant factors determining breast density; breast density decreased as BMI and number of deliveries increased. Only BMI and number of deliveries were identified as factors significantly influencing breast density. BMI was inversely correlated with breast density before and after menopause, whereas the influence of number of deliveries on breast density was significant only in postmenopausal women in their 50 and 60s.

Key words: breast cancer, mammographic breast density, life style, body mass index

Previous studies have shown an association between lifestyle and the risk of breast cancer. An expert report of the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) suggested that alcohol intake increases the risk of breast cancer in premenopausal women. Tall stature in adulthood and high birth weight may also be risk factors. In contrast, breast feeding reduces the risk of breast cancer and high levels of body fat may also decrease the risk in premenopausal women. In postmenopausal women, the risk of breast cancer is also increased by alcohol intake, and tall stature in adulthood, but in contrast to premenopausal women, the risk of breast cancer appears to increase

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as the amounts of abdominal fat and weight increase. Similarly to premenopausal women, breast feeding and exercise decrease the risk of breast cancer in postmenopausal women (http://www. dietandcancerreport. org/accessed 10/10/2012).

Higher breast density on mammography is also associated with an increased risk of breast cancer. In a meta-analysis of 42 studies, the risk in women with the highest breast density was 4.64 times greater than that in women with the lowest breast density [1]. Thus, evaluation of breast density on mammography may be important as a predictor of breast cancer risk, since it is relatively easy to perform and may serve as an objective reproducible index. If the risk of breast cancer can be evaluated accurately based on mammographic breast density, this may serve as a criterion to perform tests and advise changes in lifestyle to reduce the risk. Breast density may also serve as a surrogate parameter for interventions for prevention of breast cancer. Judgments about the final outcomes of breast cancer prevention must be based on the prevalence of breast cancer, but it takes a long time for such results to manifest. If changes in breast density induced by preventive methods can be established as a surrogate parameter of the long-term risk of breast cancer, this may reduce the cost and time of clinical studies.

Previous findings show that breast density is an important factor in breast cancer risk, but only a few studies of the relationship between breast density and lifestyle have been performed. The factors determining breast density are important to clarify if breast density is to be used as an index of breast cancer risk. In this study, we investigated the relationship between lifestyle and mammographic breast density, with the goal of identifying these factors.

Materials and Methods

Subjects. The study was performed as a cross-sectional study aimed at clarifying the association between breast density and lifestyle. The subjects were healthy women who visited Kagawa Prefectural Cancer Detection Center, Mizushima Kyodo Hospital, and Okayama Saiseikai General Hospital for mammographic screening. Subjects with a medical history of breast cancer and those in whom any abnormality was found on mammographic screening were excluded. This study was approved by the institutional ethics committee on human research. All subjects gave written consent to participation in the study.

Survey of lifestyle. Lifestyles were surveyed using a self-rating questionnaire survey. After obtaining consent, the survey was distributed and the subjects completed the form and sent it back by mail. The survey comprised the following items: current height and body weight and those at 18 years of age; 29 questions concerning cigarette smoking, alcohol drinking, and dietary habits (types and intakes of foods); 4 questions concerning physical activity in leisure time (type and frequency of current physical activity and those at 18 years of age); menstruation status and ages at first menstruation and menopause; history and number of deliveries and age at first delivery; history of breast feeding; familial history of breast cancer; presence or absence of hormone replacement therapy; working or not working; work hours; sleeping hours; and educational background. Body mass index (BMI) was calculated as the body weight (kg)/square of height (m). The Brinkman index for cigarette smoking was calculated from the answers to the survey. Alcohol ingestion was converted to intake per day (g/day). Metabolic Equivalents (METs) per week were calculated to evaluate physical activity. Family histories of breast cancer were limited to relatives of the first and second degree.

The types of food surveyed were cooked rice, bread, noodles, meat, fish, eggs, soybean products (tofu, fermented soybeans (natto), and miso soup), cow milk, dairy products (cheese and yogurt), green and yellow vegetables (carrot, pumpkin, spinach), fruits, mushrooms, cakes, ice cream, and instant foods. The frequencies of ingestion per week (4 categories: almost no ingestion, and ingested on one day, 2-4 days, and almost every day per week) were investigated for all of these foods.

Evaluation of breast density. Breast cancer screening was performed using digital mammography at all participant institutions (Kagawa Prefectural Cancer Detection Center, Mizushima Kyodo Hospital, and Okayama Saiseikai General Hospital). Digital mammography images of the subjects were exported to media and the breast density was measured on a monitor display. Two experts in reading mammographic images (S.I. and Y.I.) who had been certified by the Central Committee on Quality Control of Mammographic Screening independently judged the breast density in the mediolateral-oblique views. Breast density was classified into 4 categories following the Breast Imaging Reporting and Data System (BI-RADS) [2]: 1, breast is almost entirely fat (< 25% glandular); 2, scattered fibroglandular densities (25–50%); 3, heterogeneously dense breast tissue (51–75%); and 4, extremely dense breast tissue (> 75% glandular). The 2 examiners collated their judgments, re-evaluated mammograms in inconsistent cases, and made the final judgment after a discussion. When the density of the 2 breasts differed, the higher value was used as the final breast density.

Statistical analysis. Concordance between breast density judgments made by the two examiners was tested and a kappa coefficient was calculated. Associations between breast density and other factors were analyzed using ordinal logistic regression analysis with statistical significance set at 5%. All analyses were performed using JMP version 9.0.3 (SAS Institute).

Results

Background factors. A total of 600 subjects gave consent to participation in the study at Kagawa Prefectural Cancer Detection Center, Mizushima Kyodo Hospital, and Okayama Saiseikai General Hospital from December 2010 to December 2011. The lifestyle survey was completed by 528 subjects, yielding a response rate of 88%. Collection and analysis of mammograms were possible in 522 of the 528 subjects, and these 522 subjects were included in the analysis. The 522 subjects had a mean age of 53.3 years, a mean height of 156 cm, a mean body weight of 54.1 kg, and a mean BMI of 22.2; at the time of the survey. 219 and 303 subjects were pre- and postmenopausal, respectively. Data for cigarette smoking and alcohol drinking habits; exercise in leisure time; ages at first menstruation, menopause, and first delivery; number of deliveries; history of breast feeding, familial history of breast cancer, occupation, educational background, sleeping hours, and hormone replacement therapy are shown in Table 1.

Breast density evaluation. Breast density in the 522 subjects was evaluated in bilateral mammograms (1044 images). The results and concordance rate of the evaluations by S.I. and Y.I. are shown in Table 2. The kappa coefficient was 0.9521 (standard error: 0.008, 95% confidence interval: 0.936–0.968), showing high concordance. Breast density classifications are shown in Table 3. Of the 522 subjects, 95 (18%) were placed in category 1 (breast is almost entirely fat, < 25% glandular), 202 (18%) in category 2 (scattered fibroglandular densities, 25–50%), 192 (37%) in category 3 (heterogeneously dense breast tissue, 51–75%), and 33 (6%) in category 4 (extremely dense, > 75% glandular).

Factors influencing breast density. The results of breast density evaluation by age are shown in Fig. 1. In ordinal logistic regression analysis, the parameter estimate of age for breast density was −0.0895, the standard error was 0.0086, and the p value was < 0.0001, indicating that breast density decreases with age. There was no significant association of breast density with cigarette smoking (past and current cigarette smoking and Brinkman index) or alcohol drinking habits (type of alcoholic beverage and alcohol intake). Similarly, breast density showed no significant associations with dietary habits, including ingestion frequencies of rice, bread, noodles, meat, fish, eggs, soybean products, dairy products, green and yellow vegetables, fruits, mushrooms, sweets, and teas. METs calculated as an index of physical activity were not significantly correlated with breast density. Sleeping hours, the presence or absence of hormone replacement therapy, working or not working, work hours, and educational background also showed no significant association with breast density.

In age-adjusted univariate and ordinal logistic regression analyses, body weight, BMI, number of deliveries, history of breast feeding, age at first menstruation, and familial history of breast cancer were all significantly associated with breast density. The parameter estimates, standard errors, and p values for these factors are shown in Table 4. Breast density significantly decreased as body weight, BMI, and number of deliveries increased, and with an earlier age at first menstruation. The density was also significantly lower in subjects with a history of breast feeding and those with a familial history of breast cancer.

Influence of BMI and number of deliveries on breast density. In multivariate analysis using the significant factors in univariate analysis as explanatory variables and breast density as a response vari-

Table 1 Background factors of the subjects

		Frequency (%) or mean value ± SD		
		All (N=522)	Premenopausal (N=219)	Postmenopausal (N=303)
Age		53.3	43.8	60.2
Height (cm)		156 ± 5.6	158.1 ± 5.2	154.5 ± 5.4
Body weight (kg)		54.1 ± 8.4	54.3 ± 8.5	54 ± 8.4
BMI		22.2 ± 3.3	21.7 ± 3.0	22.6 ± 3.4
Cigarette smoking	Never	431 (83)	175 (80)	256 (84)
	Ever	53 (10)	25 (11)	28 (9)
	Current	32 (6)	19 (9)	13 (4)
	Unclear	6 (1)		6 (2)
Alcohol intake (g/day)	0	239 (46)	79 (36)	160 (53)
	≤10	146 (28)	71 (32)	75 (25)
	11-50	21 (4)	9 (4.1)	12 (4)
	≥51	105 (20)	56 (26)	49 (16)
	Unclear	11 (2)	4 (1.8)	7 (2)
MET/week		10.32 ± 20.6	7.5 ± 15.2	12.4 ± 23.6
Age at the first menstruation		12.9 ± 1.5	12.5 ± 1.2	13.3 ± 1.6
Age at menopause				49.9 ± 4.6
Age at the first delivery		26.1 ± 3.5	27.3 ± 3.7	25.3 ± 3.1
Number of deliveries	0	87 (17)	57 (26)	30 (9.9)
	1	41 (7.9)	27 (12)	14 (4.6)
	2	261 (50)	102 (47)	159 (52)
	3	98 (19)	26 (12)	72 (24)
	4	16 (3.1)	4 (1.8)	12 (4)
	5	1 (0.2)	1 (0.5)	
	Unclear	18 (3.4)	2 (0.9)	16 (5.3)
Experience of breast feeding	Absent	117 (22)	60 (27)	57 (19)
	Present	400 (77)	157 (72)	243 (80)
	Unclear	5 (1)	2 (0.9)	3 (1)
Familial history of breast cancer	Absent	444 (85)	191 (87)	253 (83)
	Present	57 (11)	18 (8.2)	39 (13)
	Unclear	21 (4)	10 (4.6)	11 (3.6)
Educational background	Junior or senior high school	222 (43)	62 (28)	160 (53)
	Junior college	163 (31)	84 (38)	79 (26)
	University or higher	134 (26)	72 (33)	62 (20)
	Unclear	3 (0.6)	1 (0.5)	2 (0.7)
Sleeping hours	3-4 h	8 (1.5)	3 (1.4)	5 (1.7)
	4-6 h	181 (35)	77 (35)	104 (34)
	6-8 h	316 (61)	136 (62)	180 (59)
	8-10 h	15 (2.9)	3 (1.4)	12 (4)
	Unclear	2 (0.4)	0 (0)	2 (0.7)
Hormone replacement therapy	Present	46 (8.8)	17 (7.8)	29 (9.6)
	Absent	470 (90)	202 (92)	268 (88)
	Unclear	6 (1.1)	0 (0)	6 (2)

able, only BMI and number of deliveries emerged as significant factors determining breast density. In multivariate analysis in premenopausal women, only BMI was a significant factor determining breast density (parameter estimate: −0.403, p value: 0.0005), and breast density decreased as BMI increased. In postmenopausal women, BMI (parameter estimate: −0.196, p value: 0.0143) and number of deliveries (parameter estimate: −0.388, p value: 0.0186) were significant factors determining breast density, and the density decreased as BMI and number of deliveries

Table 2 Concordance rate of breast density evaluation

Judgment category (breast density)		Expert 1 (S. I.)			
		1	2	3	4
Expert 2 (Y. I.)	1	218	3	0	0
	2	5	397	11	0
	3	0	8	345	1
	4	0	0	6	50

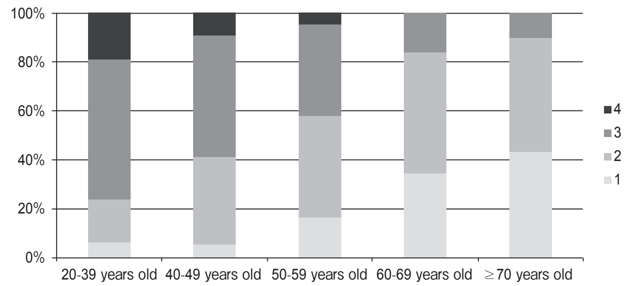

Fig. 1 Final breast density classifications by age group. Following the BI-RADS criteria, breast density was classified as 1, breast is almost entirely fat (<25% glandular); 2, scattered fibroglandular densities (25–50%); 3, heterogeneously dense breast tissue (51–75%); and 4, extremely dense (>75% glandular). Breast density tended to decrease with aging.

Table 3 Results of breast density evaluation

	Number of samples (%)		
	All N=522	Premenopausal N=219	Postmenopausal N=303
1 Breast is almost entirely fat (<25% glandular)	95 (18)	17 (8)	78 (26)
2 Scattered fibroglandular densities (25–50%)	202 (39)	64 (29)	138 (46)
3 Heterogeneously dense breast tissue (51–75%)	192 (37)	114 (52)	78 (26)
4 Extremely dense (>75% glandular)	33 (6)	24 (11)	9 (3)

Table 4 Results of analysis of factors influencing breast density

	Univariate analysis (All subjects, age-adjusted)			Multivariate analysis (All subjects)			Multivariate analysis (Premenopausal)			Multivariate analysis (Postmenopausal)		
Factor	Estimate	Standard error	p value	Estimate	Standard error	p value	Estimate	Standard error	p value	Estimate	Standard error	p value
Body weight	−0.084	0.011	<.0001	0.013	0.024	0.6006	0.043	0.039	0.2634	−0.011	0.032	0.731
BMI	−0.258	0.030	<.0001	−0.271	0.065	<.0001	−0.403	0.116	0.0005	−0.196	0.080	0.0143
Age at first menstruation	0.161	0.062	0.0092	0.118	0.068	0.0827	0.201	0.117	0.0858	0.116	0.087	0.1809
Number of deliveries	−0.365	0.090	<.0001	−0.321	0.129	0.0128	−0.340	0.223	0.1267	−0.388	0.165	0.0186
No history of breast feeding	0.205	0.103	0.0463	0.016	0.154	0.9188	0.152	0.268	0.5707	−0.068	0.197	0.7289
No familial history of breast cancer	0.289	0.135	0.0328	0.275	0.144	0.0571	0.461	0.251	0.0664	0.175	0.179	0.3281

increased.

The influences of BMI and the number of deliveries on breast density in each age group (20–30s, 40s, 50s, 60s, and ≥70 years old) were investigated by ordinal logistic regression analysis using BMI and number of deliveries as explanatory variables and breast density as the response variable (Table 5). BMI significantly influenced breast density in all women except those aged ≥70 years old. The number of deliveries mostly strongly influenced breast density in women in their 50s and 60s, but there was no significant correlation in other age groups.

Discussion

Age markedly influenced breast density in our subjects, as also previously reported [3]. Breast density showed a general decrease with aging; thus, all factors were analyzed after age adjustment. In univariate analysis, body weight, BMI, number of deliveries, history of breast feeding, age at first menstruation, and familial history of breast cancer showed a significant association with breast density. In multivariate analysis performed to account for confounding factors, only BMI and the number of deliveries remained as significant factors associated with breast density. In menopause-stratified analysis, BMI significantly influenced breast density in pre- and postmenopausal women, with the density decreasing as BMI rose. Menopause-stratified analysis has not been performed in many previous studies of the association between breast density and BMI [4–6], but one report showed no association between BMI and breast density in premenopausal women [7]. However, a significant association was found in all generations from the 20s to 60s in the age-stratified analyses in our study. This association was lost in elderly subjects aged ≥70 years old, which may have been due to an overall age-related decrease in breast density.

The number of deliveries also significantly influenced breast density in postmenopausal women, with the density decreasing as the number of deliveries increased. Age-stratified analysis showed that the number of deliveries had a particular influence on breast density in women in their 50s and 60s. There was no significant association in other age groups. An association between number of deliveries and breast density has been shown in previous studies [4, 6–8], but the menopause-stratified analysis in our study provides new details on this association.

Lifestyle factors such as dietary habits, physical activity, alcohol intake, and cigarette smoking showed no relationships with breast density. Alcohol intake is thought to increase the risk of breast cancer, and previous studies have associated alcohol intake with increased breast density [4, 7]. The type of alcoholic beverage and alcohol intake markedly vary among seasons, cultures, and regions, and these factors need to be taken into account in future investigations of the association between alcohol intake and breast density. We also found no association of breast density with any of the diet-related factors surveyed. Previous studies of various diet-related factors have suggested that olive oil and cheese ingestion reduced breast density [4] and that high-fat and high-sugar diets increased breast density [9]. We surveyed the frequency of ingestion of various types of food, but no significant association was found between the ingestion frequency of any food and breast density. However, we did not investigate the intake per single ingestion,

Table 5 Influences of BMI and number of deliveries on breast density in each age group

	BMI			Number of deliveries		
	Estimate	Standard error	*p* value	Estimate	Standard error	*p* value
20–30s	−0.281	0.087	0.0012	−0.465	0.244	0.0565
40s	−0.266	0.064	<.0001	−0.245	0.177	0.1675
50s	−0.277	0.055	<.0001	−0.336	0.160	0.0354
60s	−0.186	0.063	0.0031	−0.468	0.216	0.0302
≥70 years old	−0.194	0.109	0.0762	0.030	0.495	0.9523

which may have been a methodological limitation in the survey method that prevented identification of an association between the type of food and breast density.

High physical activity has also been suggested to reduce the breast cancer risk in postmenopausal women. However, in a previous study of the relationship between physical activity and mammographic density in postmenopausal women, breast density tended to be higher in the most physically active group, although without a significant difference. We also found no significant association between breast density and physical activity, suggesting that physical activity influences the risk of breast cancer independently of breast density. Regarding the history of breast feeding, this has been reported to be both associated [4] and not associated [6, 8] with breast density, and no consensus has been reached. Breast feeding is thought to reduce the risk of breast cancer, but it may have an association that differs from that of delivery.

In our study, breast density decreased as BMI rose regardless of age. However, the risk of breast cancer decreases as BMI increases in premenopausal women, but increases as BMI increases in postmenopausal women. This would appear to contraindicate the use of breast density as a predictor of the risk of breast cancer; it may also indicate that pre- and postmenopausal women should be separated in analyses of associations of BMI with breast density and risk of breast cancer, and that the significance of breast density as a predictor of the risk of breast cancer may be limited to premenopausal women. Alternatively, the cause of the contradiction concerning the associations of BMI with breast cancer risk and breast density may be due to the method of breast density measurement. In the BI-RADS approach used in this study, breast density was evaluated visually, whereas in other reports the percentage of high-density area was calculated by measuring the high-density and whole breast areas using computer-aided diagnosis [10]. Investigations using the whole breast may lead to different findings.

In conclusion, only BMI and number of deliveries were significant factors influencing mammographic breast density. BMI showed an inverse correlation with breast density at all ages below 70 years old, before and after menopause. The number of deliveries significantly influenced breast density in postmenopausal women in their 50 and 60s.

References

1. McCormack VA and dos Santos Silva I: Breast Density and parenchymal patterns as markers of breast cancer risk: a meta-analysis. Cancer Epidemiol Biomarkers Prev (2006) 15: 1159–1169.
2. American College of Radiology (ACR): ACR BI-RADS® Mammography; in ACR Breast Imaging Reporting and Data System, Breast Imaging Atlas, 4th Ed, American College of Radiology, Reston, VA (2003).
3. Checka CM, Chun JE, Schnabel FR, Lee J and Toth H: The relationship of mammographic density and age: implications for breast cancer screening. AJR Am J Roentgenol (2012) 198: W292–W295.
4. Masala G, Ambrogetti D, Assedi M, Giorgi D, Del Turco MR and Palli D: Dietary and lifestyle determinants of mammographic breast density. A longitudinal study in a Mediterranean population. Int J Cancer (2006) 118: 1782–1789.
5. Chen FP, Cheung YC and Soong YK: Factors that influence changes in mammographic density with postmenoposal hormone therapy. Taiwan J Obstet Gynecol (2010) 49: 413–418.
6. Tseng M, Byrne C, Evers KA and Daly MB: Dietary intake and breast density in high-risk women: a cross-sectional study. Breast Cancer Res (2007) 9: R72.
7. Jeon JH, Kang JH, Kim Y, Lee HT, Choi KS, Jun JK, Jun DK, Oh DK, Lee CT, Ko K and Park EC: Reproductive and hormonal factors associated with fatty or dense breast patterns among Korean women. Cancer Res Treat (2011) 43: 42–48.
8. Duffy SW, Jakes RW, Ng FC and Gao F: Interaction of dense breast patterns with other breast cancer risk factors in a case-control study. Br J Cancer (2004) 91: 233–236.
9. Mishra GD, dos Santos Silva I, McNaughton SA, Stephen A and Kuh D: Energy intake and dietary patterns in childhood and throughout adulthood and mammographic density: results from a British prospective cohort. Cancer Causes Control (2011) 22: 227–235.
10. Nagata C, Matsubara T, Fujita H, Nagao Y, Shibuya C, Kashiki Y and Shimizu H: Mammographic density and the risk of breast cancer in Japanese women. Br J Cancer (2005) 92: 2102–2106.