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Mammographic Density and Metabolic Syndrome in Climacteric Women

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ABSTRACT

Objective: To evaluate whether metabolic syndrome is associated with an increase in percent mammographic density, which are breast cancer risk factors.

Materials and Methods: A cross-sectional analytical study. A total of 713 climacteric women of ages between 40 and 70 were eligible to participate in our study. We performed questionnaire, general physical examination, blood test and mammogram on all participants. The participants were then classified into two groups, with and without metabolic syndrome, according to AHA/NHLBI 2005 statement. Radiologists read and categorized mammographic density by using a traditional 4-level BI-RADS density scale. We used logistic regression and mixed model statistical analysis to examine the associations of metabolic syndrome and components of metabolic syndrome with the percent mammographic density.

Results: The prevalence of metabolic syndrome in our study was 20.48%. The most common ranges of mammographic density were 50% to74% for the women with and without metabolic syndrome, respectively. We found the inverse association between metabolic syndrome and percent mammographic density. In addition, after controlling for body mass index (BMI), the inverse associations were also demonstrated between percent mammographic density and raised triglyceride.

Conclusion: Our results show that there is no association between the metabolic syndrome with an increase percent mammographic density among climacteric woman.

Keywords: metabolic syndrome, percent mammographic density, climacteric women

Introduction

Menopausal women are increasingly important since the average age of the nation's population increases. Menopause is the time of cessation of a woman's reproductive ability. At this time, there are a decrease in the ovarian function, changes in hormone level and the system of organs in the body. Some diseases are more likely to occur during this age such

as osteoporosis, cardiovascular disease, cancer, Alzheimer's disease, and sexual problems.

Insulin resistance and abdominal obesity were first mentioned by Reaven in 1988[1]. They are a group of disorders that are risk factors for heart disease and stroke, which are often found together. People with obesity increase the risk of type 2 diabetes and cardiovascular disease. The cause of metabolic syndrome is currently believed to be the result of obesity and insulin resistance[2,3]. The obesity is increasingly common in the current Department of Health. By evaluating abdominal adiposity of the residents age 15 and older, it was found that people who are obese or high waist circumference were 22.2% in 2009 and 36.5% in 2010.

Until now, there has been little attention given to the metabolic syndrome in Thailand, despite the prevalence of metabolic syndrome commonly known that it is based on age, race and gender. The increased age is lead to increase in prevalence. A total number of 1,004 people including both males and females in the age group 20 – 80 years were selected from Srichiengmai Hospital for the study. The study has shown that prevalence of this disease was 16.93%, male 17% and female 16.9% based on the third report of the National Cholesterol Education Program (NCEP ATPIII)[4]. The clinical study in postmenopausal women in Siriraj Hospital has shown that the prevalence of metabolic syndrome was between 14.9% and 16.0%, depending on the diagnostic criteria employed. The majority of prevalence was abnormalities of waist circumference or body mass index over most standards, followed by high blood pressure and lower the good cholesterol (HDL-cholesterol)[5].

Metabolic syndrome not only increases the risk of type 2 diabetes and cardiovascular disease. But the study found that it also increases prevalence of breast cancer[6]. Abdominal obesity correlated positively with triple-negative breast cancer[7], aggressive tumors[8], the recurrence of breast cancer and increased risk of death from breast cancer[9].

Epidemiological studies have reported on the relationship between breast cancer risk factors and metabolic syndrome. For example, postmenopausal women with increased triglyceride levels or low HDL-cholesterol levels associated with higher risk of breast cancer more than 60%[6], and waist circumference is associated with an increased risk of 34%[10]. An increase of fasting blood sugar level is likely to double the breast cancer risk in premenopausal women[11]. Only a few studies have been undertaken to determine the direct relationship between breast cancer and metabolic syndrome. One of the studies has reported the relationship in postmenopausal women[6], while other two studies reported no relationship[12,13].

The probability of the development of breast cancer has been calculated by using the percentage of the radiographic breast density (percent mammographic density), which could be the cause of the abnormal metabolism[14]. A study shown the percentage of the radiographic breast density is associated with an increased risk of breast cancer from four to six fold compared with high (>60%) and compared with low (<10%) density[15]. The elevated breast cancer risk may persist for an estimated 10 years after breast density assessment regardless of menopausal status or age[16]. Abdominal fat is associated with a decrease in the percentage of radiographic breast density[17]. The recent study reported the contrast relationship between percentage of breast density radiographic and the body mass index (BMI), waist circumference and higher fasting glucose. There is no relationship between other components of metabolic syndrome and percentage of radiographic breast density[18] has been reported.

Our research aims to evaluate the differences of the percentage of radiographic density of breast in menopausal women who have and who do not have metabolic syndrome. All participants were selected from health services center at Srinakarind Hospital, Khon Kaen University.

Materials and Methods

Our survey participants were selected by using quota sampling method. The analysis has been done under cross-sectional studies method. The study has examined women who attended health check at Srinakarind Hospital, Faculty of Medicine, Khon Kaen University, Thailand, during May 2012 to May 2013.

798 climacteric women of ages between 40 to 70 years participated in our study. We excluded patients who had one of the following conditions; pregnant, breasts feeding, breasts disease, psychiatric, acute renal, liver, cardiovascular disease or any other acute major illness. The remaining participants of 713 who met our selection criteria were divided into two groups, 146 participants were in metabolic syndrome and 567 participants were in without-metabolic syndrome group. Before participation in this research study, all participants completed anonymous questionnaires and signed informed consent documents as volunteers. We performed general PE, blood test and mammogram on all participants.

Mammographic density

Mammograms were taken as part of the health check and were restricted to those who has no prior breasts surgery. However, one side of breast's mammograms was accepted if another side has reported surgery (e.g., biopsy, breast augmentation, reduction or reconstruction). Film-screen mammograms were examined in batches by Jiraporn Srinakarin, an established expert in the techniques of measuring mammographic density at Srinakarind Hospital. Quantitative assessment was estimated visually by measuring the total area of the breast and the area of dense breast tissue on the craniocaudal view. Mammographic density results were classified into four traditional BI-RADS density categories and interpreted by trained radiologist.

Metabolic syndrome

The interviewer-administered questionnaires, physical exam and blood were used to determine the metabolic status in our study. Blood tests were performed in the morning after an overnight fast. Participants had venipuncture when visited. Blood pressure measurements were taken using Hybrid Sphygmomanometers when seated and after a minimum of 5 min of rest, and two sequential measurements were averaged. Waist circumferences were measured at top edge of the pelvis (iliac crest), parallel to the ground in a standing position and nonrestrictive under-garments based on NCEP-ATPIII. Biochemical assays for triglycerides, HDL-cholesterol and glucose were performed on the serum samples obtained when visited.

The metabolic syndrome was defined in accordance with American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005 (AHA/NHLBI 2005) with Asian specific cut points for waist circumference[19]. There are five major components that we used to diagnosis of metabolic syndrome. Any participants who had three or more of these components were considered to have metabolic syndrome: (a) waist circumference ≥80 cm; (b) triglycerides level ≥150 mg/dL; (c) HDL- cholesterol levels <50 mg/dL; (d) systolic blood pressure (SBP) ≥130 mmHg, diastolic blood pressure (DBP) ≥85 mmHg or self-reported use of antihypertensive medications; and (e) fasting glucose levels ≥100 mg/dL or self-reported use of antidiabetic medication (insulin or oral agents).

Statistical analysis

The characteristics of climacteric population were compared using Chi-Square test for categorical variables, Student's t-test for continuous variables and ordinal regression analysis to assess association of metabolic syndrome and percent mammographic density. The results presented as mean, maximum likelihood estimation of coefficients, standard error and p-values. The baseline characteristics included the following covariates in all adjusted models since these factors had been associated with percent mammographic density in the previous analysis (20): age, BMI, parity, menopausal status, past use of oral contraceptive hormones, smoking and physical activity. Other covariates were then added to the Metabolic syndrome models individually, including household income per month, age at menarche <12, prior use of exogenous hormones not including oral contraceptive use and alcohol consumption. Statistical computing was conducted using Stata 10.

Results

Among the 713 participants, the average age

was 52.82 years (SD = 6.93), the average BMI was <25.0 kg/m^2 (N=460, 65%). All participants were parous (100%), never smoked (99%), postmenopause (71%) (Table 1).

Table 1. Study population characteristics by Metabolic syndrome status

Characteristics	Total	Without MetS	With MetS	P
N (%)	713	567 (79.52)	146 (20.48)	-
Mean age, years (SD)	52.82 (6.93)	52.29 (6.74)	54.84 (7.25)	< 0.001
BMI (%)	-	-	-	< 0.001
< 25.0 kg/m^2	460 (64.52)	399 (70.37)	61 (41.78)	-
25.0–29.9 kg/m^2	219 (30.72)	148 (26.10)	71 (48.63)	-
≥ 30 kg/m^2	34 (4.77)	20 (3.53)	14 (9.59)	-
Household income (Baht/month)	-	-	-	0.007
1. none	7 (0.98)	4 (0.71)	3 (2.05)	-
2. <6,000	41 (5.76)	33 (5.83)	8 (5.48)	-
3. 6,000-10,000	113 (15.87)	77 (13.60)	36 (24.66)	-
4. 10,000-20,000	113 (15.87)	93 (16.43)	20 (13.70)	-
5. 20,000-30,000	116 (16.29)	101 (17.84)	15 (10.27)	-
6. >30,000	322 (45.22)	258 (45.58)	64 (43.84)	-
Menopausal status (%)	-	-	-	0.053
Premenopausal	199 (27.91)	169 (29.81)	30 (20.55)	-
Perimenopausal	5 (0.70)	3 (0.53)	2 (1.37)	-
Postmenopausal	509 (71.39)	395 (69.66)	114 (78.08)	
Past use of oral contraceptive hormone (%)	-	-	-	-
Ever use oral contraceptive	1 (0.18)	1 (0.18)	0	> 0.999
Ever use exogenous hormones	22 (3.10)	19 (3.37)	3 (2.05)	0.593
Parity (%)	-	-	-	0.033
Nulliparous	0	0	0	-
1–2	241 (33.80)	203 (35.80)	38 (26.03)	-
≥3	472 (66.20)	364 (63.31)	108 (73.97)	-
Menarche at age < 12 years (%)	14 (1.96)	12 (2.12)	2 (1.37)	0.746
Consume alcohol 1 drinks /week (%)	90 (12.64)	76 (13.43)	14 (9.59)	0.213
Smoking status (%)	missing	2 (0.35)	-	NA
1. Never	711 (99.72)	565 (99.65)	145 (100)	-
2. Former smoker	-	-	-	-
3. Current smoker	-	-	-	-
Mean sports/exercise activity (SD)	283 (39.75)	235 (41.52)	48 (32.88)	0.057
Diabetic (%)	36 (5.05)	10 (1.76)	26 (17.31)	< 0.001
Hypertension (%)	117 (16.43)	42 (7.42)	75 (51.37)	< 0.001
Dyslipidemia (%)	86 (12.06)	48 (8.47)	38 (26.03)	< 0.001

Percent mammographic density was divided into four traditional BI-RADS density categories. We found no significant difference in percent mammographic density among climacteric women who had and did not have metabolic syndrome. We found the most common range of percent mammographic density was 50 to 74% in both group. (Table 2) For the component of Metabolic syndrome, when comparing percent mammographic density who had and did not have, there were no statistically significant differences in abdominal adiposity, raised blood pressure, raised fasting plasma glucose and raised triglycerides (p<0.001) but not a reduced HDL-cholesterol (p=0.144) (Table 2). Abdominal adiposity was the most prevalent metabolic abnormalities among women with the metabolic syndrome (Table 2).

Table 2. Mean percent MD by prevalence of metabolic abnormalities

Characteristics	Total	Percent MD				P
		0-24	25-49	50-74	75-100	
	N (%)	N (%)	N (%)	N (%)	N (%)	
MetS						<0.001
No	567 (79.52)	65 (11.46)	153 (26.98)	262 (46.21)	87 (15.34)	
Yes	146 (20.48)	36 (24.66)	46 (31.51)	54 (36.99)	10 (6.85)	
Components of the MetS						
Abdominal adiposity, Asian specific waist circumference (80 cm)						0.001
No	73 (10.24)	4 (5.48)	16 (21.92)	36 (49.32)	17 (23.29)	
Yes	640 (89.76)	97 (15.16)	183 (28.59)	280 (43.75)	80 (12.50)	
Raised blood pressure (SBP 130 mm Hg, DBP 85mm Hg or taking blood pressure medication)						<0.001
No	595 (83.45)	73 (12.27)	156 (26.22)	275 (46.22)	91 (15.29)	
Yes	118 (16.55)	28 (23.73)	43 (36.44)	41 (34.75)	6 (5.08)	
Raised fasting plasma glucose (100 mg/dL or taking insulin medication)						<0.001
No	546 (76.58)	59 (10.81)	150 (27.47)	254 (46.52)	83 (15.20)	
Yes	167 (23.42)	42 (25.15)	49 (29.34)	62 (37.13)	14 (8.38)	
Raised triglycerides (150 mg/dL)						<0.001
No	548 (76.86)	65 (11.86)	146 (26.64)	252 (45.99)	85 (15.51)	
Yes	165 (23.14)	36 (21.82)	53 (32.12)	64 (38.79)	12 (7.27)	
Reduced HDL-cholesterol (< 50 mg/dL)						0.144
No	586 (82.19)	76 (12.97)	163 (27.82)	262 (44.71)	85 (14.51)	
Yes	127 (17.81)	25 (19.69)	36 (28.35)	54 (42.52)	12 (9.45)	

In multivariable analysis, we statistically control age, menopausal status, parity, sports/exercise activity. We found an inverse association of percent mammographic density was associated with the metabolic syndrome and its components (Table 3, Model 1). All associations were attenuated after adjustment for BMI. Only the association with raised triglycerides remained statistically significant (Table 3, Model 2).

Table 3. Multivariable analyses of percent mammographic density by metabolic abnormalities, regression coefficients and standard errors

Characteristics	Model 1 (without BMI adjustment) b (SE) p-value	Model 2 (with BMI adjustment) b (SE) p-value
MetS	-0.55 (0.18) 0.002	-0.26 (0.18) 0.153
Components of the MetS		
Abdominal adiposity, waist circumference (80 cm)	-0.59 (0.24) 0.013	-0.04 (0.25) 0.879
Raised blood pressure (SBP130 mmHg or DBP 85 mmHg or taking blood pressure medication)	-0.50 (0.20) 0.010	-0.19 (0.20) 0.333
Raised fasting plasma glucose (100 mg/dL or taking insulin medication)	-0.45 (0.17) 0.007	-0.32 (0.17) 0.066
Raised triglycerides (150 mg/dL)	-0.59 (0.17) 0.000	-0.42 (0.17) 0.015
Reduced HDL-cholesterol (< 50 mg/dL)	-0.42 (0.19) 0.025	-0.24 (0.19) 0.199

Values are maximum likelihood estimates of coefficients, standard error and p-values for two separate models: one with the Metabolic syndrome and a second model that included each component of the Metabolic syndrome. Model 1 represents the adjusted model including age, menopausal status, parity and sports/exercise activity, Model 2 represents Model 1 with an additional adjustment for BMI (kg/m^2).

Discussion

Among the 713 women of ages between 40 and 70 who attended health check at Srinakarind Hospital, the important finding was an inverse association between the Metabolic syndrome and percent mammographic density. However, after adjusting for BMI, the strength of this association was greatly attenuated, and it was no longer statistically significant. Five components of the metabolic syndrome also had significantly inverse association with percent mammographic density. The inverse association between the raised triglycerides and increase percent mammographic density remained statistically significant after controlling for BMI. We found an inverse association between the metabolic syndrome and percent mammographic density same as the previous study[18]. Component of Metabolic syndrome inverse association with percent mammographic density are raised triglycerides same as the studies in premenopausal women[21,22] but different from postmenopausal Caucasian women[23].

Our study about the association between metabolic syndrome and percent mammographic density is the first-time conducted in Thailand and Asian countries. The strengths of our study included, we used the newly updated criteria for diagnosis of metabolic syndrome, the interviewers and radiologists were blinded to metabolic status of the volunteers, In addition, mammographic density measurements were assessed by a single expert radiologist.

However, our study had some limitations. We didn't have the longitudinal measurement of the metabolic syndrome and percent mammographic density, therefore the strength of causal relationship was attenuated by lacking of the time or duration of exposure. Fasting blood glucose tests in our study were done without timing controls of evaluation which may have reproductive hormonal effect. In mammographic density measurements, we used traditional four-level BI-RADS density categories and interpret by a radiologist. This might affect the accuracy of percent mammographic density interpretation.

Although the metabolic syndrome is not demonstrated in our study as a breast cancer risk via the increased percent mammographic density, metabolic syndrome is still the risk factor of other important diseases in particular CVD. Therefore, we should pay attention on prevention and treatment of

metabolic syndrome. According to the result of our study, the mammogram screening in metabolic syndrome population may be not benefit over the general population.

Conclusion

The prevalence of metabolic syndrome in women ages between 40 and 70 who attended health check at Srinakarind Hospital are 20.48%. Our results show that there is no association between the metabolic syndrome and increase in percent mammographic density among climacteric woman. Although, as the percent mammographic density is considered as an intermediate outcome of breast cancer, it is still inconclusive whether metabolic syndrome is a risk factor of breast cancer or not.

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ค่าร้อยละความหนาแน่นของภาพรังสีเต้านมและโรคอ้วนลงพุงในกลุ่มผู้หญิงวัยเพศถดถอย

ณัฐพงษ์ ก้านคูณ, วรลักษณ์ สมบูรณ์พร, จิราภรณ์ ศรีนัครินทร์, สุกรี สุนทราภา, ศรีนารี แก้วฤดี

วัตถุประสงค์ : *เพื่อศึกษาความสัมพันธ์ของโรคอ้วนลงพุงกับการเพิ่มขึ้นของค่าร้อยละความหนาแน่นของภาพรังสีเต้านม ซึ่งเป็นปัจจัยหนึ่งของการเกิดโรคมะเร็งเต้านม*

วัสดุและวิธีการ : *เป็นการศึกษาวิจัยแบบภาคตัดขวางในอาสาสมัครหญิงวัยเพศถดถอยจำนวน 713 ราย อายุระหว่าง 40-70 ปี อาสาสมัครได้รับการตอบแบบสอบถาม ตรวจร่างกาย การเก็บเลือด และตรวจภาพรังสีเต้านม จากนั้นจะถูกแบ่งออกเป็น 2 กลุ่มตามเกณฑ์การวินิจฉัยโรคอ้วนลงพุง AHA/NHLBI 2005 รังสีแพทย์อ่านและแปลผลค่าร้อยละความหนาแน่นของภาพรังสีเต้านม โดยแบ่งออกเป็น 4 กลุ่ม ผู้วิจัยใช้สถิติการวิเคราะห์การถดถอยและแบบจำลองแบบผสมเพื่อทดสอบความสัมพันธ์ของโรคอ้วนลงพุงและองค์ประกอบต่างๆ ของโรคอ้วนลงพุงกับค่าร้อยละความหนาแน่นของภาพรังสีเต้านม*

ผลการศึกษา : *พบความชุกของโรคอ้วนลงพุงร้อยละ 20.48 พบค่าร้อยละความหนาแน่นของภาพรังสีเต้านมในกลุ่มโรคอ้วนลงพุงและไม่มีโรคอ้วนลงพุงมากที่สุดในช่วงร้อยละ 50 ถึงร้อยละ 74 ผู้วิจัยพบความสัมพันธ์ในทางตรงกันข้ามระหว่างโรคอ้วนลงพุงกับค่าร้อยละความหนาแน่นของภาพรังสีเต้านม ยิ่งไปกว่านั้นหลังจากควบคุมด้วยค่าดัชนีมวลกาย ความสัมพันธ์ในทิศทางตรงกันข้ามก็ยังคงพบระหว่างค่าร้อยละความหนาแน่นของภาพรังสีเต้านมกับการเพิ่มขึ้นของไขมันไตรกลีเซอไรด์*

สรุป : *ไม่พบความสัมพันธ์ระหว่างโรคอ้วนลงพุงกับการเพิ่มขึ้นของค่าร้อยละความหนาแน่นของภาพรังสีเต้านม*