CORRELATION BETWEEN MAMMOGRAPHY DETECTED BREAST ARTERIAL CALCIFICATIONS AND LIFESTYLE RISK FACTORS

Vilma Kosović[1], Ivan Krolo[2], Dijana Zadravec[2] and Petar Drviš[3]

[1]Department of Radiology, Dubrovnik General Hospital, Dubrovnik; [2]Clinical Department of Diagnostic and Interventional Radiology, Sestre milosrdnice University Hospital Center, Zagreb; [3]Clinical Department of ENT and Head and Neck Surgery, Split University Hospital Center, Split, Croatia

SUMMARY – The aim of the study was to investigate the association between some lifestyle-attributable risk factors of atherosclerosis, such as body mass index (BMI), oral contraceptives, hormone replacement therapy, smoking and alcohol consumption with breast arterial calcification (BAC) and its intensity on mammograms, and to assess the impact of these lifestyle risk factors on mammography findings of BAC. This prospective study included 300 women aged 47-69, i.e. a group of 149 women with BAC on mammograms and control group of 151 women without BAC. Self-reported BMI, use of oral contraceptives, hormone replacement therapy, smoking and alcohol consumption were recorded by medical interview. The presence of BAC and its intensity on mammography was compared according to the presence of high BMI and use of hormone therapy, smoking and alcohol consumption. The results showed the highest proportion of smokers (28.9%) in the group with mild BAC as compared with the groups without calcification (14.6%) and with intense calcification (12.1%). Women taking oral contraceptives had a higher level of calcified breast arteries but no significant between-group difference was found for high BMI, hormone therapy and alcohol consumption. Thus, study results showed the mammographic finding of BAC to be inadequate to identify women with some lifestyle-attributable risk factors such as BMI, hormone replacement therapy, smoking and alcohol consumption.

Key words: *Mammography; Lifestyle; Vascular calcification; Risk factors*

Introduction

There is a high prevalence of risk factors in healthy population due to the low level of motivation to change habits and lifestyle despite good population information on their harmfulness. Along with hyperlipidemia and hypertension, smoking is the most significant risk factor for atherosclerosis, although some researches did not establish the role of hypertriglyceridemia as an independent risk factor. High body mass index (BMI) and smoking are classified as modifiable risk factors. Together with alcohol, oral contraceptives and hormone replacement therapy, they are classified as potentially modifiable risk factors and are associated with lifestyle[1,2].

The pathogenesis, cause and clinical significance of breast arterial calcification (BAC) are not fully understood yet. BACs appear as an incidental finding on mammography and represent degenerative calcifying changes that occur in mammary artery and increase with age, so they are most pronounced in elderly women[3]. Calcifying medial sclerosis or Mönckenberg's sclerosis is a fundamental requirement for the condition called calcified breast arteries detected on mammography[4]. Medial calcifications occur indepen-

Correspondence to: *Vilma Kosović, MD*, Department of Radiology, Dubrovnik General Hospital, Roka Mišetića 2, HR-20000 Dubrovnik, Croatia
E-mail: vilmakosovic@gmail.com

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dently of atherosclerosis and can be associated with elastin and smooth muscle cells. These calcifications differ from intimal calcifications, which accumulate in the intima of large and medium-sized arteries, occur in the context of atherosclerosis, and are associated with lipid, macrophages and vascular smooth muscle blends[3,5-7].

BACs are visible on mammograms as a railroad track configuration that appears as two parallel calcific lines that accompany the tubular structure of the blood vessels[4,8]. Conventional x-ray techniques cannot with certainty distinguish medial from intimal calcifications, even though medial calcifications are finer and diffuse in small vessels compared to the large and discontinuous appearance of intimal calcifications in large and medium-sized arteries[9,10].

The aim of this study was to determine the impact of some lifestyle risk factors for atherosclerosis, such as high BMI, oral contraceptives and hormone replacement therapy, smoking and alcohol consumption, on the degree of calcifications of intramammary arteries on mammography and to demonstrate the importance of mammography findings of calcified breast arteries as an important indicator of the presence of some lifestyle risks requiring modification.

Patients and Methods

Study design

We conducted a prospective study that included 300 women aged 47 to 65 who underwent screening or diagnostic mammography. All participants were informed about the aims and methods of examinations and gave their written consent to participation according to the protocol approved by Ethics Committees of the Sestre milosrdnice University Hospital Center and Dubrovnik General Hospital. In this study, 149 women with mammography detected BAC were compared to control group of 151 women without BAC according to BMI and use of hormone therapy, either previous or current use of oral contraceptives, smoking and alcohol consumption. A history of breast operation and detected breast carcinoma were taken as exclusion criteria. Mammographic breast imaging was done on a classic mammographic unit Mammomat 300 (Siemens, Erlangen, Germany) and digital mammographic unit Sophia-PlanMed (Shimadzu, Helsinki, Finland) at Sestre milosrdnice University Hospital Center, and on a digital mammographic unit Mammomat 1000 (Siemens, Munich, Germany) at Dubrovnik General Hospital. Most of the mammograms had two views: mediolateral oblique and craniocaudal view of each breast.

Two radiologists who interpreted the mammograms independently also evaluated BACs, which are benign calcifications and are not usually reported on mammogram analysis. BACs were evaluated as positive or absent on a mammogram, and if positive, they were classified according to the degree of shadows as mild and intense calcifications.

Data on self-reported BMI, calculated from body height and weight (m^2/kg), were collected from study subjects by medical interview, along with data on the previous use of oral contraceptives and hormone replacement therapy. Smoking was considered positive if women were current smokers. Alcohol consumption was positive if the participant reported taking alcohol daily.

The correlation between mammography detected BAC and BMI, previous use of oral contraception and hormone therapy, smoking and alcohol consumption was determined using variance analysis if the variables were measured on the interval or metering scales. If the measures were measured by dichotomous scales, the χ^2-test was calculated. Statistical analyses were performed with the IBM SPSS Statistic 20. The level of statistical significance was set at $p<0.05$.

Results

We enrolled 149 participants with BAC and 151 participants without BAC on mammograms. The study group of 149 women with mammography detected BAC was divided into two subgroups: a subgroup of 83 (56%) women with mild calcifications and a subgroup of 66 (44%) women with intense calcifications. According to lifestyle risk factors, there were 18% of current smokers, 13.7% used oral contraceptives, 2.7% were taking hormone replacement therapy and 2.3% were taking alcohol daily.

Body mass index is a simple index of weight-for-height that is commonly used to classify underweight, overweight and obesity in adults. It is defined as the weight in kilograms divided by the square of the height in meters (kg/m^2). The normal BMI range is

18.5-24.99. According to the International Classification, overweight is defined as BMI ≥25, pre-obesity as BMI 25-29.99, and obesity as BMI ≥30[11].

In this study, the mean BMI was 25.58±3.11, range 14.4-40.51 (Table 1).The mean age of all study subjects was 61.95±6.41, range 47-69 years (Table 1).

Table 1. Descriptive data on body mass index (BMI) in all study subjects

	Age (yrs)	BMI
N	300	300
Arithmetic mean	61.95	25.58
Central median	63	24.80
Standard deviation	6.41	3.11

Table 2. Distribution of study subjects according to smoking habit and alcohol consumption

		Frequency	%
Smoking	No	246	82.0
	Yes	54	18.0
	Total	300	100.0
Alcohol consumption	No	293	97.7
	Yes	7	2.3
	Total	300	100.0

Table 3. Distribution of study subjects according to use of oral contraception and hormone replacement therapy

		Frequency	%
Oral contraception	No	259	86.3
	Yes	41	13.7
	Total	300	100.0
Hormone replacement therapy	No	292	97.3
	Yes	8	2.7
	Total	300	100.0

Smoking was the only of the three variables observed (smoking, oral contraceptives and hormone therapy) that was not distributed equally in the study groups defined according to mammography findings (χ^2=9.450, p<0.05). The highest proportion of smokers (28.9%) was recorded in the mild BAC subgroup as compared with the group without calcification (14.6%) and the subgroup with intense calcification (12.1%).

Table 4. Correlation of mammography results and smoking

		Mammography			Total
		Calcification			
		None	Mild	Intense	
Smoking	No	129	59	58	246
	Yes	22	24	8	54
Total		151	83	66	300

χ^2=9.450; p<0.05

Table 5. Correlation of mammography results and use of oral contraception

		Mammography			Total
		Calcification			
		None	Mild	Intense	
Oral contraception	No	137	68	54	259
	Yes	14	15	12	41
Total		151	83	66	300

χ^2=0.868; p>0.05

Table 6. Correlation of mammography results and other variables

	Mammography
Smoking	0.033
Body mass index	-0.007
Oral contraception	0.116*
Hormone replacement therapy	-0.024
Alcohol consumption	0.006

*p<0.05

As shown in Table 6, correlation of mammography results and other variables yielded only one variable, oral contraceptives, as being statistically significant (p<0.05); thus, there was positive correlation between BAC and use of oral contraceptives.

Discussion

The prevalence of BAC increases with increasing age and has been observed in 9%-12% of women older than 50 years[12,13]. The majority of studies suggest BAC to be associated with the age of women[14-17]. Most pre-

vious studies investigated the relationship between BAC and risk factors for cardiovascular disease, such as hyperlipidemia, hypertension and diabetes, and its role as a potential marker for cardiovascular disease. Some of these studies demonstrated significant association between BAC and main atherosclerotic risk factors, such as hypertension, diabetes mellitus and hyperlipidemia, suggesting that BAC could be related to the risk of cardiovascular disease[18-22].Some studies showed that BACs were an independent risk factor for coronary artery disease, especially in women with diabetes mellitus, as compared with women without BAC[14,18,21,23]. In a study by Baum *et al*., the results suggested that arterial calcification on mammograms might be a sign of coexisting diabetes[19]. Markopoulos *et al*. report on significant correlation between BAC detected by mammography and atheromatous changes of carotid and femoral arteries, proposing BAC as a marker of systemic vascular atherosclerosis[24]. This connection between BACs and atherosclerosis is not understood, concerning different accumulation of intimal calcifications of atherosclerotic arterial changes and medial calcifications of breast arteries. Furthermore, other studies report different results on the impact of these risk factors of atherosclerosis on mammography detected BAC. So, some studies found no association between BAC and main cardiovascular risk factors[25-28]. A study by Almeida *et al*., which included 197 menopausal women, found no significant association between BAC and cardiovascular risk factors, such as hypertension, diabetes mellitus, previous stroke and acute coronary syndrome, smoking and high BMI[29]. In a study by Akinola *et al*., there was no connection found between BAC and lifestyle risk factors, such as smoking, alcohol and hormone replacement therapy either[30], reporting results consistent to our study. Zafar *et al*. report results similar to ours, recording no relationship between BAC and high BMI and hormone therapy, but they did find connection with oral contraceptives[31]. In our study, we investigated the impact of some lifestyle risk factors on BAC development; according to the results, the women taking oral contraception appeared to have a higher degree of calcifications on mammography. Similar results have been reported by Leinster *et al*.[32] In our study, there was no association between BAC and excess body weight as defined by BMI, and similar results were found in the studies by Kataoka *et al*.[25], Almeida *et al*.[29] and Zafar *et al*.[31].

This study had several limitations. One of the study limitations might be that it was focused on the general female population older than 47 because the study population was mostly recruited from screening mammography. Self reported BMI might differ from the actual BMI if the participant did not know her exact height and weight. Another limitation of the study was that the participants were assessed for smoking, which was positive if the participant was current smoker but not previous smoker. Also, women drinking alcohol on a daily basis may have decided not to admit it on the interview.

In conclusion, in this study, we found no statistically significant differences in the association of BAC and lifestyle risk factors of atherosclerosis, such as high BMI, smoking, alcohol consumption, but there was a significant association with oral contraceptives. These results also indicate that additional studies on a larger sample are needed to confirm or reject these findings and to explore the pathogenesis of BAC, which is still unclear.

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Sažetak

KORELACIJA ARTERIJSKIH KALCIFIKACIJA DOJKE NA MAMOGRAMU S ČIMBENICIMA RIZIKA POVEZANIM S NAČINOM ŽIVOTA

V. Kosović, I. Krolo, D. Zadravec i *P. Drviš*

Istraživala se povezanost određenih čimbenika rizika ateroskleroze povezanih s načinom života poput indeksa tjelesne mase (ITM), uzimanja oralnih kontraceptiva, hormonske nadomjesne terapije, pušenja i konzumiranja alkohola s arterijskim kalcifikacijama dojke i njihovim stupnjem intenziteta na mamografiji. Ova prospektivna studija je uključila 300 žena u dobi od 47 do 69 godina, od kojih je skupina od 149 žena imala arterijske kalcifikacije dojki na mamografiji, a druga kontrolna skupina od 151 žene je bila bez arterijskih kalcifikacija. Medicinskim intervjuom dobiveni su podaci o tjelesnoj težini i visini ispitanica, prema kojima se izračunao ITM te anamnestički podaci o prethodnoj uporabi oralnih kontraceptiva, hormonske nadomjesne terapije, pušenju i konzumiranju alkohola. Uspoređen je nalaz arterijskih kalcifikacija dojki i njihovog stupnja na mamografiji s ITM i uporabom hormonske terapije te pušenjem i konzumiranjem alkohola. U skupini žena s blažim kalcifikacijama dojki bio je najveći udio pušača (28,9%) u odnosu na skupinu bez kalcifikacija (14,6%) ili skupinu s intenzivnim kalcifikacijama (12,1%). Rezultati su pokazali statistički značajnu povezanost arterijskih kalcifikacija dojki s oralnom kontracepcijom, dok nije nađena statistički značajna povezanost između arterijskih kalcifikacija dojki na mamogramu i uporabe hormonske nadomjesne terapije, ITM, pušenja i konzumiranja alkohola. Dakle, mamografski nalaz arterijskih kalcifikacija dojki nije dostatan za identificiranje žena s nekim čimbenicima rizika ateroskleroze povezanim s načinom života, odnosno nalaz istih na mamogramu ne upućuje na čimbenike rizika na koje se može utjecati, kao što su visok ITM, uporaba hormonske terapije, pušenje i konzumiranje alkohola.

Ključne riječi: *Mamografija; Način života; Vaskularna kalcifikacija; Rizični čimbenici*