

# Evolution of Intima Media Thickness and Breast Arterial Calcifications as Cardiovascular Risk Factor, Effect of Pregnancy and Breast Feeding

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## ABSTRACT:

Evolution of intima media thickness and breast arterial calcifications as cardiovascular risk factor, effect of pregnancy and breast feeding

**Objective:** The aim of retrospective study was to evaluate intima media thickness (IMT) of common carotid artery and breast arterial calcifications (BAC) as indicator of cardiovascular risk factors. We also aimed to evaluate contribution of pregnancy count and total time spent on breast feeding to BAC and IMT.

**Material and Method:** This study included 40 patients with BCI and 40 patients without BCI, referred to Taksim Research and Education Hospital Radiology Clinic. All individuals cardiovascular risk factors were noted and common carotid artery IMT was measured with color doppler imaging. Number of pregnancies and time spent on breast feeding were also noted.

**Results:** There was statistically significant relation between age and IMT, BCI both. Patients with increased IMT had higher cardiovascular risk factors compared to normal cases (1.82 against 1.33). There was not different cardiovascular risk factor value between BAC positive and negative patients (Same as 1.675). We could not find any effect of number of pregnancies and time spent on breast feeding to IMT and BAC.

**Conclusion:** IMK was a better indicator of cardiovascular disease compared to BAC. We could not find any effect of number of pregnancies and time spent on breast feeding to IMT and BAC.

**Keywords:** Breast arter calcifications, cardiovascular risk, intima media thickness

## ÖZET:

İntima-media kalınlığı ve meme arter kalsifikasyonlarının kardiyovasküler risk faktörü olarak değerlendirilmesi, gebelik ve emzirmenin rolü

**Amaç:** Retrospektif çalışmamızda ana karotid arterde intima media kalınlığı ölçümünün ve meme arter kalsifikasyonlarının, kardiyovasküler risk belirteci olarak değerlendirilmesini, gebelik sayısı ve emzirme süresinin katkısını ölçmeyi amaçladık.

**Gereç ve Yöntem:** Çalışmaya, Taksim Eğitim ve Araştırma Hastanesi Radyoloji Kliniği'ne başvuran ve mammografide meme arter kalsifikasyonu bulunan 40, meme arter kalsifikasyonu (MAK) bulunmayan aynı sayıda olgular katıldı. Tüm olguların kardiyovasküler risk faktörleri not edildi. Karotis arter intima media kalınlıkları (İMK) ölçüldü. Gebelik ve emzirme süreleri kaydedildi.

**Bulgular:** Yaş ile MAK ve İMK arasında anlamlı ilişki saptandı. İMK artışı olan olgularda kardiyovasküler risk faktörleri daha yüksek bulundu (1.82 ye karşın 1.33). MAK bulunan olgularda bulunmayanlar ile karşılaştırıldığında artmış kardiyovasküler risk faktörü bulunmadı (Her iki grupta 1.675 olarak hesaplandı). Gebelik ve emzirme süresinin İMK ve MAK ilişkisi saptanmadı.

**Sonuç:** Kardiyovasküler risk belirteci olarak İMK artışı MAK a kıyasla daha güvenilir bir parametredir. Gebelik sayısı ve emzirme süresi İMK ve MAK üzerine etkisi bulunmamaktadır.

**Anahtar kelimeler:** Meme arter kalsifikasyonları, kardiyovasküler risk, intima media kalınlığı

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## INTRODUCTION

Today, the current theory on the plaque formation is based on the atherosclerosis, being a response to the damage of endothelial cells that line the arteries. Three stages occur in the plaque formation. Initially, the blood lipids accumulate under the endothelium. Second, the lipid material is ingested by the macrophages, and foam cells form, which take their names from their microscopic foamy appearance. Finally, the smooth muscle cells migrate to subendothelial layer from the muscular layer and transformed into fibroblasts (1). Inflammation plays a crucial role in plaque formation. The ongoing inflammation causes the destruction of foamy cells and the other components of the plaque and accumulation of inflammatory debris. The thickening of the intima-media complex indicates a subtle plaque formation, but of course, the plaque can be visualized directly with ultrasound when it reaches the sufficient size to reach the carotid artery lumen. Intima-media thickness (IMT) and the prevalence of plaque increase with age (2-4). In addition, IMT also increases as a response to the early plaque formation. Therefore, increased IMK is used as an indicator of cardiovascular risk in various clinical settings (5).

Breast arterial calcifications (BACs) due to atherosclerosis are the parallel calcified lines that characteristically correspond to the artery wall and can easily be recognized. The early arterial calcifications may mimic the linear calcifications in ductal in situ carcinoma. The presence of non calcified vascular structure that may cause suspected calcifications leads to correct diagnosis. Magnification images show the tram route-like arterial calcifications between the two parallel lines (6). Arterial calcification is a common feature in degenerative atherosclerotic disease and subclinical atherosclerosis may be understood by modern imaging techniques (7,8). With conventional radiology techniques such as mammography (MG), the calcium deposits in the arterial wall can be seen. But the clinical significance of these calcifications remains yet unexplained (9,10).

In this study, it is aimed to evaluate the IMT and BAC as cardiovascular risk factors, and to discuss the role of pregnancy and breastfeeding.

## MATERIAL AND METHOD

The patients with detected breast vessel wall calcification, who presented between December 2009-April 2010 to Taksim Training and Research Hospital, Department of Radiology with MG request, were chosen. Forty cases with BAC present and the same number of subjects with no BAC formed the study and control groups.

Mammography was performed with Agfa CR 35-X (Agfa Corporation Greenville, Belgium) device. Mammography option is performed with a special software and 18x24 cm and 24x30 cm mammography cassettes with 20 pixels/mm.

Color Doppler examination was performed with a GE Logiq Q9 (General Electric, New York, USA) model device.

The mammograms and carotid color Doppler examinations were evaluated by 2 radiologists with 11 and 12 years of experience (GD and BDÖ), respectively. In both right and left breasts at the mammograms, the calcium deposits along the contour of breast arteries were defined as vessel wall calcifications.

Three diastolic measurements at each location were performed in carotid color Doppler examination; the thickest intima-media in both major carotid arteries, the proximal part of the bulb and the proximal parts of the artery from the arcus aorta on the left, and from the brachiocephalicus on the right. The mean value of these measurements were noted as IMT.

In assessment of the cardiovascular risk factors of the cases, diabetes mellitus (DM) hypertension (HT), hypercholesterolemia, family history of any heart diseases and the body mass index (BMI) have been questioned.

The patients with levels of fasting blood glucose more than 140 mg/dl twice or patients with previously diagnosed with DM joined the diabetic group.

Patients who were previously diagnosed with hypercholesterolemia or patients with blood total cholesterol levels more than 210 mg/dl were considered as hypercholesterolemia.

Patients who were previously diagnosed with HT or patients with systolic/diastolic blood pressure levels over 200/140 mm/Hg were included in the hypertensive group.

Patients with body mass index (BMI) levels over 25 were evaluated in the increased BMI group.

Patients with at least one heart disease in their first and second-degree relatives were included in the group of patients with heart disease in the family.

The number of 5 cardiovascular risk factors that these cases have, were noted for statistical analysis.

The total duration of breastfeeding and the number of pregnancies of all cases were noted.

## RESULTS

The mean age of 40 cases with BAC ranged between 40-84 years, with a mean value of 62.6 years. The mean age of 40 cases without BAC ranged between 40-78 years, with a mean value of 60.5 years. The difference was statistically significant.

When the distribution of the risk factors were assessed; Seven cases of 80 in our study had family history of heart disease (8.75%),

Twenty-four had hypertension (30%),

Twenty-one had DM (26.25%)

Fifty-eight had hypercholesterolemia (72.5%)

Twenty-two had increased BMI (27.5%) (Table-1).

**Table-1: The distribution of the risk factors of the patients participating in the study**

Risk factors	Number of cases	Rate
Family history of heart diseases	7	8.75
Hypertension	24	30
Diabetes mellitus	21	26.25
Hypercholesterolemia	58	72.5
Increased body mass index	22	27.5

The mean age of cases with BAC was 61.3, without BAC was 58.5, and the difference inbetween is statistically significant ( $p=0.047$ ).

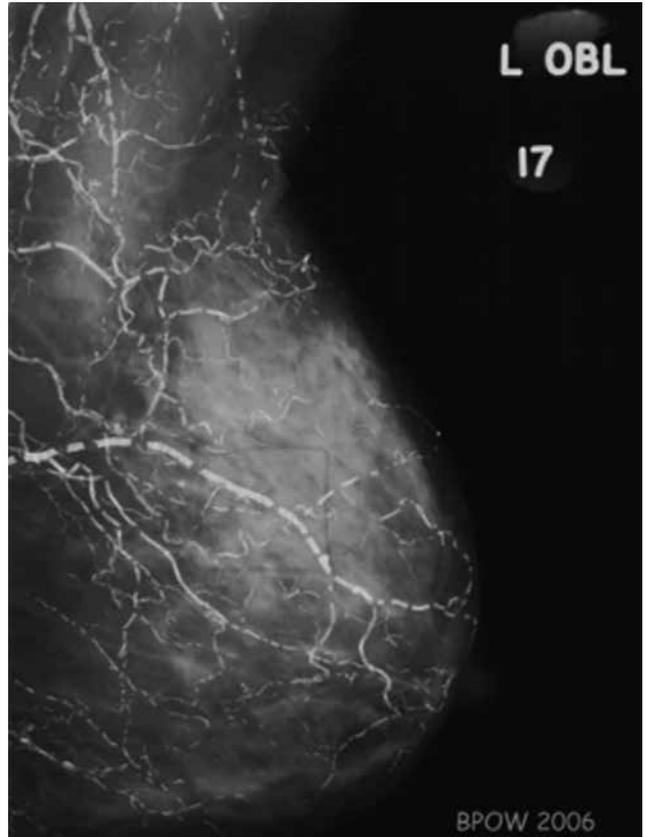
The mean risk factor in cases with BAC was calculated as 1.675, without BAC as 1.675.

The average duration of breastfeeding in cases with BAC was 43 months, without BAC was 41.5 months. The difference inbetween was not statistically significant ( $p=0.33$ ).

The mean number of pregnancies in cases with BAC was 5.15, without BAC was 4.75. The difference inbetween was not statistically significant ( $p=0.09$ ) (Table-2).

**Table-2: The comparison of demographic data, average risk factors, pregnancy and breastfeeding in patients with and without BAC**

	BAC present	BAC absent	p
Age distribution	40-84	40-78	
Mean value	61.6	58.5	0.047
Mean number of risk factors	1.675	1.675	x
Mean breast-feeding time	43	41.5	0.33
Mean number of pregnancy	5.15	4.75	0.09

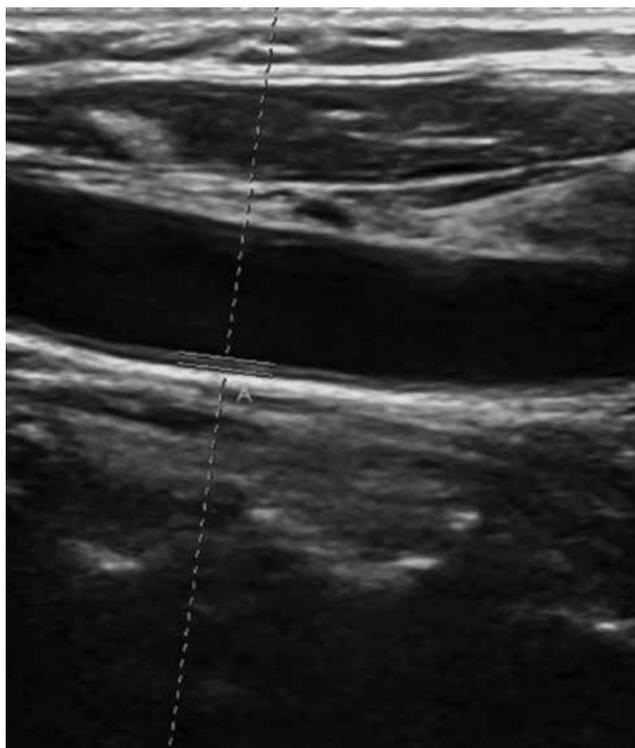


**Figure-1: Breast artery calcifications**

The number of cases with increased IMT was 47, with a ratio to all cases 68.75%. The number of cases with normal IMT was 33, with a ratio to all cases 41.25%.

The mean age of cases with normal IMT was 57.3 years, and of cases with increased IMT, 61.78 years. The difference inbetween was statistically significant ( $p<0.01$ ).

The mean risk factor in cases with normal IMT was found as 1.33, and in cases with increased IMT, as 1.82. The difference inbetween was statistically



**Figure-2:** Measurement of intima media thickness

**Table-3:** The comparison of demographic data, average risk factors, pregnancy and breastfeeding in patients with normal and increased IMT

	Normal IMT	Increased IMT	p
Age distribution	40-84	40-78	
Mean value	57.3	61.78	<0.01
Mean number of risk factors	1.33	1.82	<0.01
Mean breast-feeding time	41.85	43.5	0.26
Mean number of pregnancy	5.2	4.75	0.08

significant ( $p < 0.01$ ).

The average duration of breastfeeding in cases with normal IMT was 41.85 months, and in cases with increased IMT, 43.5 months, with no statistically significant difference ( $p = 0.26$ ).

The mean number of pregnancies in cases with normal IMT was 5.2, and in cases with increased IMT, it was 4.75, with no statistically significant difference ( $p = 0.08$ ) (Table-3).

## DISCUSSION

Atherosclerosis can be seen as a means of vascular aging. It is impossible to prevent this process, even

the advanced medical level we reached today. Both genetic heritage, as well as the lifestyle may accelerate or slow down this process. In our study, as an indicator of the genetic background, the family history of heart disease was questioned and added to the findings.

In the partly changable factors with lifestyle of our study group; high cholesterol, diabetes mellitus (DM), increased systolic and diastolic blood pressure (hypertension) and increased BMI existed.

Smoking may be included in the questionable risk factors. However, because of the relatively small number of cases in our study group, and the uncommon habit of women smoking in our society, it is considered that there will be no adequate statistical data obtained, so this criteria was excluded. Of course, it is also gratifying for the society that smoking is not common.

The distribution of the risk factors in the cases in the study, given that the cases were over 40 years old with MG, may be said that they have predictable rates. However, what is prominent here, is the presence of high cholesterol levels with such high rate as 72.5%. In our study, 210 mg/dl level was used as the reference. However, this value has been revised several times in the recent years. These revisions tend to withdraw the total cholesterol levels. Recently, up to 200 mg/dl was defined as normal, 200-240 mg/dl as borderline, and 240 mg/dl and more as high cholesterol levels (11).

IMT is a dynamic entity, which tends to increase with age. Beşir et al. (12) in their study involving 2298 cases with ages between 18-92 years, reported that the mean IMT shows a mean increase of 0.066 mm per decade after 20 years old. In our study, the age distribution of the participants was 40-84 years, with a reported normal value of 0.492-0.793 for this age group. Sedighi et al. (13) in their study involving 537 cases, they defined low cardiovascular risk in the group with IMT:0.6, and moderate risk in the group with IMT:0.6-0.8. We determined the IMT reference value as 0.8, considering that the participants in our study were over the age of 40.

In our study, the number of pregnancies and the mean duration of breastfeeding were not evaluated in the risk factors category. However, the contribution

of these factors to BAC and IMT formation was examined. In the statistical analysis, we didn't observe a significant contribution of these factors to BAC and IMT formation. Similarly, Büyükkaya et al. (14), in their study with 105 cases, reported that pregnancies and the duration of breastfeeding didn't contribute to BAC development.

In our study, we found a statistically significant increase in both IMT and BAC, with age. IMT increase in the arteries with advancing age due to atherosclerosis and vascular wall calcifications in all vessels, also in the breast, are the expected results of atherosclerosis (3,6).

In our study, we found that the cardiovascular risk factors were higher in cases with increased IMT. Hester et al. (15), in their meta-analysis including 14 cohort studies and 45828 participants in total, stated that 01. mm of increase in IMT brings 1.12% of increased myocardial infarction and cerebrovascular event risk in women, and in men 1.08% of increased risk.

In our study, in patients with BAC, no increased risk factors were detected compared to patients without BAC. Different results were obtained in previous studies on this subject. Shah et al. (16), in their meta-analysis study including 19 studies and

33583 cases in total, they stated no relationship between BAC and coronary artery disease (CAD) risk in 4 studies, significant relationship in 13 studies, and significant relationship in cases with more than 50% stenosis in 2 studies. This meta-analysis included 1 study with premenopausal women.

The most important limitation of our study is the relative small number of cases. In addition, with the prediction of getting inadequate statistical data, because smoking is not common among women, we couldn't include smoking as a risk factor.

## CONCLUSION

Pregnancy and the duration of breastfeeding were found to have no effect on BAC and IMT development which were both defined as the cardiovascular disease markers. Advanced age has significant effect on these two data. Cardiovascular risk factors increase IMT significantly, while this was not the case for BAC. The presence of BAC was controversial to be a cardiovascular risk marker also in the previous studies. We believe that IMT increase is a more reliable and strong indicator of this issue. New studies with greater number of patients will contribute to the subject.

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