Factors Associated with Breast Arterial Calcification on Mammography
Aasma Nudrat Zafar1, Shamrez Khan1 and Saemah Nuzhat Zafar2

ABSTRACT
Objective: To determine the frequency of breast arterial calcifications (BAC) as seen on mammographic examination and to determine the association between BAC and hypertension, age, parity and weight of the person.
Study Design: Cross-sectional analytic study.
Place and Duration of Study: Department of Diagnostic Radiology, Military Hospital, Rawalpindi, from January 2006 to January 2007.
Methodology: Two hundred patients undergoing mammography were studied to evaluate the association of BAC with raised blood pressure, age and parity. Previous history of lactation and the patients’ weight were also recorded. Proportions of classes were compared using chi-square test.
Results: 13.5% of the subjects (n = 200) were positive for BAC on mammograms. Mean age of the BAC positive subjects was higher than their counterparts found negative for BAC. Women bearing 5–6 children showed the highest frequency of BAC. Seventy seven (10.38%) of the BAC positive cases had previous history of lactation, whereas 15.44% (n = 123) had not breast fed their children and showed BAC. No significant association of presence of BAC was noted with the weight of the subjects.
Conclusion: The frequency of presence of BAC on mammography was associated with systemic hypertension and higher age. It also increased with the reproductive parameters of a woman.


INTRODUCTION
Breast self-examination, clinical assessment, X-ray mammography and fine-needle aspiration cytology are the basics of detecting breast disease.1,2 Calcium deposition in breast arteries is commonly seen on mammograms. Mammographically visible breast intraarterial calcification (BAC) is positively related to high parity. It occurs most often with advancing age.3 It is controversial whether it is an independent risk factor for multiple cardiovascular outcomes among women.4 The altered mineral metabolism during pregnancy and lactation is presumably the most important causative factor in the occurrence of BAC. Pregnancy is associated with major changes in the calcium metabolism to meet the high requirements for fetal growth and for breast-milk production. Some biochemical proteins of bone resorption and formation (e.g. osteocalcin, a bone morphogenic protein) are elevated in the first months of lactation and are also found in calcified vascular tissues.5

The objectives of this study were to determine the frequency of BAC on mammography and the association between BAC and systemic hypertension, advanced age, lactation and the number of children born to a female.

METHODOLOGY
The study was carried out at the Department of Diagnostic Radiology, Military Hospital, Rawalpindi, from January 2006 to January 2007. Two hundred patients were included in this cross-sectional analytic study. Purposive, non-probability sampling was undertaken after informed consent. Approval for the study was taken from the Ethics Review Board of this institution. All female patients, regardless of their age, undergoing unilateral or bilateral screening/diagnostic/follow-up mammography were included and all male patients were excluded.

BAC were defined as calcifications in the arteries on mammograms varying from small particles in a single breast artery to thick columns of calcium along an entire artery and its side branches, looking like a railroad track. All other cases of mammographically detectable calcification were excluded e.g. in mass lesions in breast tissue, muscle or axilla, skin lesions like tattoos and keloid, etc.

Hypertensive patients included all those patients who were diagnosed cases of raised blood pressure, whether

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or not they were on medication. Parity was defined as all pregnancies, including abortions. Breast feeding was defined as having breastfed at least one child.

Mammograms were conducted in accordance with established breast cancer screening protocols and obtained in two standard projections, craniocaudal and mediolateral oblique, for each breast on Siemens Mammomat 300/3000 RX dedicated mammographic unit. After an informed consent, a demographic profile of age, parity and blood pressure was recorded.

Mammograms of 200 patients were studied over a period of 01 year for prevalence of BAC. The data was collected for association of raised blood pressure, age and parity with arterial calcifications on a specially designed proforma.

The data of both groups was entered in Statistical Package for Social Sciences (SPSS) version 10 for analysis. A p-value of < 0.05 was considered statistically significant. Chi-square test was used to measure the association between BAC and hypertension, age, weight and parity.

### RESULTS

Out of the 200 subject, 13.5% were found positive for BAC on mammograms, while 86.5% did not show arterial calcification on mammography.

One hundred (50%) of the total subjects were normotensives and the rest were hypertensive (p = 0.023). Mean age of the BAC positive cases was 56.56 ± 13.098 years (ranging from 28 to 70 years), whereas BAC negative cases had a mean age of 44.38 ± 10.873 years (ranging from 18 to 79 years). The association of higher age with the occurrence of BAC was highly significant with p-value less than 0.001 (Table I).

Association of BAC on mammograms and parity of the subject was significant (p < 0.001), in contrast to its association with history of lactation (p = 0.308).

Mean weight of the subjects positive for mammographically detected BAC was 71.52 ± 13.874 kilograms (ranging from 40 to 93 kilograms). It was 70.40 ± 12.608 kilograms in the BAC negative subjects (ranging from 40 to 130 kilograms). Relationship of BAC occurrence with weight was not significant (p = 0.501) as well.

### DISCUSSION

Intramammary vascular calcifications are benign findings that are incidentally found on mammograms. X-ray

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### Table I: Evaluation of association of breast arterial calcification with hypertension, age and parity.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>BAC present</th>
<th>BAC negative</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure (mm of Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Hypertensive</td>
<td>19</td>
<td>81</td>
<td>100</td>
<td></td>
<td>0.023</td>
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<tr>
<td>normotensive</td>
<td>08</td>
<td>92</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>03</td>
<td>61</td>
<td>64</td>
<td></td>
<td>&lt; 0.001</td>
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<tr>
<td>Group 2</td>
<td>05</td>
<td>74</td>
<td>79</td>
<td></td>
<td></td>
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<tr>
<td>Group 3</td>
<td>12</td>
<td>28</td>
<td>40</td>
<td></td>
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<tr>
<td>Group 4</td>
<td>02</td>
<td>09</td>
<td>11</td>
<td></td>
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<tr>
<td>Group 5</td>
<td>04</td>
<td>01</td>
<td>05</td>
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<tr>
<td>Group 6</td>
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<tr>
<td>Parity</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>05</td>
<td>24</td>
<td>29</td>
<td></td>
<td>0.501</td>
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<tr>
<td>Group 2</td>
<td>13</td>
<td>110</td>
<td>123</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 3</td>
<td>09</td>
<td>36</td>
<td>45</td>
<td></td>
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<tr>
<td>Group 4</td>
<td>0</td>
<td>02</td>
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<tr>
<td>Group 5</td>
<td>0</td>
<td>01</td>
<td>01</td>
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<tr>
<td>Lactation</td>
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</tr>
<tr>
<td>Positive</td>
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<td>69</td>
<td>77</td>
<td></td>
<td>0.308</td>
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<tr>
<td>Negative</td>
<td>19</td>
<td>104</td>
<td>123</td>
<td></td>
<td></td>
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<tr>
<td>Weight (kilograms)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Group 1</td>
<td>05</td>
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<td>Group 2</td>
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<td>Group 5</td>
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BAC: Breast Arterial Calcification; P-values are based on Chi-square test
mammography is the only examination capable of adequately depicting various types of calcifications in the breast. This is one of the major reasons that no other radiological diagnostic test, including sonography, magnetic resonance imaging (MRI), scintimammography etc., has replaced this imaging modality for their depiction.6 Medial calcifications are seen in small or medium-sized arteries and are considered less important.7 From pathological studies, it is known that breast arterial calcifications are located in the media of the vessel wall and are created unequally; intimal calcifications are seen in elastic and large arteries and are clinically important. The latter type is seen in systemic vascular disorders.8 It was assumed that when calcium is well available in the breast circulation, like during pregnancy and lactation, vascular smooth muscle cells can become activated and promote mineralization.

This research was aimed at investigating whether arterial calcifications seen on mammograms may serve as a screening tool for atherosclerotic risk assessment in women. The simultaneous use of mammograms for breast disease or screening and atherosclerotic disease could be very cost-effective.

BAC were identified on screening mammograms in 9.1% of Canadian women.9 13.5% subjects in the present study showed arterial calcifications on mammograms; however, this study is not directly comparable with the international study because mammograms were performed on a smaller sample size.

Circulating estrogen levels are inversely associated with the calcium content of atherosclerotic plaques. This is the reason that BAC are seen in the peri-menopausal years. A direct association of increasing age with BAC was found in this study.

The amount of calcium present in the coronary arteries has shown to be a strong marker of plaque burden and is currently used for assessment of future coronary heart disease (CHD) risk in asymptomatic patients. In women, calcium scores are lower in all age groups compared to disease (CHD) risk in asymptomatic patients. In women, circulating estrogen levels are inversely associated with BAC.8 In a study undertaken in The Netherlands, significant association was noticed between BAC and hypertension. The results also revealed that BAC seen on screening mammography was associated with disorders related to increased or accelerated arterio-

sclerosis.13 In a recent study, however, no association could be found between the presence of BAC and atherosclerotic lesions at coronary angiography.14 Due to limited resources, there was no follow-up of the hypertensive BAC positive patients by this invasive procedure.

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The findings of BAC may be related to hypertensive end-organ damage.15 The prevalence of BAC in hypertensive retinopathy, which is regarded as a marker of systemic vascular disease, is statistically higher than in those without retinopathy.16,17 In the present study, fundoscopic examination was not carried out in the hypertensive subjects.

Since the incidence of atherosclerotic heart disease increases with age, its manifestation in arteries of breast also rises. The present results show that average age of patients showing BAC on mammographic examination was higher than in patients with mammograms negative for BAC. In peri-menopausal period, calcium scores in coronary arteries in women are comparable to men of their age due to the loss of protective effect of circulating estrogens on the vascular wall during the fertile period of life. An increasing prevalence of BAC with higher age was seen in a study carried out in the United Kingdom.18 Since increasing age contributes to adipose tissue replacing the glandular parenchyma, faint vascular calcifications are very well visualized in the lucent background due to reduction in glandular tissue i.e. age positively correlates with BAC but negatively with breast density.

The present study revealed that parity and presence of BAC were significantly associated. A positive relationship of parity and BAC was found in a study conducted in the USA in recent years.3 Analysis of screening mammograms of postmenopausal patients in The Netherlands showed that parity and BAC had linear relationship.11 Enhancement of vascular calcification in pregnant women may be caused by elevated levels of parathyroid hormone-related protein (PTHrP). PTHrP is expressed in a variety of bone and vascular tissues and causes hypercalcaemia.20 Significant association of parity with both coronary artery calcification (CAC) and BAC is reported in literature, whereas breast feeding is associated with BAC, but not with CAC.19 However, this study did not show significant association of BAC with the history of lactation.

Although we did not encounter a significant relationship of BAC with the weight of the subjects, in a recent two-year study undertaken in the USA, it was shown that older women with a smaller body size had a higher probability of having BAC than women of the same age with a larger body size.20

In a retrospective study conducted on 228 women, who had both mammography and BMD evaluation during 2001-2003 in the USA, showed that osteoporosis and
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arterial calcification are strongly and independently correlated. Evaluation of the bone mineral density was not part of this study due to limited resources.

Role of mammography in primary investigation of cardiovascular diseases is questionable, but it may be a useful indicator to categorize the patients who need further evaluation, particularly if they are seen at an early age, with nulliparity or decreased parity. They can be advised to exercise and adopt risk modifying life-style aggressively.

Certain limitations of this study prevent generalization of results. Subjects who were illiterate or less educated were not sure of their age. Cardiovascular risk factors could not be evaluated fully by invasive techniques.

Further research regarding the role of screening mammography as an inexpensive tool to identify women at cardiovascular risk is required. This may include correlation of BAC seen mammographically with degree of generalized arterial calcification diagnosed by angiography (conventional or computed tomography). Also, if mammograms have to serve as useful tools for detection of CVS risk factors, standards will have to be set so as to identify women who need further risk evaluation.

CONCLUSION

BAC seen on mammograms are indicative of a generalized arterial calcification occurring in old age, due to loss of estrogens after menopause; they are not a reliable screening sign for evaluating cardiovascular risks. They are associated with increasing age, hypertension and parity.

REFERENCES