Original Article

Assessing the Stress Echocardiography in Women With Breast Arterial Calcification

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Abstract

Objective: breast arterial calcification (BAC) is one of the most prevalent mammographic findings and has been debated as a marker of cardiovascular disease (CVDs). The present study aimed to assess the findings of stress echo in women with BAC.

Materials and methods: This cross-sectional study was conducted on women who undergo mammography for routine breast cancer screening at Imam Reza hospital, western Iran from March 2018 to July 2018. The patients underwent stress echocardiography to evaluate the probability of myocardial ischemia (MI). Chi-square and independent t-tests were used to assess the differences between subgroups.

Results: BAC was present in 61 (15.2%) women. The mean age of the patients with BAC was significantly higher than the patients without BAC (58.59± 7.82 vs. 55.32±6.57, p =0.003). Prevalence rates of the menopause (88.5% vs. 71.1%, p=0.009), hypertension (29.5% vs. 17.7%, p=0.032), and hypercholesterolemia (24.6% vs. 13.0, p=0.018) were significantly higher in the patients with BAC compared to the patients without BAC. The prevalence rate of MI symptoms in the patients with BAC was equal to 24.6%. Significantly, more women with BAC were positive for myocardial ischemia compared to the women without BAC (24.6% vs. 8.5%, p<0.001). The prevalence rates of the diabetes mellitus, hypertension, hypercholesterolemia, and history of CVDs were significantly higher in the patients who were positive for MI.

Conclusion: It was found that BACs are correlated with an increased occurrence rate of CVDs. Our results illustrated that the patients who were positive for MI were more plausible to be diabetic, hyperlipidemic, hypertensive, and having a history of CVDs.

Keywords: Breast; Arteries; Echocardiography; Myocardial Ischemia; Women

Introduction

Cardiovascular diseases (CVDs), as the most common chronic non-communicable diseases, are responsible for 15.52% of total DALYs and 32.84% of total deaths worldwide according to the Global Burden of Disease (GBD) study (1). CVDs are known as the leading causes of death, especially in women (2). Gender-based differences in the CVDs

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risk factors, pathophysiological features, and symptoms onset are well defined (3, 4). Therefore, continuous investigations of the CVDs markers, disaggregated by gender, are essential. These markers play an important role in recognizing, managing and decision making regarding cardiovascular events (5).

Breast arterial calcification (BAC) is known as a marker of CVDs (6). BAC is defined as deposition of calcium in breast tissue. BAC is recognized by mammograms and it is more prevalent after menopause. Mammographic images show these deposits, as white dots or lines, which are small and untouchable. BAC is usually noncancerous and benign, although, certain patterns of breast calcification - such as compressed and irregular shapes may indicate breast cancer (7).

Given the existence of contradictory findings regarding the relationship between the BAC and CVDs, it remains important to determine the association between the BAC and CVDs (8-11). Until now, no study has been done to assess the findings of stress echocardiography in patients with BAC in Kermanshah, thus the current study was undertaken to address this research gap.

Therefore, this study was conducted to investigate the findings of stress echo in women with the BAC.

Materials and methods

Setting: Kermanshah, in western Iran, with a population of 1,980,351 (978,344 women), is a megacity with many deprived people. Imam Reza Hospital (IRH) affiliated with Kermanshah University of Medical Sciences (KUMS), Kermanshah, Kermanshah province, Iran, was selected for our study. This hospital, as a mega general hospital, with 750 active beds, provides advanced care and diagnostic services in almost all medical fields (e.g. mammography). Doctors in IRH visit patients with any illness, regardless of the severity of diseases, and socioeconomic status who come from the city and countryside.

Study design and sampling: This cross-sectional study was conducted on 400 women who undergo mammography for routine breast cancer screening from March 2018 to July 2018. We chose this number because a similar study (12) had reported that 58% of women who underwent mammography had BAC and, using a confidence level of 95% and a marginal error of 5%, the computed sample size was 364. However, considering a 5-10% possible non-response rate, a sample size of 400 was considered appropriate. Finally, patients were randomly selected using simple randomization. In this regard, we used computer-generated random numbers.

$$n=((z_{(1-\alpha/2)})^2 (p)(1-p))/(d)^2 =((1.96)^2 (0.58)(0.8))/(0.05)^2 \simeq 364$$

Inclusion criteria: Women, who undergo mammography for routine breast cancer screening, were selected to participate in the study.

Exclusion criteria: Participants were excluded from the study if they did not formally consent to participate and/or those were non-residential and/or those were hemodynamically unstable, and/or those were pregnant.

Instrument and data collection: The eligible patients, that signed consent forms, underwent mammography for possible BAC. Planmeca full digital mammography machine was used for BAC assessment. A radiologist interpreted the mammograms. Cases were defined as BAC if the disease had been confirmed by the radiologist and/or the individuals had experienced at least unilateral BAC. Then, data were obtained by a trained nurse using a questionnaire. We developed a validated questionnaire based on the study's objectives to gather data on socio-demographic and clinical characteristics such as age, history of breastfeeding, parity, body mass index (BMI), menopause, hypertension, hypercholesterolemia, diabetes mellitus, and history of CADs. The reliability of the questionnaire was assessed and approved by obtaining experts' opinions, including two radiologists, and a cardiologist. The validity of questionnaire was measured using a pilot study with 10 participants (face validity). All questionnaires were checked and verified by a general physician who was responsible for quality control.

To conduct the stress echocardiography, patients were referred to Imam Ali Hospital affiliated with the KUMS, Kermanshah, Kermanshah province, Iran. The patients underwent echocardiography, and all the walls and 16 segments of the heart were assessed for regional movement disorder. In women who had regional movement disorder, stress echocardiography was not performed due to the possibility of ischemia. Other patients underwent exercise test/treadmill test (TMT). For women who are unable to undergo TMT, dobutamine infusion was given at a dose of 5-40 micro/kg/min. In stress echo, wall motion abnormalities, chest pain and electrocardiogram (ECG) changes were considered as indicators of myocardial ischemia.

Statistical Methods: Statistical analysis was performed by the statistical package for social sciences (SPSS) statistical software (Version 23.0; IBM Corporation, Chicago, USA). Quantitative variables (e.g., age) were described using mean ± standard deviation (SD) and qualitative/categorical variables (e.g., diabetes mellitus) were expressed as frequencies and percentages. Differences between groups were evaluated using the Chi-Square test (or Fisherṡ exact test) for categorical variables, and Independent-Samples t-Test for continuous and normally distributed variables. All the analyses were considered to be significant at P<0.05.

Ethic: The Research Ethics Committee at the Deputy of Research of the KUMS approved the study protocol and monitored the research process (IR.KUMS.REC.1397.087). Further, the participants were given the participant information statement and signed the written consent form. Individual personal information was kept confidential.

Results

Four hundred women were evaluated. BAC was present in 61 (15.2%) women. Demographic and baseline characteristics of the patients with and without BAC were summarized in Table 1. Mean±SD of age for the patients with BAC was equal to 58.59±7.82 years old, and for the patients without BAC, it was equal to 55.32±6.57 years old (p =0.003). Prevalence rates of the menopause (88.5% vs. 71.1%, p=0.009), hypertension (29.5% vs. 17.7%, p=0.032), and hypercholesterolemia (24.6% vs. 13.0, p=0.018) were significantly higher in the patients with BAC compared to the patients without BAC. Significantly, more women with BAC were positive for myocardial ischemia compared to the women without BAC (24.6% vs. 8.5%, p<0.001).

In Table 2, the demographic and baseline variables are compared between the women who were positive for MI and those who were negative for MI. Table 2 shows that the prevalence rates of the diabetes mellitus (36.4% vs. 19.7%, p=0.010), hypertension (47.7% vs. 16.0%, p<0.001), hypercholesterolemia (29.5% vs. 12.9, p=0.003), and history of CADs (47.7% vs. 9.3, p<0.001) were significantly higher in the patients who were positive for MI compared to those who were negative for MI.

Figure 1 shows a mammographic image of BAC case.

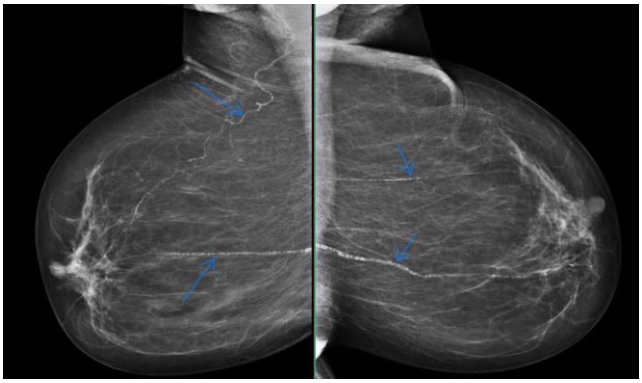

Figure 1: A mammographic image of BAC case. The calcifications are shown by blue arrows

Discussion

In our study, the prevalence rate of BAC was determined as 15.2%. The prevalence rate of BAC reported in previous studies is variable. Rotter et al. from the United States reported a prevalence of 14% in 2004 (6), Ferreira and colleagues reported a prevalence of 8.5% in Brazilian postmenopausal women (13), Schnatz et al. found a prevalence of 16.3% (14), Abou-Hassan and colleagues reported rates of around 58.4% (12), Hendriks et al. found that the prevalence of BAC was 8.6% (15).

Table 1: Demographic and baseline characteristics of the women with and without breast arterial calcification (BAC) (n=400)

Characteristic	With BAC (n=61) N (%)/ mean ± SD	Without BAC (n=339) N (%)/ mean ± SD	P-value
Age (year)¶	58.59± 7.82	55.32±6.57	0.003*
BMI¶	24.19±2.81	24.03±2.65	0.680*
History of breastfeeding	30 (49.2)	163 (48.1)	0.874**
Menopause	54 (88.5)	241 (71.1)	0.009**
Hypertension	18 (29.5)	60 (17.7)	0.032**
Hypercholesterolemia	15 (24.6)	44 (13.0)	0.018**
Diabetes mellitus	15 (24.6)	61 (18.0)	0.226**
History of CVDs	9 (14.8)	45 (13.3)	0.755***
Positive for myocardial ischemia	15 (24.6)	29 (8.5)	0.001>**

N, Number; BMI, body-mass index; CVD, cardiovascular disease.
Continuous variables expressed as mean ± SD, otherwise n (%).
* T-test, ** chi-square test, *** Fisherṡ Exact test.

Table 2: Demographic and baseline characteristics of the women who were positive for myocardial ischemia and those who were negative for myocardial ischemia (n=400)

Characteristic	Positive for myocardial ischemia (n=44) N (%)/ mean ± SD	Negative for myocardial ischemia (n=356) N (%)/ mean ± SD	P-value
Age (year)¶	57.64± 6.34	57.13± 5.98	0.786*
BMI¶	25.03±2.89	24.46±2.36	0.496*
Parity	4.54±2.45	3.98±2.05	0.433**
History of breastfeeding	23 (52.3)	170 (47.7)	0.571**
Menopause	35 (79.5)	260 (64.6)	0.354**
Hypertension	21 (47.7)	57 (16.0)	0.001>**
Hypercholesterolemia	13 (29.5)	46 (12.9)	0.003***
Diabetes mellitus	16 (36.4)	70 (19.7)	0.010**
History of CVDs	21 (47.7)	33 (9.3)	0.001>**

N, Number; BMI, body-mass index; CVD, cardiovascular disease.
Continuous variables expressed as mean ± SD, otherwise n (%).
* T-test, ** chi-square test, *** Fisherś Exact test.

Our results demonstrated that the women with BAC were older, and with a higher prevalence of hyperlipidemia, hypertension, and menopause, compared to those without BAC. Ferreira et al. showed that the patients with BAC were older than those without BAC (13). Crystal and colleagues illustrated an association between BAC and age, hypertension, history of CVD, dyslipidemia and diabetes mellitus (16). Hendriks et al. reported that advanced age, diabetes mellitus, nulliparity are associated with the higher prevalence rate of BAC (15). Trimboli et al. found that age, parity, diabetes, and hyperlipidemia were correlated with BAC (17). Rotter et al. showed that women with BAC were more likely to be older, hyperlipidemic, hypertensive, diabetic and menopausal (6).

Besides, it was found that BAC was significantly associated with CVDs. In line with our results, Maas et al. from Netherlands indicated that BAC was strongly associated with the development of calcifications in the coronary arteries in 2006, they used multislice computed tomography to evaluate coronary artery calcifications (18). Rotter et al. illustrated that BACs are correlated with an increased prevalence rate of CVDs (6). Conversely, Penugonda et al. in 2010 reported that there was no difference in the prevalence rate of coronary artery disease (CAD) between patients with and without BAC, they used angiography to evaluate CAD (19). Likewise, Henkin et al. found that BAC was not associated with CAD, they used angiography to assess CAD (20).

In our study, the prevalence of myocardial ischemia symptoms in patients with BAC was determined to be 24.6%. Several prior studies have examined the relationship between BAC and CVDs. Ferreira et al. reported that the prevalence of CVDs in women with BAC was equal to 23.1% in 2009 (13). Kataoka et al. found that there were 2.54 increased odds of CVDs in patients with BAC seen on mammography (21). Schnatz et al showed that the prevalence of CVDs in women with BAC was equal to 20.8%.(14). Fathala et al. illustrated that 17% of women with BAC were positive for MI, they used computed tomography to evaluate MI (8). Rafeh et al. reported that there was a 1.59 increased odds of coronary heart disease (CHD) in women with BAC in 2012, they used angiography to assess CHD (22). In our study, the mean age of women was 58. Although we reported relatively high prevalence (25%) of CVDs in patients with BAC, this result might be ascribed to the effects of advanced age. It means that the prevalence of BAC and CVDs might be increased with advanced age; and hence, older women are more susceptible to have both BAC and CVDs. In the other words, most CVDs risk factors are associated with advanced age, and BAC is also associated with advanced age.

Our results illustrated that the BAC patients who were positive for myocardial ischemia were more probable to be diabetic, hyperlipidemic, hypertensive, and having history of CADs.

In the end, results from previous studies may not be applicable worldwide; rather, we can mention ‘studies based on population’ which needs to be illuminated for every population. According to our knowledge, until now similar studies have not been done in Kermanshah. This is an important advantage for our study.

Our study had several limitations. First, its design is cross-sectional; thus, no associations over time can be inferred. There was no long-term follow-up, as well as no control for cardiovascular risk factors such as age; thus, for evaluating causality, longitudinal studies with an extended follow-up should be performed. Second, our data were obtained from Kermanshah province; therefore, our participants may not be representative of the whole patients with BAC. The relatively small number of participants is one of the limitations of this study.

Conclusion

Our results showed that in the studied population, the prevalence rate of myocardial ischemia symptoms in the patients with BAC was equal to 24.6%. It was found that BACs are associated with an increased prevalence of CVDs. Our results illustrated that the patients who were positive for myocardial ischemia were more common to have diabetes, hyperlipidemia, hypertension, and a history of CADs. Accordingly, future studies are needed to tailor longitudinal design with an extended follow-up. Finally, the current study provides a foundation for future studies that should be conducted in the other ethnic groups residing in different parts of Iran.

Conflict of Interests

Authors have no conflict of interests.

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