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Evaluation of the Correlation Between Breast Artery Calcification and Coronary Artery Calcium Scores in Predicting the Risk for Cardiovascular Disease

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Abstract

Aim: Coronary artery calcium (CAC) score is a scoring system used in the stratification of coronary risks. Breast artery calcification (BAC) is a type of medial artery calcification that can be visualized using mammography and is also known as arteriosclerosis. It has been reported that a significant correlation exists between BAC and CAC and that the presence of BAC improves the ability of detecting women with CAC. This study aimed to evaluate the relationship between mammographically-detected BAC and CAC.

Materials and Methods: A total of 31 patients who presented to our hospital for diagnostic or screening mammography and who underwent CAC scoring between 2015 and 2018 were included in the study. Agatston method was used to determine the CAC score. Total BAC, which varies from 0 to 12, was measured based on the number and length of calcified vessels and the severity of mammographically-visualized calcification.

Results: The mean BAC scores were found to be 0 in 1 patient, 1-3 in nine patients and 4-12 in 21 patients. The mean CAC scores were found to be 0 in eight patients, 11-100 in 12 patients, 101-400 in eight patients and >400 in three patients. There was a statistically significant positive correlation between the BAC and CAC scores.

Conclusion: This study revealed a positive correlation between the BAC and CAC scores. It was found that mammographic calcification scoring, which is already commonly used as a screening tool and is more advantageous than tomography, can be used for the early determination of intermediate risk groups for cardiovascular diseases.

Keywords: Breast artery calcification, coronary artery calcium score, mammography, cardiovascular disease, screening

Introduction

Cardiovascular diseases (CVDs) are the leading cause of death worldwide with approximately 17.9 persons died from CVD in 2016 (1). Similarly, in our country also CVDs rank first among the causes of death. According to the data of the Turkish Statistical Institute, deaths due to CVDs are the leading among all causes of death by 39.8% (2). In the Western countries, yearly rate of CVD mortality has been reported as 2-8/1000 in men and 0.6-3/1000 in women aged between 45 and 74 years. In our country, this rate has been reported as 7.6/1000 in men and 3.8/1000 in women in the same age group (3). Identification of asymptomatic persons who are at a higher risk for future cardiovascular events is the basis of implementing preventive strategies. Coronary artery calcium (CAC), score which is a scoring system based on the measurement of the amount of calcium in the arterial walls that supply heart muscle is used for the stratification of cardiovascular risk. Several studies have shown that CAC score is significantly associated with major cardiovascular events (all causes mortality, cardiac mortality, and nonfatal myocardial infarction) in middle and long term follow up (4). However, currently CAC score is not used in routine screening. The use of CAC is based on clinical findings and a history of genetic predisposition. Nevertheless, CAC occurs in the intima of the vessels, and is closely associated

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with aterosclerotic plaque burden. Therefore, the presence of CAC is in fact a diagnostic factor for cardiovascular disease (5).

Breast cancer is the most common type of cancer in women in the developed and developing countries, and is among the most important global healthcare problems (6). It ranks second following lung cancer worldwide (7), accounting for nearly 30% of all cancers seen in women (8). On the other hand, it is stated that the chance for healing is high when breast cancer is recognized in an early period.

Breast Cancer Screening Program National Standards prepared by the Ministry of Health Public Health Institution recommend screening every 2 years with mammography in women aged between 40 and 69 years (9). Breast Cancer Screening Guidelines by the Turkish Radiology Association accept the age of starting mammographic screening as 40 years, and recommend yearly follow up (10). According to these guidelines, it is advisable to discontinue screening between 70 and 74 years old if life expectancy is under 5 years depending on the age and presence of other comorbidities.

Breast artery calcification (BAC) is a type of medial artery calcification, which can be seen on mammography, and is also named as arteriosclerosis that is known as Monckeberg arteriosclerosis (11,12). Recently, BAC has been shown to be a potential women specific risk factor for both coronary artery disease and cardiovascular disease (13). However, unfortunately the presence or absence of BAC is often neglected in mammographic evaluation. Studies have shown that subclinical atherosclerosis and cardiovascular disease can be assessed with mammography (14,15). It has been reported that there is a significant relationship between BAC and CAC, and the presence of BAC improves the ability for detection of women with CAC (16).

Mammography provides an important alternative screening technique to determine the risk of coronary artery disease in women. Given that millions of women over 40 years old have mammography, a significant correlation between BAC and CVD will provide improvement in risk stratification without additional costs and radiation exposure (17). The objective of this study was to evaluate the relationship between BACs on mammography and CAC score.

Materials and Methods

Among the women who presented to our hospital for screening or diagnosis with mammographic evaluation, a total of 31 women aged between 40-74 years who recently presented for coronary calcium scoring between October 2015 and June 2018 were included in this study. Women aged under or over the specified age range, those with a history of stroke, transient ischemic or coronary artery disease, patients with coronary stents, advanced coronary calcification, those undergone breast surgery, and patients with chronic inflammatory diseases such as infection or autoimmune diseases, hepatic and/or renal failure were excluded from the study. All BAC and CAC evaluations were performed by a radiologist specialized on this topic.

Before the beginning of the study, the necessary approval was received from the local ethics committee with 2/2019.K-018 numbered decision. Patients included in the study were informed about the objective of the study and given written and verbal consents. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Coronary Artery Calcium Scoring

CAC is a pathognomonic finding of atherosclerosis (18). CAC may be observed in any stage of atherosclerosis. Therefore, determination of CAC level is not only a measurement of calcified plaque burden, but it is also an indicator of the non-calcified plaque burden of the existing atherosclerotic disease. The most common method in the measurement of CAC is Agatston score. This score was described by Agatston et al. (19) in 1990 as the first practically applicable quantitative CAC protocol. In this method, any structure with a density of 130 HU or higher and an area of 1 mm^2 or higher is considered as a calcified focus, and the foci found in the anatomic regions of coronary arteries as calcified plaques. Each calcified focus is scored between 1-4 points based on the peak density. Total Agatston score of each person is calculated with summation of the scores of each focus (Table 1).

Coronary artery calcium examinations were performed with visualization between tracheal bifurcation and heart vessel at early mid-diastole, using a 120-sections computed tomography device (Siemens Somatom 2015).

Table 1. Risk stratification according to Agatston score

CAC score	Plaque burden	Cardiovascular risk	Likelihood of obstructive disease
0	No detectable plaque	Very low	Very low <5%
1-10	Minimal plaque	Low	Low <10%
11-100	Mild plaque	Moderate	Mild stenosis
101-400	Moderate plaque	Moderate-to-high	Likelihood of both non-obstructive and obstructive disease
>400	Diffuse atherosclerotic plaque	High	Likelihood of at least one significant stenosis (≥90%)

CAC: Coronary artery calcium

Breast Artery Calcification

Arterial calcification in the breast is a type of medial calcification, which can be easily detected on mammography, and is seen as parallel lines and railways on mammography. Calcification of the arterial intima is considered as coronary calcification and is usually accompanied by plaques consisting of lipid deposits. Whereas BAC occurs in the middle layer of the artery, and known as Mönckeberg medial calcific sclerosis. BAC is a novel potential risk stratification tool for CVD.

Total BAC score differs between 0-12 points, and is produced based on three elements on mammography: the number of calcified vessels (0-6 points), the severity of artery calcification (0-3 points) and the length of calcified vessels (0-3 points). Accordingly, the total scores are divided into three categories with 0 point indicates the absence of BAC, 1-3 points mild calcification, and 4-12 points significant calcifications (Table 2).

Mammography was performed by acquiring mediolateral oblique and craniocaudal images including tomosynthesis (Siemens Mammomat Inspiration 2015).

Statistical Analysis

Data obtained in the study were analysed using SPSS Version 20.0 (SPSS 20.0 for Windows IBM, Virginia, USA) statistical software. Normality of the data was tested and normal distribution value was calculated with Skewness-Kurtosis test. Continuous numerical variables are expressed median (minimum-maximum) values as appropriate, and categorical variables as percentage (%). Paired Student's t-test was used in the comparison of continuous variables. The correlation between continuous variables was studied with Pearson's correlation analysis. P<0.05 values were considered statistically significant.

Table 2. BAC scoring system

Number of vessels		Length of vessels		Severity of calcification	
1	1	1/3 involvement	1	Spot calcification	1
2	2	1/3 - 2/3 involvement	2	Spot calcification in the lumen	2
3	3	>2/3 involvement	3	Intense calcification in the vessel including tangential walls and lumen	3

BAC: Breast artery calcification

Table 3. Correlation between BAC and CAC scores

	No BAC	Mild calcification	Significant calcification	Total	p value
No CAC	1	7	-	8	0.001
Minimal plaque	-	-	-	-	
Mild plaque	-	2	10	12	
Moderate plaque	-	-	8	8	
Diffuse atherosclerotic plaque	-	-	3	3	
Total	1	9	21	31	

BAC: Breast artery calcification, CAC: Coronary artery calcification

Results

A total of 31 women were included in the study. The median age of the participants was 57 (40-74) years. BAC scores were found as 0 in one (3.2%) patient, 1-3 in nine (29.0%) patients, and 4-12 (67.7%) in 21 patients. Both BAC and CAC scores were increased as the age of the patients increased.

CAC scores were found as 0 in eight (25.8%) patients, 11-100 in 12 (38.7%) patients, 101-400 in eight (25.8%) patients and >400 in three (9.2%) patients. Sample of the study mostly consisted of the patients with a CAC score between 11-100 and a BAC score between 4-12.

CAC score was 0 in a patient with a BAC score of 0, while seven (77.8%) of patients with BAC scores of 1-3 were in CAC 0 group, and the remaining two patients were in CAC 11-100 group. Of the 21 patients in BAC 4-12 group, 10 (47.6%) were in CAC 11-100 group, eight (38.1%) in CAC 101-400 group and 3 (9.68%) in CAC >400 group. Accordingly, the highest rate of patients was found in BAC 4-12 and CAC 11-100 groups by 47.6% (Chart 1).

When the results of t-test and mean values of the groups were evaluated together, CAC scores were found to be more effective. Effect of BAC scores on CAC scores was found as 63%. The correlation between BAC and CAC scores was statistically significant (r=0.796 p<0.005) (Table 3). When cardiovascular risk factors related to BAC were examined; Diabetes mellitus was found in 19 (61.29%), hypertension in 17 (54.83%), hyperlipidemia

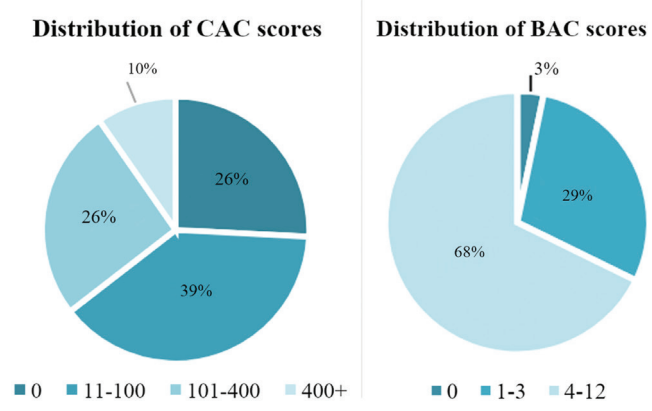

Chart 1. Distribution of CAC and BAC scores

BAC: Breast artery calcification, CAC: Coronary artery calcification

in 16 (51.61%), smoking in four (12.90%), chronic kidney disease in two (6.45%) patients and family history in one (3.22%) patient. The relationship between the presence of BAC and cardiovascular risk factors was given in Table 4.

Samples of moderate and moderate-advanced stage coronary artery and breast vascular calcifications are given in Figures 1 and 2.

Discussion

CAC scoring has been a risk estimation tool for coronary artery calcification as an indicator of subclinical heart disease (19). Higher CAC scores are associated with a higher risk of coronary events. In addition, the presence of CAC has been used to justify modification treatments with a more aggressive CAD risk factor such as aspirin, statins and lifestyle changes (20). Studies have shown that the extent of CAC is strongly associated with the rate of future cardiac events, and that high prevalence of CAC in patients with coronary heart disease make percutaneous coronary intervention difficult (4).

Table 4. Relationships between the presence of BAC and cardiovascular risk factors

	BAC scores	
	BAC -	BAC +
Number of patients (n)	1	30
Age at mammography (mean ± SD)	54 (7.5)	59 (8)
Presence of BAC	1	30
Diabetes mellitus	12	19
Hypertension	14	17
Smoking	4	4
Hyperlipidemia	15	16
Chronic kidney disease	0	2
Family history	0	1

BAC: Breast artery calcification, SD: Standard deviation

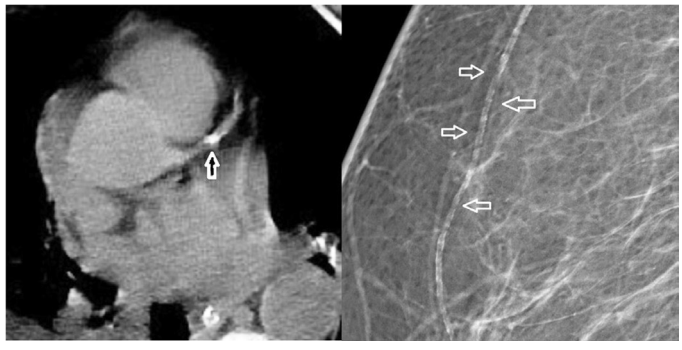

Figure 1. Mild calcification in the left anterior descending coronary artery of a 56-year-old woman with BAC score 4

BAC: Breast artery calcification

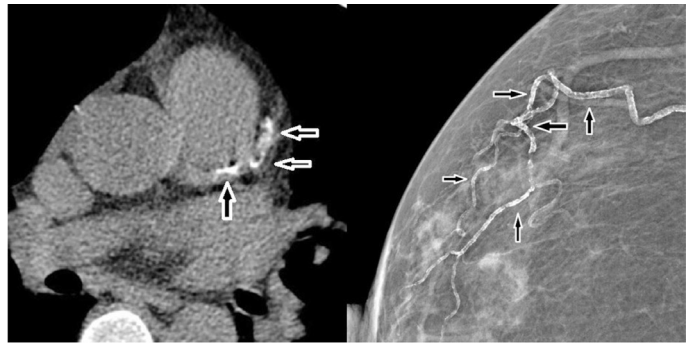

Figure 2. Moderate calcification in the left anterior descending coronary artery of a 74-year-old woman with BAC score 9

BAC: Breast artery calcification

Mammography screening has been widely used in early detection of breast cancer. BAC is a benign finding on mammography especially in elderly women. It has been proposed that this incidental finding can be used as an indicator of vascular disease (21). Therefore, relationships between BAC and cardiovascular disease markers and potential risk factors and CAC scores (22,23).

In the present study the relationship between BAC and CAC was evaluated. As a result of the evaluations and analyses, a strong correlation was found between BAC and CAC. In a study by Pecchi et al. (16) in 2003, a strong correlation was found between BAC and CAC. In 2007, Maas et al. (24) reported a strong correlation between BAC and CAC in 499 women at the end of 9-year follow up. More recently, in a retrospective study by Chadashvili et al. (25) with 145 women who were referred for coronary computed tomography within one year after mammography screening; a significant association was found between the presence of CAC>11 and BAC.

BAC rates increase in patients as CAC scores increase. In our study, BAC scores were found in the range of 4-12 in three patients with a CAC score >400. In a study by Matsumura et al. (26) in 2013, BAC scores were significantly increased in women with a CAC score >400. However, there is currently no exact consensus on this issue in the literature. In a cross-sectional study by Moradi et al. (27), the relationship between BAC and CAC was investigated in 150 Iranian women aged >40 years, and no significant correlation could be found. The authors stated that BAC and the presence of significant coronary stenosis might be independently associated with age, and therefore older women were more susceptible for both BAC and CAC. In our study also, both BAC and CAC scores were increased as the age of the patients increased.

Several factors might have affected these contradictory results. Different study designs might be the major factor affecting the differences between these results. The effect of cardiac risk factors on coronary arteries should be kept in mind.

In a study by Wendling (28) in 2016, CAC was found by 47.6% among 292 women. The authors reported a significant correlation between CAC and BAC. In our study, moderate cardiovascular risk was found by 47.6% among the participants. In addition, we found a strong correlation between CAC and the elements of BAC (number of calcified vessels, length of calcified vessels, and severity of calcification). In a study by Fathala et al. (29), similar results were reported. In addition, in another prospective study by Dale et al. (30) including 1000 women, the likelihood of CAC was found as 6.2 times higher in women with BAC compared to those without BAC in all age groups. The results of that study which has a high number of participants and those of the other studies indicate that mammography could be a helpful tool for the screening of coronary vascular disease. Likewise, previous studies except for the study by Moradi et al. (27), in our study also a significant correlation was found between BAC and CAC scores. However, the reported results should be cautiously interpreted. Because there is difference between sample sizes of the studies, and participants have already presented for computed tomography screening in most of these studies. In addition, different methods and threshold values were used for the measurement of CAC scores among the studies. Sensitivity of BAC in prediction of CAC on mammography is variable and is reported between 17% and 91%. Again, specificity of BAC score is reported between 54% and 94% in different studies. Therefore, further studies with larger cohorts are needed for establishing a definitive consensus on the relationship between these two scores in the literature and introduction of BAC score in routine clinical practice for the prediction of CAC.

Study Limitations

This study has several limitations. First, the number of patients was relatively small. Second, we included only the women who presented for CAC score evaluation. Finally, the study has no long term follow up data. However, we believe that our results would provide contribution to the future consensus on this issue in the literature.

Conclusion

We found a positive correlation between BAC and CAC scores in the studied sample. This correlation between BAC and CAC scores could be used as a diagnostic tool in asymptomatic women. Criteria of this diagnostic method could be determined with further studies including a larger series of patients and longer follow-up.

Ethics

Ethics Committee Approval: Before the beginning of the study, the necessary approval was received from the local ethics committee with 2/2019.K-018 numbered decision.

Informed Consent: Patients included in the study were informed about the objective of the study and given written and verbal consents. The study was conducted in accordance with the principles of the Declaration of Helsinki

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: I.Y., Concept: I.Y., Design: F.N., Data Collection or Processing: F.N., Analysis or Interpretation: F.N., Literature Search: F.N., Writing: I.Y.

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References

1. World Health Organization 2017, cardiovascular disease, viewed 21 January 2019. <https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)>
2. TÜİK Haber Bülteni, Ankara Sayı:24572, 27 Nisan 2017 http://www.tuik.gov.tr/HbPrint.do?id=24572 (Accessed on: 25/03/2019).
3. TÜİK Haber Bülteni, Ankara Sayı:16050, 30 Nisan 2014, http://www.tuik.gov.tr/PreHaberBultenleri.do%3Fid%3D16050
4. Greenland P, Bonow RO, Brundage BH, Matthew J Budoff, Mark J Eisenberg, Scott M Grundy, et al. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography) developed in collaboration with the Society of Atherosclerosis Imaging and Prevention and the Society of Cardiovascular Computed Tomography. J Am Coll Cardiol. 2007;49:378-402.
5. Nasir K, Bittencourt MS, Blaha MJ, Blank-stein R, Agatson AS, Rivera JJ, et al. Implications of Coronary Artery Calcium Testing Among Statin Candidates According to American College of Cardiology/American Heart Association Cholesterol Management Guidelines: MESA (Multi-Ethnic Study of Ath. erosclerosis). Journal of the American College of Cardiology. 2015;66:1657-68.
6. Yiğit A. Mamografi Sağlık Teknolojisi ile Meme Kanseri Tarama Programının Klinik Etkililiğinin Meta Analiz Yöntemiyle Değerlendirilmesi. SBE Dergisi. 2017;28:401-30.https://sbedergi.sdu.edu.tr/assets/uploads/sites/343/files/28-sayi-yazi22-20112017.pdf
7. Topuz, E. Meme Kanseri. Tanı-Tedavi-Takip. In: Nobel Tıp Kitapevleri, İstanbul, Aydıner A, İğci A, editors, 2006.
8. Aslan FE, Gürkan A. Kadınlarda Meme Kanseri Risk Düzeyi. Meme Sağlığı Dergisi. 2007;3:63-8.
9. Meme Kanseri Tarama Programı Ulusal Standartları. https://hsgm.saglik.gov.tr/tr/kanser-tarama-standartlari/listesi/meme-kanseri-tarama-program%C4%B1-ulusal-standartlar%C4%B1.html
10. TRD Yeterlilik Kurulu, Rehber ve Standartlar Komitesi-Meme Kanseri Tarama Rehberi, 2011. https://www.turkrad.org.tr/assets/standartlar/meme-tarama-rehberi.pdf
11. Everhart JE, Pettitt DJ, Knowler WC, Rose FA, Bennett PH. Medial arterial calcification and its association with mortality and complications of diabetes. Diabetologia. 1988;31:16-23.

12. Shanahan CM, Cary NR, Salisbury JR, Proudfoot D, Weissberg PL, Edmonds ME. Medial localization of mineralization-regulating proteins in association with Monckeberg's sclerosis: evidence for smooth muscle cell-mediated vascular calcification. Circulation. 1999;100:2168-76.
13. Jiang X, Clark M, Singh RK, Juhn A, Schnatz PF. Association of breast arterial calcification with stroke and angiographically proven coronary artery disease: a metaanalysis. Menopause. 2015;22:136-43.
14. Hendriks EJ, de Jong PA, van der Graaf Y, Mali WP, van der Schouw YT, Beulens JWJ. Breast arterial calcifications: a systematic review and meta-analysis of their determinants and their association with cardiovascular events. Atherosclerosis. 2015;239:11-20.
15. Shah N, Chainani V, Delafontaine P, Abdo A, Lafferty J, Abi Rafeh N. Mammographically detectable breast arterial calcification and atherosclerosis. Cardiol Rev. 2014;22:69-78.
16. Pecchi A, Rossi R, Coppi F, Ligabue G, Modena MG, Romagnoli R. Association of breast arterial calcifications detected by mammography and coronary artery calcifications quantified by multislice CT in a population of postmenopausal women. Radiol Med. 2003;106:305-12.
17. Yoon YE, Kim KM, Han JS, Khang SH, Chun EJ, Ahn S, et al. Prediction of subclinical coronary artery disease with breast arterial calcification and low bone mass in asymptomatic women: Registry for the Women Health Cohort for Breast, Bone, and Coronary Artery Disease Study. Jacc Cardiovasc Imaging. 2018;12:1202-11.
18. Budoff MJ, Gul KM. Expert Review on Coronary Calcium. Vasc Health Risk Manag. 2000;4:315-24.
19. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte Jr M, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Colle Cardiol. 1990;15:827-32.
20. Taylor AJ, Bindeman J, Feuerstein I, Le T, Bauer K, Byrd C, et al. Community-based provision of statin and aspirin after the detection of coronary artery calcium within a community-based screening cohort. J Am Coll Cardiol. 2008;51:1337-41.
21. Markopoulos C, Mantas D, Revenas K, Kouskos E, Tzonou A, Liapis C, et al. Breast arterial calcifications as an indicator of systemic vascular disease. Acta Radiol. 2004;45:726-9.
22. Pidal D, Sánchez Vidal MT, Rodríguez JC, Corte MD, Pravia P, Guinea O, et al. Relationship between arterial vascular calcifications seen on screening mammograms and biochemical markers of endothelial injury. Eur J Radiol. 2009;69:87-92.
23. Sedighi N, Radmard AR, Radmehr A, Hashemi P, Hajizadeh A, Taheri AP. Breast arterial calcification and risk of carotid atherosclerosis: focusing on the prefentially affected layer of vessel wall. Eur J Radiol. 2011;79:250-6.
24. Maas AH, van der Schouw YT, Atsma F, Beijerinck D, Deurenberg J, Mali W, et al. Breast arterial calcifications are correlated with subsequent development of coronary artery calcifications, but their aetiology is predominantly different Eur J Radiol. 2007;63:396-400.
25. Chadashvili T, Litmanovich D, Hall F, Slanetz PJ. Do breast arterial calcifications on mammography predict elevated risk of coronary artery disease? Eur J Radiol. 2016;85:1121-4.
26. Matsumura ME, Maksimik C, Martinez MW, Weiss M, Newcomb J, Harris K, et al. Breast artery calcium noted on screening mammography is predictive of high risk coronary calcium in asymptomatic women: a case control study. GefaÃàsskrankheiten J Vas Dis. 2013;42:429-33.
27. Moradi M, Atoosa A, Abedi M. Relationship between breast arterial calcification on mammography with CT Calcium scoring and coronary CT angiography results. Adv Biomed Res. 2014;3:79.
28. Wendling P. Breast Arterial Calcification on Mammography IDs Atherosclerotic CVD Risk. https://www.medscape.com/viewarticle/861029
29. Fathala AL, Alabdulkarim FM, Shoukri M, Alanazic M. Association between breast arterial calcifications found on mammography and coronary artery calcifications in asymptomatic Saudi women. Ann Saudi Med. 2018;38:433-8.
30. Dale PS, Mascarhenas C, Richards M, Mackie G. Mammography as a screening tool for coronary artery disease. J Surg Res. 2008;148:1-6.