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Hand

Distal Upper Extremity Arterial Calcification as a Predictor for Subclinical Coronary Artery Disease by Coronary Artery Calcium Scoring

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Summary: Several studies have linked calcification of the thoracic and lower extremity arterial trunks to an increased risk of developing coronary artery disease (CAD). Calcifications of the radial and/or ulnar artery are regularly identified in hand/wrist x-rays; however, the clinical relevance of these findings as related to identifying subclinical CAD is not well understood. Associations between CAD and upper extremity calcifications have been reported, but the timeline is unclear. The purpose of this study was to evaluate the association between upper extremity arterial calcifications on hand radiographs with CAD by coronary artery calcification (CAC) scoring in patients with no known history of CAD. This is a pilot single-center, prospective, matched cohort study. We included patients with no known history of CAD, related symptoms, or major risk factors. We recruited five patients with calcifications (cal+) and five patients matched by age, race, sex, and medical history but without calcifications (cal–). CAC scores were determined from computed tomography scanning, and lipid profile was evaluated. In the cal+ group, the mean CAC total score was 244.1; in the control (cal–) group, it was 85.2. The mean total cholesterol levels were 220.8 mg per dL and 167 mg per dL in the cal+ and cal– groups, respectively. Two cal+ patients with CAC scores of 937 and 669 died shortly after being enrolled in our study. Preliminary findings suggest that calcifications in the radial or ulnar artery in otherwise asymptomatic patients with no history of CAD may be an independent sign of CAD. *(Plast Reconstr Surg Glob Open 2024; 12:e5768; doi: 10.1097/GOX.0000000000005768; Published online 24 April 2024.)*

THE CLINICAL PROBLEM

Asymptomatic individuals with underlying coronary artery disease (CAD) are at risk for cardiac events, including myocardial infarction. Early detection using laboratory testing as well as studies such as myocardial stress testing and coronary artery imaging may further evaluate individuals at risk. Coronary artery calcification (CAC) distribution is an independent predictor of incident major coronary events,[1] and CAC detection using non-contrast computed tomography is a strong predictor of an individual's absolute risk of atherosclerotic cardiovascular disease (ASCVD) events.[2]

Extracoronary calcifications visualized on routine CAC computed tomography scanning, including those in the thoracic aorta, aortic valve, and mitral valve, have been independently associated with ASCVD events and mortality.[3] Radial artery calcifications or ulnar artery calcifications are regularly identified in plain film radiographs of the hand; however, the clinical relevance of these upper extremity (UE) calcifications are not well understood. Studies reporting on UE calcifications as related to CAD have not looked at the temporal relationship.[4] It remains unclear if the calcifications precede the diagnosis or events of CAD. If they do, it may provide a preventative health opportunity for any provider that evaluates hand x-rays. We sought to evaluate the association of arterial calcifications on plain film hand/wrist radiographs with subclinical CAD based on CAC scoring in asymptomatic patients.

PRELIMINARY COHORT STUDY

This study was conducted at The Curtis National Hand Center (CNHC) at MedStar Union Memorial Hospital.

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The study cohort consisted of patients seen at CNHC, with no history of CAD, who were found to have UE arterial calcifications on hand radiographs and were successfully recruited to participate (cal+). We then recruited a matched control cohort (cal−), each with a similar age (± 3years), sex, race and medical history to one of our cal+ patients but without arterial calcifications on hand/wrist radiographs and with no history of CAD (Table 1). None of the patients had diabetes. Given the difficulty of recruiting participants, some comorbidities including hyperlipidemia, hypertension, or smoking status were not included in the matching criteria.

Any patient found to have UE arterial calcification on hand/wrist x-rays was reviewed for demographic information (age, sex, race, and body mass index), presence of CAD (based on medical history), and other medical comorbidities (hypertension, hyperlipidemia, diabetes, chronic kidney disease, stroke, and smoking status). Patients meeting the inclusion criteria were then contacted and asked about history or current symptoms of chest pain, exertional dyspnea, exercise intolerance, referral to a cardiologist, or known cardiovascular disease. They were also asked if they had ever taken nitroglycerin for chest pain or discomfort, and if they had ever undergone procedures such as cardiac catheterization, angioplasty, coronary artery bypass graft, pacemaker or defibrillator implantation, or any other cardiac surgery. These patients with UE arterial calcification and no history of CAD then underwent CAC scoring. Patients without a lipid profile test within the past year had their blood test completed as well. Continuous variables were presented as mean ± SD using two-sided paired z-test analysis.

During nearly 18 months of recruitment, most of the patients with UE calcifications were not eligible (27 of 36). Seven of the remaining nine with UE calcifications were eligible and were successfully recruited. These formed our cal+ cohort (Fig. 1). As we enrolled each cal+ patient, we focused on recruitment of a matched patient with hand radiographs and no calcifications (cal− group; Table 2). Of the 46 cal− patients we approached, six were recruited. A total of 13 subjects were enrolled: seven cal+ and six cal−. We properly matched five of the recruited cal+ with five cal−.

Detailed demographic information on participants is summarized in Table 2. Average age in both cohorts was very similar at 65.8 and 66.2 years, respectively. The average body mass index in the cal− group was 26.1 kg per m^2 and in the cal+ group it was 28.6 kg per m^2. Mean total CAC scores were different at 244.1 in the cal+ group versus 85.2 in the cal− group. The cal+ group had borderline high mean total cholesterol levels of 220.8 mg per dL, whereas the total cholesterol for the cal− group was in the desirable range of 167 mg per dL (Table 3). All comparisons were not statistically significant ($P > 0.05$).[5]

Of note, during the 2-year study period, two participants who had radial artery calcifications died. One patient with a CAC score of 937 died 7 months after recruitment. Another patient with a CAC score of 669 had cardiac arrest with ventricular fibrillation and acute inferior myocardial infarction 11 days after recruitment.

Takeaways

Question: Do arterial calcifications visible on routine hand/wrist x-rays indicate coronary artery disease (CAD) or related cardiac pathology in patients with no prior cardiac history? Is this an opportunity for identifying a major health risk in asymptomatic patients?

Findings: In our pilot matched prospective cohort study (five per group), those with upper extremity calcifications had higher coronary artery calcium scores and higher total cholesterol. Two of the five upper extremity calcification patients, both with high coronary artery calcium scores, died shortly after enrollment.

Meaning: Presence of calcifications in the radial/ulnar artery among individuals with no previous history of CAD might serve as an isolated indicator of CAD.

DISCUSSION

The purpose of this study was to assess for a temporal relationship between calcifications in ulnar or radial arteries and higher CAC scores in cardiovascular asymptomatic individuals. Although other extracoronary calcifications (thoracic aorta and cardiac valves and lower extremities[3]) can be suitable predictors of CAC, there is limited literature investigating the role of UE calcifications in predicting or indicating CAD/ASCVD. What has been reported for UE calcifications shows an association between UE calcifications and CAD,[4] but no temporal relationship could be evaluated in that retrospective study.

Based on our preliminary data, incidental findings of radial artery calcifications and/or ulnar artery radial artery calcifications on plain film radiographs may suggest the importance of further evaluation for ASCVD and/or hyperlipidemia. Our results demonstrate overall differences in total CAC scores and cholesterol levels in control and positive groups, although we were underpowered for further statistical analyses. Our results were somewhat skewed by

Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Subject ages from 45 to 85 years • Patients who underwent plain radiograph of hand or wrist with arterial calcification • Patients of CNHC and other MedStar Health sites where CHNC providers treat patients	• Patients with CKD or ESRD • Patients with any history of CAD or stroke • Patients with any history of chest pain, dyspnea on exertion, or other signs/symptoms of possible CAD even without the diagnosis • Pregnant women

CKD = chronic kidney disease; ESRD = end-stage renal disease; CAD = coronary artery disease.

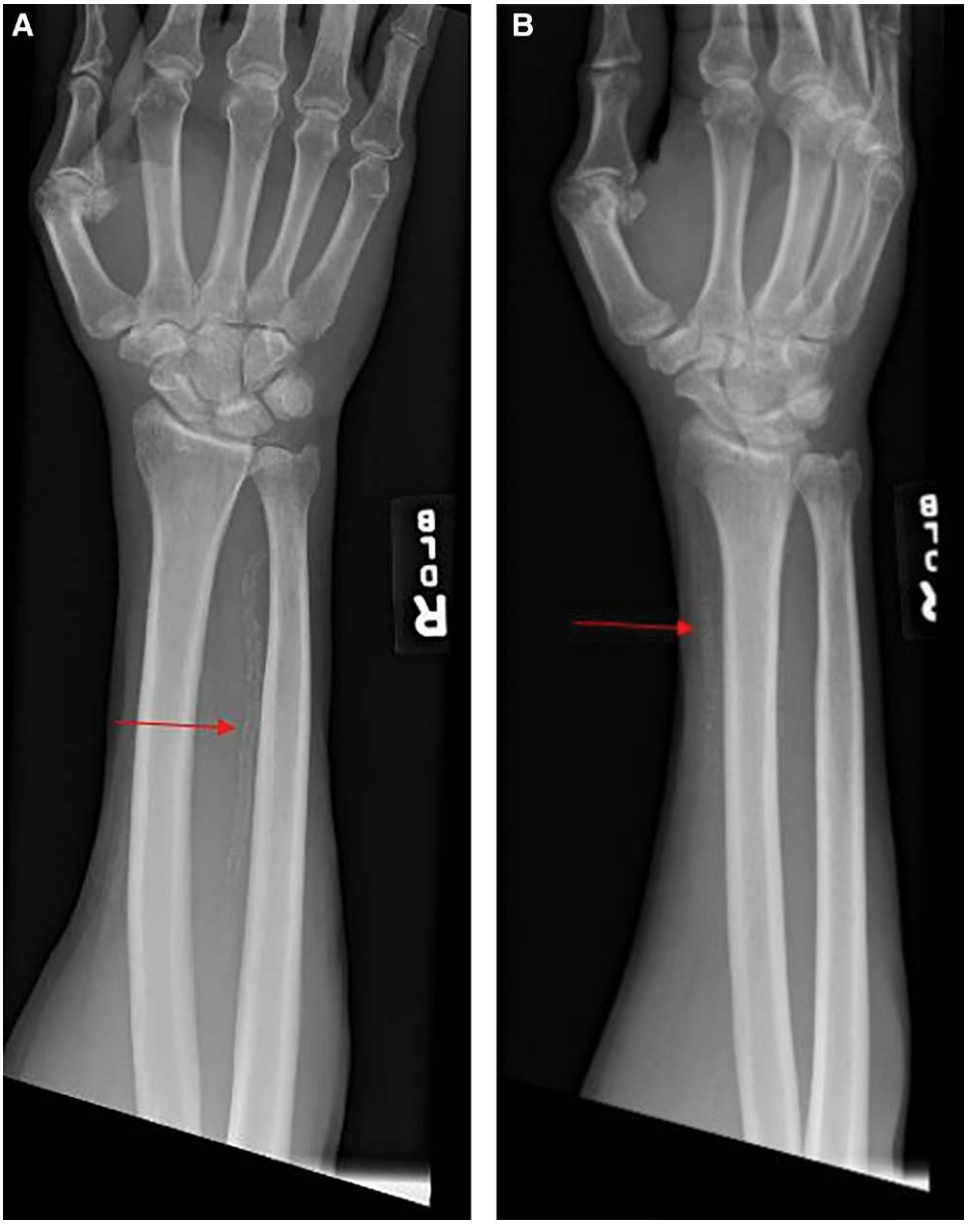

Fig. 1. Hand radiographs of ulnar and radial calcifications. A, Ulnar calcification. B, Radial calcification.

three cal+ patients with very high CAC levels, indicating that UE calcifications may not be directly predictive of CAC but may indicate an increased likelihood of severe CAC findings. It is concerning that two of the cal+ participants with high CAC levels died of cardiac related ailments. The differences in lipid profile results also suggest that UE calcifications might be an indication to evaluate lipid levels and may reflect an elevated lipid profile in some patients.

Our study has limitations. It was underpowered. To achieve statistical significance in both groups, post hoc analysis showed we would need 64 participants. Recruitment was very difficult; asymptomatic UE calcification patients are rare, and many control patients did not want to participate. Also, it is important to mention that hyperlipidemia might be a confounding element in this study, as it is commonly known to be a risk factor for developing CAD and cardiovascular events,[6] and perhaps UE calcifications are more an indicator of hyperlipidemia than specifically an indicator for CAD. However, we are underpowered to clarify this issue further.

There are various measuring technologies and scoring systems that are used in different fields of surgery for predicting risks and outcomes, for example wound management, flap venous congestion, or urological surgical care.[7–10] Whether UE calcifications can be added to that list remains unclear. However, these preliminary results suggest that UE calcifications found on plain radiographs in asymptomatic generally healthy patients may be critical clinical indicators of underlying CAD and referral for additional evaluation may be appropriate.

Table 2. Participant Demographics

Characteristic	Positive Cohort (Cal+)	Control Cohort (Cal–)	Overall
No. participants	5	5	10
Age (mean)	66.2	65.8	65.1
BMI	28.6	26.1	27.4
Sex			
Male	2	2	4
Female	3	3	6
Race			
White	4	4	8
African American	1	1	2
Ethnicity			
Non-Hispanic	5	5	10
Hispanic	0	0	0

BMI = body mass index; cal+ = with calcifications; cal– = without calcifications.

Table 3. Comparisons between cal+ and cal– Groups

Characteristic	Cal– Mean	Cal+ Mean	Mean of Paired Differences	SD of Paired Differences	*P*
Age	65.8	66.2	0.4	2.6	0.75
BMI	26.1	28.6	2.5	6	0.41
CAC total score	102	208	105.8	300.3	0.48
Cholesterol	167	220.8	53.8	55.2	0.09
Triglyceride	91	120.6	29.6	31.2	0.1
HDL	87.4	60	-27.4	43.5	0.23
LDL	77	140.2	63.2	59.1	0.07
Percentile	0.534	0.372	-0.162	0.4	0.41

BMI = body mass index; HDL = high-density lipoprotein; LDL = low-density lipoprotein; cal– = without calcifications; cal+ = with calcifications.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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