Association between Aortic Arch Calcification Detected on Plain Chest X-Ray and Myocardial Scarring Detected on Cardiac Magnetic Resonance Imaging in Coronary Heart Disease Patients

Thanapon Nilmoje MD*, Jitladda Wasinrat MD**,
Ahthit Yindeengam BSc***, Rungroj Krittayaphong MD*

** Division of Cardiology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
*** Division of Diagnostic Radiology, Department of Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
**** Department of Research Promotion, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Background: *Coronary heart disease requires advanced investigations. However, findings of fundamental investigations are sometimes underused and/or neglected, such as plain chest X-ray (CXR) and electrocardiography (ECG). A previous study found an association between aortic calcification and coronary artery disease, but there are no studies that have investigated association between aortic arch calcification in CXR and coronary artery disease consequences, such as myocardial viability (scarring).*

Objective: *To investigated association between aortic arch calcification detected on plain CXR and myocardial scarring detected on cardiac magnetic resonance imaging (CMRI) in coronary heart disease patients*

Material and Method: *one hundred eighty-seven eligible patients aged ≥18 years and diagnosed as coronary heart disease by CMRI at Siriraj Hospital between January 2008 and December 2014 study periods were enrolled. We retrospectively reviewed aortic arch calcification from plain CXR, demographic data, hospitalization data, underlying disease, medications used, and CMRI parameters.*

Results: *There was no significant association between aortic arch calcification from CXR and myocardial scar by CMRI. Aortic arch calcification was detected in 86 (45.98%) and 78 (41.70%) of patients with and without myocardial scar by CMRI (p = 0.981). There was no significant correlation between calcium grading and calcium thickness from CXR and the presence or absence of myocardial scar by CMRI. Myocardial scar was detected in 52.2%, 47.8%, 51.4%, and 59.1% in patients with calcium grade 0, 1, 2, and 3 respectively (p =0.751).*

Conclusion: *There was no association found between aortic arch calcification detected on plain CXR and myocardial scarring detected on CMRI.*

Keywords: *Calcification, Aorta, Magnetic resonance imaging, Coronary heart disease*

J Med Assoc Thai 2016; 99 (9): 982-7
Full text. e-Journal: *http://www.jmatonline.com*

In 2004, coronary heart disease was the highest cause of death worldwide up to 7.2 million related deaths[1]. Trends relating to heart disease are similar in many countries, including Asian populations[2-6]. Coronary heart disease risk factors include diabetes, smoking, family history, high LDL-cholesterol, high blood pressure, and perhaps obesity. Consequences of atherosclerotic coronary heart disease caused by long-term cardiovascular burden includes chronic heart failure, stroke, and/or a dependent state that requires more frequent hospital admissions; all of which create a burden on national healthcare budget[4].

There are now more advanced cardiac investigation tools for diagnosis and management of coronary artery heart disease. Plain chest radiography is now performed in nearly every case of coronary heart disease. The ability to derive more information from standard investigation techniques may provide the practitioner with early ideas regarding a grossly defined prognosis of coronary heart disease. Previous research suggested an association between coronary artery disease risk and aortic calcification detected from plain chest radiography[7]. There are no studies that demonstrate whether myocardial scarring is associated

Correspondence to:
Krittayaphong R, Division of Cardiology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.
Phone: +66-81-8059992, Fax: +66-2-4127412
E-mail: rungroj.kri@mahidol.ac.th

with aortic arch calcification, as detected on plain chest radiography. The aim of this research was to investigate association between aortic arch calcification detected on plain chest X-ray (CXR) and myocardial scarring detected on cardiac magnetic resonance imaging (CMRI) in coronary artery disease patients.

Material and Method

Study population

Two hundred thirty nine patients were diagnosed as coronary disease by CMRI at Siriraj Hospital between January 2008 and December 2014. Of 239 diagnosed patients, 52 were excluded for lack of necessary information. Leaving 187 patients enrolled in the study. Plain CXRs and medical records were reviewed and clinical and demographic data were collected and recorded.

Inclusion criteria were, as follows: aged 18 years and older, diagnosis of coronary heart disease by CMRI at Siriraj Hospital, and having plain CXR in patient medical record. Patients who lacked important basic information in their medical records that was germane to this study were excluded.

Study protocol

We retrospectively reviewed coronary heart disease patients diagnosed by CMRI according to the following criteria: presence of perfusion defect in coronary artery distribution, presence of abnormal coronary magnetic resonance angiography (MRA), and/or presence of abnormal stent placement. CMRI results were interpreted by a cardiology imaging expert in routine practice. The following CMRI data was collected: left ventricular ejection fraction (LVEF), left ventricular mass index, and myocardial scar. Plain CXRs for all enrolled patients were collected and interpreted by an expert radiologist and categorized into 4 grades according to calcium thickness of aortic arch calcification for purposes of identifying potential associations: grade 0 = no visible calcification, grade 1 = calcification less than 25% of circumference, grade 2 = calcification 25 to 50% of circumference, and grade 3 = calcification more than 50% of circumference[8]. The radiologist who reviewed the plain CXRs was blinded to the CMRI results.

The protocol for this study was approved by the Siriraj Institutional Review Board (SIRB).

Statistical analysis

Subject characteristics were described using descriptive statistics, including frequency and percentage for categorical variables. Continuous variables were reported as mean, standard deviation for normally distributed variables and median (minimum to maximum) for non-normally distributed variables. Normality of distribution of variables was examined by the Kolmogorov-Smirnov or Shapiro-Wilk test. Association of aortic arch calcification, calcium grading, and calcium thickness with myocardial scarring were analyzed by Chi-square test. Factors for predicting myocardial scarring were evaluated by Student's t-test or Mann-Whiney U test for continuous variables and by Chi-square test or Fisher's exact test for categorical variables. Variables found to be significant (p-value <0.2) in univariate analysis, were further analyzed using multivariate backward stepwise logistic regression. Calcium parameters were included irrespective of statistical significant. The logistic method was referred by backward eliminate of variable was contributing significant is for fit of the model. For all tests, a two-tailed p-value <0.05 was considered statistically significant. SPSS version 18.0 statistical software (SPSS Inc., Chicago, IL, USA) was used for all statistical analysis.

Results

Enrolled patients were diagnosed as coronary heart disease by CMRI between January 2008 and December 2014. We reviewed CMRI results from 239 patients and found 187 patients who met the inclusion criteria. Most subjects were more than 60 years old. There was no statistical significance between absence or presence of myocardial scarring and age, blood pressure, underlying disease (diabetic mellitus, dyslipidemia), and beta-blocker or statin usage.

There was significantly higher prevalence of scarring in patients who had the following: male genders, history of smoking, history of non-ST-segment elevation myocardial infarction (NSTEMI), ST-segment elevation myocardial infarction (STEMI), percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass graft (CABG), heart failure, peripheral artery disease (PAD), stroke, diuretic and clopidogrel usage, and abnormal Q wave in electrocardiography (ECG) (Table 1).

Table 2 showed that there was no significant association between myocardial scar by CMRI and aortic arch calcification from CXR measured by calcium grade and calcium thickness.

The initial multivariable model includes: gender, body mass index (BMI), PAD, stroke, heart

failure, smoking, STEMI, NSTEMI, PTCA, CABG, clopidogrel, diuretics, abnormal Q wave, LVEF, LV mass index, calcium grade, calcium thickness.

Multivariate analysis revealed the statistically significant risk markers for myocardial scarring to be: history of peripheral artery disease (OR 10, 95% CI 1.25-79.75, $p = 0.011$), history of NSTEMI (OR 28.54, 95% CI 3.77-215.92, $p = 0.001$), and LVEF by CMRI (OR 0.91, 95% CI 0.89-0.94, $p<0.001$). We also included aortic arch calcification parameters even

Table 1. Patient characteristics at baseline

Factor	Absence of scar (n = 89)	Presence of scar (n = 98)	*p*-value
Gender (male), n (%)	35 (38.0)	57 (62.0)	0.010
Age (year), mean ± SD	74.31±8.93	72.60±9.82	0.215
Body mass index (kg/m^2), mean ± SD	26.18±4.44	25.03±3.89	0.003
SBP (mmHg), mean ± SD	136.99±16.29	136.40±22.89	0.849
DBP (mmHg), mean ± SD	73.11±11.59	73.11±13.30	1.000
GFR (mL/minute/1.73 sqm), mean ± SD	52.80±21.29	49.34±24.63	0.357
GFR (mL/minute/1.73 sqm)			0.512
>66	30 (50.8)	29 (49.2)	
30-59	36 (54.5)	30 (45.5)	
15-29	6 (40.0)	9 (60.0)	
<15	5 (35.7)	9 (64.3)	
Medical history, n (%)			
Diabetic mellitus	52 (46.4)	60 (53.6)	0.697
Hypertension	85 (48.3)	91 (51.7)	0.442
Dyslipidemia	63 (45.0)	77 (55.0)	0.220
Peripheral artery disease	1 (9.1)	10 (90.9)	0.008
Stroke	2 (13.3)	13 (86.7)	0.006
Heart failure	6 (17.1)	29 (82.9)	<0.001
Smoking	3 (18.8)	13 (81.2)	0.016
History of coronary heart disease, n (%)			
STEMI	1 (9.1)	10 (91.9)	0.008
NSTEMI	1 (4.0)	24 (96.0)	<0.001
Unstable angina	10 (41.7)	14 (58.3)	0.516
PTCA	16 (29.6)	38 (70.4)	0.002
CABG	7 (24.1)	22 (75.9)	0.006
Medication, n (%)			
ASA	57 (44.9)	70 (55.1)	0.280
Clopidogrel	26 (35.1)	48 (64.9)	0.006
ACEI	17 (44.7)	21 (55.3)	0.693
ARB	35(48.6)	37 (51.4)	0.826
Beta-blocker	61(48.4)	65 (51.6)	0.663
CCB	38 (48.7)	40 (51.3)	0.795
Statin	65 (44.2)	82 (55.8)	0.073
Diuretic	17 (27.0)	46 (63.0)	<0.001
Oral hypoglycemic drug	34 (45.3)	41 (54.7)	0.553
ECG parameter, n (%)			
Abnormal Q wave	12 (30.0)	28 (70.0)	0.002
CMRI parameter, mean ± SD			
LVEF (%)	71.71±9.78	54.61±18.49	<0.001
LV mass index (gm/sqm)	78.01±24.62	94.92±25.53	<0.001

SBP = systolic blood pressure; DB = diastolic blood pressure; GFR = glomerular filtration rate; ECG = electrocardiography; CCB = calcium channel blocking agent; ASA = aspirin; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; NSTEMI = non-ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; CABG = coronary artery bypass graft; CMRI = cardiac magnetic resonance imaging; LVEF = left ventricular ejection fraction; LV mass index = left ventricular mass index

Table 2. Aortic arch calcification parameters

Aortic arch calcification parameter (%)	Absence of scar (n = 89)	Presence of scar (n = 98)	*p*-value
Calcium grade			0.751
Grade 0	11 (47.8)	12 (52.2)	
Grade 1	2.4 (52.2)	22 (47.8)	
Grade 2	36 (48.6)	38 (51.4)	
Grade 3	18 (40.9)	26 (59.1)	
Calcium thickness (mm)			0.733
0	11 (47.8)	12 (52.2)	
<2 mm	26 (51.0)	31 (49.0)	
2-2.8 mm	29 (48.3)	30 (51.7)	
>2.8 mm	23 (43.4)	30 (56.6)	

Table 3. Multivariate analysis of risk markers for myocardial scarring

Factors	Multivariate odds ratio (CI)	*p*-value
PAD	10.00 (1.25-79.75)	0.001
NSTEMI	28.54 (3.77-215.92)	0.001
LVEF	0.91 (0.89-0.94)	<0.001
Calcium grade: ref = 0		0.41
1	0.84 (0.3-2.29)	
2	0.97 (0.38-2.47)	
3	1.32 (0.48-3.65)	
Calcium thickness (mm)		0.792
1.9-2.8	1.11 (0.56-2.22)	
2.8-11	1.24 (0.62-2.49)	

NSTEMI = non-ST-segment elevation myocardial infarction; PAD = peripheral artery disease; LVEF = left ventricular ejection fraction

they had no significant correlation with myocardial scar from univariate analysis. Calcium grade (1-3, ref 0) [Grade 1 (OR 0.84, 95% CI 0.3-2.29), Grade 2 (OR 0.97, 95% CI 0.38-2.47), Grade 3 (OR 1.32, 95% CI 0.48-3.65), $p = 0.41$], and calcium thickness 1.9-2.8 and 2.8-11 mm [(OR 1.11, 95% CI 0.56-2.22) and (OR 1.24, 95% CI 0.62-2.49), $p = 0.792$], respectively (Table 3).

There was no association between aortic arch calcification detected on plain CXR and myocardial scarring detected on CMRI. From our study, 164 patients (87.68%) had aortic arch calcification from CXR and 98 patients (52.4%) had myocardial scar from CMRI.

Discussion

Vascular calcifications are risk markers for atherosclerosis and amount of calcium is associated with atherosclerotic burden. Coronary calcium burden was applied to define atherosclerotic burden. As such, measurement of coronary artery calcification (CAC) by electronbeam computed tomography (EBCT) was used to predict silent myocardial ischemia[9]. Moreover, a correlation was reported between coronary calcium and complex percutaneous coronary intervention (PCI) [10]. A complex lesion such as chronic total occlusion (CTO) with high coronary calcium may be associated with silent myocardial damage, which is detectable on CMRI up to 86% of cases[11]. It can be said that more calcium in the coronary arteries there is a tends to cause a high atherosclerotic burden, which leads to silent myocardial damage, as reported in a previous study[11].

Eisen et al[12] showed the association of coronary and aortic calcification in the elderly as a diffusion of atherosclerosis. Aortic calcification detected on plain CXR also shows atherosclerotic risk prediction, such as the association with coronary artery disease[7,8]. We wondered whether presence of aortic calcification represents diffuse atherosclerosis and whether it is associated with silent myocardial damage like CAC or not. Although we graded aortic arch calcification in four grades, there was no association with myocardial scarring as we anticipated there might be. This may be explained by myocardial scarring being modified by not only calcium burden but by multiple factors including history of myocardial infarction (MI) and repeated myocardial damage. Perhaps these are the main factors that contribute to myocardial scarring. We may also have overestimated aortic calcification because in both groups we included high prevalence of aortic calcification. This was notably the case in the renal failure group, which patient glomerular filtration rate (GFR) was <60 in up to 49.4% of the group with absence of scar and 50.6% in the group with presence of scar. This may be associated by chance with aortic calcification and myocardial scarring. One of the atherosclerotic mechanisms is medial matrix remodeling; a process that converts medial smooth muscle cells into osteogenic cells. We also evaluated calcium thickness to ascertain whether or not it was correlated with scarring. Although we observed a tendency toward association between calcium thickness and myocardial scarring, the correlation was no statistical significant. According to our grading, calcium thickness in the aortic arch is more strongly associated with myocardial scarring than is diffusion of calcium in the aortic arch.

Other factors that demonstrated an association with myocardial scarring were male gender, history of smoking, NSTEMI, STEMI, PTCA, CABG, heart failure, PAD, stroke, diuretic, clopidogrel and statin

usage, abnormal Q wave in ECG, and the group with a higher ejection fraction (EF) associated with lower myocardial scar all as anticipated. Our study showed the potential of patients with higher BMI to be associated with lower myocardial disease as described in previous study as "the obesity paradox"[13]. In multivariate analysis, only history of peripheral artery disease, NSTEMI, and LVEF showed an association with myocardial scarring.

Our study has some limitations. First, we included only patients from diagnoses as coronary heart disease by cardiac MRI, instead of including all coronary artery patients who had CXR showing both positive and negative aortic arch calcification. Many coronary artery patients had CXR, but did not have CMRI. As such, patients that did not have both diagnostic investigations could not be in our study. However, we were able to extrapolate which patients included in our study were high-risk patients. A diagnosis of coronary heart disease by CMRI failed to show an association between aortic arch calcification and myocardial scarring in our patients. It can then, therefore, be assumed that this association would not be demonstrated in lower-risk patients either.

In conclusion, there was no association found between aortic calcification detected on plain CXR and myocardial scarring detected on CMRI. Patients with more calcium thickness had more myocardial scarring, but the increase was not statistically significant.

What is already known on this topic?

Aortic arch calcification from CXR reflects atherosclerotic process and myocardial scar from CMRI is the consequence of myocardial infarction.

What this study adds?

This study confirmed that aortic arch calcification is not associated with myocardial scar burden. The association between BMI and myocardial scarring characterized "obesity paradox" as previously reported.

Potential conflicts of interest

None.

References

1. World Health Organization. The global burden of disease: 2004 update [Internet]. 2008 [cited 2015 Mar 26]. Available from http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf
2. Heron M, Sutton PD, Xu J, Ventura SJ, Strobino DM, Guyer B. Annual summary of vital statistics: 2007. Pediatrics 2010; 125: 4-15.
3. Tatsanavivat P, Klungboonkrong V, Chirawatkul A, Bhuripanyo K, Manmontri A, Chitanondh H, et al. Prevalence of coronary heart disease and major cardiovascular risk factors in Thailand. Int J Epidemiol 1998; 27: 405-9.
4. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. Circulation 2001; 104: 2746-53.
5. Kolh P, Wijns W, Danchin N, Di Mario C, Falk V, Folliguet T, et al. Guidelines on myocardial revascularization. Eur J Cardiothorac Surg 2010; 38 (Suppl): S1-52.
6. Ueshima H, Sekikawa A, Miura K, Turin TC, Takashima N, Kita Y, et al. Cardiovascular disease and risk factors in Asia: a selected review. Circulation 2008; 118: 2702-9.
7. Li J, Galvin HK, Johnson SC, Langston CS, Sclamberg J, Preston CA. Aortic calcification on plain chest radiography increases risk for coronary artery disease. Chest 2002; 121: 1468-71.
8. Iijima K, Hashimoto H, Hashimoto M, Son BK, Ota H, Ogawa S, et al. Aortic arch calcification detectable on chest X-ray is a strong independent predictor of cardiovascular events beyond traditional risk factors. Atherosclerosis 2010; 210: 137-44.
9. He ZX, Hedrick TD, Pratt CM, Verani MS, Aquino V, Roberts R, et al. Severity of coronary artery calcification by electron beam computed tomography predicts silent myocardial ischemia. Circulation 2000; 101: 244-51.
10. Gökdeniz T, Kalaycıoğlu E, Aykan AÇ, Boyacı F, Turan T, Gül İ, et al. Value of coronary artery calcium score to predict severity or complexity of coronary artery disease. Arq Bras Cardiol 2014; 102: 120-7.
11. Choi JH, Chang SA, Song YB, Hahn JY, Choi SH, Oh J, et al. Cardiac magnetic resonance imaging unveils hidden myocardial damage that cannot be evaluated by echocardiography or electrocardiography in patients with chronically occluded coronary artery. J Am Coll Cardiol 2012; 59: E1079.
12. Eisen A, Tenenbaum A, Koren-Morag N, Tanne D, Shemesh J, Golan A, et al. Coronary and aortic calcifications inter-relationship in stable angina pectoris: A Coronary Disease Trial Investigating

Outcome with Nifedipine GITS (ACTION)--Israeli spiral computed tomography substudy. Isr Med Assoc J 2007; 9: 277-80.
13. Jensen JC, Hyes B, Parker M, Wagner A, Lombardi M, Schwitter J, et al. Relationship between obesity and unrecognized myocardial infarction: a EuroCMR multi-center study. J Cardiovasc Magn Reson 2013; 15 (Suppl 1): O76.

ความสัมพันธ์ของการเกิดแคลเซียมบริเวณหลอดเลือดแดงเอออร์ตาที่วินิจฉัยจากเอกซเรย์ปอดกับการเกิดพังผืดของหัวใจที่วินิจฉัยจากเครื่องตรวจหัวใจด้วยคลื่นแม่เหล็กไฟฟ้าในผู้ป่วยหัวใจโคโรนารี

ธนพล นิลโมจน์, จิตรลัดดา วะศินรัตน์, อาทิตย์ ยินดีงาม, รุ่งโรจน์ กฤตยพงษ์

ภูมิหลัง: *การวินิจฉัยโรคหลอดเลือดหัวใจทำได้หลายวิธี การตรวจขั้นพื้นฐาน ได้แก่ เอกซเรย์ปอด (CXR) และคลื่นไฟฟ้าหัวใจ (ECG) แต่ยังไม่มีข้อมูลว่าแคลเซียมบริเวณหลอดเลือดแดงเอออร์ตามีความสัมพันธ์กับการเกิดพังผืดของหัวใจที่เป็นผลจากโรคหลอดเลือดหัวใจหรือไม่*

วัตถุประสงค์: *เพื่อศึกษาความสัมพันธ์ของการเกิดแคลเซียมบริเวณหลอดเลือดแดงเอออร์ตาที่วินิจฉัยจาก CXR กับการเกิดพังผืดของหัวใจที่วินิจฉัยจากเครื่องตรวจหัวใจด้วยคลื่นแม่เหล็กไฟฟ้า (CMRI) ในผู้ป่วยหัวใจโคโรนารี*

วัสดุและวิธีการ: *CXR จากผู้ป่วย 187 ราย ที่อายุมากกว่า 18 ปี ที่ได้รับการวินิจฉัยหัวใจโคโรนารีด้วย CMRI ในโรงพยาบาลศิริราช ตั้งแต่ เดือนมกราคม พ.ศ. 2551 ถึง ธันวาคม พ.ศ. 2557 ได้รับการประเมินรายละเอียดแคลเซียมบริเวณหลอดเลือดแดงเอออร์ตาและเก็บข้อมูลทาง CMRI เพื่อจะดูในเรื่องของความสัมพันธ์ของการเกิดแคลเซียมบริเวณหลอดเลือดแดงเอออร์ตาและพังผืดของหัวใจ รวมไปถึงข้อมูลพื้นฐานอื่น ๆ ที่อาจมีความสัมพันธ์กันกับแคลเซียมบริเวณหลอดเลือดแดงเอออร์ตา*

ผลการศึกษา: *ความสัมพันธ์ของการเกิดแคลเซียมบริเวณหลอดเลือดแดงเอออร์ตาจาก CXR และการเกิดพังผืดของหัวใจจาก CMRI นั้น พบว่าในกลุ่มที่มีแคลเซียมบริเวณหลอดเลือดแดงเอออร์ตามีสัดส่วนของการพบพังผืดและไม่พบพังผืดจาก CMRI เป็น 86 (45.98%) และ 78 (41.70%) ตามลำดับ ไม่พบความสัมพันธ์ระหว่างแคลเซียมบริเวณหลอดเลือดแดงเอออร์ตากับการพบพังผืดจาก CMRI โดยพบพังผืดที่หัวใจ 52.2%, 47.8%, 51.4% และ 59.1% ในผู้ป่วยที่มี calcium grade 0, 1, 2 และ 3 ตามลำดับ (p = 0.751)*

สรุป: *ไม่มีความสัมพันธ์กันของการเกิดแคลเซียมบริเวณหลอดเลือดแดงเอออร์ตาที่ วินิจฉัยจากเอกซเรย์ปอดกับการเกิดพังผืดของหัวใจที่วินิจฉัยจากเครื่องตรวจหัวใจด้วยคลื่นแม่เหล็กไฟฟ้าในผู้ป่วยหัวใจโคโรนารี*