Association of abdominal aortic calcium with coronary artery calcium and obstructive coronary artery disease

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ABSTRACT

This study sought to determine the association of abdominal aortic calcium [AAC] with coronary artery calcium [CAC] and obstructive coronary artery disease [CAD]. This study included 110 patients [mean age 58.09 years, 51.8% males] who underwent a non-contrast abdominal computed tomography [CT] scan and 64-slice CCTA. A total AAC score using Agatston method was calculated in the abdominal aorta from the takeoff of the celiac artery to the aortic bifurcation. The results were analyzed using the IBM SPSS analytic software. A total of 58/110 [52.73%] patients had AAC. Patients with AAC were older with no differences in other baseline characteristics. Only 17.3% the patients with a zero, and 89.6% of those with a positive AAC score had obstructive CAD. Thus, an AAC score of zero had an 82.7% negative predictive value [NPV] and a positive AAC score had 89.6% positive predictive value [PPV] for the detection of obstructive CAD, in addition to 84.6% NPV and 82.7% PPV for detection of any coronary calcium plaque. Using multivariate linear regression, AAC score was an independent predictor of CAC score after adjusting for age [P < 0.001]. In our analysis, AAC score correlates with CAC score and has a high NPV to rule out CAD. Abdominal aortic calcium [AAC] score strongly correlates with coronary artery calcium [CAC] score and has a high NPV for the absence of obstructive CAD.

Keywords: Influenza virus, Antiviral peptide, Molecular docking, Nuraminidase, Hemagglutinin

رابطة كالسيوم الشريان الأورطى البطنى مع كالسيوم الشريان التاجى ومرض انسداد الشريان التاجى

سعت هذه الدراسة إلى تحديد ارتباط الكالسيوم الأورطي البطني (AAC)مع كالسيوم الشريان التاجي (CAC) ومرض الشريان التاجي الانسدادي (CAD) تضمنت هذه الدراسة 110 مريضاً متوسط العمر 58.09 عامًا ، 51.8٪ ذكور خضعوا لفحص التصوير المقطعي المحوسب للبطن (CT)غير المتباين و 64 شريحة CCTA تم حساب مجموع نقاط خضعوا لفحص التصوير المقطعي المحوسب للبطن (CT)غير المتباين و 64 شريحة CCTA تم حساب مجموع نقاط خضعوا لفحص التصوير المقطعي المحوسب للبطن (CT)غير المتباين و 64 شريحة CCTA تم حساب مجموع نقاط المريان البائي الأبهر. تم تحليل AAC باستخدام طريقة Agatston في الشريان الأورطي البطني من إقلاع الشريان البطني إلى تشعب الأبهر. تم تحليل النتائج باستخدام طريقة MSPSS في الشريان الأورطي البطني من إقلاع الشريان البطني إلى تشعب الأبهر. تم تحليل المرضى الذين يعانون من AAC أكبر سناً مع عدم وجود اختلافات في خصائص خط الأساس الأخرى فقط 17.3٪ من المرضى الذين لديهم محمو عد 17.8% من المرضى الذين لديهم CAD معرقلة. وبالتالي ، المرضى الذين لديهم محمو مع 10.5% (QCD) وكانت النتيجة الإيجابية كان لديهم AAC معرقلة. وبالتالي ، المرضى الذين لديهم محمو محود اختلافات في خصائص خط الأساس الأخرى فقط 17.3% من المرضى الذين لديهم محمو ، و 8.05% من أولئك الذين لديهم درجة AAC إيجابية لا يديهم CAD معرقلة. وبالتالي ، المرضى الذين لديهم محمو ، و 8.05% من أولئك الذين لديهم درجة AAC إيجابية لا يحمو مع ومود (QCD) وكانت النتيجة الإيجابية لا AAC معرقلة. وبالتالي ، المرضى الذين لديهم محمو ، و 8.05% (QCD) وكانت النتيجة الإيجابية لا AAC معرقلة. وبالتالي ، المرضى الذين لديهم درجة AAC الو و 2.25% وQCD لي الكرى في وحمة المرعوم التاجية. وQCD الكساف عن CAD الإضافة إلى 8.46% (QCD) وكانت النتيجة الإيجابية ال 20.5% معوم المرعى الوحة يعامة درجة AAC الو و من QCD الكشوم و ورحة المعنور الو و 2.25% ورحى الكشوم و 2.25% ولي الموعة الي معمور الكشف من أي لوحة (QCD) وكانت درجة AAC الو و 2.25% ولي الو و الوحة الكالسيوم التاجية. وQCD الكش عمد دامة عمود المتغيرات ، كانت درجة AAC موشراً مستقلاً لدرجة CAC ولي الحك ولي الحك ولي ورحى ولي ورفي و 4.25% ولي الكالي و و 9.05% ولي الكامي ولي مالي ولي ورحى ولي مالي ولي والي الولي الو والي المح ولي مالي ولي ولي والي الموى والي الو والي الو ولي ولي والي الو والي الو و

1. INTRODUCTION

Cardiovascular disease [CVD] remains the leading cause of mortality and major cause of morbidity worldwide, with underlying atherosclerosis as one of the key elements. In more than 90% of cases, the cause of myocardial ischemia is atherosclerotic plaque progression and rupture which leads to thrombus formation and obstruction of blood flow in the coronary arteries. More than 50% of patients die without clinical symptoms. To identify asymptomatic individuals at highest risk, attempts have been made on developing tools to risk-stratify individuals with subclinical atherosclerosis [1].

Atherosclerotic coronary artery calcifications are most frequently found as calcium lumps in advanced atherosclerotic lesions but may occur as small deposits of calcium in earlier lesions [2, 3]. Coronary artery calcium [CAC] is a marker of subclinical atherosclerosis [4, 5]. Recent investigation suggests that calcium content of the plaque may be proportional to the risk of rupture until a certain point, at which the evolving plaque becomes a more stable plaque [6]. Risk prediction may be improved by use of noninvasive tests of atherosclerosis such as assessment of CAC by electron-beam tomography [EBT] scan, which is known to predict cardiovascular disease [7].

Until recently, cardiac Computed Tomography [CT] applications were almost exclusively directed at detection and quantification of coronary calcium deposits, mainly using EBCT [8-10]. Nevertheless, with development of multi-slice spiral CT [MSCT] scanners, coronary CT angiography [CTA] is now a feasible and minimally invasive technique for detecting and characterizing asymptomatic coronary plaques at a high sensitivity, specificity, and accuracy, and has been suggested as an effective filter before catheter angiography [11, 12]. Simultaneous performance of Ca-scoring and coronary CTA has resulted in feasibility of comparison of both data to determine agreement between their findings [13, 14].

Aortic calcification [AC] is frequently seen on CT scans, although its importance is not well understood [15, 16]. Cardiovascular disease risk factors are modestly associated with CAC. Although aortic calcification may also be associated with the overall burden of atherosclerosis in this vessel, its relationship to cardiovascular disease has been even less frequently studied [17]. However, abdominal aortic calcification [AAC] is associated with incident myocardial infarction or stroke [18]. Its presence is a marker of both subclinical atherosclerotic disease and arteriosclerosis, and is also an independent predictor of cardiovascular morbidity and mortality [19, 20].

There is a moderate concordance between the presence of CAC and aortic calcification, however, calcification may be detectable years earlier in the aorta than in the coronary arteries [21]. Several noninvasive methods are available to detect and measure the degree of aortic vascular calcification. Computed tomography [CT] constitutes the gold standard for quantification of vascular calcification and, being the most effective and widely available with reproducible measurements [22, 23].

2. MATERIALS AND METHODS

Materials

A population of 110 patients agreed to receive coronary and abdominal calcium scans during the baseline [precontrast] period, [57 males and 53 females] aged 50 to 80 years with clinical indication for non-invasive CT angiographic study of coronary arteries was enrolled in this study in AL Najaf cardiovascular center at Al Sader Medical City. The most frequent inclusion criteria were chest pain and equivocal findings in exercise test]. The exclusion

criteria were tachycardias, arrhythmias, inability to hold breath, impaired renal function or history of any allergic reaction to contrast agent.

The study was performed using a 64-slice CT scanner [Aquillon 64, V4.51 ER 010, Toshiba Medical Systems, Tochigi, Japan] with ECG gating.

Methods

Scanning for calcium scores of the coronary arteries and abdominal aorta was performed at the start of imaging. A non-ionic contrast medium was then administered intravenously. Reconstructed images were transferred to another workstation [Vitrea 2 workstation, Vital Images Inc., Plymouth, Minne-sota, USA], where image analysis was performed. All CT examinations were reviewed by one radiologist experienced in cardiovascular radiology. Measurement of Stenosis: The origin, course, and caliber of the major coronary arteries and their branches were evaluated. Stenosis levels were automatically calculated. The coronary artery stenosis was expressed as a percentage of stenotic / non stenotic coronary diameter. To determine the extent of coronary involvement, 50% narrowing of the luminal diameter was considered significant [In clinical studies of coronary disease, some groups have defined 50% narrowing of the luminal diameter as significant] [24]. We classified Patients' coronary Cascore category according to Agatston score as follows: [1] Zero Ca-Score; [2] Ca-score more than zero and less than 100; [3] Ca-score equal to or greater than 100 indicating none, minimal-mild, and moderate-significant calcification, respectively. Then in a similar way we categorized abdominal aorta Ca-score into three groups: [0, 1 to 99, and equal to or greater than 100], based on guidelines for CAC [25, 26]. Calcium-score was automatically calculated on a wizard workstation.

3. RESULTS

Of the 110 subjects, 53 [48.2%] were females and 57 [51.8%] were males. Their ages ranged from 50 to 80 years [mean: 58.09 ± 6.252 years]. Of those patients only 34 [68%] of them had a positive serology, Table 1. Approximately 49 subjects [44.545%] had no CCTA detectable coronary artery stenosis, 13 subjects [11.8%] had non-significant, and 48 subjects [43.64%] had significant stenosis [figure 1].

[1]: calcium contents of abdominal aorta and coronary arteries.								
Characteristics	Range	Mean	St. Deviation					
Abd. aorta calcium	0-4700	420.66	905.732					
Coronary artery calcium	0-2000	113.73	270.851					

Table [1].



Figure [1]: Shows the distribution of coronary stenosis in the study group.

The presence of CAC or AAC [defined as values > 0] was relatively common in this study group, with 51 % and 52.73% of subjects demonstrating coronary and abdominal aorta calcium respectively. The vascular calcification was quantified using equivalent Agatston score.

Patients with higher levels of CAC or AAC were older, pearson correlation coefficient [r] was 0.348 for age and coronary artery score, and 0.353 for age and abdominal aorta score with significant correlation between abdominal aorta and coronary artery calcium scores [r= 0.679] and highly significant p values for these three relations [p=0.000] [table 2].

Stain	r	P value	
Age and abd. aorta score	0.353	< 0.001	
Age and coronary artery score	0.348	< 0.001	
Abd. aorta and coronary artery score	0.679	< 0.001	

 Table [2]: Correlation between age, abdominal aorta calcium score and coronary artery calcium score.

The patients were first divided into two groups, 54 subjects [49.09 %] with CAC scores equal to zero [CAC=0] and 56 subjects [50.90 %] with scores greater than zero [CAC>0]. Similar groups were divided according to the presence [58 subjects, 52.73 %] or absence [52 subjects, 47.27 %] of AAC. Among those with negative coronary Ca scoring only 8 subjects [14.81%] had significant stenosis, with negative abdominal aorta Ca scoring only 6 subjects [11.54%] had significant coronary stenosis, while among patients with positive coronary Ca scoring or abdominal aorta Ca scoring, 40 subjects [71.43%] and 42 subjects [72.41%] had significant coronary stenosis respectively, and this was statistically significant [P=0.000] ie, CAC has 71.43% PPV and 85.2% NPV for significant coronary stenosis, this means that patients are nearly 71.43% and 72.41% at risk of having significant coronary artery stenosis when the CT scan showed positive CAC or AAC respectively, Conversely, the lack of CAC or AAC was associated with low risks [14.81% and 11.54%] and high NPVs [85.2% and 88.5%] for significant coronary stenosis respectively. The number and percentage of those with significant coronary stenosis among these two groups are shown in [table 3].

Table [3]: Number and percentage of significant coronary s	stenosis associated with negative and positive
calcium groups in coronary arteries and abdominal aorta.	

Calcium	Coronary artery			Abdominal aorta			
content	total	significant		total	significant		
	number	coronary stenosis		number	coronary stenosis		
	CAC	number	percent	AAC	number	percent	
Negative	54	8	14.81%	52	6	11.54%	
Positive	56	40	71.43%	58	42	72.41%	
	X2=35.825 p=0.000			X2=41.321 p=0.000			

While comparing between presence and absence of AAC in our study population we find that cases with negative AAC had low incidence of CAC, any coronary obstruction and significant coronary artery stenosis as compared with the high figures of these three parameters when AAC was present [figure 2].



Figure [2]: Prevalence of CAC, significant stenosis and any coronary stenosis according to the presence of AAC

Furthermore we categorized CAC and AAC into three groups [0, 1 to 99 and \geq 100] indicating none, minimal-mild, and moderate-significant calcification, respectively, based on guidelines for CAC. Fifty four [49.09 %] of our patients out of 110 had zero coronary Ca scoring, 27 [24.54 %] had <100 Ca-scores, and 29 [26.36 %] had \geq 100 Ca-scores. In the first group [Ca score=0], only 8 patients [14.8%] had significant stenosis, while 14 patients [51.85%] in the second [Ca-score <100] and 26 patients [89.65%] in the third [Ca score \geq 100] groups had significant coronary artery stenosis [P=0.002] [Figure 3].



Figure [3]: showing classification of patients according to coronary artery calcium score groups [ratio of patients with significant coronary stenosis to total number of patients in each calcium score group].

Similarly 52/110 patients [47.27%] had zero AAC scoring, 13/110 patients [11.82 %] had <100 Ca-scores, and 45/110 patients [40.91 %] had \geq 100 Ca-scores. In the first group [Ca score=0], 6 patients [11.54%] had significant stenosis, 7 patients [53.85%] in the second [Ca-

score <100] and 35 patients [77.78%] in the third [Ca score \geq 100] group had significant coronary artery stenosis [P=0.001] [Figure 4].



Figure [4] showing classification of patients according to abdominal aorta calcium score groups [ratio of patients with significant coronary stenosis to total number of patients in each calcium score group].

Thus higher scores of abdominal aortic calcium and higher scores of coronary calcium are similarly associated with higher rates of coronary artery Stenosis. The number and percentage of those with significant coronary stenosis among the three groups for each of the coronary arteries and abdominal aorta are shown in [table 4] and [figure 5].



Figure [5] correlation of the risk of significant coronary stenosis with increasing CAC and AAC scores

4. **DISSCUSION**

Many symptomatic and asymptomatic patients are evaluated on a \+yearly basis for cardiac risk stratification in the hospital or in a physician's office. Although, there are many tools to evaluate CAD risk, a significant number of first myocardial infarctions occur in patients that would be considered low risk by routine methods [27, 28]. In addition, billions of dollars are spent on an annual basis evaluating patients with possible acute coronary syndromes with time consuming and expensive serial troponin testing, chest pain center observations, stress

testing and cardiac catheterizations. This suggests a need for additional methods to timely and efficiently evaluate patients presenting with a need for cardiac risk stratification.

Coronary artery calcium has been shown by histopathologic studies to correspond with presence of atherosclerosis [29-31]. Increasing CAC score can predict coronary events independently of other coronary risk factors in asymptomatic men and women [32, 33]. In addition, the absence of CAC portends an excellent cardiovascular prognosis. Patients with CAC score of zero have been shown to have a cardiovascular event rate of 0.4% over 3–5 years and a negative predictive value [NPV] of 96–100% for presence of obstructive CAD [34, 35], in our study, those with CAC score zero were 54 patients [49.09%] and only 8 patients [14.81%] had significant atherosclerotic stenosis in CCTA [NPV=85.2% for detection of significant stenosis].

The presence of AAC on lateral lumbar radiographs has been identified as a predictor of cardiovascular morbidity and mortality [19, 36]. Lateral lumbar radiographs can likely only identify patients with a largeburden of calcium in later stages of atherosclerosis. It has never been demonstrated before if smaller amounts of AAC seen on abdominal CT correlates with CAC and obstructive CAD. The aim of this study is to determine whether AAC qualitatively and quantitatively correlate with CAC and obstructive CAD on CCTA.

Multiple studies have shown that CAC score can predict cardiovascular events independent of other cardiac risk factors [32, 33]. Our study demonstrated that AAC score correlates with CAC score and thus may potentially be another marker for coronary artery disease and coronary events.

A total of 52 patients had no detectable AAC, of them only six patient [11.54%] had significant obstructive CAD. Among patients with AAC, 52/58 [89.65%] had coronary obstruction and 42/58 [72.42%] had significant coronary stenosis, and 48/58 [82.76%] had detectable CAC. Thus, AAC had an 82.7% NPV and 89.6% positive predictive value [PPV] for the detection of obstructive coronary artery disease and, 88.5% NPV and 72.4% positive predictive value [PPV] for the detection of significant coronary obstruction and an 84.6% NPV and 82.7% PPV for detection of any coronary calcium plaque. In addition, there was a linear correlation between AAC score and CAC score, r = 0.679, P < 0.0001.

Lack of coronary calcium has been shown to have an excellent negative predictive value for presence of obstructive disease and a low likelihood for development of cardiac events.[33,37,38] Our study showed that absence of abdominal aortic calcium on non-contrast abdominal CT had a NPV of 89.6% for obstructive CAD and 82.76% NPV for presence of any coronary calcification these are nearly comparable with previous study results which was 100% for obstructive CAD and 80% NPV forpresence of any coronary plaque [37]. We demonstrated that evaluating the abdominal aorta for absence of calcifications may help rule out presence of obstructive CAD.

Arterial calcification is thought to occur in later stages of atherosclerosis development and mostly present in older individuals. The patients in this study that had no AAC were significantly younger with a mean age of $[55.36 \pm 4.68]$. However, even when adjusting for age, AAC score predicted CAC score.

An important drawback of this study was its lack of correlation with fluoroscopic invasive quantitative coronary angiography as the gold standard. This was mainly relevant to that significant proportion of our patients had normal findings, resulting in their exclusion from an invasive catheter coronary angiography. Furthermore, due to the radiation burden AAC scoring cannot be performed routinely. Another limitation was lack of Picture archiving and communication system [PACS] which allow reference to previous abdominal CTS of the patients.

4. CONCLUSION

Abdominal aortic calcium [AAC] score strongly correlates with coronary artery calcium [CAC] score and has a high NPV for the absence of obstructive CAD.

CONFLICT OF INTEREST

No conflict of interest.

PATIENT CONSENT

Consents were obtained from Al-Hussein Medical City and Kerbala Health Directorate.

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