Journal of Cardiovascular Computed Tomography xxx (2017) 1–6

Contents lists available at ScienceDirect

Journal of Cardiovascular Computed Tomography

journal homepage: www.JournalofCardiovascularCT.com

Research paper

Quantifying Aortic Valve Calcification using Coronary Computed Tomography Angiography

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ARTICLE INFO

Article history:
Received 28 June 2016
Received in revised form
18 January 2017
Accepted 25 January 2017
Available online xxx

Keywords:
Aortic valve calcification
Aortic stenosis
Cardiac CT angiography

ABSTRACT

Introduction: Aortic valve calcification (AVC) has been associated with major adverse cardiovascular events and all-cause mortality. We sought to develop and validate a method to quantify AVC using coronary CT angiography (CTA).

Methods: Of 59 patients who underwent both non-contrast and contrast enhanced coronary CTA, 25 patients served as the derivation cohort and 34 patients served as the validation cohort. For non-contrast enhanced CT, quantification of AVC was performed using the Agatston method for coronary artery calcification (CAC). For contrast enhanced coronary CTA, a region of interest (ROI) was placed in the ascending aorta and the mean aortic attenuation value (HU_{Aorta}) and standard deviation (SD) were measured. Using a calcium threshold of mean HU_{Aorta} + 2SD, the AVC_{CTA} was calculated. All other Agatston score parameters (weighting factors and area calculations) remained unchanged.

Results: In the derivation cohort, the correlation between AVC_{CAC} and AVC_{CTA} was excellent (r = 0.982). Using the line of best fit, a correction factor was calculated enabling the conversion of AVC_{CTA} results to a AVC_{CAC} equivalent ($AVC_{Corrected}$ = 1.868 × AVC_{CTA}). Using this correction in the validation cohort, the correlation and agreement between AVC_{CAC} and $AVC_{Corrected}$ were good (ICC = 0.939; 95% CI: 0.881–0.969; kappa = 0.700; 95% CI: 0.469–0.931).

Conclusion: The quantification of $AVC_{Corrected}$ using contrast enhanced CTA is feasible using a systematic approach with very good reliability and good agreement with AVC_{CAC}. Larger-scale validation studies are needed to determine whether the use of AVC_{CAC} can be eliminated in favour of $AVC_{Corrected}$.

1. Introduction

Aortic valve calcification (AVC) has been associated with major adverse cardiovascular events and all-cause mortality.[1] In patients with aortic stenosis (AS), severity of AVC has been associated with severity of stenosis and mortality.[2–4] Quantification of AVC has been performed using the Agatston method with non-contrast enhanced ECG-gated computed tomography (CT) images.[3,4] With the adoption of transcatheter aortic valve implantation (TAVI), pre-TAVI contrast enhanced ECG-gated CT is routinely performed for prescription of valve sizes. Using current techniques, the quantification of AVC and pre-TAVI planning would require 2 separate image acquisitions. The ability to acquire all clinical information with a single study would be desirable. The quantification of AVC using contrast-CT studies is not routinely performed. We sought to develop and validate a method to quantify AVC using coronary CT angiography (CTA).

2. Methods

Between 2008 and 2010, 64 AS consecutive patients underwent coronary CTA and 59 had underwent both non-contrast and contrast enhanced coronary CTA. Of these, 25 patients with varying degrees of AS, were prospectively enrolled into a substudy of the Aortic Stenosis Progression Observation: Measuring Effects of Rosuvastatin (ASTRONOMER) trial[5,6] and were used as the derivation cohort. The ASTRONOMER trial included both male and female

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http://dx.doi.org/10.1016/j.jcct.2017.01.007
1934-5925/

patients between the ages of 18 and 82 that had mild to moderate AS (defined by peak Doppler aortic valve velocities of 2.5–5 m/s) and had baseline LDL-C values within targeted level for the risk category.[5] An additional 34 patients with aortic stenosis who were referred for both non-contrast and contrast enhanced cardiac CT were identified to have AVC from institutional CT registry and served as the validation cohort. The study was approved by the local institutional review board.

3. Non-contrast and contrast enhanced cardiac CT

Non-contrast and contrast enhanced ECG-gated CT were acquired as per local clinical routine.[7,8] Prior to scanning, patients received metoprolol targeting a heart rate to ≤65 bpm and in the absence of severe aortic stenosis, sublingual nitroglycerin (0.8 mg) was administered. Using the GE Volume CT scanner (General Electric Healthcare, Milwaukee, WI, USA), a non-contrast enhanced, prospective, ECG-triggered image acquisition (400–800 mA, 120 kVp) was performed at the 70% phase and images were reconstructed with a 2.5 mm slice thickness and 25 cm field of view.

For coronary CTA, a triphasic contrast (Visipaque 320 or Omnipaque 350, GE Healthcare, Princeton, NJ, USA) bolus protocol was used (100% contrast, 40%/60% contrast/saline, and saline). Prospective ECG-triggered or retrospective ECG-gated images (with X-ray tube modulation) were acquired using the GE Volume CT scanner (64 × 0.625 mm slice collimation, 400–800 mA, 100–120 kVp) and coronary CTA data sets were reconstructed with a slice thickness of 0.625 mm.

4. Quantification of Aortic Valve Calcification

Quantification of AVC was calculated from non-contrast and contrast enhanced CT images using the Aquarius iNtuition software (Version 4.4.7, TeraRecon Inc, San Mateo, CA, USA) by two experienced independent reviewers blinded to all clinical information.

For non-contrast enhanced CT, quantification of AVC was performed using the Agatston method.[9] The Agatston score of the aortic valve was calculated by carefully including the aortic valve only and excluding calcified non-aortic valve structures (such as the aorta, mitral annulus, and coronary arteries). All other Agatston score parameters (weighting factors and area calculations) remained unchanged.

Using coronary CTA images, a region of interest (ROI) was placed in the ascending aorta at the transaxial level between the origins of the right coronary artery and left main coronary artery. The mean aortic attenuation value (HU_{Aorta}) and standard deviation (SD) were measured and used to determine the threshold for calcium detection (mean HU_{Aorta} + 2SD).[10] Using this threshold for defining calcium, the AVC_{CTA} was calculated using the same quantification software used for the non-contrast enhanced CT (Fig. 1). All other Agatston score parameters (weighting factors and area calculations) remained unchanged.

The mean scores from the two readers were averaged and used for analysis. In cases where there were wide discrepancies, measured values were resolved through consensus reading. To determine agreement between AVC and severity of AS, the thresholds previously published by Clavel and his colleagues were used.[3] An AVC score of ≥1274 HU (Hounsfield units) in female and ≥2065 HU in male were used to define severe AS.[3]

5. Statistical analysis

Statistical analyses were performed using SAS (version 9.2, SAS Institute, Inc., Cary, NC, USA). Statistical significance was defined as $p < 0.05$. Continuous variables were expressed as means with SDs. Categorical variables were expressed as frequencies with percentages. To generate the correction factor, the ability for coronary CTA to predict severe valvular calcification was evaluated using a linear regression model.

To measure reliability of continuous data, intra-observer and inter-observer reliability for AVC_{CAC} and AVC_{CTA} measures were assessed using intra-class correlation coefficients (ICC). The reliability between AVC_{CAC} and AVC_{CTA} was also evaluated graphically using a Bland–Altman plot which demonstrates both the overall degree of agreement and whether the agreement is related to the underlying value of the item.[11] The agreement between categorical AVC_{CAC} and AVC_{CTA} was expressed using the weighted kappa with 95% confidence intervals. Likewise, Kappa statistics was also used to evaluate the agreement between categorical AVC_{CAC} and AVC_{CTA} measures of calcium in the validation cohorts.

6. Results

A total of 25 patients (age = 62.6 ± 12.5 years, 56% men) and 34 patients (age = 69.8 ± 12.3 years, 58% men) were analyzed in the derivation and validation cohorts, respectively (Table 1).

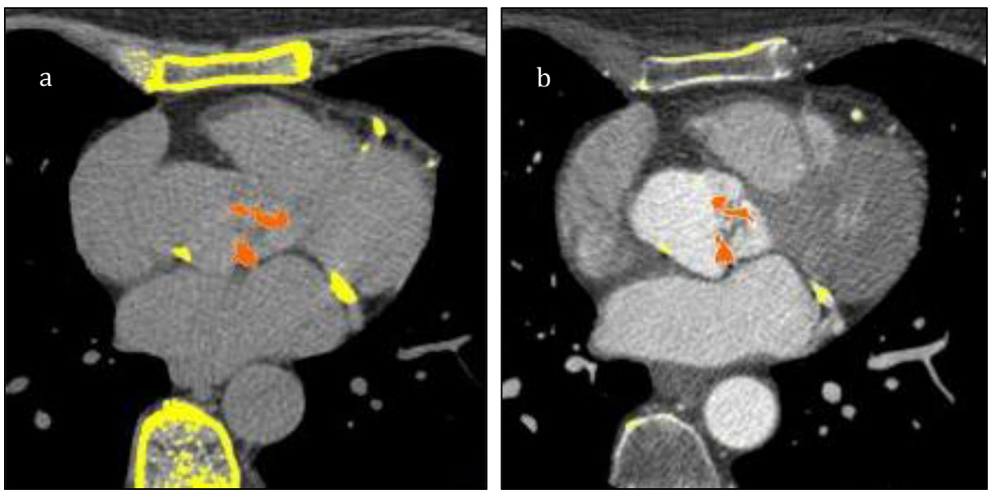

Fig. 1. Aortic Valve Calcification (orange) using (a) Non-Enhanced Cardiac CT, and on (b) Contrast Enhanced CT (using a threshold of 614 (= mean ascending aorta + 2SD)) Hounsfield units.

Please cite this article in press as: Alqahtani AM, et al., Quantifying Aortic Valve Calcification using Coronary Computed Tomography Angiography, Journal of Cardiovascular Computed Tomography (2017), http://dx.doi.org/10.1016/j.jcct.2017.01.007