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Prognostic value of multi-detector computed tomography in asymptomatic aortic valve stenosis☆

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ABSTRACT

Background: Multi-Detector Computed Tomography (MDCT) is a high-resolution imaging technique with potential additive value in the evaluation of patients with aortic valve stenosis (AS). We aimed to assess the prognostic value of MDCT in asymptomatic patients with AS compared to conventional transthoracic echocardiography (TTE).

Methods: 116 patients with asymptomatic AS (Vmax > 2.5 m/s assessed by clinical screening TTE, LVEF > 50%) were examined with TTE (Vivid e9) and MDCT (Aquilion 320) on the same day. The treating physician was blinded for research protocol defined imaging results. Outcome was defined as indication for aortic valve replacement (AVR) determined by the treating physician or sudden cardiac death.

Results: The mean age was 72 (8) years, 27% were women, mean AVA by TTE was 1.01 (0.30) cm^2. Median follow up time was 27 (IQR 19–44) months. Forty seven patients (41%) developed indication for AVR. No patients suffered a sudden cardiac death. AVA and aortic valve calcification were significant univariable predictors of AVR when measured by both TTE and MDCT, whereas left ventricular mass was only significant measured by MDCT. Significant coronary artery disease by MDCT tended to predict future indication for AVR, but this did not reach statistical significance (HR: 1.79 (95% CI 0.96–3.44), p = 0.08).

Conclusion: MDCT derived AVA can be of use as an alternative to TTE derived AVA in patients with asymptomatic AS to predict future clinical indication for AVR.

1. Introduction

Aortic valve replacement (AVR) is indicated in patients with severe aortic valve stenosis (AS) and related symptoms (exertional dyspnea, angina, dizziness, or syncope). In patients without symptoms prediction of future need for AVR is challenging. Currently, risk stratification relies primarily on echocardiographic parameters such as aortic valve area (AVA), left ventricular ejection fraction (LVEF), excessive left ventricular hypertrophy and the grade of valve calcification [1]. However, some patients have poor acoustic windows limiting conclusive transthoracic echocardiographic (TTE) examination. Multi-detector computed tomography (MDCT) is a relatively new high-resolution imaging technique with potential additive functional and structural information on top of TTE in the evaluation of patients with AS. This includes comorbidity such as ischemic heart disease which could present with similar symptoms as AS.

Retrospective contrast-enhanced MDCT imaging of a single heart beat provides information about AVA [2,3], aortic root geometry [4], left ventricular (LV) volumes [5], myocardial mass, and coronary artery disease (CAD). Furthermore, aortic valve calcification (AVC) estimated by the Agatston method on non-enhanced images has been shown to be closely related to the physical calcific burden of the valve [6] and previous studies have related the degree of calcification to the severity of stenosis [7,8]. AVC load has also been shown to differ between sexes

Abbreviations: AS, aortic valve stenosis; AU, Agatston units; AVA, aortic valve area; AVAi, aortic valve area indexed by BSA; AVC, aortic valve calcification; AV Vmax, aortic valve peak velocity; AVR, aortic valve replacement; BSA, body surface area; CACS, coronary artery calcification score; CAD, coronary artery disease; LV, left ventricular; LVEF, left ventricular ejection fraction; LVMi, left ventricular mass indexed by BSA; MDCT, multi-detector computed tomography; TAVI, transcatheter aortic valve implantation; TTE, transthoracic echocardiographic; VTI, volume time integral.

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[9] and AVC indexed by aortic annulus size (AVC density) [10] and with separate cut-off for women and men has been shown to have independent prognostic value for predicting overall mortality at diagnosis of AS.

We hypothesized that MDCT derived measures could contribute to a better prognostic assessment of patients with asymptomatic AS compared to clinical and conventional echocardiographic measures.

2. Methods

2.1. Study population

From September 2009 to January 2012 one hundred and sixteen patients with asymptomatic AS were included in the study. Prevalent patients with the diagnosis AS at six hospitals (Roskilde Hospital, Herlev Hospital, Bispebjerg Hospital, Hillerød Hospital, Gentofte Hospital and Rigshospitalet) in the area of Greater Copenhagen were screened for inclusion and exclusion criteria. See flow chart in Fig. 1. Eligible patients were offered participation in the study. Inclusion criteria were AS defined by echocardiographic aortic valve peak velocity (AV Vmax) >2.5 m/s, asymptomatic status as defined by the treating physician at the local hospital, and informed consent to participate in the study. Patients with p-creatinine >130 mmol/l, allergy to contrast, LVEF <50% on echocardiography, or a known malignant disease were excluded. All potential participants were contacted by letter and then by phone and all included patients gave informed consent in writing. The study complies with the Declaration of Helsinki and was approved by the local Research and Ethics Committee (J.nr.H-B-2009-027). The treating physicians were blinded for research protocol defined imaging results and all clinical decision making including referral for AVR was performed independently by the clinical heart team. TTE was performed immediately after the MDCT scan on the same day.

2.2. MDCT

Image acquisition was performed using a 320-detector CT (Aquilion 320, Toshiba, Japan) with 320 detector collimation, 100–120 kV tube voltage, 380–500 mA tube current, and 350–400 ms gantry rotation time. Tube voltage and current were adjusted according to the patient's body mass index. The MDCT scan consisted of a non-contrast enhanced coronary artery calcium score (CACS) followed by a cardiac angiography. Intravenous contrast (Visipaque 320, GE Healthcare, UK) was infused with a flow rate of 5 ml/s followed by a 50 ml saline chaser. The automatic bolus triggering technique was used for initiating image acquisition. The scanning was conducted as an ECG-triggered, retrospective, single beat, single rotation scan. Only one heart cycle was scanned if the heart rate was optimal (<65 bpm). In case of irregularity or heart rate >65 bpm, 2 or 3 heart cycles were acquired. The scanning was performed as a dual Z-axis volume covering the heart and the aortic arch. The MDCT images were reconstructed with 2 mm slice thickness and an increment of 0.3 mm. The acquisition was done without dose modulation and with FBP reconstruction.

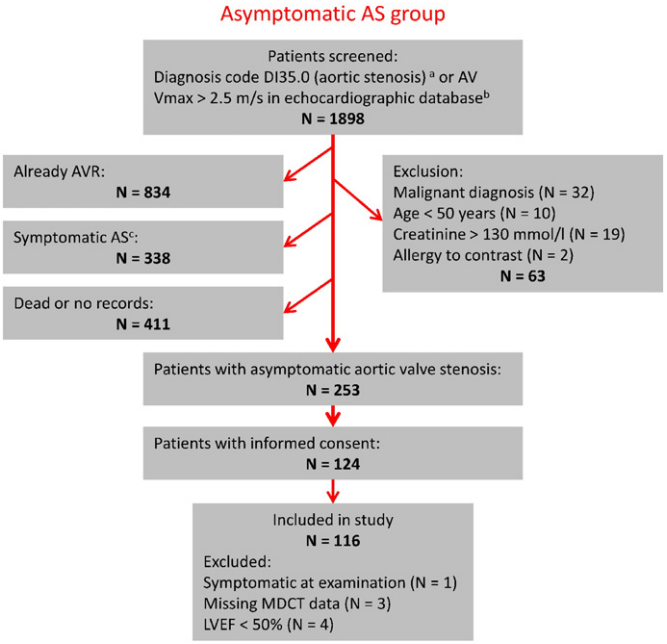

Fig. 1. Flow chart over the inclusion and exclusion of patients in the study. a = Bispebjerg, Roskilde, Hillerød and Gentofte Hospital; b = Rigshospitalet, Bispebjerg and Herlev Hospital; c = referred for additional examination prior to AVR OR awaiting operation OR assessed to have indication but the patient declined operation OR assessed to have indication for AVR but found to have too much comorbidity.

To optimize image quality beta-blocker (Metoprolol 100 mg) was administered orally if the heart rate was >65 bpm and systolic blood pressure >110 mm Hg (n = 57). In cases of low body weight (<50 kg) the dose was reduced.

2.3. MDCT image processing and analysis

All data were transferred to an external workstation (Vitrea2 FX version 6.3, Vital Images, Plymouth, Minnesota, USA). One observer (LHL) performed the analysis of AVA, aorta annulus, LV volume, LV mass, and calcification scores. Another observer (KFK) performed the coronary angiography analysis. Image analysis was performed blinded to research protocol defined TTE data and clinical outcome data.

AVA was measured in accordance with a previously published study partly based on the same study population [11]. In addition LV volume and mass were measured based on functional images with volumetric planimetry using the Vitrea2 FX software for three chamber analysis [12]. The software was manually corrected to ensure detection of correct volumes. LV mass and AVA was indexed by body surface area (BSA) giving LVMi and AVAi by MDCT. AVC was indexed by aorta annulus area (AVC density), and severe AVC density was defined as >300 Agatston units (AU)/cm^2 for women and >475 AU/cm^2 for men. Coronary artery calcification and aortic valve calcification was quantified using Agatston score on the non-contrast enhanced coronary artery calcium score images. CACS was defined as the combined Agatston score for the left main artery, the left anterior descending artery, the circumflex artery and the right coronary artery including the posterior descending artery. AVC by Agatston was defined as the calcification of the aortic leaflets including the attachment points of the leaflets. Also calcification of the aortic wall immediately connected to the calcification of the aortic valves was included in AVC. Careful consideration was given to avoid including calcification arising from the ostium of the coronary arteries, the mitral annulus and mitral valve. Multi-planar reformatting was used to ensure correct measurement in all cases. Coronary computed tomography angiography analyses were performed according to the American Society of Cardiovascular Computed Tomography guidelines [13]. A coronary lesion was considered significant if the stenosis was >70% of the luminal diameter.

2.4. TTE

All examinations were performed on a Vivid e9 scanner (General Electric, Horten, Norway) with a 3.5-MHz transducer. Images were obtained and digitally transferred to a remote workstation for offline analysis (Echopac BT 11.1.0, General Electric, Horten, Norway). All examinations were performed by one operator (LHL) and analyses were performed by a single image reader (HGC) without knowledge of the MDCT analyses.

2.5. TTE image acquisition and analysis

LV mass was calculated by the Devereux formula. LVEF was measured using the biplane method of disks (modified Simpsons' rule) in the apical-four chamber and apical-two chamber [14]. AVA calculation was based on the volume time integral (VTI) using the continuity equation in accordance with EAE/ASE recommendations [15]. Stroke volume was calculated with the Doppler method as: stroke volume = cross sectional area in the left ventricular outflow tract × VTI in the left ventricular outflow tract. Four different flow patterns were assessed: normal flow/low gradient (normal flow ≥ 35 ml/m^2 and mean gradient < 40 mm Hg), normal flow/high gradient: (normal flow ≥ 35 ml/m^2 and mean gradient ≥ 40 mm Hg), low flow/low gradient: (low flow < 35 ml/m^2 and mean gradient < 40 mm Hg) and low flow/high gradient: (low flow <35 ml/m^2 and mean gradient ≥40 mm Hg) [16,17]. All measurements were averaged over three cardiac cycles. LV mass and AVA were indexed by BSA giving LVMi and AVAi by TTE. AVC was assessed visually and classified as: 1 (no calcification); 2 (mildly calcified, small isolated spots); 3 (moderately calcified, multiple larger spots); and 4 (heavily calcified, extensive thickening and calcification of all cusps) according to Rosenhek [18]. Patients with an AVC grading of 4 were reported as having severe AVC.

2.6. Follow up

The predefined outcome was a composite of sudden cardiac death and indication for AVR as determined by the clinical heart team. MDCT data acquired as part of the research protocol were not made available for the clinical heart team. Information on mortality and indication for AVR were obtained from a systematic review of hospital contacts (ambulant and acute admissions) after the baseline examination. Follow up was conducted by September 2013. Events were reviewed by two researchers who reached consensus on cause of death and whether indication for AVR had been established. Indication for AVR was used as event instead of AVR to include patients who were found to have an indication, but who refused operation or were found to have too much comorbidity to undergo AVR (either surgical or transcatheter). Patients were censored from the study if they died from a non-cardiac cause (n = 7). The minimal uneventful follow up period was 19 months and differences in clinical characteristic between groups with and without event were displayed on the truncated follow up time of 19 months.

2.7. Statistics

Statistical analysis was performed using IBM SPSS software (version 20) and R (Version 2.15.2; Vienna, Austria). Continuous variables with normal distribution were presented as means and standard deviations (SD). Those with non-normal distribution were