A New Three-Dimensional Echocardiography Method to Quantify Aortic Valve Calcification

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Background: Aortic valve calcification (AVC) quantification is computed from multidetector computed tomography (MDCT). The aim of this study was to test the hypothesis that three-dimensional (3D) transthoracic echocardiography can be used to provide a bedside method to assess AVC.

Methods: The study included 94 patients (mean age, 78 ± 12 years; mean aortic valve [AV] area, 1.0 ± 0.6 cm^2) referred for MDCT and echocardiography for AV assessment. Apical 3D full-volume data sets focused on the AV region were acquired during transthoracic echocardiography, and a region-growing algorithm was applied offline to compute 3D transthoracic echocardiographic AVC (AVC-3DEcho). AVC-3DEcho was compared with AVC by MDCT and with calcium weight in the subgroup of patients referred for surgery, with explanted AVs analyzed by a pathologist (n = 22).

Results: In the explanted valve group, AVC-3DEcho score exhibited fair correlations with MDCT score (r = 0.85, P < .001), calcium load (r = 0.81, P < .001), and peak AV velocity (r = 0.64, P < .001). In the overall population, AVC-3DEcho score correlated modestly with MDCT score (r = 0.61, P < .001) but had similar accuracy to identify severe aortic stenosis (area under the curve = 0.94). AVC-3DEcho > 1,054 mm^3 identified severe aortic stenosis with specificity of 100% and sensitivity of 76%. In addition, AVC-3DEcho was associated with the presence of significant paravalvular regurgitation after transcatheter aortic valve implantation. Finally, intraobserver and interobserver variability for AVC-3DEcho score was 4.2% and 8.9%, respectively.

Conclusions: AVC-3DEcho correlated with calcium weight obtained from pathologic analysis and MDCT. These data suggest that a bedside method for quantifying AV calcification with ultrasound is feasible. (J Am Soc Echocardiogr 2018;■:■-■.)

Keywords: Aortic valve stenosis, Calcium scoring, 3D echocardiography

Degenerative aortic valve stenosis (AVS) shares a common pathophysiology with coronary artery disease, particularly in the initial phases. An inflammatory process related to atherosclerosis and calcium homeostasis imbalance are suspected to be involved in the mechanism of aortic valve (AV) thickening and calcification.[1,2] AV calcification (AVC) was first qualitatively assessed using two-dimensional (2D) transthoracic echocardiography (TTE),[3] and its clinical value for predicting aortic stenosis (AS) progression and outcome was proposed by Rosenhek *et al.*[4] Accurate quantification of AVC has become possible thanks to multidetector computed tomography (MDCT), which provides three-dimensional (3D) imaging of the AV and a clear differentiation of calcified tissues.[5-7] Large population-based studies confirmed the correlation between AVC quantified using MDCT (MDCT score), AVS severity, and patient outcomes.[8-10] Small studies demonstrated the association between MDCT score and significant paravalvular regurgitation (PVR; grade ≥ II) after transcatheter AV implantation (TAVI).[11] These data suggested that AVC assessment should be a part of AVS investigation when discrepancies exist between clinical functional status and echocardiographic markers.[5,12] However, AVC quantification is not a bedside method and requires referring the patient for MDCT, which is time consuming. To overcome this issue, we propose a new method based on 3D TTE for assessing AVC. The purpose of this study was to compare an AVC score derived from 3D TTE with the MDCT score and echocardiographic criteria for AVS.

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Conflicts of Interest: None.

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Abbreviations

2D = Two-dimensional

3D-TTE = Three dimensional transthoracic echocardiography

AS = Aortic stenosis

AU = Arbitrary unit

AV = Aortic valve

AVA = Aortic valve area

AVC = Aortic valve calcification

AVC-3DEcho = Three-dimensional transthoracic echocardiographic aortic valve calcification

AVS = Aortic valve stenosis

MDCT = Multidetector computed tomography

PVR = Paravalvular regurgitation

TAVI = Transcatheter aortic valve implantation

TTE = Transthoracic echocardiography

METHODS

Population

In this single-center study, we prospectively screened 110 consecutive patients referred for MDCT and 3D TTE for AVC assessment and quantification between March 2015 and May 2017. Patients with adequate 3D TTE and MDCT available for postprocessing were included. We excluded patients with poor acoustic windows or inadequate 3D image quality ($n = 10$), histories of AV dilation or replacement ($n = 5$), and histories of aortic endocarditis ($n = 1$). Ultimately, 94 patients were enrolled, and all patients provided written informed consent to participate in the study.

Echocardiographic Acquisition

Echocardiographic acquisitions were performed using a Vivid E9 with a commercially available 3D array transducer probe (4V-D; GE Vingmed Ultrasound, Horten, Norway). Standard 2D echocardiography included a parasternal view for left ventricular outflow tract measurement, 2D apical views (four-chamber, two-chamber, and three-chamber) for left ventricular ejection fraction assessment, left ventricular outflow tract pulsed Doppler, and continuous aortic Doppler flow from the apical and modified right parasternal views. AV area (AVA) was computed using the continuity equation. Severe AVS was defined as AVA < 1 cm^2 and/or mean AV gradient > 40 mm Hg and/or peak AV velocity ≥ 4 m/sec. Full-volume 3D AV images were acquired from apical views using single- or multibeat mode with a standardized setting (volume rate > 10 frames/sec, frequency = 1.7/3.3 MHz, gain = 14, compression = 11, reject = 0, and dynamics parameters = 6).

AVC by 3D Echocardiography

Three-dimensional transthoracic echocardiographic AVC (AVC-3DEcho) score was computed from a full-volume data set of the AV region during the systolic period. Image processing was automatically computed using dedicated software developed in MATLAB version 7.12 (The MathWorks, Natick, MA). After a semiautomatic delineation of the aortic annular region, high signal structure was identified automatically by applying the region-growing algorithm[13,14] (see Supplemental Figures 1 and 2, available at www.onlinejase.com). Binary transformed images were used to compute AVC-3DEcho score (expressed as cubic millimeters), which provides a quantification of AV calcium volume.

Computed Tomography AVC Score

Electrocardiographically gated noncontrast MDCT (Discovery CT 750HG; GE Healthcare, Little Chalfont, United Kingdom) was used to quantify MDCT calcium score. A standardized acquisition protocol was used, acquiring 64 contiguous transverse slices (thickness = 2.5 mm, 120 keV, 5 mAs, rotation time 0.35 s, field of view = 25 cm). AVC measurements were performed offline on a dedicated workstation (GE Smartcore 2007) by an experienced operator (J.-F.D.) blinded to echocardiographic and pathologic data. Calcification was defined as four adjacent pixels with density > 130 Hounsfield units. Preoperative in vivo MDCT score (expressed as arbitrary units [AUs]) was obtained using the Agatston method by manually selecting calcified structure belonging to the AV from transverse slices.

Ex Vivo and Pathologic Data

In the group of patients referred for surgical AV replacement, 22 explanted AVs were analyzed in the pathology department. Before analysis, all explanted valves were scanned to assess ex vivo MDCT calcium score. Then the valve was dried and a validated soft tissue removal method (timed bleaching technique) from formalin-fixed valves allowed tissue digestion. Residual calcium was rinsed with water, dried overnight, and directly weighed the following day by a pathology technician unaware of the results of MDCT and echocardiography.

PVR after TAVI

All patients who underwent TAVI were systematically evaluated on predischarge TTE. According to the Valve Academic Research Consortium 2, the circumferential extent of PVR assessed on a parasternal short-axis view was used to grade the severity of aortic regurgitation after TAVI. PVR was categorized as mild, moderate, or severe when the circumferential extent was <10%, 10% to 30%, and ≥30 %, respectively.

Statistical Analysis

All statistical analyses were performed using SPSS for Windows (SPSS, Chicago, Illinois). Data are presented as mean ± SD or as percentages. Comparisons between groups were performed using Student's *t* test or variance analysis for continuous variables and the χ^2 test for dichotomous variables. Comparisons between small groups ($n < 30$) were performed by using nonparametric tests (Mann-Whitney *U* test for continuous variables and χ^2 test with the Fisher correction for dichotomous variables). AVC-3DEcho and MDCT scores were compared with AVS markers using the logarithmic or linear regression method. Area under the receiver operating characteristic curve was used to determine the accuracy of 3D AV signal score index for identifying severe AS. Mean absolute differences over the mean difference between two repeated measurements was used to evaluate reproducibility of AVC-3DEcho measurements. *P* values $< .05$ were considered to indicate statistical significance.

RESULTS

Baseline Characteristics of Patients

Of the 94 patients included (mean age, 78 ± 12 years; mean AVA, 1.0 ± 0.6 cm^2; mean AVA index, 0.5 ± 0.3 cm^2/m^2), 84% ($n = 79$) had severe AVS on 2D TTE. Most patients were symptomatic (80% [$n = 75$]), and left ventricular ejection fraction averaged 54 ± 11% (29% with left ventricular ejection fraction < 50%). AV