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## Accuracy of device landing zone calcium volume measurement with contrast-enhanced multidetector computed tomography



Won-Keun Kim <sup>a,b,c,\*,1</sup>, Matthias Renker <sup>a,b,1</sup>, Andreas Rolf <sup>a,c</sup>, Christoph Liebetrau <sup>a,c</sup>, Arnaud Van Linden <sup>b</sup>, Mani Arsalan <sup>b</sup>, Mirko Doss <sup>b</sup>, Julian Rieck <sup>d</sup>, Maksymilian P. Opolski <sup>e</sup>, Helge Möllmann <sup>f</sup>, Thomas Walther <sup>b</sup>, Christian W. Hamm <sup>a,c</sup>

<sup>a</sup> Kerckhoff Heart Center, Department of Cardiology, Bad Nauheim, Germany; DZHK (German Centre for Cardiovascular Research), partner site Rhein-Main, Frankfurt am Main, Germany

<sup>b</sup> Kerckhoff Heart Center, Department of Cardiac Surgery, Bad Nauheim, Germany <sup>c</sup> Justus-Liebig University of Giessen, Department of Cardiology, Giessen, Germany

<sup>d</sup> Angio Consult, Speyer, Germany

<sup>e</sup> Institute of Cardiology, Department of Interventional Cardiology and Angiology, Warsaw, Poland

<sup>f</sup> St. Johannes Hospital, Department of Cardiology, Dortmund, Germany

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### ABSTRACT

Background: The extent of aortic valve calcification is an important determinant of procedural success in transcatheter aortic valve implantation (TAVI). We sought to validate device landing zone calcium volume (DLZ-CV) measurements on contrast-enhanced multidetector computed tomography (MDCT) with non-contrast-enhanced scans as reference.

Methods: We determined DLZ-CV in 141 patients undergoing transfemoral TAVI. Non-contrast-enhanced images were analyzed using a threshold of 130 HU as reference ( $DLZ-CV_{130}$ ). For contrast-enhanced scans, we applied various thresholds including 450 HU (DLZ-CV<sub>450</sub>), 850 HU (DLZ-CV<sub>850</sub>), mean aortic attenuation (Atten<sub>Ao</sub>) + 2 SD  $(DLZ-CV_{2SD})$ , Atten<sub>Ao</sub> + 4 SD  $(DLZ-CV_{4SD})$ , Atten<sub>Ao</sub> + 4 SD + 5 mm<sup>3</sup> volume filter  $(DLZ-CV_{4SD+})$ , and based on visual estimation (DLZ-CVvis). We compared DLZ-CV values between patients with versus without paravalvular leak (PVL), and between patients with versus without post-dilatation stratified by the type of prosthesis.

Results: All DIZ-CV measurements on contrast-enhanced scans significantly differed from DIZ-CV<sub>130</sub> (p < 0.001 for all comparisons). The best approximation to DLZ-CV $_{130}$  was achieved with DLZ-CV $_{4SD+}$  (508 mm<sup>3</sup> [332–772]; Pearson correlation: R = 0.87, p < 0.001; Bland-Altman: mean difference 1339 mm<sup>3</sup> [limits of agreement 79;2600]). Moreover, DLZ-CV<sub>4SD+</sub> allowed for discrimination of PVL ≥1° or the need for post-dilatation in patients receiving self-expanding prostheses. Procedural outcome using balloon-expandable prostheses was independent of DLZ-CV. Conclusion: Measurement of DLZ-CV using contrast-enhanced scans with unadjusted thresholds results in incorrect estimation of the calcium volume. The use of a scan-specific individual HU threshold including a volume filter (DLZ-CV<sub>4SD+</sub>) provides the best approximation to the reference and allows for discrimination of PVL  $\geq$  1° in patients receiving the Acurate neo prosthesis.

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#### 1. Introduction

Transcatheter aortic valve implantation (TAVI) has become an important therapeutic option for patients with severe aortic stenosis and high operative risk [1,2]. There are sustained efforts to optimize screening, imaging, and outcomes of TAVI. The severity and distribution of device landing zone calcification have been identified as important determinants of procedural outcome [3–7]. Traditionally, measurement

\* All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

E-mail address: w.kim@kerckhoff-klinik.de (W.-K. Kim).

<sup>1</sup> These authors contributed equally.

Abbreviations: AVCV, aortic valve calcium volume; DLZ-CV, device landing zone calcium volume; DLZ-CV<sub>130</sub>, DLZ-CV with threshold at 130 HU on non-contrast-enhanced scans; DLZ-CVvis, DLZ-CV with visually adjusted threshold; DLZ-CV450, DLZ-CV with threshold at 450 HU; DLZ-CV850, DLZ-CV with threshold at 850 HU; DLZ-CV250, DLZ-CV with threshold determined according to aortic attenuation +2 SD; DLZ-CV<sub>4SD</sub>, DLZ-CV with threshold determined according to aortic attenuation +4 SD; DLZ-CV<sub>4SD</sub>, DLZ-CV with threshold determined according to aortic attenuation +4 SD and additional volume filter set at 5 mm<sup>3</sup>; HU, Hounsfield Unit; MDCT, multidetector computed tomography; LVOT-CV, left ventricular outflow tract calcium volume; PVL, paravalvular leak; TAVI, transcatheter aortic valve implantation.

Corresponding author at: Kerckhoff Heart Center, Department of Cardiology/Cardiac Surgery, Benekestr. 2-8, 61231 Bad Nauheim, Germany.

of device landing zone calcification has been performed according to the method described by Agatston et al. [8] using non-contrastenhanced multidetector computed tomography (MDCT) scans and is considered the reference standard. Since this method requires additional image acquisition along with increased radiation dose and examination time, in recent years it has become common practice to determine the device landing zone calcium volume (DLZ-CV) using contrast-enhanced MDCT scans that are routinely performed for TAVI screening [3,9–11]. However, this approach is controversial, as the amount of calcification may be overestimated due to inappropriate detection of contrast material [12]. Whereas some authors use prespecified thresholds irrespective of the scan parameters, with often arbitrarily selected values ranging between 450 and 1050 Hounsfield Units (HU) [3,4,10,13,14], there are also more customized approaches that take into account the individual scan-specific aortic attenuation [9,15]. Watanabe et al. have been the only group to adjust the threshold to match the calcification under visual control; however, their method was not validated with a reference measurement [16]. The aim of the present study was to compare and validate different methods of threshold selection for quantifying DLZ-CV on contrastenhanced MDCT scans against the reference of DLZ-CV measurement derived from non-contrast-enhanced scans.

#### 2. Methods

#### 2.1. Patients and procedure

Consecutive patients with severe aortic stenosis undergoing transfemoral TAVI with implantation of the Sapien 3 (Edwards Lifesciences, Irvine, CA, USA) or Acurate neo (Symetis SA, Ecublens, Switzerland) transcatheter heart valve (THV) between June and December 2016 in a high-volume center were retrospectively included. The only exclusion criteria were the lack of or non-diagnostic quality of pre-procedural MDCT scans of the aortic root. Patient selection for TAVI was based on current guidelines [17], and details of the implantation techniques have been described elsewhere [18,19]. Post-procedural paravalvular leakage (PVL) was assessed by transthoracic echocardiography according to established criteria [20]. Two experienced cardiologists who were blinded to clinical characteristics independently reviewed all echocardiographic images, and in case of disagreement mutual consent was achieved. The study was approved by the institutional ethics committee and was conducted in accordance with the principles of the Declaration of Helsinki.

#### 2.2. Multidetector computed tomography

All MDCT examinations were performed using a third-generation dual-source system (Somatom Force; Siemens Healthcare, Forchheim, Germany) with a detector collimation of 2  $\times$  192  $\times$  0.6 mm and gantry rotation time of 0.25 s. Further details are provided in the Supplements.

All datasets were analyzed offline on a dedicated workstation (Syngo via, Siemens, Forchheim, Germany) or FDA-approved software (3mensio, Pie Medical, The Netherlands) by a single reader with profound experience in cardiac imaging who was blinded to clinical data. The image quality of the MDCT datasets were evaluated as previously described [21].

#### 2.3. DLZ-CV measurements

On the Syngo via workstation, the DLZ-CV was measured according to the Agatston method using a threshold of 130 HU (DLZ-CV<sub>Agats</sub>) [8]. The region of interest included the aortic valve and adjacent calcium deposits within the left ventricular outflow tract. Regions that were incorrectly denoted as valvular calcium (e.g. coronary artery plaques) were cropped manually.

Using 3mensio, segmentation of the aortic root and ascending aorta was executed automatically for contrast-enhanced scans. For non-contrast-enhanced scans, segmentation was performed manually. Subsequently, we identified the hinge points of the three aortic cusps in order to determine the annular plane, and standard aortic root measurements were performed as previously described [22]. The DLZ-CV was measured semiautomatically within a pre-specified region of interest encompassing the aortic valve at the highest level of the commissures and the left ventricular outflow tract 5 mm below the annular plane. Furthermore, we separately measured calcifications of the leaflets above the annular plane (AVCV) and the left ventricular outflow tract below the annular plane (LVOT-CV). Calcifications at the sinotubular junction and the coronary ostia were excluded.

For non-contrast-enhanced scans, a threshold of 130 HU (DLZ-CV<sub>130</sub>) according to the Agatston method was applied. For contrast-enhanced images, constant thresholds at 450 HU (DLZ-CV<sub>450</sub>) and 850 HU (DLZ-CV<sub>850</sub>) as well as scan-specific individual thresholds were employed. The latter included values derived from the mean attenuation of the ascending aorta (Atten<sub>A0</sub>) + 2 standard deviations (DLZ-CV<sub>25D</sub>), +4 standard deviations (DLZ-CV<sub>45D</sub>), and an individual setting of the threshold (HU<sub>vis</sub>) according to visual estimation of the calcifications by the observer (DLZ-CV<sub>sis</sub>) (Fig. 1). For DLZ-CV<sub>vis</sub>, the threshold was adjusted in steps of initially 50 HU, and subsequently 20 HU, until false negative detection of contrast material was not noticed any more, and the boundaries of calcium deposits were identified properly. For DLZ-CV<sub>4SD</sub>, we applied an additional volume filter with a threshold of 5 mm<sup>3</sup> (DLZ-CV<sub>4SD+</sub>) as previously described [9]. All DLZ-CV measurements were stratified according to tertiles of Atten<sub>A0</sub>. Furthermore, by manual adjustment we identified the "ideal" threshold (HU<sub>kef</sub>) that would be required to match DLZ-CV<sub>130</sub> as reference. False positive or detection of contrast material or false negative detection of calcium deposits were assessed visually.

In addition, we calculated the cover index  $[=100 \times (\text{prosthesis diameter} - \text{MDCT} annulus size) / \text{prosthesis diameter}], annular eccentricity [maximum/minimum annular]}$ 



**Fig. 1. Determination of aortic valve calcification on contrast-enhanced computed tomography using various thresholds.** Short-axis view of aortic valve (A) with calcifications at the non- and left coronary cusp. Measurement of device landing zone calcium volume (DLZ-CV) using various thresholds with calcium deposits marked in red color, resulting in either overestimation (B: DLZ-CV<sub>450</sub>; C: DLZ-CV<sub>450</sub>) or underestimation (F: DLZ-CV<sub>1050</sub>). Proper segmentation of the calcified region can be achieved by using an additional volume filter (D: DLZ-CV<sub>45D+</sub>) that eliminates small areas of falsely positive detected contrast material, or by visual estimation by individual setting of the HU threshold (E: DLZ-CV<sub>vis</sub>). However, with increasing aortic attenuation and/or enhanced detection of false positive contrast material, a high HU threshold may be required that could lead to slight underestimation.

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