

iMAIL

LETTER TO THE EDITOR

Severe Left Ventricular Outflow Tract Calcification Is Associated With Poor Outcome in Patients Undergoing Transcatheter Aortic Valve Replacement

Presence of moderate or severe left ventricular outflow tract (LVOT) calcification (SCA_{LVOT}) in patients undergoing transcatheter aortic valve replacement (TAVR) has been linked to adverse outcomes (1,2). However, calcium quantification in contrast-enhanced computed tomography (CTA) scans remains challenging, and previous studies were limited by implementation of uncorrected calcium quantification methods using different Hounsfield (HU) thresholds. In this single-center study, we aimed to determine the impact of SCA_{LVOT} on outcome in patients undergoing TAVR with balloon-expandable valves (BEV) by using a novel standardized calcium quantification method.

Overall, 587 consecutive patients with native severe aortic stenosis (AS) undergoing transfemoral TAVR with either third-generation Sapien 3 (n = 455) or second-generation Sapien XT (n = 132) between January 2013 and December 2015 were analyzed. Primary outcome was a nonhierarchical composite of all-cause death, any cerebrovascular event, prosthesis dislocation, annulus rupture, or more than mild paravalvular leakage (PVL) at 30 days. Receiver-operating curve statistics revealed an ideal cut-off of 609 mm³ LVOT calcium volume with respect to the composite endpoint (area under the curve = 0.75).

Pre-procedural image acquisition was performed using dual-source computed tomography (CT) system (Somatom Definition Flash or Somatom Force, Siemens AG, Forchheim, Germany) with an electrocardiogram-triggered high-pitch spiral acquisition. Parameters for the reference tube current, reference voltage, and reference pitch value were set to 320 mAs, 120 kVp, and 3.4, respectively. All patients received 60 ml iodinated contrast media (Iomeron 350, Bracco, Milan, Italy) injected at a rate of 4 ml/s followed by a saline chaser of 100 ml.

Pre-interventional CT images were analyzed using dedicated 3mensio Medical imaging software (Version 8.1, Pie Medical Imaging, Maastricht, the Netherlands). The LVOT region was defined as

the region between the basal ring and 15 mm inferior into the left ventricle. The optimal HU threshold was determined by analyzing the data of 110 patients who underwent both nonenhanced and CTA scans. First we quantified the calcium volume in the non-enhanced scans. Second, the mean attenuation values (HU) inside of the ascending aorta of the CTA scans were determined. For calcium quantification in CTA scans, a threshold of individual aortic attenuation + 100% of the individual attenuation was identified as the optimal HU threshold, allowing for correct automatic detection of calcium without misinterpretation of contrast medium as calcium. Using this algorithm, an individual HU threshold level was defined for every single patient in accordance to his aortic contrast medium attenuation.

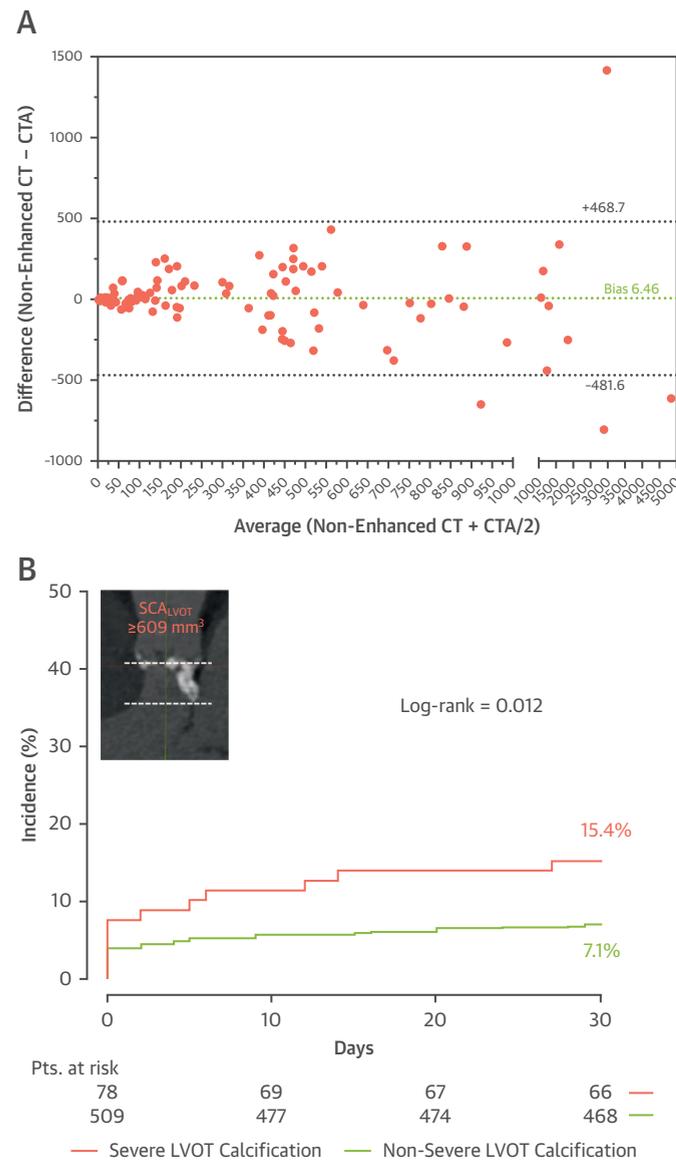
In this dataset (n = 110), we performed a linear regression model depending on the individual HU threshold and the ratio between the calcium measurements in CTA and nonenhanced scans. The regression line showed a slope of -0.0003 and an intercept with the Y-axis at 0.4065. Hence, the calibration factor (CF) for calcium quantification in CTA scans was calculated as follows:

$$\text{calibration factor} = \frac{1}{(\text{individual HU threshold} \times \text{slope}) + \text{Y-axis intercept}}$$

The derived CTA volumes of aortic calcifications using the +100% HU threshold above the intravascular density were then multiplied by the individual CF. For validation purposes, the accuracy of this approach was determined in additional 100 consecutive patients undergoing CT for TAVR planning (Figure 1A).

Overall, 78 patients (13.3%) presented with SCA_{LVOT} . The composite clinical endpoint occurred more frequently in the SCA_{LVOT} group (Figure 1B). Furthermore, patients with SCA_{LVOT} showed higher incidence of more than mild PVL (2.4% vs. 6.4%, p = 0.046) and were at higher risk of 30-day and 2-year all-cause mortality (2.4% vs. 9.0%, log-rank p = 0.001; 22.6% vs. 32.8%, log-rank p = 0.019, respectively). In multivariate model, SCA_{LVOT} was identified as independent predictor of the 30-day composite endpoint (hazard ratio [HR]: 2.44; 95% confidence interval [CI]: 1.26 to 4.73) and 2-year mortality (HR: 1.86; 95% CI: 1.17 to 2.93).

Although the threshold of 609 mm³ LVOT calcium volume was derived and validated in the same cohort,

FIGURE 1 Method Validation and Short-Term Outcome in Patients With Severe LVOT Calcification

(A) Bland-Altman plot for agreement between calcium volume measured by nonenhanced computed tomography (CT) and calibrated contrast-enhanced computed tomography (CTA). **(B)** Incidence of the composite clinical endpoint according to severity of left ventricular outflow tract (LVOT) calcification.

additional confirmation in an independent population is required. In addition, our results have to be interpreted within the context of a specific contrast protocol on specific scanner platforms. However, by application of this novel standardized method for calcium quantification from CTA images, we were able to confirm SCA_{LVOT} as important risk factor of 30-day adverse events as well as short-term and mid-term mortality in patients undergoing TAVR with BEV. This finding underlines the important clinical role of accurate pre-TAVR assessment and risk stratification by CT taking SCA_{LVOT} into account.

David Jochheim, MD*
 Simon Deseive, MD
 Bernhard Bischoff, MD
 Magda Zadrozny, MD
 Sebastian Hausleiter
 Moritz Baquet, MD
 Christian Tesche, MD
 Hans Theiss, MD
 Christian Hagl, MD
 Steffen Massberg, MD
 Julinda Mehilli, MD
 Jörg Hausleiter, MD

*Department of Cardiology
 Munich University Clinic (LMU)
 Marchioninistr. 15
 Munich 81377
 Germany

E-mail: David.Jochheim@med.uni-muenchen.de

<https://doi.org/10.1016/j.jcmg.2018.06.008>

Please note: Drs. Mehilli and Hausleiter have received lecture fees and institutional research grants from Edwards Lifesciences and Abbott Vascular. All other authors have no conflicts of interest to disclose.

REFERENCES

- Maeno Y, Abramowitz Y, Yoon SH, et al. Relation between left ventricular outflow tract calcium and mortality following transcatheter aortic valve implantation. *Am J Cardiol* 2017;120:2017-24.
- Barbanti M, Yang TH, Rodès Cabau J, et al. Anatomical and procedural features associated with aortic root rupture during balloon-expandable transcatheter aortic valve replacement. *Circulation* 2013;128:244-53.