

Quantity and Location of Aortic Valve Complex Calcification Predicts Severity and Location of Paravalvular Regurgitation and Frequency of Post-Dilation After Balloon-Expandable Transcatheter Aortic Valve Replacement

Omar K. Khalique, MD,* Rebecca T. Hahn, MD,* Hemal Gada, MD,* Tamim M. Nazif, MD,* Torsten P. Vahl, MD,* Isaac George, MD,* Bindu Kalesan, PhD, MPH,* Molly Forster, BA,* Mathew B. Williams, MD,* Martin B. Leon, MD,* Andrew J. Einstein, MD, PhD,* Todd C. Pulerwitz, MD,* Gregory D. N. Pearson, MD, PhD,* Susheel K. Kodali, MD*

ABSTRACT

OBJECTIVES This study sought to determine the impact of quantity and location of aortic valve calcification (AVC) on paravalvular regurgitation (PVR) and rates of post-dilation (PD) immediately after transcatheter aortic valve replacement (TAVR).

BACKGROUND The impact of AVC in different locations within the aortic valve complex is incompletely understood.

METHODS This study analyzed 150 patients with severe, symptomatic aortic stenosis who underwent TAVR. Total AVC volume scores were calculated from contrast-enhanced multidetector row computed tomography imaging. AVC was divided by leaflet sector and region (Leaflet, Annulus, left ventricular outflow tract [LVOT]), and a combination of LVOT and Annulus (AnnulusLVOT). Asymmetry was assessed. Receiver-operating characteristic analysis was performed with greater than or equal to mild PVR and PD as classification variables. Logistic regression was performed.

RESULTS Quantity of and asymmetry of AVC for all regions of the aortic valve complex predicted greater than or equal to mild PVR by receiver-operating characteristic analysis (area under the curve = 0.635 to 0.689), except Leaflet asymmetry. Receiver-operating characteristic analysis for PD was significant for quantity and asymmetry of AVC in all regions, with higher area under the curve values than for PVR (area under the curve = 0.648 to 0.741). On multivariable analysis, Leaflet and AnnulusLVOT calcification were independent predictors of both PVR and PD regardless of multidetector row computed tomography area cover index.

CONCLUSIONS Quantity and asymmetry of AVC in all regions of the aortic valve complex predict greater than or equal to mild PVR and performance of PD, with the exception of Leaflet asymmetry. Quantity of AnnulusLVOT and Leaflet calcification independently predict PVR and PD when taking into account multidetector row computed tomography area cover index. (J Am Coll Cardiol Intv 2014;7:885-94) © 2014 by the American College of Cardiology Foundation.

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**ABBREVIATIONS
AND ACRONYMS****AnnulusLVOT** = annulus and left ventricular outflow tract**AUC** = area under the curve**AVC** = aortic valve calcification**Ca** = calcification**CT** = computed tomography**HU** = Hounsfield units**LVOT** = left ventricular outflow tract**MDCT** = multidetector row computed tomography**PD** = post-dilation**PVR** = paravalvular regurgitation**ROC** = receiver-operating characteristic**TAVR** = transcatheter aortic valve replacement**TEE** = transesophageal echocardiography**THV** = transcatheter heart valve

Transcatheter aortic valve replacement (TAVR) is an expanding alternative to surgical replacement for patients with high operative risk (1-3). Paravalvular regurgitation (PVR) is an important complication of TAVR that has been shown to be associated with increased mortality (4-8). Thus, there is a growing body of literature regarding the determinants of PVR (4,9-18). Aortic valve calcification (AVC) has

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been proposed as one of these determinants; however, the location and pattern of calcification differ significantly between patients. The impact of calcification in various regions of the aortic valve complex (leaflets, annulus, and left ventricular outflow tract [LVOT]) is incompletely understood. In theory, calcification impairs the seal of the transcatheter heart valve (THV) to the aortic annulus and LVOT, resulting in PVR.

In the present study, our aim was to identify the impact of calcification of different locations of the aortic valve complex on the severity of PVR and to determine whether quantification of AVC by location accurately predicts the location of PVR. Additionally, we sought to determine whether calcification predicts the need for balloon post-dilation (PD), an important surrogate for PVR.

METHODS

PATIENT POPULATION AND PROCEDURE. This analysis included patients who underwent TAVR with a balloon-expandable Edwards Sapien or Sapien XT THV (Edwards Lifesciences, Irvine, California) in a single academic medical center from October 1, 2011 to July 31, 2013. All patients entering the analysis were required to have undergone both pre-procedural multidetector row computed tomography (MDCT) and intraprocedural transesophageal echocardiography (TEE) and were therefore nonconsecutive. After review of 218 charts, 150 patients were included in the final analysis on this basis. No patients were excluded from the analysis on the basis of imaging quality. The procedural access route was determined by the treating physicians. THV sizing was determined at the discretion of the treating physicians with the use of all available imaging modalities (MDCT and 3-dimensional TEE). All patients gave informed consent and the study was approved by the institutional review board for human research. The

need for PD was decided by the treating physicians and was typically on the basis of the immediate post-deployment TEE imaging of more than mild PVR.

IMAGE ACQUISITION. Echocardiography. Patients underwent intraprocedural TEE using commercially available equipment (iE33, Philips Medical Imaging, Andover, Massachusetts). A complete 2-dimensional and 3-dimensional TEE was performed pre- and post-THV implantation as recommended by the American Society of Echocardiography guidelines (19).

MDCT. Our methodology for MDCT acquisition with a 320-slice scanner (Aquilion ONE, Toshiba Medical Systems, Otawara, Japan) has been previously described (18). Prior to April 27, 2013, iodixanol 320 mg I/ml (124 patients) was used; thereafter, iohexol 350 mg I/ml (26 patients) was used. Intravenous contrast was injected at a rate of 3.5 ml/s. Datasets were transmitted to a dedicated workstation and analyzed using 3mensio Valves software (version 5.1, Pie Medical Imaging, Maastricht, the Netherlands).

MDCT AORTIC ANNULUS MEASUREMENTS. The aortic annulus was defined as a virtual plane containing the basal attachment points of the 3 aortic valve leaflets in the LVOT. Annular area was planimetered directly in the short-axis plane. The area cover index representing the percentage of oversizing of the THV as compared with the measured annulus size was calculated using the formula $(\text{Nominal THV area} - \text{measured area}) / \text{nominal THV area} \times 100\%$. All annulus measurements were performed in mid-systole.

MDCT QUANTIFICATION OF AORTIC VALVE

CALCIFICATION. AVC was quantified using calcium volume scoring on contrast-enhanced images in keeping with recent investigations (9,14) and in light of the increased reproducibility compared with Agatston scoring (20,21). Contrast imaging allows for higher spatial resolution than do noncontrast images to delineate different leaflets and regions within the aortic valve complex. Quantification was performed by a cardiologist board-certified in cardiac CT who had previously reviewed at least 300 TAVR cases (O.K.K.). The late-diastolic phase with the best visually assessed image quality was used. An empiric CT number cutoff of 550 Hounsfield units (HU) was used for AVC quantification for most patients. However, given the variability of luminal enhancement in contrast-enhanced images, for patients with luminal attenuation <200 HU (11 patients), a cutoff of 300 HU was used for AVC quantification; for patients with luminal attenuation >500 HU (36 patients), a cutoff of 50 HU greater than the luminal attenuation

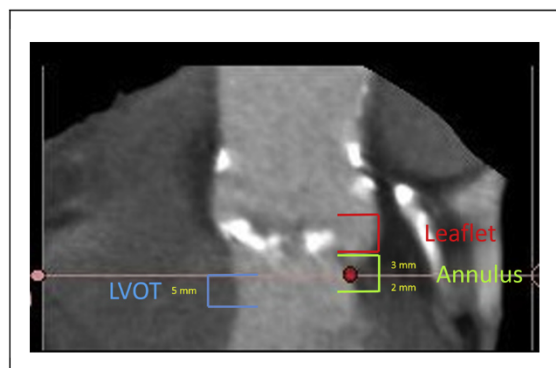


FIGURE 1 Regions of the Aortic Valve Complex

The left ventricular outflow tract (LVOT) region (blue bracket) is defined as the cross-sectional region 5 mm inferior to the annular plane to the annular plane (pink line). The Annulus region (green bracket) is defined as the cross-sectional region 2 mm inferior to the annular plane to 3 mm superior to the annular plane. The Leaflet region (red bracket) is defined as the cross-sectional region 3 mm superior to the annular plane to the cranial portion of the leaflets. The AnnulusLVOT (not shown) section encompasses the Annulus and LVOT regions.

was used. The region of interest was cropped as needed to optimize assessment. The aortic valve complex was separated in the craniocaudal axis along the double oblique long-axis of the LVOT/aortic valve into the following regions: LVOT (from 5 mm inferior to annular plane to the annular plane); Annulus (from 2 mm inferior to the annular plane to 3 mm superior to the annular plane); AnnulusLVOT (from 5 mm inferior to annular plane to 3 mm superior to annular plane, encompassing Annulus and LVOT regions); Leaflet (from 3 mm superior to

annular plane to the superior edge of leaflets) (Fig. 1); and Total (encompassing all of the above). Volume of calcification (CA) (in mm³) was recorded for each region (LVOTCa, AnnulusCa, AnnulusLVOTCa, LeafletCa, and TotalCa). Each section was divided into 3 sectors to correspond to each leaflet distribution: left; right; and noncoronary (Fig. 2). Asymmetry was assessed using the maximum absolute difference in volume scores between any 2 leaflet sectors for each region (Δ LVOTCa, Δ AnnulusLVOTCa, Δ AnnCa, Δ LeafletCa).

POST-PROCEDURAL PVR ASSESSMENT. PVR was defined as present if it remained after all interventions (including THV implantation and balloon PD where applicable) were completed. Assessment was performed via intraprocedural TEE post-TAVR deployment using a modification of the VARC-2 (Valve Academic Research Consortium-2) guidelines (22), and planimetry of 3-dimensional color Doppler reconstruction with planimetry of vena contracta (Fig. 3) was the method of choice (23-26) with the following cutoffs: trace: 0 to 4 mm²; mild: 5 to 9 mm²; moderate: 10 to 19 mm²; moderate-severe: 20 to 29 mm²; and severe: ≥ 30 mm². When 3-dimensional color Doppler reconstruction was not possible, assessment was performed by a combination of visual estimation of 2-dimensional color Doppler imaging and quantitative Doppler assessment of relative stroke volumes across the LVOT and right-ventricular outflow tract (22). The location of the PVR jets was retrospectively determined by a board-certified echocardiographer (O.K.K.) experienced in periprocedural TAVR imaging, and then was assigned to a coronary leaflet sector. Only the jet compromising most of the PVR was analyzed. If jets in 2 different

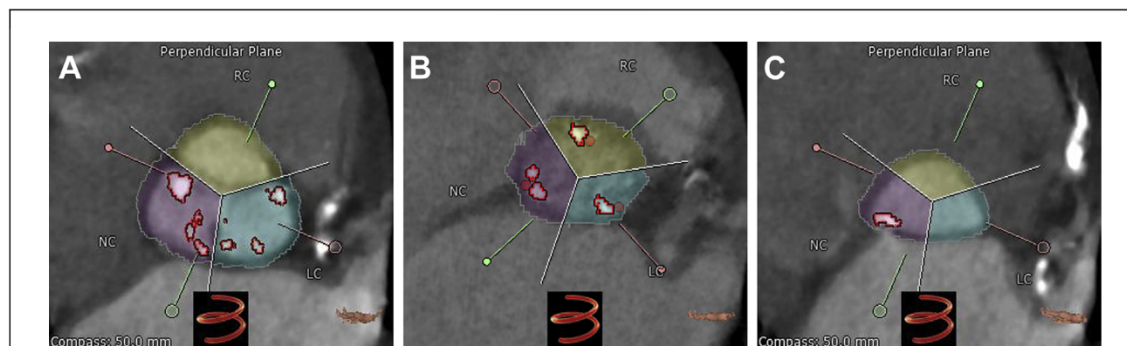
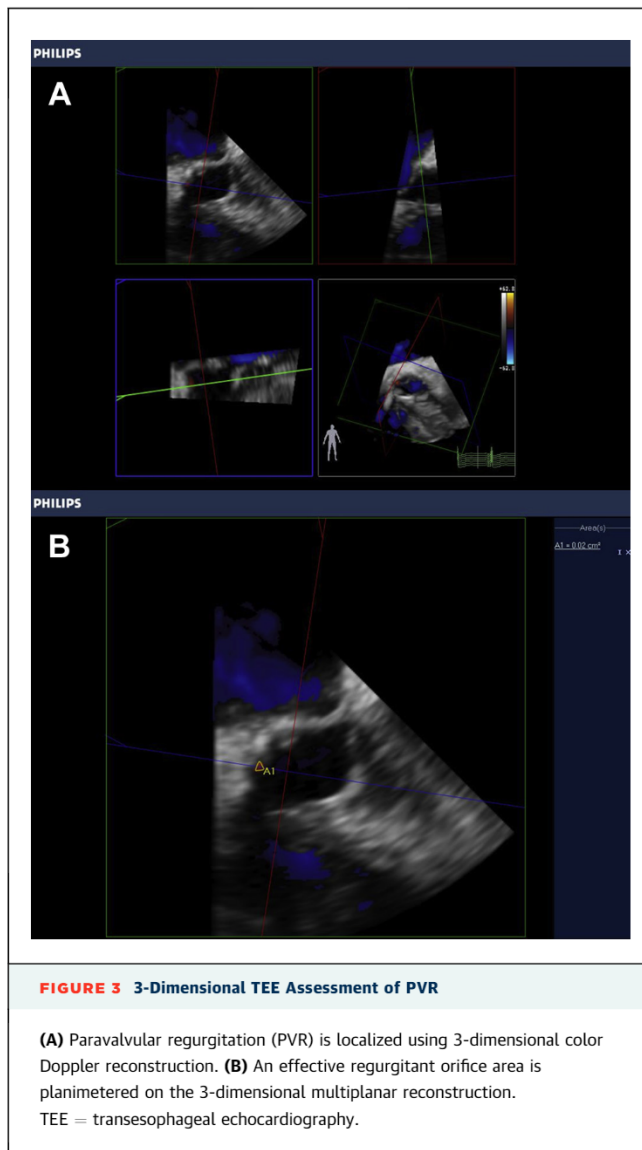


FIGURE 2 Aortic Valve Calcium Quantification by Leaflet Sector

(A) Calcium quantification by leaflet sector at the leaflet level is shown. (B) Calcium quantification by leaflet sector near the annulus level is shown. (C) Calcium quantification by leaflet sector at the LVOT level is shown. LC = left coronary; LVOT = left ventricular outflow tract; NC = noncoronary; RC = right coronary.



sectors were deemed equally large, either was counted as the major jet. Echocardiographers performing PVR analysis were blinded to the results of calcium scoring.

TABLE 1 Distributions of Calcium Volume (mm³) by Leaflet Sector

	Left	Right	Non	Total
LVOTCa	23 ± 52	7 ± 21	19 ± 61	49 ± 94
AnnulusCa	56 ± 66	33 ± 49	62 ± 80	151 ± 144
AnnulusLVOTCa	69 ± 91	35 ± 54	71 ± 96	175 ± 176
LeafletCa	284 ± 225	304 ± 240	407 ± 271	993 ± 610

Values are mean ± SD.

AnnulusCa = volume of calcification 2 mm inferior to the annulus to 3 mm superior to the annulus; AnnulusLVOTCa = volume of calcification 5 mm inferior to the annulus to 3 mm superior to the annulus; LeafletCa = volume of calcification 3 mm superior to the annulus to the cranial portion of the leaflets; LVOTCa = volume of calcification 5 mm inferior to the annulus extending to the level of the annulus.

STATISTICAL ANALYSIS. Analyses were performed using Stata/SE (version 12, StataCorp LP, College Station, Texas), and MedCalc (version 12.4.0.0, MedCalc Software, Mariakerke, Belgium). Statistical significance was defined as $p < 0.05$. Continuous variables are reported as mean ± SD. Normality of distributions for continuous variables was tested using the Shapiro-Wilk test. Hypothesis testing was then performed accordingly, using the appropriate t -test or nonparametric test (the Wilcoxon test for paired samples or the Mann-Whitney U test for independent samples). The intraclass correlation coefficient was used to assess interobserver (O.K.K. and H.G.) and intraobserver (O.K.K.) variability (27). Receiver-operating characteristic (ROC) curves were generated using greater than or equal to mild PVR and PD, respectively, as classification variables, employing the method of DeLong et al. (28), and the area under the curve (AUC) was calculated. Cutoff values from the ROC analysis with the highest combination of sensitivity and specificity were chosen. Multivariable logistic regression was used to determine independent predictors of greater than or equal to mild PVR and performance of PD.

RESULTS

STUDY POPULATION. The study population included 69 men and 81 women with a mean age of 83.3 ± 8.2 years. The mean calculated aortic valve area and peak velocity were 0.66 ± 0.17 cm² and 4.0 ± 0.7 m/s, respectively. TAVR was performed via the following access points: transfemoral in 125 patients (83%); transaortic in 13 patients (9%); and transapical in 12 patients (8%). The following THV sizes were implanted: 23 mm in 45 patients (30%); 26 mm in 82 patients (55%); and 29 mm in 23 patients (15%). The Sapien THV was implanted in 90 patients (60%) and the Sapien XT in 60 patients (40%). Balloon PD was performed in 37 patients (25%).

MDCT PARAMETERS. The average tube potential setting was 105 ± 10 kV and the average tube current setting was 406 ± 133 mA (data only available for 86 patients). The average volume of contrast used was 49 ± 5 ml.

PARAVALVULAR REGURGITATION. Sixty-nine patients (46%) had PVR at the end of the procedure, and 81 patients (54%) had no PVR. Of those patients with PVR, 9 (6%) had moderate, 19 (13%) had mild, and 41 (27%) had trace regurgitation. No patient had severe PVR. Of the 28 patients (19%) with greater than or equal to mild PVR, 26 were graded by 3-dimensional color

TABLE 2 Calcium Volume Scores (mm³) and Asymmetry in Patients With Greater Than or Equal to Mild PVR Versus Less Than Mild PVR and in PD Versus Non-PD Patients

	PVR No/Trace	PVR \geq Mild	p Value	No PD	PD	p Value
LVOTCa	42 \pm 94	79 \pm 87	0.01	30 \pm 67	104 \pm 135	<0.0001
Δ LVOTCa	30 \pm 69	65 \pm 81	0.013	22 \pm 51	78 \pm 105	<0.0001
AnnulusCa	136 \pm 130	215 \pm 183	0.0007	126 \pm 123	232 \pm 173	0.0001
Δ AnnulusCa	67 \pm 64	125 \pm 101	0.002	63 \pm 58	125 \pm 100	0.0002
AnnulusLVOTCa	158 \pm 164	249 \pm 209	0.006	140 \pm 149	281 \pm 209	<0.0001
Δ AnnulusLVOTCa	79 \pm 87	152 \pm 126	0.002	72 \pm 76	158 \pm 130	<0.0001
LeafletCa	941 \pm 589	1,216 \pm 657	0.026	863 \pm 523	1,386 \pm 689	<0.0001
Δ LeafletCa	276 \pm 209	304 \pm 185	0.243	253 \pm 170	367 \pm 271	0.007

Values are mean \pm SD.

Δ = maximum difference PD = post-dilation; PVR = paravalvular regurgitation; other abbreviations as in Table 1.

Doppler reconstruction, 1 was qualitatively graded by 2-dimensional color Doppler, and 1 was graded by a combination of qualitative color Doppler and quantitative Doppler. Among the 28 patients with greater than or equal to mild PVR, 12 had 1 jet, 15 had 2 jets, and 1 had 3 jets.

AVC DISTRIBUTION. The average luminal MDCT attenuation was 416 \pm 163 HU. The average total volume of calcium (including all regions) was 1,167 \pm 722 mm³. The distribution of calcium by sector was as follows: left (328 \pm 249 mm³); right (332 \pm 261 mm³); and non (458 \pm 292 mm³) coronary

distributions (p < 0.0001 for noncoronary vs. left or right coronary). Table 1 shows calcium scores by sector. Inter- and intraobserver reproducibility was excellent (intraclass correlation coefficient = 0.89 to 0.94) (Online Table 1) for these measurements.

AVC QUANTITY AND ASYMMETRY STRATIFIED BY PVR AND PD. Table 2 compares AVC volume scores and asymmetry for different regions dichotomized by level of PVR and performance of PD. Figure 4 compares volume scores by region using box-and-whisker plots. For all regions, patients with greater than or equal to mild PVR had significantly more calcium

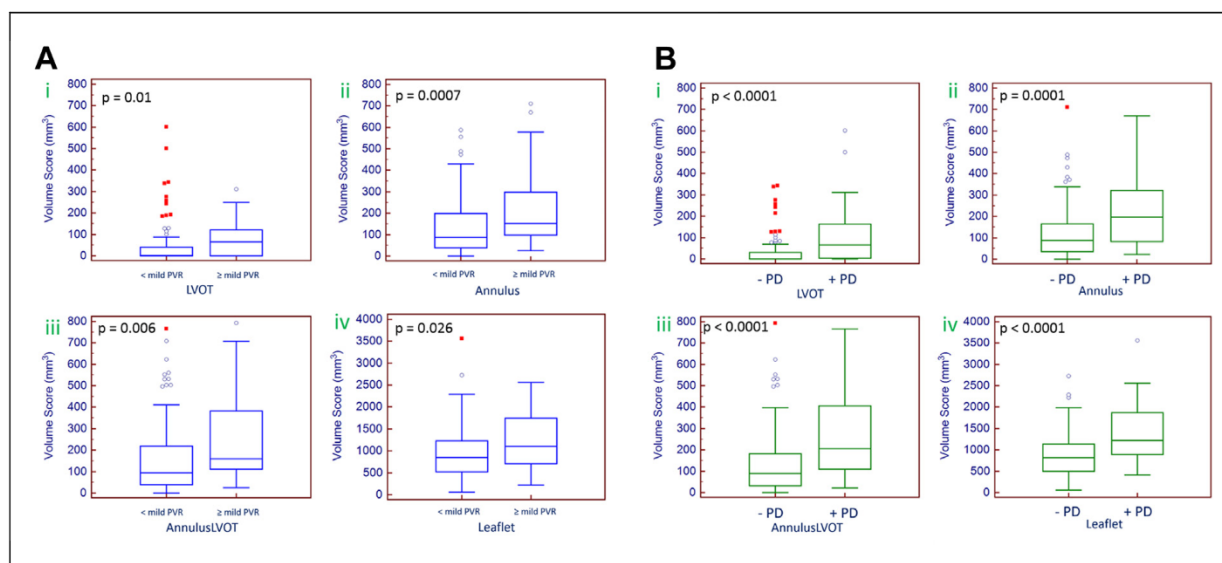
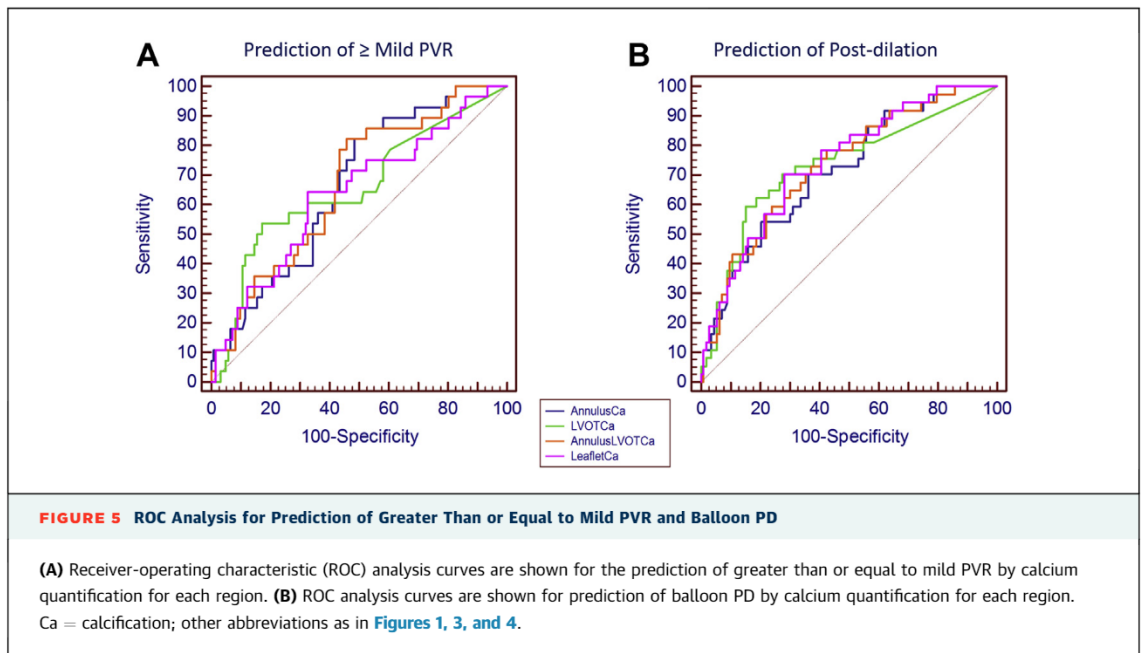


FIGURE 4 Comparison of Calcium Volume Scores Dichotomized by PVR and PD

(A) Volume scores in patients with less than mild PVR and greater than or equal to mild PVR are compared and the associated p values are shown. Panel B compares volume scores in those patients who did not undergo balloon post-dilation (-PD) to those in patients who underwent balloon PD (+PD). For each panel, calcification in the LVOT (i), Annulus (ii), AnnulusLVOT (iii), and Leaflet (iv) locations is compared. Data for 150 patients; 28 patients had greater than or equal to mild PVR and 37 had +PD. Outside (blue or green circles) and far out (red dots) values are also displayed. Abbreviations as in Figures 1 and 3.



than those with less than mild PVR. For all regions, patients who received balloon PD had significantly more calcium than non-PD patients did. Patients with greater than or equal to mild PVR and those who received PD had more asymmetry in all regions, with the exception of Δ Leaflet for PVR ($p = 0.243$).

AVC QUANTITY AND ASYMMETRY PREDICTION OF GREATER THAN OR EQUAL TO MILD PVR AND PD. ROC curves for AVC in predicting PVR are shown in Figure 5A (p is not significant for comparison of ROC curves shown). Table 3 shows AUC values with corresponding cutoffs for calcification and asymmetry in predicting greater than or equal to mild PVR. All ROC analyses were significant for the prediction of greater than or equal to mild PVR with the exception of Δ LeafletCa. ROC curves for AVC in predicting PD are

shown in Figure 5B (p is not significant for comparison of ROC curves shown). Table 4 shows AUC values with corresponding cutoff values for calcification and asymmetry in predicting PD. All ROC analyses were significant for the prediction of PD.

SECTOR WITH HIGHEST CALCIUM LOAD VERSUS LOCATION OF PVR. Among the 28 patients with greater than or equal to mild PVR, 3 had the major jet in a commissure (i.e., could not be attributed to a particular leaflet sector). Among the remaining 25 patients, 14 had the major jet in the left-coronary, 4 in the right-coronary, and 12 in the noncoronary sector. The proportion of PVR jets corresponding with the sector demonstrating the highest level of calcification was 19 of 25 (76%) for AnnulusLVOT and 9 of 25 (36%) for Leaflet ($p = 0.01$).

INDEPENDENT PREDICTORS OF PVR AND PD. Multivariable analysis results are shown in Table 5. AnnulusLVOTCa, LeafletCa, and CT area cover index (with binary cutoffs determined from ROC analysis) were analyzed to determine whether leaflet calcium and calcium at the anchoring zone were independent predictors of PVR and PD when taking relative sizing into account. All were independent predictors of both greater than or equal to mild PVR and PD.

DISCUSSION

The main findings of our study are the following: 1) calcification in all regions of the aortic valve complex predicts greater than or equal to mild PVR

TABLE 3 AVC prediction of Greater Than or Equal to Mild PVR Using ROC Analysis

	AUC	Cutoff (mm ³)	Sensitivity	Specificity	p Value
LVOTCa	0.652	17.6	61	67	0.013
Δ LVOTCa	0.648	17.6	57	67	0.017
AnnulusCa	0.663	107.2	71	57	0.002
Δ AnnulusCa	0.687	19.9	71	64	0.002
AnnulusLVOTCa	0.666	107.2	79	57	0.0019
Δ AnnulusLVOTCa	0.689	69.9	71	62	0.0015
LeafletCa	0.635	988.9	64	67	0.025
Δ LeafletCa	0.571	NS	NS	NS	0.252

AUC = area under the curve; AVC = aortic valve calcification; NS = non-significant; ROC = receiver-operating characteristic; other abbreviations as in Tables 1 and 2.

immediately post-TAVR; 2) calcification of the aortic valve complex predicts the need for PD; 3) LeafletCa and AnnulusLVOTCa are independent predictors of PVR and PD when taking into account CT area cover index.

PARAVALVULAR REGURGITATION. PVR is an important complication of TAVR and is associated with increased mortality (4-8,29). Research focusing on AVC in relation to PVR has yielded mixed results. Several previous papers (9-12,16,30) have shown that AVC predicts PVR. However, another paper (31) has contradicted this. There have been variable data regarding the location of PVR in regard to distribution of calcification (9-11,16). Ewe et al. (9) showed that aortic wall calcification near the annulus was more important than leaflet calcification in predicting PVR. Koos et al. (11) demonstrated that asymmetry of calcium distribution did not predict severity of post-TAVR PVR. Marwan et al. (16) found that commissural calcium did not differ between patients with and without significant PVR. Gripari et al. (32), however, showed that by TEE, commissural calcification was a significant determinant of PVR. More recently, Freuchtner et al. (33) found that protruding calcium (>4 mm) was predictive of PVR following TAVR.

The current study examined both severity of PVR and location of PVR in relation to aortic valve complex calcification. Asymmetry of calcification was also analyzed. Patients with greater than or equal to mild PVR had significantly greater calcification in all regions of the aortic valve complex and more asymmetry in the Annulus and LVOT regions. However, Leaflet asymmetry was not significantly different regardless of severity of PVR. Additionally, when Leaflet asymmetry was analyzed using ROC curves, analysis for greater than or equal to mild PVR was not significant. These findings suggest that asymmetry at the annulus and LVOT anchoring zone is more important than leaflet asymmetry for predicting PVR.

In the current study, a significantly higher proportion of paravalvular regurgitant jets corresponded with the coronary leaflet sector with the highest level of calcification in the AnnulusLVOT anchoring zone as opposed to the Leaflet region (Fig. 6). This correlates with previous findings by Ewe et al. (9) and Haensig et al. (10) that PVR location corresponds to the location of AVC. However, Ewe et al. did not specify the extent of LVOT calcification included in their analysis, and Haensig et al. (10) did not analyze LVOT calcification. The importance of annular and subannular calcification in predicting the location of PVR in the current study supports the

TABLE 4 AVC Prediction of PD Using ROC Analysis

	AUC	Cutoff (mm ³)	Sensitivity	Specificity	p Value
LVOTCa	0.729	17.6	70	73	<0.0001
ΔLVOTCa	0.729	17.6	70	73	<0.0001
AnnulusCa	0.712	118.4	70	64	<0.0001
ΔAnnulusCa	0.707	59.3	68	59	<0.0001
AnnulusLVOTCa	0.732	139.0	70	65	<0.0001
ΔAnnulusLVOTCa	0.734	80.6	68	67	<0.0001
LeafletCa	0.741	988.9	70	72	<0.0001
ΔLeafletCa	0.648	255.4	68	60	<0.0001

Abbreviations as in Tables 1 to 4.

theory that malapposition of the THV stent at the annulus/LVOT region is responsible for PVR.

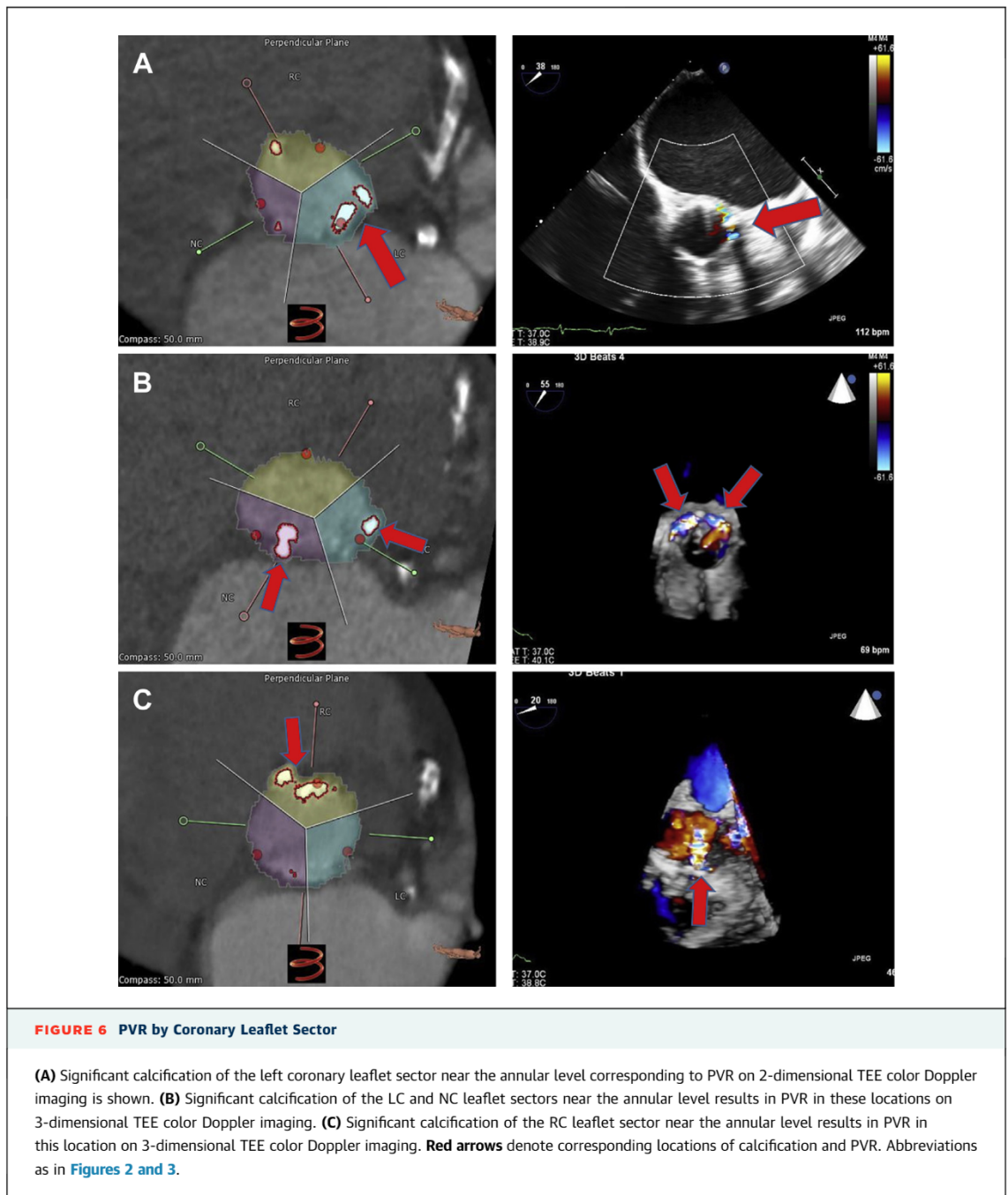
BALLOON POST-DILATION. There have been limited data regarding the predictive factors for PD after THV deployment. PD is an important surrogate for PVR, as it is only performed if significant PVR is seen after the THV implantation. Schultz et al. (34) and John et al. (30) demonstrated that AVC was related to the need for PD of the self-expanding THV. Nombelo-Franco et al. (35) found that more calcification predicted grade 2 or higher PVR which did not respond to PD after balloon-expandable TAVR. However, neither study included the LVOT nor were the annulus and leaflets analyzed separately. In the current study, absolute calcium volume and degree of asymmetry were higher in patients on whom PD was performed. ROC analysis was significant for all regions for calcium volume and asymmetry. The AUC values for PD were generally higher than for prediction of PVR at the conclusion of the procedure. In a separate ROC analysis that included patients in whom PD was performed and those in whom PD was not performed but had greater than or equal to mild PVR post-TAVR, AUC was not as high as for prediction of PD alone. These findings suggest that PD may mitigate some of the effects of AVC in causing PVR.

TABLE 5 Multivariate Predictors of Greater Than or Equal to Mild PVR and PD

	Univariate OR*	p Value	Multivariate OR	p Value
≥ Mild PVR, n = 28				
AnnulusLVOTCa ≥107.2 mm ³	4.8 (1.8-12.6)	0.0016	3.5 (1.2-9.8)	0.019
LeafletCa ≥988.9 mm ³	3.57 (1.51-8.40)	0.004	2.6 (1.0-6.7)	0.045
CTAreaCI ≤10.7%	4.02 (1.67-9.66)	0.0019	4.1 (1.6-10.2)	0.003
PD, n = 37				
AnnulusLVOTCa ≥139.0 mm ³	4.3 (1.9-9.6)	0.0004	3.2 (1.3-7.9)	0.012
LeafletCa ≥988.9 mm ³	5.73 (2.54-12.9)	<0.0001	4.7 (1.9-11.5)	0.0008
CTAreaCI ≤9.2%	3.71 (1.71-8.05)	0.0009	3.2 (1.3-7.8)	0.0009

*Odds ratios are presented with 95% confidence intervals.

CTAreaCI = area cover index by multidetector row computed tomography; OR = odds ratio; other abbreviations as in Tables 1 and 2.



INDEPENDENT PREDICTORS. Importantly, LeafletCa and AnnulusLVOTCa were independent predictors for greater than or equal to mild PVR and PD when taking into account area cover index by MDCT. It appears likely that calcification in the annulus and LVOT are important factors in the outcomes of PVR and PD; however, the finding that LeafletCa is an independent predictor for these outcomes when taking into account AnnulusLVOTCa and relative THV-to-

annulus sizing suggests that perhaps overall LeafletCa contributes to other factors (such as inaccurate stent positioning, noncoaxiality, and incomplete deployment), which may lead to THV stent malapposition and PVR. Further study is needed in this regard. Regardless of balloon-expandable THV sizing relative to annulus size, calcification appears to play an important role in post-procedural PVR and the need for balloon PD.

STUDY LIMITATIONS. PVR in the right-coronary sector may be underestimated on TEE due to acoustic shadowing from more posterior structures. Given the limited number of patients with greater than or equal to moderate PVR in our cohort, we were not able to use this as a primary outcome. The HU cutoffs for calcium assessment on contrast MDCT have not been well-established and attenuation can vary significantly across scans. We attempted to mitigate this by meticulous verification of calcium detection and adjustment of HU cutoffs. Commissural calcium was not analyzed separately. The multivariable analyses were limited given the relatively limited numbers of events. As meta-analyses have suggested, there is likely an interplay of multiple factors leading to PVR, including implantation depth, coaxiality, positioning, and valve type (balloon-expandable vs. self-expanding), of which all were not studied in this analysis (4). The current study was performed only on patients who underwent TAVR with balloon-expandable devices.

CONCLUSIONS

Calcification of all regions of the aortic valve complex predicted greater than or equal to mild PVR at the end of the TAVR procedure and also predicted the need for PD. Asymmetry of the annulus and LVOT may be more important than that of the leaflets for predicting PVR and the need for PD post-TAVR. PD may lower the impact of calcification in causing PVR. The location of PVR corresponds more closely with heavily calcified annulus and LVOT locations than with heavily calcified leaflet locations. LeafletCa and AnnulusLVOTCa were independent predictors of greater than or equal to mild PVR and PD when factoring in MDCT annulus area cover index.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Susheel K. Kodali, Columbia University Medical Center/New York-Presbyterian Hospital, 177 Fort Washington Avenue, New York, New York 10032. E-mail: skodali@columbia.edu.

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KEY WORDS aortic regurgitation, aortic stenosis, calcification, multidetector computed tomography, transcatheter aortic valve replacement

APPENDIX For the supplemental table, please see the online version of this article.