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Original Article

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Calcium Distribution Patterns of the Aorta as Predictors of Significant Coronary Artery Disease in Patients with Moderate to Severe Aortic Stenosis

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ABSTRACT

OBJECTIVE Computed tomography (CT) of the aortic valve and aorta has gained a greater role in planning for aortic valve replacement (AVR). However, when AVR is planned, invasive coronary angiography remains the standard investigation. Whether the calcium distribution pattern in the aorta predicts the significant presence of coronary artery disease (CAD) in patients undergoing AVR remains unclear. This study evaluated the correlation between the calcium distribution pattern from the CT aorta to predict significant CAD in patients with symptomatic moderate to severe aortic stenosis undergoing AVR.

METHODS This retrospective study included candidates for AVR either with transcatheter replacement (TAVR) or surgical replacement (SAVR) at a single tertiary-care center between 2017 and 2022. The calcium distribution patterns from the left ventricular outflow tract up to the descending aorta were analyzed from the non-contrast CT of the aorta. Significant CAD was identified from invasive coronary angiography and was defined as 50% diameter stenosis (DS) of the left main and 70% DS of the proximal left anterior descending artery. Multivariate logistic regression analysis was performed to identify the calcification pattern associated with the significant CAD.

RESULTS In total, 110 patients were included in the analysis. Among them, 40 patients (36.4%) were candidates for TAVR, while 70 patients (63.6%) were candidates for SAVR. The prevalence of significant CAD was 12.7%. Baseline characteristics were similar between patients with and without CAD, with the exception of a higher prevalence of chronic kidney disease in the CAD group (42.9% vs. 19.8%, $p = 0.01$). The presence of calcium at the ostium of the coronary artery and descending aorta was an independent predictor of significant CAD (OR 3.44, 95% CI1.30-9.10, $p = 0.01$ and OR 12.03, 95% CI 1.14-126.84, $p = 0.04$).

CONCLUSIONS This pilot study showed that calcium at the ostium of the coronary artery and descending aorta from non-contrast CT aorta was associated with significant CAD in patients with moderate to severe AS. Further study with more subjects be needed to confirm the findings.

KEYWORDS calcium distributions; aortic stenosis; coronary artery disease; computed coronary angiography

INTRODUCTION

Computed tomography (CT) of the aortic valve and aorta has increasingly played a significant role in planning for aortic valve interventions. The aortic valve calcification load from CT can aid in determining the severity of aortic valve stenosis (1) and serve as a prognostic factor for survival (2) and complications related to the procedure (3, 4), especially for transcatheter aortic valve replacement (TAVR).

Presently, a dedicated CT protocol is mandatory for patients with aortic stenosis who are candidates for TAVR (5, 6). The main purpose of CT angiography for TAVR planning is to evaluate the aortic valve, annulus, vascular access routes and any potential obstacles that could affect the procedure (6, 7). It appears that CT is not limited to TAVR planning: for modern minimally invasive aortic valve surgery, CT of the aorta is also important in planning the procedure (8). The complex anatomy is associated with prolonged operation times (8).

In addition to concern about aortic valve disease, coronary artery disease (CAD) is also one of the comorbidities that influence the treatment plan. The severity of CAD can change the approach from surgical aortic valve replacement (SAVR) to TAVR or vice versa, depending on the surgical risk (6). The prevalence of CAD in patients who underwent TAVR ranged from 30.0% to 74.9% (9, 10), whereas in patients who underwent SAVR, it ranged from 48.9% to 52.2% (11, 12). According to the 2021 ESC/EACTS Guidelines for the management of valvular heart disease, invasive coronary angiography (ICA) remains the standard investigation when aortic valve intervention is planned (6).

Concerning the fact that ICA can be costly and carries the risk of complications, there have been attempts to optimize the use of data obtained from the CT. Recently, Kondoleon and colleagues performed coronary reconstruction from the computed tomography angiography (CTA) for TAVR planning and reported that CTA could reduce the need for ICA in 51.8% of patients (13). This finding could be explained by the high negative predictive values of the CTA, which were up to 97-99% (13).

Despite the positive data supporting CTA for TAVR planning in evaluating CAD, clinical guidelines limit the use of CTA to patients who are at low risk of atherosclerosis (6). Additionally, the presence of heavy calcification of the coronary trees hampers the diagnostic accuracy of CTA (14). Our hypothesis posited that the distribution of calcium along the aorta could serve as a predictor for the presence of significant proximal CAD. In the current study, we sought to maximize the use of CT data irrespective of the procedural plan, image protocol and atherosclerotic risk in identifying patients with significant CAD before undergoing aortic intervention.

METHODS

Study design and study population

This retrospective pilot study included patients with moderate to severe aortic stenosis (defined as a mean gradient ≥ 20 mmHg, peak aortic jet velocity (Vmax) ≥ 3 m/s, or aortic valve area (AVA) ≤ 1.5 cm^2) (6) who had indications of aortic valve intervention. We excluded patients with a history of coronary artery bypass graft (CABG) and those with a history of percutaneous coronary intervention (PCI) performed more than 2 years prior. Data was collected from January 2017 to January 2022 at Maharaj Nakorn Chiang Mai Hospital. The study was granted an ethics exemption by the Institutional Review Board (study number: MED-2565-08783). Informed consent was waived as the data collection was retrospective and without patient identifiers.

CT acquisition protocol

All patients were scanned using a third-generation dual source CT scanner (SOMATOM Force, Siemens AG, Munich, Germany). A non-contrast prospective ECG-gating transaxial scan of the heart between the level of the tracheal carina and the diaphragm was performed using ultra-high-pitch spiral acquisition with a tube voltage of 120 kV and adaptive tube current. The images were reconstructed using a standard filtered-back projection algorithm with 3.0-mm slice thickness and 2.5-mm slice increment. The acquisition was from the bottom of the valve to the level of the sinotubular junction and the thoracic aorta. These regions were determined 2-dimensionally using data sets on a Syngovia workstation.

CT calcium distribution analysis

The calcium distribution patterns were analyzed offline by two interventional cardiologists (T.T. and S.D.) using the hospital picture archiving and communication system (PACS) system. Figure 1 illustrates the aortic segments being evaluated. The calcification pattern was visually assessed in five zones from the left ventricular outflow to the descending aorta as follows: zone i) left ventricular outflow, zone ii) aortic annulus to junction, zone iii) coronary ostium and ascending aorta, zone iv) aortic arch, and zone v) descending aorta. The definition of each segment of the aorta follows the aortic segmentation according to the 2022 ACC/AHA Guideline for the Diagnosis and Management of Aortic Disease (15). The presence of calcium in the aortic segments of each patient was recorded as presence or absence. There was no volumetric analysis of the calcification due to the lack of a valid method for assessing calcium at the aortic wall. All calcified plaques were identified by visual estimation. The analysts were blinded to the results of the ICA study.

Invasive coronary angiography

All patients included in the analysis underwent ICA before aortic valve intervention. The procedures were performed using 5 French diagnostic catheters with standard techniques and projection planes. The severity of stenosis was gauged by visual estimation by experienced interventional cardiologists in multiple views. Significant CAD was defined as diameter stenosis ≥ 50% for the left main coronary artery and ≥ 70% of the proximal left anterior descending artery (LAD) (16).

Statistical analysis

Descriptive analysis results are presented as frequency and percentage for qualitative data, and as mean plus standard deviation (SD) for quantitative data. For comparative analysis, Fisher's exact and Chi-square tests were used to compare discrete data, while Student's T-test was used to compare normally distributed continuous data.

The association between the calcium distribution pattern and significant left main and proximal LAD stenosis was analyzed using univariate and multivariate logistic regression analysis. The correlation is presented as an adjusted odds ratio and 95% confidence interval. Statistical analyses were performed with IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). A two-sided $p < 0.05$ was considered to indicate statistical significance.

RESULTS

Baseline characteristics

From January 1, 2017 through January 31, 2022, 179 patients were scheduled for aortic valve intervention and underwent ICA. Of these, 69 patients (38.5%) were excluded from the analysis due to incomplete data. Among the remaining patients, 96 (87.3%) did not have significant CAD, while 14 (12.7%) did have significant CAD. The baseline characteristics of the patients with and without significant CAD are summarized in Table 1. The baseline characteristics were not different between the two groups, with the exception that the CAD group had a higher prevalence of chronic kidney disease compared to the non-CAD group (42.9% vs. 19.8%, $p = 0.01$). In addition, mitral regurgitation was significantly more common in patients without CAD than those with CAD, with rates of 56.1% and 28.5%, respectively ($p = 0.01$). Mean aortic valve gradient was also significantly greater in patients without CAD compared to those with CAD. (53.4±22.1 vs. 38.5±14.0 mmHg, $p = 0.02$). (Table 2)

Calcium distribution pattern and predictors of significant CAD

The univariate and multivariate analysis of the calcium distribution patterns and the significant presence of CAD in the left main and proximal coronary arteries is shown in Table 3. A notable

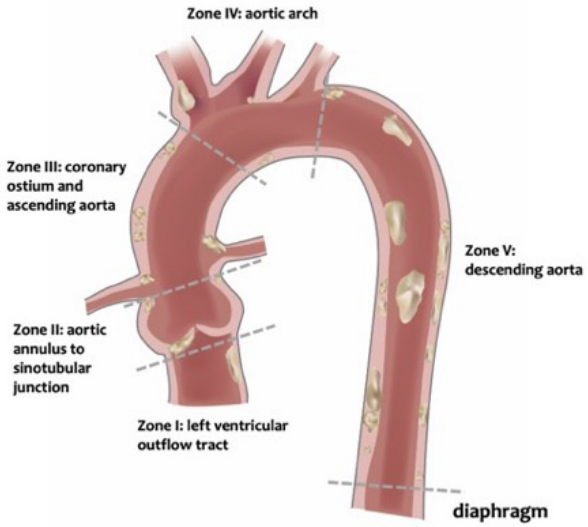

Figure 1. Assessment of the calcification pattern in the aorta

Table 1. Baseline characteristics of patients with and without CAD

Baseline characteristics	Without CAD (N=96)	CAD (n=14)	*p*-value
Age, years	71.7±9.5	71.2±14.9	0.92
Men, n (%)	49 (51.0)	8 (57.1)	0.45
Body mass index, kg/m^2	23.6±3.7	24.8±4.5	0.38
NYHA functional class, n (%)			0.29
Class I	7 (10.3)	0 (0.0)	
Class II	45 (66.2)	5 (55.6)	
Class III	13 (19.1)	4 (44.4)	
Class IV	3 (4.4)	0 (0.0	
Underlying diseases, n (%)			
Hypertension	58 (60.4)	10 (71.4)	0.56
Diabetes mellitus	28 (29.2)	7 (50.0)	0.13
Dyslipidemia	45 (46.9)	8 (57.1)	0.57
Atrial fibrillation	16 (16.7)	2 (14.3)	1.00
Cerebrovascular accident	5 (5.2)	2 (14.3)	0.22
History of heart failure	39 (40.6)	5 (35.7)	0.78
Chronic lung disease	9 (9.4)	1 (7.1)	1.00
Liver disease	2 (2.1)	0 (0.0)	1.00
Carotid artery stenosis	1 (1.0)	0 (0.0)	1.00
Chronic kidney disease			0.01
Without dialysis	10 (10.4)	6 (42.9)	
With dialysis	9 (9.4)	0 (0.0)	
Labs and Investigations			
Baseline hemoglobin, g/dL	11.9±1.9	11.9±2.7	0.94
Baseline serum creatinine, mg/dL	1.6±1.9	1.3±0.5	0.58
Baseline eGFR (CKD-EPI)	62.3±26.7	57.9±25.9	0.58
Electrocardiography			
Baseline PR interval, ms	177.8±34.7	168.2±40.1	0.45
Baseline QRS duration, ms	99.0±19.1	95.2±17.4	0.58

Data are shown as n (%) or mean±SD

CAD, coronary artery disease; CKD-EPI, CKD epidemiology collaboration; eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association, QRS duration, the time it takes for an electrical impulse to travel through the ventricles of the heart; PR interval, the period, measured in milliseconds, that extends from the beginning of the P wave until the beginning of the QRS complex

association with significant CAD was observed for calcium located at the ostial of the coronary artery (odds ratio [OR] 4.17, 95% confidence interval [CI] 1.73-10.05, $p = 0.002$) and the descending aorta (OR 11.23, 95% CI 1.40-90.38, $p = 0.01$). Calcium distribution at the origin of the coronary artery and in the descending aorta remained significantly associated with significant CAD in multivariate regression analysis (OR 3.44, 95% CI 1.30-9.10, $p = 0.01$, and OR 12.03, 95% CI 1.14-126.84, $p = 0.04$, respectively).

Comparison of characteristics of patients undergoing TAVR and SAVR

We further explored the differences in baseline characteristics between patients undergoing TAVR and those undergoing SAVR. There were 40 (36.4%) eligible candidates for TAVR and 70 (63.6%) suitable candidates for SAVR. Patients scheduled for TAVR were older than those scheduled for SAVR (79.4±6.4 years and 67.1±9.4 years, respectively, $p < 0.01$). Additionally, patients scheduled for TAVR had a higher incidence of co-morbidities than those with SAVR (Table 4).

The echocardiographic findings are shown in Table 5. The left ventricular ejection fraction (LVEF) in the TAVR group was significantly lower than that in the SAVR group (51.6±18.9% vs. 61.4±14.3%, $p = 0.01$). Remarkably, there was a distinct difference in the morphology of the aortic valve between the two groups. Trileaflet aortic valve were commonly observed in patients scheduled for TAVR (TAVR 80.0% vs. SAVR 48.6%), while bicuspid leaflets were more frequently seen in patients scheduled for SAVR (TAVR 20.0% vs. SAVR 51.4%). However, other valve pathology did not differ between the two groups of patients.

Table 2. Echocardiographic findings in patients with and without CAD

Baseline characteristics	Without CAD (n=96)	CAD (n=14)	*p*-value
Left ventricular ejection fraction (%)	57.9±16.5	56.8±19.1	0.84
Aortic valve disease etiology, n (%)			1.00
Degenerative	95 (99.0)	14 (100.0)	
Rheumatic	1 (1.0)	0 (0.0)	
Aortic valve morphology, n (%)			0.78
Trileaflet	57 (59.4)	9 (64.3)	
Bileaflet	39 (40.6)	5 (35.7)	
Aortic stenosis severity, n (%)			0.17
Moderate	4 (4.2)	2 (14.3)	
Severe	92 (95.8)	12 (85.7)	
Aortic regurgitation severity, n (%)			0.39
No	46 (47.9)	10 (71.4)	
Mild	29 (30.2)	3 (21.4)	
Moderate	19 (19.8)	1 (7.1)	
Severe	2 (2.1)	0 (0.0)	
Mitral stenosis severity, n (%)			0.52
No	93 (96.9)	13 (92.9)	
Mild	2 (2.1)	1 (7.1)	
Moderate	1 (1.0)	0 (0.0)	
Mitral regurgitation severity, n (%)			0.01
No	44 (45.8)	10 (71.4)	
Mild	32 (33.3)	2 (14.3)	
Moderate	20 (20.8)	1 (7.1)	
Severe	0 (0.0)	1 (7.1)	
Tricuspid regurgitation severity, n (%)			0.93
No	48 (50.0)	8 (57.1)	
Mild	29 (30.2)	3 (21.4)	
Moderate	13 (13.5)	2 (14.3)	
Severe	6 (6.3)	1 (7.1)	
Aortic valve area, cm^2	0.67±0.3	0.66±0.3	0.95
Mean aortic valve gradient, mmHg	53.4±22.1	38.5±14.0	0.02
Aortic valve peak velocity, m/s	4.5±0.8	4.0±0.9	0.13

Data are shown as n (%) or mean±SD
CAD, coronary artery disease

Table 3. Univariate and multivariate regression analysis of the calcium distribution pattern of predictors of significant coronary artery disease in the left main and proximal arteries

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Calcium in left ventricular outflow tract	1.44	0.45-4.60	0.570	1.79	0.44-7.35	0.420
Calcium in aortic valve annulus	-	-	0.460	-	-	-
Calcium in ostial of coronary artery	4.17	1.73-10.05	0.002	3.44	1.30-9.10	0.010
Calcium in sinus of valsalva	3.02	0.87-10.49	0.080	2.64	0.62-11.22	0.190
Calcium of sinotubular junction	0.81	0.37-1.77	0.690	0.41	0.15-1.09	0.070
Calcium in ascending aorta	1.80	0.83-3.90	0.170	1.63	0.65-4.04	0.300
Calcium in aortic arch	3.20	0.83-12.34	0.140	0.92	0.18-4.80	0.920
Calcium in descending aorta	11.23	1.40-90.38	0.010	12.03	1.14-126.84	0.040

CI, confidence interval; OR, odd ratio

Table 4. Baseline characteristics of patients undergoing TAVR and SAVR

Baseline characteristics	TAVR (n=40)	SAVR (n=70)	*p*-value
Age, years	79.4±6.4	67.1±9.4	< 0.010
Men	20 (50.0)	37 (52.9)	0.770
Body mass index, kg/m^2	23.2±4.4	24.0±3.4	0.320
NYHA functional class, n (%)			0.010
Class I	1 (3.0)	6 (13.6)	
Class II	18 (54.5)	32 (72.7)	
Class III	11 (33.3)	6 (13.6)	
Class IV	3 (9.1)	0 (0.0)	
Underlying diseases, n (%)			
Hypertension	26 (65.0)	42 (60.0)	0.600
Diabetes mellitus	14 (35.0)	21 (30.0)	0.590
Dyslipidemia	20 (50.0)	33 (47.1)	0.770
Coronary artery disease	10 (25.0)	0 (0.0)	< 0.010
Atrial fibrillation	8 (20.0)	10 (14.3)	0.440
Cerebrovascular accident	6 (15.0)	1 (1.4)	0.010
History of heart failure	27 (67.5)	17 (24.3)	< 0.010
Chronic lung disease	7 (17.5)	3 (4.3)	0.020
Liver disease	0 (0.0)	2 (2.9)	0.280
Carotid artery stenosis	1 (2.5)	0 (0.0)	0.180
Chronic kidney disease			0.010
Without dialysis	11 (27.5)	5 (7.1)	
With dialysis	4 (10.0)	5 (7.1)	
Labs and Investigations			
Baseline hemoglobin, g/dL	11.3±2.2	12.3±1.8	0.030
Baseline serum creatinine, mg/dL	1.8±1.7	1.5±1.8	0.370
Baseline eGFR (CKD-EPI)	50.8±25.4	68.4±25.1	0.001
Electrocardiography			
Baseline PR interval, ms	179.5±41.3	174.4±30.9	0.540
Baseline QRS duration, ms	99.5±20.3	98.0±18.0	0.710

Data shows n (%) or mean±SD

CKD-EPI, CKD Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association; TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement

Table 6 shows angiographic characteristics of TAVR and SAVR candidates. There were no significant differences in the number of diseased vessels, left main stenosis ≥ 50%, or proximal LAD artery stenosis ≥ 70% between the two groups. Overall, significant CAD was observed in 14 patients (12.7%). One-half of the patients in the TAVR group had significant CAD that required PCI, which was performed before TAVR in 6 patients and at the index TAVR procedure in 5 patients. Among SAVR patients, 27.5% received coronary artery bypass graft surgery in the index procedure.

Table 7 summarizes the findings of CT angiography of the aorta between the two groups. The parameters of the aortic valve annulus were well matched. The aortic valve calcium score in the SAVR group was significantly higher than that observed in the TAVR group (2,878.4±1,626.7 vs. 3,908.7±2,145.2, p = 0.04). The TAVR group had significantly higher rates of calcification than the SAVR group in almost every aortic zone, except the left ventricular outflow tract zone which was comparable between the two groups.

DISCUSSION

This study focuses on examining the correlation between calcium distribution in the adjacent areas of the aortic valve and the aorta in patients with moderate to severe aortic valve stenosis who are candidates for aortic valve implantation or replacement to determine the incidence of significant CAD. To our knowledge, the present study is the first report that illustrates a correlation between calcium distribution patterns from non-contrast CT and the presence of

Table 5. Echocardiographic findings in patients undergoing TAVR and SAVR

Baseline characteristics	TAVR (n=40)	SAVR (n=70)	*p*-value
Left ventricular ejection fraction (%)	51.6±18.9	61.4±14.3	0.010
Aortic valve disease etiology, n (%)			1.000
Degenerative	40 (100.0)	69 (98.6)	
Rheumatic	0 (0.0)	1 (1.4)	
Aortic valve morphology, n (%)			0.001
Trileaflet	32 (80.0)	34 (48.6)	
Bileaflet	8 (20.0)	36 (51.4)	
Aortic stenosis severity, n (%)			1.000
Moderate	2 (5.0)	4 (5.7)	
Severe	38 (95.0)	66 (94.3)	
Aortic regurgitation severity, n (%)			0.700
No	20 (50.0)	36 (51.4)	
Mild	13 (32.5)	19 (27.1)	
Moderate	7 (17.5)	13 (18.6)	
Severe	0 (0.0)	2 (2.9)	
Mitral stenosis severity, n (%)			0.740
No	39 (97.5)	67 (95.7)	
Mild	1 (2.5)	2 (2.9)	
Moderate	0 (0.0)	1 (1.4)	
Mitral regurgitation severity, n (%)			0.700
No	14 (35.0)	40 (57.1)	
Mild	17 (42.5)	17 (24.3)	
Moderate	8 (20.0)	13 (18.6)	
Severe	1 (2.5)	0 (0.0)	
Tricuspid regurgitation severity, n (%)			0.080
No	15 (37.5)	41 (58.6)	
Mild	13 (32.5)	19 (27.1)	
Moderate	7 (17.5)	8 (11.4)	
Severe	5 (12.5)	2 (2.9)	
Aortic valve area, cm^2	0.68±0.30	0.66±0.25	0.680
Mean aortic valve gradient, mmHg	44.3±20.5	55.9±21.4	0.010
Aortic valve peak velocity, m/s	4.0±0.9	4.6±0.8	0.010

Data shows is n (%) or mean±SD

TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement

significant CAD in moderate to severe aortic stenosis (AS) patients who underwent aortic valve (AV) interventions. Many previous studies have explored the usefulness of CT aorta in identifying significant CAD. However, it should be noted that those studies focused on the comparison between CT angiography for TAVR planning or CT coronary angiography in detecting significant CAD from ICA (13). The present analysis was conducted using the non-contrast phase CT to simplify the method. This approach made it easier to evaluate for both interventional cardiologists and cardiothoracic surgery (CVT) surgeons, especially considering that not every center has dedicated software for CT analysis.

The proportion of significant CAD in the present study was found to be 12.7%, which is similar to the previously reported rate of 11.4% (13). However, it is important to note that the previous report conducted a lesion-level analysis, whereas the present study used a patient-level analysis. Additionally, the definition of significant CAD varies across studies, e.g., encompassing criteria such as all proximal segments of epicardial arteries with 70% stenosis or 50% stenosis of the left main (13), or including only proximal LAD and left main stenosis of 70% and 50%. As a result, direct comparisons of results among the trials may be challenging.

Table 6. Angiographic findings of patients undergoing TAVR and SAVR

	Total (n=110)	TAVR (n=40)	SAVR (n=70)	*p*-value
Number of diseased vessels				0.420
Not significant	61 (55.5)	19 (47.5)	42 (60.0)	
1	18 (16.4)	8 (20.0)	10 (14.3)	
2	13 (11.8)	4 (10.0)	9 (12.9)	
3	18 (16.4)	9 (22.5)	9 (12.9)	
LM stenosis ≥ 50%	5 (4.6)	1 (2.6)	4 (5.7)	0.650
Proximal LAD stenosis ≥ 70%	10 (9.1)	4 (10.0)	6 (8.6)	1.000
Significant CAD*	14 (12.7)	5 (12.5)	9 (12.9)	1.000
Location of diseased vessel				
LAD	42 (38.2)	19 (47.5)	23 (32.9)	0.160
Proximal LAD ≥ 70%	10 (9.1)	6 (10.0)	6 (8.6)	
LCX	24 (21.8)	12 (30.0)	12 (17.1)	0.150
Proximal LCX ≥ 70%	7 (6.4)	4 (10.0)	3 (4.3)	
RCA	31 (28.2)	12 (30.0)	19 (27.1)	0.830
Proximal RCA ≥ 70%	7 (6.4)	2 (5.0)	5 (7.1)	
Any LM disease or proximal coronary artery disease	22 (20.0)	8 (20.0)	14 (20.0)	1.000
Revascularization				
PCI	11 (10.1)	10 (25.0)	1 (1.4)	<0.001
CABG	19 (17.4)	0 (0.0)	19 (27.5)	<0.001

Data shows is n (%) or mean±SD

*significant CAD defined as left main diameter stenosis ≥ 50% and proximal LAD stenosis ≥ 70%

CABG, coronary artery bypass graft surgery; CAD, coronary artery disease; LAD, left anterior descending; LCX, left circumflex; LM, left main; PCI, percutaneous coronary intervention; RCA, right coronary artery TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement

Table 7. Computed tomography angiography of aorta and calcification pattern in patients undergoing TAVR and SAVR

	TAVR (n=40)	SAVR (n=70)	*p*-value
Aortic valve size	27.3±3.8	27.8±3.2	0.530
Maximum aortic valve annulus diameter, mm	20.9±2.9	21.7±3.0	0.370
Minimum aortic valve annulus diameter, mm	4.4±1.1	3.9±0.5	0.490
Aortic valve annulus area, cm^2	76.8±10.5	78.6±7.0	0.500
Aortic valve annulus perimeter, mm	2,878.4±1,626.7	3,908.7±2,145.2	0.040
Aortic valve calcium score*	2,019.6±1,816.4	2,001.8±2,783.1	0.980
Coronary calcium score**			
Calcium distribution pattern			
Zone i) LVOT	3 (7.5)	10 (14.3)	0.368
Zone ii) aortic annulus to STJ	22 (55.0)	18 (25.7)	0.004*
Zone iii) coronary ostium/ascending aorta	24 (60.0)	21 (30.0)	0.003*
Zone iv) aortic arch	39 (97.5)	58 (82.9)	0.029*
Zone v) descending aorta	40 (100.0)	58 (82.9)	0.004*

Data shows is n (%) or mean±SD, *aortic valve calcium score was assessed in 31 (77.5%) and 32 (45.0%) patients in the TAVR and SAVR, respectively, **coronary calcium score was assessed in 13 (32.5%) and 22 (31.4%) patients in the TAVR and SAVR, respectively.

LVOT, left ventricular outflow tract; TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; STJ, sinotubular junction

In the current study, patients with bicuspid aortic valves constituted 32.7% of the overall population, and the majority (81.0%) underwent SAVR. The high proportion of SAVR in bicuspid AS patients can be explained by their age at presentation. Wanchaitanawong et al. reported that patients with bicuspid AS had higher AV calcium scores than those with degenerative AS (17). This

could explain why in the present study the mean AV score of patients who underwent SAVR was higher than that of the TAVR group.

We excluded patients who underwent PCI for more than 2 years as we wanted to ensure that the major cause of dyspnea leading to AV intervention was primarily AS rather than concomitant obstructive CAD. Including patients who had already undergone revascularization could reflect that their symptoms were primarily the consequence of AS.

In the present analysis, calcium at the coronary ostium and descending aorta were the predictors of significant CAD. These findings are in line with the report by Kälsch and colleagues (18) that observed a correlation between descending aorta calcification and coronary calcium score. On the contrary, Wong (19) and colleagues reported that calcification in the thoracic aorta was not found to correlate with the coronary calcium score or the presence of coronary heart disease in asymptomatic patients.

The association between the presence of calcification in the descending aorta and significant CAD may be attributable to differences in the tissue composition between the descending and ascending aorta. The wall thickness of the thoracic aorta is generally less than that of the ascending aorta. Furthermore, the ascending aorta contains a higher proportion of collagen and elastin compared to the descending aorta. Additionally, the smooth muscle cells (SMCs) in the ascending aorta originate from the ectoderm, while those in the descending aorta originate from the mesoderm. This is similar to the origin of SMCs in the coronary artery which stem from the proepicardium and are also derived from the mesoderm. It has also been reported that the elastin fiber in the descending aorta has the same compontents as the aortic valve. This elastin plays a role in generating sclerosis leading to AS, calcium deposition in the descending aorta and in CAD (20-23).

In previous studies, AV calcium scores have been reported to be associated with the prevalence and extent of obstructive CAD as assessed by CT coronary angiography (24). However, we did not include the aortic valve calcium score or the coronary artery calcium score in the regression analysis due to missing data on the non-systematic assessment of both scores in the study population.

According to our findings, non-contrast CT of the aorta is associated with significant CAD and therefore could be used as screening tool for patients who are appropriate candidates for invasive coronary angiogram. The implementation of a strategy based on CT of the aorta may enable the avoidance of ICA in a significant subset of patients undergoing aortic valve interventions.

Recent cumulative data has shown that performing PCI either in the same session as or after transcatheter aortic valve implantation is better than performing it before transcatheter aortic valve implantation. Pre-TAVR PCI is associated with risks of contrast-induced nephropathy, bleeding, and stroke. No evidence supports that pre-TAVR PCI provides more clinical benefit than post-TAVR PCI (25, 26). Moreover, PCI after TAVR was associated with improved 2-year clinical outcomes compared with before or index TAVR procedures (27). Thus, there is no requirement to admit the patient for the diagnosis or treatment of CAD before TAVR. Notably, that statement does not align with the current guideline recommendation (6). The findings of the present study can guide physicians when patients with severe AS are in an unstable condition that is not suitable for CT angiography and ICA, but who require emergency TAVR. These findings can shorten the waiting time for the procedure, as the ICA can be done during the TAVR procedure.

This study encountered several limitations. Primarily, the absence of a standardized protocol for conducting CTA of the aorta in all patients scheduled for SAVR led to the exclusion of nearly 50 patients from the SAVR group due to ineligibility based on the inclusion criteria. Addressing and accounting for this limitation should be considered in future research endeavors. In the present analysis, we did not demonstrate a correlation between the degree of calcification and the severity of coronary stenosis as the volumetric analysis of calcium in the aortic wall was not performed. This limitation was due to the lack of a valid method and the requirement for dedicated software for calculating the calcium aortic wall score. Such software is expensive and requires trained physicians to perform the analysis, which means it is often not feasible in real practice since not all centers can acquire such a product. Future multicenter studies with larger numbers of participants dedicated exclusively to TAVR candidates, sys-

tematic assessment of AV calcium scores, coronary calcium scores and, calcium distribution patterns would help to confirm the study findings. Additionally, the long-term clinical outcomes and calcium distribution patterns should be further explored.

CONCLUSION

The study identified an association between significant CAD and calcium at the ostial of the coronary and descending aorta as revealed by non-contrast CT of the aorta. The calcification pattern may assist in identifying patients with a heightened likelihood of CAD, especially TAVR candidates. Further studies are needed prior to endorsing the use of CT data in evaluating CAD in patients with moderate to severe AS undergoing aortic valve intervention.

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CONFLICTS OF INTEREST

All the authors declare that they have no conflict of interests.

ADDITIONAL INFORMATION

Authors' contributions

T.T.: provided substantial contributions to the conception or design of the work, performed data collection and statistical analysis, prepared the manuscript and tables; S.D.: performed data collection, statistical analysis and prepared tables. PS interpreted the data and drafted the manuscript; S.K.: critically revised the data and manuscript for important intellectual content and the acquisition, analysis, and interpretation of the data. All authors agreed to be accountable for all aspects of the work and in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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