Association of Thoracic Aorta Calcium Score With Left Ventricular Hypertrophy and Clinical Outcomes in Patients With Severe Aortic Stenosis After Aortic Valve Replacement

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Background. **Substantial aortic calcification is known to be associated with aortic stiffening and subsequent left ventricular (LV) hypertrophy. This study examined whether the thoracic aorta calcium score (TACS) is related to LV hypertrophy and whether it leads to an adverse prognosis in patients with severe aortic stenosis (AS) after aortic valve replacement (AVR).**

Methods. **We retrospectively reviewed 47 patients (mean age, 64 ± 11 years) with isolated severe AS who underwent noncontrast computed tomography of the entire thoracic aorta and who received AVR. TACS was quantified using the volume method with values becoming log transformed ($_{log}$[TACS+1]). Transthoracic echocardiography was performed before and 1 year after the operation.**

Results. **Preoperative LV mass index (LVMI) displayed significant positive correlations with male gender ($r = 0.430$, $p = 0.010$) and $_{log}$(TACS+1) ($r = 0.556$, $p = 0.003$). In multivariate linear regression analysis, only $_{log}$(TACS+1) was independently associated with LVMI, even after adjusting for age, gender, transaortic mean pressure gradient, and coronary or valve calcium score. Independent determinants for postoperative LVMI included $_{log}$(TACS+1) and preoperative LVMI after 1 year of follow-up echocardiography, adjusting for age, gender, indexed effective orifice area, and coronary or valve calcium score. During a median follow-up period of 54 months after AVR, there were 10 events (21%), which included 4 deaths from all-causes, 3 strokes, 2 inpatient admissions for heart failure, and 1 myocardial infarction. The event-free survival rate was significantly lower for patients with TACS of 2,257 mm^3 or higher compared with those whose TACS was lower than 2,257 mm^3 (log-rank $p < 0.001$).**

Conclusions. **High TACS was associated with increased LVMI among patients with severe AS. Further, high TACS usefully predicted less regression of LVMI and poor clinical outcomes after AVR. TACS may serve as a useful proxy for predicting LV remodeling and adverse prognosis in patients with severe AS undergoing AVR.**

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Calcific aortic stenosis (AS) is the most commonly acquired valvular disorder found in developed countries [1]. Aortic valve stenosis induces left ventricular (LV) hypertrophy (LVH) as an adaptive response to the chronic overload of the LV and is considered to be the causal link between AS and myocardial ischemia as well as diastolic dysfunction and ventricular arrhythmia associated with sudden death [2]. LVH is linked with an increased risk of postoperative death after aortic valve replacement (AVR) in AS patients [3]. AVR is typically followed by a decline in LVH. Prior studies have further documented gender, preoperative LV mass, and prosthesis-patients mismatch are among the factors that act as independent predictors of postoperative LV mass regression [4, 5].

To date, AS is considered a complex disease associated with the ability of the LV to adapt to increased afterload, the severity of valvular obstruction, and reduced arterial compliance, rather than isolated aortic valve disease [6]. Measurements that integrate the ventricular, vascular, and valvular components of the disease have been reported to advance risk stratification in patients with AS [6], and a close association between arterial stiffness and LV filling pressure or clinical symptoms has further been reported in AS patients [7].

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Numerous cohort studies have acknowledged an overlap in several clinical factors (ie, dyslipidemia or hypertension) that are associated with atherosclerosis and AS [1]. To this end, atherosclerosis is one of the central factors that leads to the development of vascular calcification. We have previously reported that heavy aortic calcification and resultant arterial stiffening might underlie LVH and diastolic dysfunction in elderly male patients with hypertension [8]. AS is relatively frequent among older patients (predominantly in men) [9] and shares common risk factors with atherosclerosis.

Notably, patients with severe AS reflect a population that is most at risk for heavy aortic calcification and resultant LVH, with the exception of the severity of valvular disease. Despite this, the effect of aortic calcification on LVH and its regression after AVR remains to be investigated in an AS setting. This study sought to test the hypothesis that heavy aortic calcification may result in a more profound LVH and in a worse prognosis after AVR in patients presenting with severe AS.

Patients and Methods

The Institutional Review Board of Yonsei University, Severance Hospital, Seoul, Korea, approved this study.

Study Population

We retrospectively reviewed data of 119 patients who underwent noncontrast computed tomography (CT) of the entire aorta and who received isolated AVR as a consequence of degenerative calcific AS at Severance Cardiovascular Hospital between January 2009 and May 2014. All patients underwent preoperative and postoperative echocardiography. After excluding 10 patients with significant mitral valve dysfunction or aortic regurgitation on preoperative or postoperative echocardiography, 47 patients who underwent concurrent aortic arch replacement along with 15 patients who required concurrent bypass operations, the remaining 47 patients constituted the analytic sample.

Kidney function was ascertained by estimating the glomerular filtration rate (GFR) using the formula according to the Modification of Diet in Renal Disease (MDRD) study as follows [10]: GFR ($mL/min/1.73m^2$) $= 186.3 \times (\text{serum creatinine } [mg/dL]^{-1.154} \times age^{-0.203}$ ($\times$ 0.742, if female). Hypertension was defined as systolic blood pressure of 140 mm Hg higher, diastolic blood pressure of 90 mm Hg or higher, or treatment with antihypertensive agents. Diabetes was defined as treatment with hypoglycemic agents or insulin, or fasting glucose of 126 mg/dL or higher.

The primary end point was defined as the composite of all-cause death, stroke, myocardial infarction, and urgent admission due to heart failure during follow-up. The occurrence of a clinical event was ascertained by review of hospital records and by telephone interview if necessary.

Echocardiographic Measurement

Echocardiography was performed in all 47 patients within 15 $\pm$ 15 days before AVR (range, 1 to 48 days) and within 14 $\pm$ 2 months after AVR (range, 11 to 19 months). The LV dimensions and the ejection fraction were measured as recommended [11]. Septal and LV posterior wall thickness were measured at end diastole. The LV mass was calculated using the formula as recommended [11], and the LV mass index (LVMI) was defined as LV mass indexed for the body surface area. The left atrial (LA) volume was calculated using standard criteria based on the American Society of Echocardiography recommendations, and the LA volume index was defined as the LA volume indexed for the body surface area. Mitral inflow velocities were obtained by pulse-wave Doppler in the apical 4-chamber view. The mitral early diastolic velocity (E) was also measured, whereby peak early diastolic mitral annular (E′) velocity was recorded from the septal mitral annulus. We then calculated the E/E′ ratio, which is a measure of the LV filling pressure.

CT Imaging Protocol and Analysis

CT was performed in all 47 patients within 36 months from the AVR (within –8 $\pm$ 13 months; range, –36 to 12 months). Patients were scanned using a 64-section Sensation 64 CT scanner (Siemens Healthcare, Forchheim, Germany). For calcium scanning, unenhanced CT was performed with prospective electrocardiography-triggered acquisitions in middiastole using 120 to 140 kV with 150 to 220 mAs, depending on the patient's size; 240 ms exposure time per rotation; 330 ms gantry rotation time; and 64-mm $\times$ 0.6-mm slice collimation. Calcium scans were reconstructed at 70% of the R-R interval using a slice thickness of 3 mm with an increment of 3 mm.

Coronary artery, aortic valve, and thoracic aorta calcium scoring were performed on reconstructed images. Foci of coronary artery, aortic valve, and thoracic aorta were identified using semiautomatic Vitrea 2.0 software (Vital Images, Minnetonka, MN) and scored by an experienced technician who was masked to the patient's medical records, as well as being verified by imaging cardiologists (H.J.C. and R.H.) with level 3 clinical competence in cardiovascular CT imaging, in a masked fashion [12].

An objective volume-scoring method included in the system software was determined, which provided a score in cubic millimeters [8]. Lesion-specific calcium scores were summed across all lesions identified within the left main, left anterior descending, left circumflex, and right coronary arteries for estimating the coronary artery calcium score (CACS). Calcification corresponding to the aortic valve leaflets was identified to calculate the aortic valve calcium score (AVCS). The thoracic aorta calcium score (TACS) included calcium scored in the ascending aorta, aortic arch, and descending aorta to the diaphragm level.

Statistical Methods

Variables are reported as percentages or as means $\pm$ SD for normally distributed variables and as the median (interquartile [25% to 75%] range) for nonnormally distributed variables. The nonnormally distributed variables of TACS, CACS, and AVCS were transformed before analysis by adding 1 and obtaining the natural

logarithm of the value (eg, $_{log}$[TACS+1], $_{log}$[CACS+1], and $_{log}$[AVCS+1]) to achieve normality of these variables. A paired *t* test was performed to compare the values of the preoperative and postoperative hemodynamic and echocardiographic data. To determine whether LVMI correlated with the other clinical parameters, we calculated Pearson correlation coefficients. We also evaluated linear relationships using simple linear regression analysis to determine independent correlates of LVMI. Variables that had a *p* value of less than 0.2 in univariable analysis were entered into the multivariate linear regression model.

Receiver operating characteristic curves were also plotted to determine the sensitivity and specificity of different TACSs for predicting events and to determine the optimal cutoff value. Multivariable Cox proportional hazard analysis was used to determine independent variables for potential predictors of cardiac events, with the variables showing statistical significance in univariate analysis, age and gender, as covariates. Kaplan-Meier survival curves were used to plot all clinical events according to the time to the first event. A *p* value of less than 0.05 was considered statistically significant.

Results

The 47 patients (27 men, 20 women) included in this study were a mean age of 64 ± 11 (Table 1). All patients survived the operation without any worsening of their clinical status. Hypertension was present in 20 patients (42.6%) and diabetes mellitus in 1 patient (2.1%). The median value of the TACS in the study population was 1,036 mm^3 (interquartile range, 345 to 3,735 mm^3) and the mean value of $_{log}$(TACS+1) was 6.8 ± 2.0. Representative cases for low and high TACS are shown in Figure 1.

Table 2 reports preoperative and postoperative hemodynamic and echocardiographic data. Systolic blood pressure (119 ± 15 vs 127 ± 20 mm Hg, $p = 0.046$) and diastolic blood pressure (73 ± 9 vs 78 ± 12 mm Hg, $p = 0.030$) were both increased after the follow-up period. Conversely, LV end-diastolic dimension (50.9 ± 6.2 vs 48.1 ± 4.7 mm, $p < 0.001$), LV end-systolic dimension (34.3 ± 7.3 vs 31.7 ± 5.3 mm, $p = 0.006$), and LVMI (151.4 ± 30.0 vs 121.2 ± 30.5 g/m^2, $p < 0.001$) were decreased. No significant change was reported in the LV ejection fraction after the operation. The preoperative mean aortic valve area index was 0.42 ± 0.13 cm^2/m^2, and postoperative indexed effective area was 1.13 ± 0.28 cm^2/m^2.

Figure 2 demonstrates the correlation between TACS and LVMI before and 1 year after AVR. A significant positive correlation was found between the preoperative LVMI and $_{log}$(TACS+1) ($r = 0.430$, $p = 0.003$) and was somewhat stronger between the postoperative LVMI and $_{log}$(TACS+1) ($r = 0.556$, $p < 0.001$). Regression analyses for the determinant of preoperative LVMI are reported in Table 3. Preoperative LVMI demonstrated a significant positive correlation with male gender ($r = 0.430$, $p = 0.010$) and $_{log}$(TACS+1) ($r = 0.556$, $p = 0.003$).

Table 1. Clinical Characteristics and Calcium Scores

Variable[a]	Value (n = 47)
Age, y	64 ± 11
Men	27 (57.4)
Body surface area, m^2	1.62 ± 0.23
Hypertension	20 (42.6)
Diabetes mellitus	1 (2.1)
Medication	
ACE inhibitor/ARB	26 (55.3)
β-Blocker	10 (21.3)
Calcium antagonists	12 (25.5)
Diuretics	18 (38.3)
Laboratory values	
Calcium, g/mL	9.1 ± 0.5
Phosphorus, g/mL	3.8 ± 0.6
Triglyceride, g/mL	115.0 ± 61.7
HDL cholesterol, g/mL	45.0 ± 12.8
LDL cholesterol, g/mL	103.3 ± 35.4
GFR, mL/min/1.73m^2	77.4 ± 22.9
CT calcium score	
CACS, mm^3	29 (0–184)
AVCS, mm^3	4,286 (2,432–5,563)
TACS, mm^3	1,036 (345–3,735)

[a] Continuous data are presented as mean ± SD or as the median (interquartile [25%–75%] range) and categoric data as number (%).

ACE = Angiotensin-converting enzyme; ARB = angiotensin receptor blocker; AVCS = aortic valve calcium score; CACS = coronary artery calcium score; CT = computed tomography; GFR = glomerular filtration rate; HDL = high-density lipoprotein; LDL = low-density lipoprotein; TACS = thoracic aorta calcium score.

In multivariate linear regression analysis, $_{log}$(TACS+1) emerged as the only independent variable associated with LVMI, even after adjusting for age, gender, transaortic mean pressure gradient, and $_{log}$(TACS+1) ($p = 0.019$). A similar independent association was observed between $_{log}$(TACS+1) and LVMI, even after adjusting for age, gender, transaortic mean pressure gradient, and $_{log}$(AVCS+1) ($p = 0.009$).

Table 4 reports the univariable and multivariate linear regression analyses for the determinants of postoperative LVMI. Variables associated with postoperative follow-up LVMI were male gender ($p = 0.039$), preoperative LVMI ($p < 0.001$), $_{log}$(AVCS+1) ($p = 0.010$), and $_{log}$(TACS+1) ($p < 0.001$). After adjustment in the multivariate model, $_{log}$(TACS+1) ($p = 0.049$) and preoperative LVMI ($p = 0.015$) remained as independent predictors of postoperative LVMI, after adjusting for age, gender, indexed effective orifice area, and $_{log}$(CACS+1). Independent associations continued between postoperative LVMI and $_{log}$(TACS+1), even after adjusting for age, gender, LVMI, and $_{log}$(AVCS+1) ($p = 0.045$). Figure 3 reports the percentage change in LVMI after AVR, demonstrating a significant correlation with $_{log}$(TACS+1) ($r = 0.315$, $p = 0.031$).

During a median follow-up of 54 months (interquartile range, 20 to 71 months) after AVR, there were 10 adverse events (21%), including 4 deaths from all-causes, 3

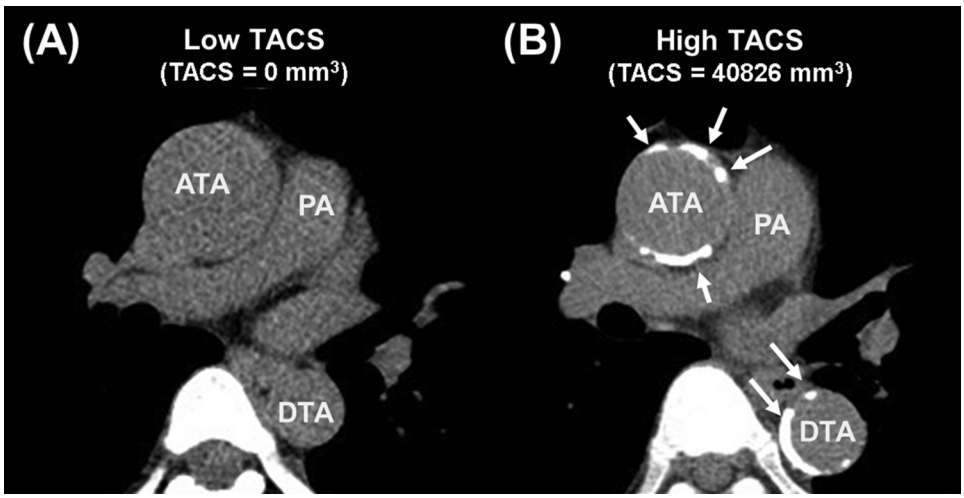

Fig 1. Representative scans show (A) low and (B) high thoracic aortic calcium scores (TACS). The white arrows indicate aorta calcifications. (ATA = ascending thoracic aorta; DTA = descending thoracic aorta; PA = pulmonary artery.)

strokes, 2 inpatient admissions for heart failure, and 1 myocardial infarction. All events were in different patients. Because there are no accepted thresholds or cutoffs for TACS risk categories, we chose to divide the TACS according to receiver operating characteristic curve analysis. The TACS (≥2,257 mL/m^2) cutoff point exhibited a sensitivity of 81.8% and specificity of 77.8% for prediction of all events, with an area under the curve of 0.816.

Table 2. Preoperative and Postoperative Hemodynamic and Echocardiographic Data

Variable	Preoperative (n = 47) (Mean ± SD)	Postoperative (n = 47) (Mean ± SD)	*p* Value
Hemodynamic			
Systolic BP, mm Hg	119 ± 15	127 ± 20	0.046
Diastolic BP, mm Hg	73 ± 9	78 ± 12	0.030
Echocardiographic			
LV end-diastolic dimension, mm	50.9 ± 6.2	48.1 ± 4.7	<0.001
LV end-systolic dimension, mm	34.3 ± 7.3	31.7 ± 5.3	0.006
LV ejection fraction, %	63.6 ± 13.0	66.1 ± 7.9	0.163
LV mass index, g/m^2	151.4 ± 30.0	121.2 ± 30.5	<0.001
LA volume index, mL/m^2	35.9 ± 12.4	33.3 ± 11.7	0.041
Aortic valve area, cm^2	0.67 ± 0.16	…	…
Aortic valve area index, cm^2/m^2	0.42 ± 0.13	…	…
Peak aortic velocity, m/sec	4.8 ± 0.6	…	…
Transaortic mean pressure gradient, mm Hg	58.9 ± 15.6	…	…
Effective orifice area, cm^2	-	1.85 ± 0.48	…
Indexed effective orifice area, cm^2/m^2	-	1.13 ± 0.28	…

BP = blood pressure; LA = left atrial; LV = left ventricular.

Table 5 reports the univariate and multivariate analysis of variables as potential predictors of cardiac events in patients with severe AS after AVR. In univariate analysis, high postoperative LVMI and high TACS predicted all-cause events ($p = 0.008$ and $p = 0.002$, respectively). Among these, high TACS (≥2,257 mL/m^2) was the only independent predictor for all-cause events, even after adjusting for age, gender, and postoperative LVMI ($p = 0.031$). In Figure 4, Kaplan-Meier curves revealed that the event-free survival rate was significantly lower for patients presenting with a TACS of 2,257 mm^3 or higher than for those who had a TACS below 2,257 mm^3 (log-rank $p < 0.001$).

Comment

To our knowledge, this is the first study to demonstrate an association between TACS and LVH among patients with severe AS after AVR. This study supports the contention that AS is not merely an isolated aortic valve disease but rather a complex disease related to the LV, the valve, and the arterial system. Foremost, the measurement of TACS by noncontrast CT may serve useful toward assessing LV overload caused by the aorta and may also prove important in the prediction of adverse cardiovascular prognosis and LV mass regression after correction of the valvular component of the disease.

Arterial Stiffness in AS Patients

Long-standing AS causes chronic pressure overload to the LV by the stenotic valve and leads to compensatory remodeling of the LV. Compensated pathologic LVH leads to impairment of vascular compliance and elevated LV diastolic pressure [7]. Moreover, arterial stiffening adversely affects the LV through increased afterload. This mechanism, termed as ventricular-vascular coupling, has been proposed as one of the important factors in the development of LVH [13]. Arterial stiffening is associated with atherosclerosis, and increased arterial stiffness is a

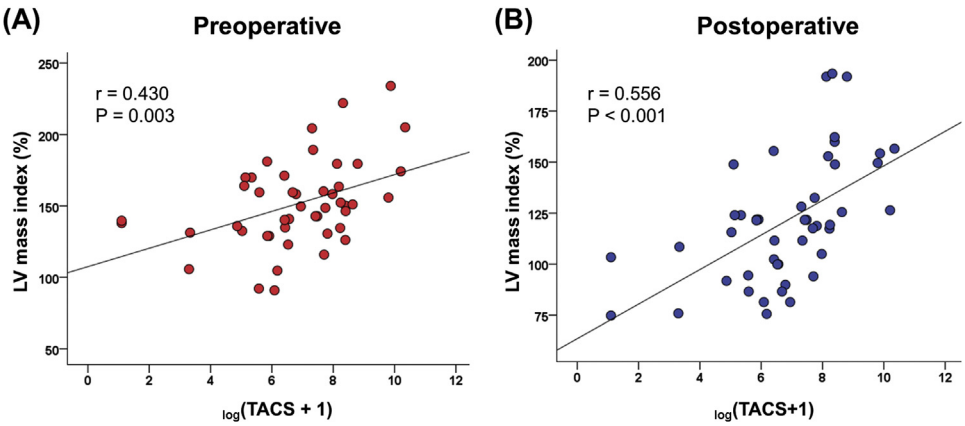

Fig 2. Correlation between the thoracic aorta calcium score (TACS) and the (A) preoperative and (B) postoperative left ventricular (LV) mass index.

common finding in AS patients who are relatively older and who often present with traditional risk factors for atherosclerosis. Aside from valvular stenosis, reduced aortic compliance contributes to the increased systolic load, and this double load initiated by the valvular and arterial systems may have a combined detrimental effect on LV function [14].

Aorta Calcification and Arterial Stiffness

The mechanisms that lead to increased arterial stiffness are thought to primarily involve structural alterations within the media and deposition of collagen [15]. Another plausible mechanism is vascular calcification [16]. A positive proportional correlation between pulse wave velocity and aortic calcification from animal and human studies has highlighted vascular calcium deposition as a mechanism underlying arterial stiffening [15, 17]. Notably, AS patients tend to be relatively old, often present with numerous conventional risk factors for atherosclerosis, and are therefore more prone to vascular calcification and arterial stiffening.

TACS for AS Patients

Calcification of the aorta is relatively straightforward to assess by use of a noncontrast CT scan. For those undergoing valve operations, the role of CT is rapidly emerging as a gatekeeper or as an alternative for invasive coronary angiography for ruling out the presence of coronary stenosis [18]. TACS can be easily assessed concomitantly with coronary CT angiography, which is taken preoperatively. However, the role of CT angiography is still limited to the assessment of coronary AS and the measurement of the thoracic aortic diameter for ruling out aortic aneurysm, and the clinical implications of the calcium score assessment in severe AS have yet to

Table 3. Univariable and Multivariate Linear Regression Analysis for the Determinant of Preoperative Left Ventricular Mass Index

	Univariate		Multivariate	
Variable	β	*p*	β	*p*
Mode1 1				
Age, years	–0.117	0.435	–0.223	0.157
Female gender	–0.370	0.010	–0.156	0.383
Aortic valve area index, cm^2/m^2	–0.201	0.176	–0.051	0.742
$_{log}$(CACS+1), mm^3	0.258	0.099	0.073	0.650
$_{log}$(TACS+1), mm^3	0.325	0.003	0.448	0.019
Mode1 2				
Age, years	–0.117	0.435	–0.251	0.120
Female gender	–0.370	0.010	–0.107	0.520
Aortic valve area index, cm^2/m^2	–0.201	0.176	–0.067	0.690
$_{log}$(AVCS+1), mm^3	0.244	0.102	0.038	0.819
$_{log}$(TACS+1), mm^3	0.325	0.003	0.468	0.009

AVCS = aortic valve calcium score; CACS = coronary artery calcium score; TACS = thoracic aorta calcium score.

Table 4. Univariable and Multivariate Linear Regression Analysis for the Determinant of Postoperative Left Ventricular Mass Index

	Univariate		Multivariate	
Variable	β	*p*	β	*p*
Mode1 1				
Age, years	0.087	0.561	–0.037	0.814
Female gender	–0.303	0.039	–0.020	0.897
Preoperative LV mass index, g/m^2	0.603	<0.001	0.412	0.015
Indexed effective orifice area, cm^2/m^2	–0.325	0.053	–0.175	0.210
$_{log}$(CACS+1), mm^3	0.237	0.131	0.197	0.385
$_{log}$(TACS+1), mm^3	0.556	<0.001	0.342	0.049
Mode1 2				
Age, years	0.087	0.561	–0.050	0.753
Female gender	–0.303	0.039	0.015	0.922
Preoperative LV mass index, g/m^2	0.603	<0.001	0.417	0.015
Indexed effective orifice area, cm^2/m^2	–0.325	0.053	–0.173	0.224
$_{log}$(AVCS+1), mm^3	0.378	0.010	0.070	0.490
$_{log}$(TACS+1), mm^3	0.556	<0.001	0.274	0.045

AVCS = aortic valve calcium score; CACS = coronary artery calcium score; LV = left ventricular; TACS = thoracic aorta calcium score.

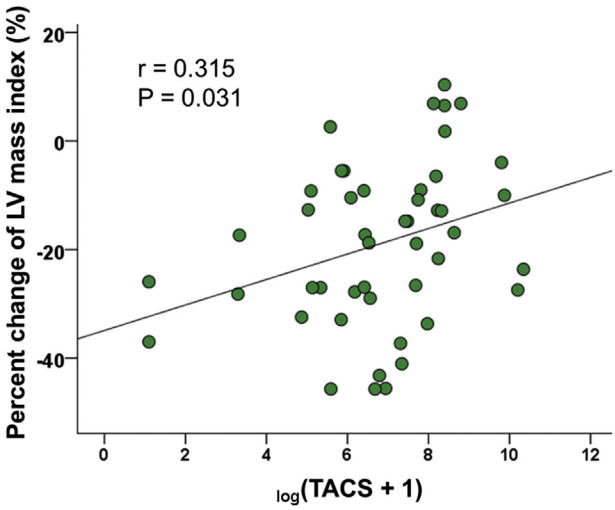

Fig 3. Correlation between the thoracic aorta calcium score (TACS) and the percentage change of the left ventricular (LV) mass index after aortic valve replacement.

be fully elucidated. In the presence of a porcelain aorta (ie, extensive calcification of the ascending aorta or aortic arch that can be completely or near completely circumferential), AVR is considered to be technically demanding and associated with a heavy burden of morbidity and death [19]. Nevertheless, a predictive role for the quantitative measurement of aortic calcium remains to be investigated in AS patients.

Prior studies have speculated that the aortic calcium score is an independent predictor of cardiovascular events in angina pectoris patients and asymptomatic adults [20, 21]. Hermann and colleagues [22] also reported that thoracic aortic calcification was associated with the incident of stroke in the general population in addition to established risk factors. Our data further suggest that TACS can additionally be used as a predictor for clinical outcomes as well as LV mass regression among severe AS patients after AVR. Interestingly, it has been recently reported that calcification of the descending aorta relates to the presence of peripheral arterial disease, which is a well-known predictor of poor long-term outcomes [23]. Whether the presence of peripheral artery disease was associated with poor outcomes in the current study is not clear because data regarding the prevalence of peripheral artery disease were unavailable in the current study sample. Further studies designed to investigate the potential association between TACS and peripheral artery disease are warranted.

Given CT is performed more frequently as a preoperative evaluation for coronary stenosis before aortic valve operations in clinical practice, the additional measurement of TACS could perhaps be clinically beneficial for patients with severe AS preparing for an operation, although additional studies are needed to support this notion.

Study Limitations

A key limitation is the small study sample due to the enrollment of a particular population who underwent CT and postoperative follow-up echocardiography. Inaccuracy of the linear regression model and widening of the confidence intervals of the hazard ratios in Cox proportional analysis cannot be discounted owing to the relatively small study sample used during analyses. Nevertheless, data related to LVMI and clinical prognosis persistently displayed similar results that signified poor outcomes in patients with high TACS, which in turn supports the current study hypothesis.

In addition, the current study findings were based on a retrospective analysis; albeit we carefully reviewed the medical records along with CT and echocardiography reports to avoid any possible biases that may have arisen. CT imaging was not performed during the same time period for all patients, although it bears mentioning that all scans were obtained within a 36-month period, and over time, aortic calcification quite often manifests in an indolent manner.

We dichotomized TACS according to receiver operating characteristic curve analysis using the patients

Table 5. Multivariate Cox Proportional Hazard Analysis of Variables as Potential Predictors of the Composite of All Cardiac Events[a]

	Univariate		Multivariate	
Variable	Hazard Ratio (95% Confidence Interval)	*p*	Hazard Ratio (95% Confidence Interval)	*p*
Age, years	1.03 (0.96–1.10)	0.365	0.99 (0.94–1.06)	0.912
Female gender	0.65 (0.17–2.46)	0.522	1.18 (0.24–5.73)	0.837
Hypertension	3.36 (0.89–12.72)	0.074	...	...
Post-op LV mass index ≥126 g/m^2	6.01 (1.59–22.81)	0.008	2.03 (0.43–9.63)	0.374
High CACS (≥61 mm^3)	3.25 (0.95–11.14)	0.061	...	...
High AVCS (≥3,752 mm^3)	6.69 (0.85–52.99)	0.072	...	...
High TACS (≥2,257 mm^3)	11.17 (2.41–51.81)	0.002	7.94 (1.21–51.88)	0.031

[a] Events included including all-cause death, stroke, myocardial infarction, and urgent admission due to heart failure in patients with severe aortic stenosis after aortic valve replacement.

AVCS = aortic valve calcium score; CACS = coronary artery calcium score; LV = left ventricular; Post-op = postoperative; TACS = thoracic aorta calcium score.

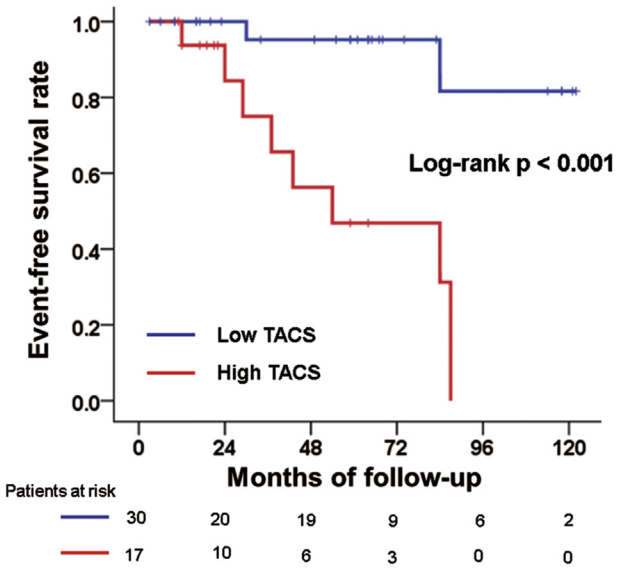

Fig 4. Kaplan-Meier curves display differences in event-free survival among patients with aortic stenosis who underwent aortic valve replacement according to low (blue line) and high (red line) thoracic aorta calcium score (TACS).

included in the current study. Hence, caution should be taken when extrapolating this cutoff value, which might be considered arbitrary based on the current limited population. Despite this, it bears mentioning that the primary purpose of this study was to explore and verify the hypothesis that TACS may be a predictor of future adverse events in AS patients after AVR. Although clearly, in light of the current study limitations, further larger prospective studies are warranted for the purpose of consolidating our hypothesis and discovering accepted thresholds or cut-off points for TACS risk categories. In this study, CACS, a well-known predictor of cardiac events [24], failed to demonstrate statistical significance in predicting all cardiac events. We may add, however, that the lack of a significant association could be partly due to our highly particular population after omitting those with coronary artery disease who required concurrent bypass operations.

Conclusions

High TACS was associated with increased LVMI among patients with severe AS. A major finding is that TACS further predicted less regression of LV mass and poor clinical outcomes after AVR. As such, TACS should be considered a useful surrogate for the prediction of LV remodeling along with an adverse prognosis in patients with severe AS undergoing AVR.

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INVITED COMMENTARY

In this issue of *The Annals*, Cho and colleagues [1] reported the association of thoracic aorta calcium score (TACS) to left ventricular (LV) hypertrophy and clinical outcomes in patients with severe aortic stenosis (AS). The main finding of the study was that high TACS was associated with LV hypertrophy, and it predicted less regression of LV mass and poor clinical outcomes following aortic valve replacement. This observation timely recalls that LV remodeling, a major determinant of outcome, is a complex pathophysiologic process. It interplays the inherited ability of the LV to adapt to increased afterload, the severity of valvular obstruction, and the reduced arterial compliance. The contribution of the vascular compliance to the LV remodeling through the so-called ventriculoarterial coupling is a well-known phenomenon. Increased arterial stiffness as estimated by an increase in pulse wave velocity has recently been shown to be associated with decreased quality of life and cognition after aortic valve replacement [2, 3]. The clinical relevance of these reports [2, 3], in line with the study by Cho and colleagues [1], is to place AS within a degenerative vascular disease continuum that involves the arterial tree from the aortic valve and the large arteries toward the arterioles, sharing common risk factors.

While carotid–femoral pulse wave velocity is the gold standard measure of arterial stiffness, with validated normal reference range values [4], TACS only remains an indirect and potentially late measure of the vascular compliance. The methodology for TACS has to be standardized and widely tested for interscan, scan-rescan, and interobserver reproducibility. TACS normative values for age, sex, and ethnicity have to be compiled before it can enter the clinical armamentarium. Nevertheless, unenhanced computed tomography used for TACS has the advantage of comprehensively evaluate broadly the calcification load, including coronary and valve calcification scores that are inaccessible to other techniques, which respectively are risk markers for coronary artery stenosis and of postoperative outcomes in patients with AS [5]. Cho and colleagues [1] failed to replicate the former finding because the patients with notorious coronary vascular disease were excluded from the cohort. On a clinical view, the study by Cho and colleagues [1] provided no sufficient evidence to change how we care for patients with AS, because of limited study sample and inherent composite input limitations pertaining to its retrospective nature. However, they should be congratulated for indicating how it could be important to redefine the risk factors in patients with AS using vascular compliance assessment, both for disease severity and prognosis-based operative decision making. Their report thus paves the way for larger prospective and controlled trials to improve stratification of AS using vascular compliance and calcification scores.

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