Usefulness of Thoracic Aortic Calcium to Predict 1-Year Mortality After Transcatheter Aortic Valve Implantation

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In patients who underwent transcatheter aortic valve implantation (TAVI), vascular disease is associated with increased risk of mortality. Thoracic aortic calcification (TAC), an objective surrogate of vascular disease, could be a predictor of mortality after TAVI. We aimed to analyze the association between TAC burden and 1-year all-cause mortality in patients who underwent TAVI in a US population. From July 2015 through July 2017, a retrospective review of TAVI procedures was performed at Baylor Scott & White-The Heart Hospital, Plano, Texas. Patients were analyzed for comorbidities, cardiac risk factors, and 30-day and 1-year all-cause mortality. Restricted cubic splines analysis was used to define low, moderate, and high TAC categories. The association between TAC and survival was evaluated using unadjusted and adjusted Cox models. A total of 431 TAVI procedures were performed, of which TAC was measured in 374 (81%) patients. Median (interquartile range) age was 82 (77, 87) years, and 51% were male. Median (interquartile range) STS PROM was 5.6 (4.1, 8.2) %. Overall 30-day and 1-year all-cause mortality was 1% and 10%, respectively. TAC was categorized as low (<1.6 cm^3), moderate (1.6 to 2.9 cm^3), and high (>2.9 cm^3). At 1 year, all-cause mortality was 16% in patients with high TAC compared with 6% in the low and moderate TAC categories (p = 0.008). Unadjusted and adjusted Cox regression analysis showed a significant increase in mortality for patients with high TAC compared with low TAC (hazard ratio 2.98, 95% confidence interval [1.34−6.63]), but not significant compared with moderate TAC group. TAC is a predictor of late mortality after TAVI. In conclusion, adding TAC to preoperative evaluation may provide an objective, reproducible, and potentially widely available tool that can help in shared decision-making. **(Am J Cardiol 2021;140:103−109)**

Transcatheter aortic valve implantation (TAVI) has emerged as an effective treatment for patients with severe symptomatic aortic stenosis across all surgical-risk profiles.[1−4] Common models used to assess procedural risk include the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM), the logistic EuroSCORE, and EuroSCORE II.[5,6] These models have limited applicability in patients who underwent TAVI since they were developed and validated in patients who underwent surgical procedures. Therefore, a TAVI-specific risk model to predict in-hospital mortality was developed from the STS/American College of Cardiology (ACC) Transcatheter Valve Therapy (TVT) Registry.[7] Despite significantly decreased TAVI mortality, 1-year mortality is 11% to 26% in all-comer analyses.[4,8] Thus, pre-TAVI evaluation has shifted focus toward identifying patients who, despite surviving TAVI, will not be alive at 1 year. Thoracic aortic calcification (TAC) was recently shown, and validated in 2 European cohorts, to be a strong predictor of cardiac outcomes after TAVI.[9−11] In the present study, we aimed to validate the prognostic value of TAC to predict 1-year all-cause mortality after TAVI in a US population.

Methods

From July 2015 through July 2017, 431 patients underwent TAVI at Baylor Scott & White-The Heart Hospital, Plano, Texas. Patients with prior available computed tomography (CT) data were included in the study. Patients' demographics, baseline characteristics, and in-hospital outcomes were defined and coded according to the TVT

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registry (Supplemental Table 1). Preoperative grip strength, KATZ Index of Independence in Activities of Daily Living, 5-m walk test, and albumin were recorded as markers of patient frailty. Follow-up mortality data were obtained from clinic visits, direct phone communication, or by query of the Social Security Death Index according to a previously validated methodology.[12] This study was approved by the Baylor Scott & White Health Research Institute Institutional Review Board.

TAC was measured from the preoperative CT scan (Figure 1). CT scans were performed with a Revolution 256-CT scanner (GE Healthcare, Waukesha, WI) or a Definition Flash 256-CT dual-source scanner (Siemens Healthcare, Malvern, PA) using electrocardiogram (ECG) gating and 100 to 140 kV tube voltage with adapted mAs. The axial slice reconstruction parameters ranged from 0.625 to 0.8. All images were made anonymous, transferred to a core lab, and analyzed by one operator who was blinded to outcomes data.

The whole thoracic aorta was studied in each examination. A semiautomated dedicated software based on an open-source environment was used to extract calcifications.[13] Briefly, the rater delineated the ascending, horizontal, and descending thoracic aorta with the placement of at least 3 points. The aorta's main axis was calculated using a third-order b-spline. An adjustable tube encompassing the entire aorta was created, and calcifications were detected using an initial threshold of 550 Hounsfield Units (HU), which could be adapted to improve algorithm performance, within the tube (Figure 1). The results of the segmentation were visually postulated, and the user manually adjusted and verified the calcification. A graph-theory-based connectivity algorithm was then applied to segment each calcification. After setting the threshold, this algorithm was a simple recursive function initialized in the center of each calcification. For each pixel, the 28 neighboring pixels were checked. If a pixel's true value was above the threshold, the algorithm was re-run. Only TAC from the aortic sinus to the diaphragmatic hiatus was calculated; valvular calcifications were excluded.

Two TAVI systems were used: balloon-expandable (Edwards SAPIEN valves, Edwards Lifesciences, Irvine, CA) and self-expandable (Medtronic CoreValve system, Medtronic, MN).

The median, first, and third quartiles of quantitative and the absolute and relative frequencies of qualitative characteristics were presented. Patient characteristics according to 1-year vital status were compared using Wilcoxon, chi-square, or Fisher exact tests as appropriate for the data type.

A Cox model with restricted cubic spline (RCS) was used to evaluate the association of TAC with the log-hazard ratio without the assumption of linearity using a Wald test. RCS, a sum of smooth piece-wise polynomial functions of the independent variable, provides greater flexibility to investigate nonlinear relationships.[14] RCS was defined using 3 knots at the recommended 5th, 50th, and 95th percentiles after the initial evaluation by an independent statistician who was not involved in the initial standard linear survival analysis.[15]

TAC was categorized into 3 categories using the regions of low, moderate, and high risk based on the association of the RCS with the log-hazard ratio. While blinded to clinical outcomes, cutoffs were prespecified to be selected according to the corresponding TAC measurements where the 95% confidence band is less than and greater than a hazard ratio of 1 surrounding median TAC. Patients with a follow-up greater than 1-year were censored at 365 days post-TAVI. Time to event was defined as the time from TAVI to expiration, last follow-up, or 365 days, whichever occurred earlier.

Patient characteristics and outcomes were compared between TAC categories using Kruskal-Wallis, chi-square, or Fisher exact tests according to data type. Correlation of categorized TAC with frailty markers was estimated using the nonparametric Spearman Rank correlation. The association of categorized TAC with survival was assessed with a log rank test, and risk of mortality was compared between the 3 groups based on the hazard ratio from the Cox model. The proportional hazards assumption was evaluated by visually inspecting the Schoenfeld residuals against time

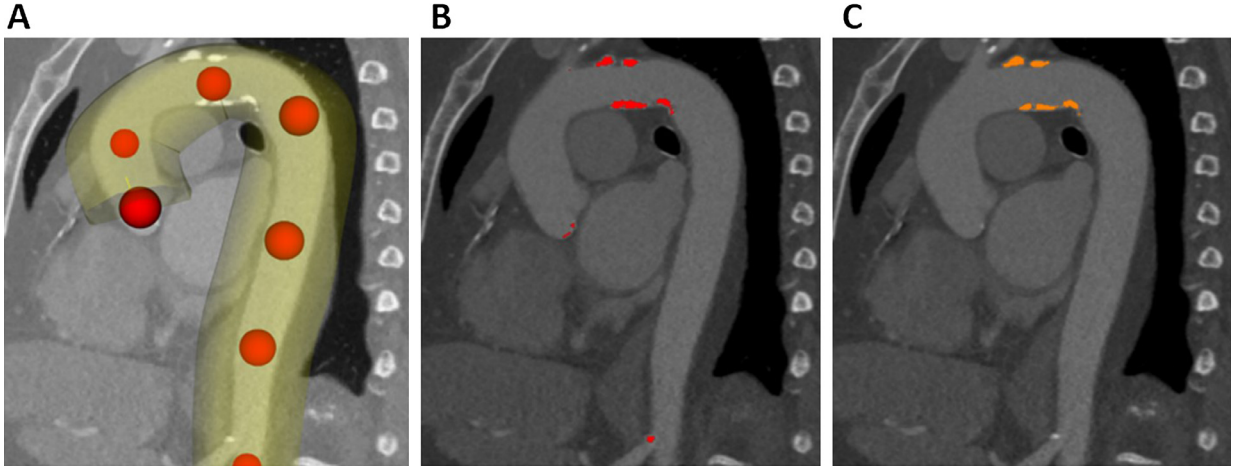

Figure 1. Thoracic aortic calcification measurement. (*A*) By placing several points (red spheres) a 3-dimensional tube containing the whole thoracic aorta is created. (*B*) After adjusting the threshold (initially set at 550 HU) the software automatically selects the calcifications within the tube. (*C*) The operator manually adjusts each calcification.

plot and using the Schoenfeld residual test. The association of TAC with mortality was investigated alongside traditional cardiac mortality risk factors in 2 predetermined adjusted models: STS-PROM score (Model 1), and age, gender, coronary artery disease (CAD), diabetes mellitus, New York Heart Association (NYHA) Class >II, peripheral vascular disease, ejection fraction, and TAVI route (Model 2). A third model adjusting for all factors significantly associated with categorized TAC ($p < 0.1$) was also investigated: age, body mass index (BMI), glomerular filtration rate (GFR), peripheral vascular disease, CAD, postoperative mean aortic gradient, right ventricular pressure, and STS PROM (Model 3). A supplemental multivariable logistic regression analysis was performed investigating the association of TAC categories with 1-year survival adjusted for potential confounders based on variables that were significantly different ($p < 0.10$) between survival status at 1 year. Prosthesis type was collapsed as Edward valves compared with other valves to facilitate inclusion in the model. All statistical tests and confidence intervals were calculated 2-sided with a significance threshold set at 0.05. Analyses were performed in R (version 3.6.1).

Results

Of 431 patients who underwent TAVI, 374 (81%) met the inclusion criteria with a quality CT scan (Figure 2). The median (interquartile range) age was 82 (77, 87) years, and 51% were men. Co-morbidities included: PAD (31%), CAD (63%), diabetes (45%), and advanced heart failure with NYHA Class III and IV (69%). TAVI procedures were predominantly performed via the femoral route (94%) and with balloon-expandable valves (81%).

The all-cause mortality rate was 1% (4/374) at 30 days and 10% (37/374) at 1 year. Vascular complications occurred in 9% (32/374) of patients and 30-day stroke/TIA in 3% (11/374) of patients with no significant differences between survival status. In contrast, the 30-day readmission rate was 13% greater in deceased patients compared with those alive at 1 year (24% vs 11%; $p = 0.03$). STS-PROM score did not differ significantly between alive and deceased groups (Table 1). Compared with the deceased patients, alive patients had markedly lower TAC measurements (median; 2.1 vs 3.6; $p < 0.01$), higher BMI (median; 27.8 vs 25.0; $p = 0.01$), longer 5-m walk times (median; 7.6 vs 6.3; $p = 0.03$), lower albumin (median; 3.4 vs 3.6; $p < 0.01$), higher postoperative mean aortic gradient (median; 8 vs 6; $p = 0.03$), were less likely to report a high KATZ score ≥5 (78% vs 92%; $p < 0.01$), and were more likely to receive a balloon-expandable valve (83% vs 62%; $p = 0.007$; Table 2).

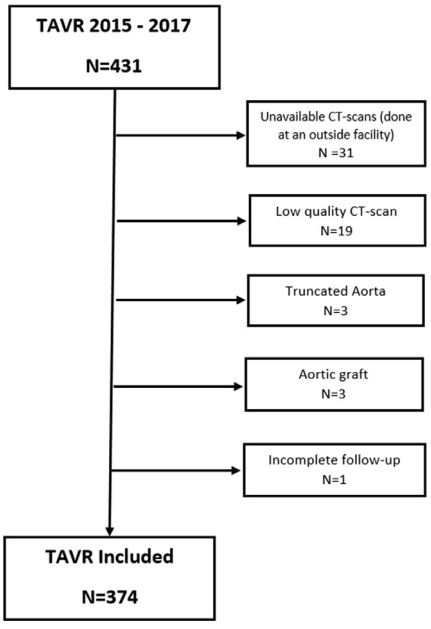

Figure 2. Flow chart of the included TAVR patients.

The Cox model with RCS showed that TAC had a significant nonlinear association with mortality (Wald Test of Association $p = 0.02$; Wald Test of Linearity $p = 0.02$; Figure 3). The risk of mortality increased linearly on a log-scale with increasing TAC up to an inflection point at 2.9 cm^3. Beyond 2.9 cm^3, the hazard ratio increased at a decreasing rate to a peak of 5.9 cm^3, above the third quartile of TAC. Low-, moderate-, and high-risk TAC categories were determined by the 2 points where the confidence bands cross a hazard ratio of 1 surrounding the median indicated at 1.6 and 2.9 cm^3 (Figure 3).

Of 374 patients, 142 (38%) presented with low TAC < 1.6 cm^3, 79 (21%) with moderate TAC between 1.6 and 2.9 cm^3, and 153 (41%) with high TAC >2.9 cm^3. Patients presenting within a higher TAC category were significantly associated with lower age, higher BMI, higher creatinine, lower GFR, and higher STS-PROM score (Table 2); whereas no significant differences and weak to no correlation were found between TAC categories and frailty markers including grip strength (Spearman $r = -0.08$; $p = 0.12$), proportion of patients with KATZ score ≥5 ($r = -0.07$; $p = 0.17$), duration on 5-m walk test ($r = 0.03$; $p = 0.62$), and serum albumin levels ($r = -0.03$; $p = 0.57$). Co-morbidities in the high TAC group were more prevalent than in the moderate and low TAC groups. Vascular complications were significantly increased among patients in the high TAC group compared with those in the moderate and low TAC groups (Table 2). Furthermore, 24 of 153 (16%) patients with high TAC expired within 1 year compared with 14 out of 221 (6%) in the low and moderate TAC categories ($p = 0.008$).

The Kaplan-Meier curves in Figure 4 illustrate that the 3 risk categories of TAC were associated with mortality (log rank $p = 0.002$). TAC > 2.9 cm^3 was associated with greater than double the risk of 1-year all-cause mortality compared with low TAC <1.6 cm^3 (hazard ratio [HR], 95% confidence interval [CI]: 2.98, 1.34 to 6.63; $p = 0.008$); whereas high versus moderate TAC of 1.6 to 2.9 cm^3 did not reach statistical significance ($p = 0.06$). There was no significant difference in the risk of mortality comparing patients with moderate TAC compared with low TAC in the long term ($p = 0.93$). Adjustment for STS-PROM score (model 1), traditional cardiac risk factors (model 2), and potential confounding factors (model 3) did not change the association of greater than double the risk of mortality for high TAC above 2.9 cm^3compared with low TAC below 1.6 cm^3 (Table 3). However, adjusting for traditional cardiac risk

Table 1.
Comparison of demographic and clinical variables by 1-year vital status

Variable	Overall (n = 374)	1-year vital status		p value
		Alive (n = 337)	Deceased (n = 37)	
Age (years)	82 [77, 87]	82 [77, 87]	82 [79, 86]	0.61
Body mass index (kg/m^2)	27.5 [24.1, 32.6]	27.8 [24.4, 32.9]	25.0 [22.2, 29.3]	0.01
Men	189 (51%)	174 (52%)	15 (41%)	0.27
NYHA > II	257 (69%)	228 (68%)	29 (78%)	0.25
Grip strength (kg)	18.0 [12.7, 23.7]	18.2 [12.9, 23.7]	17.3 [12.0, 22.8]	0.44
KATZ score ≥ 5	340 (91%)	311 (92%)	29 (78%)	0.004
5-minute Walk test (seconds)	6.4 [4.8, 8.6]	6.3 [4.6, 8.4]	7.6 [5.6, 10.2]	0.03
Albumin (g/dL)	3.6 [3.4, 3.8]	3.6 [3.4, 3.8]	3.4 [3.2, 3.8]	0.008
Glomerular filtration rate (ml/min/1.73m^2)	47.7 [36.1, 65.9]	48.2 [36.3, 66.5]	39.3 [32.2, 58.0]	0.08
Chronic obstructive pulmonary disease	71 (19%)	62 (18%)	9 (24%)	0.52
Diabetes mellitus	168 (45%)	149 (44%)	19 (51%)	0.51
Peripheral artery disease	117 (31%)	103 (31%)	14 (38%)	0.47
Coronary artery disease	237 (63%)	217 (64%)	20 (54%)	0.29
Cerebrovascular disease	95 (25%)	84 (25%)	11 (30%)	0.66
STS PROM	5.6 [4.1, 8.2]	5.6 [4.1, 8.2]	6.7 [3.8, 10.2]	0.25
Ejection fraction (%)	60 [53, 60]	60 [55, 65]	60 [50, 60]	0.67
Baseline mean transvalvular gradient (mm Hg)	45 [40, 54]	45 [40, 54]	50 [41, 56]	0.24
Postoperative mean transvalvular gradient (mm Hg)	8 [6, 11]	8 [6, 11]	6 [4, 9]	0.03
Right ventricular pressure (mm Hg)	41 [33, 52]	40 [34, 50]	48 [33, 62]	0.08
Mitral regurgitation (mild, moderate, or severe)	56 (15%)	49 (15%)	7 (19%)	0.64
TAC (cm^3)	2.2 [1.0, 5.0]	2.1 [1.0, 4.9]	3.6 [2.2, 6.8]	0.007
TAVR route (femoral)	353 (94%)	317 (94%)	36 (97%)	0.71
Prosthesis type				0.007
Edwards	304 (81%)	281 (83%)	23 (62%)	
CoreValve	55 (14%)	41 (12%)	11 (30%)	
Other	18 (5%)	15 (4%)	3 (8%)	
Vascular complications	32 (9%)	28 (8%)	4 (11%)	0.54
Readmitted, 30 days	46 (12%)	37 (11%)	9 (24%)	0.03
Stroke/TIA, 30 days	11 (3%)	8 (2%)	3 (8%)	0.08

Values are median (first quartile, third quartile) or absolute count (percentage) as appropriate.

factors (model 2) including age, gender, coronary artery disease, diabetes mellitus, NYHA>II, peripheral vascular disease, ejection fraction, and TAVI route altered the statistical significance comparing the risk of mortality of patients with high TAC to those with moderate TAC (HR 2.66, 95% CI [1.14 to 6.22]; p = 0.02). Regarding the association of TAC categories with survival up to 1 year, Cox regression analysis was in agreement with a multivariable logistic regression analysis adjusting for significantly different factors found through comparison of survival status at 1 year (Supplemental Table 2).

Discussion

TAC is an important determinant of the stiffness of the aorta and has been considered an important marker of vascular aging.[16] Recently, we showed that the TAC burden measured on preoperative CT improved the accuracy of a model to predict cardiovascular and all-cause mortality after TAVI.[10] In the present study, we applied the same TAC quantification methodology used in our previous multicenter French study, and demonstrated its strong prognostic significance in a US cohort. Patients with high TAC >2.9 cm^3 were associated with greater than double the risk of long-term all-cause mortality compared with those with low TAC <1.6 cm^3 (HR 2.98, 95% CI [1.34 to 6.63], p = 0.008).[10] These findings have 2 implications; first, TAC can be used as an objective tool for risk stratification; second, poor vascular status is a marker of poor long-term survival. The findings were consistent after adjusting for STS-PROM, traditional cardiac risk factors, and potential confounding factors (Table 3).

Lantelme et al reported a new scoring system to help predict 1-year cardiovascular and all-cause mortality in patients being considered for TAVI in France based on TAC, patient demographics and co-morbidities, atherosclerotic disease, and cardiac function.[10] The addition of TAC to the other factors significantly improved the prediction of cardiovascular and all-cause mortality. An increase of 1 cm^3 in TAC was associated with a 6% increase in cardiovascular mortality (HR: 1.06; 95%CI: 1.01 to 1.10) and a 4% increase in all-cause mortality (HR: 1.04; 95% CI: 1.00 to 1.08). These findings were validated in an independent Dutch cohort in which each 1,000 Hounsfield unit increment in TAC was found to be significantly associated with increased all-cause mortality (HR: 1.046; 95% CI: 1.015 to 1.077; p = 0.045) after adjusting for multiple baseline variables.[11] These results were similar to those reported by Lantelme et al.[10]

The ability to predict 1-year outcomes after TAVI is important for patient selection and informed shared decision-making.[17] Combining traditional risk scores with

Table 2.
Comparison of demographic and clinical variables by TAC category

Variables	TAC category			p value
	Low (<1.6 cm^3) (n = 142)	Moderate (1.6 to 2.9 cm^3) (n = 79)	High (>2.9 cm^3) (n = 153)	
Age (years)	81 (72, 85)	83 (79, 87)	84 (79, 88)	<0.001
Body mass index (kg/m^2)	29.2 (25.3, 35.1)	27.2 (23.9, 32.9)	26.7 (23.8, 30.6)	0.003
Gender, male	74 (52%)	40 (51%)	75 (49%)	0.87
NYHA > II	92 (65%)	61 (77%)	104 (68%)	0.16
Grip strength (kg)	18.6 (13.9, 24.5)	18.0 (11.6, 24.7)	17.2 (12.6, 22.6)	0.27
KATZ score ≥ 5	132 (93%)	73 (92%)	135 (88%)	0.40
5-meter Walk test (seconds)	6.3 (4.8, 8.2)	6.4 (4.7, 9.2)	6.6 (4.9, 8.5)	0.85
Albumin (g/dL)	3.7 (3.4, 3.9)	3.6 (3.4, 3.8)	3.6 (3.4, 3.8)	0.47
Glomerular filtration rate ($ml/min/1.73m^2$)	57.7 (43.1, 77.3)	45.3 (37.3, 58.3)	41.4 (33.2, 55.1)	<0.001
Chronic obstructive pulmonary disease	28 (20%)	15 (19%)	28 (18%)	0.95
Diabetes mellitus	68 (48%)	32 (41%)	68 (44%)	0.57
Peripheral vascular disease	31 (22%)	23 (29%)	63 (41%)	0.002
Coronary artery disease	82 (58%)	46 (58%)	109 (71%)	0.03
Cerebrovascular disease	28 (20%)	18 (23%)	49 (32%)	0.04
STS PROM	4.8 (3.5, 7.3)	5.6 (4.4, 8.0)	6.7 (4.8, 9.5)	<0.001
Ejection fraction (%)	60 (51, 60)	60 (53, 60)	60 (55, 65)	0.98
Mean aortic gradient (mm Hg)	45 (41, 53)	47 (40, 59)	44 (40, 54)	0.47
Post-Mean aortic gradient (mm Hg)	9 (6, 12)	8 (6, 11)	8 (5, 11)	0.03
Right ventricular pressure (mm Hg)	39 (30, 48)	45 (36, 54)	43 (35, 54)	0.007
Mitral regurgitation (mild, moderate, or severe)	21 (15%)	13 (16%)	22 (14%)	0.91
TAC (cm^3)	0.8 (0.4, 1.1)	2.2 (1.8, 2.5)	5.8 (4.1, 8.8)	NA
TAVR route (femoral)	137 (96%)	74 (94%)	142 (93%)	0.35
Prosthesis type				0.17
Edwards	121 (85%)	67 (85%)	116 (76%)	
CoreValve	17 (12%)	10 (13%)	25 (16%)	
Other	4 (3%)	2 (2%)	12 (8%)	
Vascular complications	6 (4%)	5 (6%)	21 (14%)	0.01
Readmitted, 30 days	18 (13%)	11 (14%)	17 (11%)	0.81
Stroke/TIA, 30 days	5 (4%)	0 (0%)	6 (4%)	0.21
Mortality, 30 days	0 (0%)	2 (3%)	2 (1%)	0.16
Mortality, 1 year	8 (6%)	5 (6%)	24 (16%)	0.008

Values are median (first quartile, third quartile) or absolute count (percentage) as appropriate.

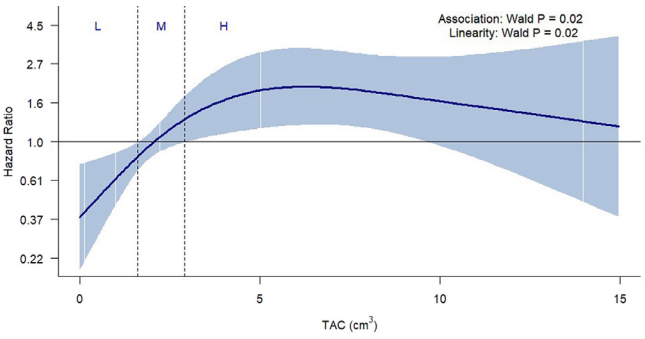

Figure 3. Association of TAC modeled as a restricted cubic spline with three knots at the 5th, 50th, and 95th percentiles with the hazard ratio of mortality. Three categories of TAC (low < 1.6, moderate 1.6 to 2.9, high > 2.9) cm^3 are selected based on the points where the 95% confidence band of the hazard ratio relative to the median TAC measurement is less than (<1.6 cm^3) and greater than (>2.9 cm^3) a hazard ratio of 1 (dashed lines). L, low; M, moderate; H, high.

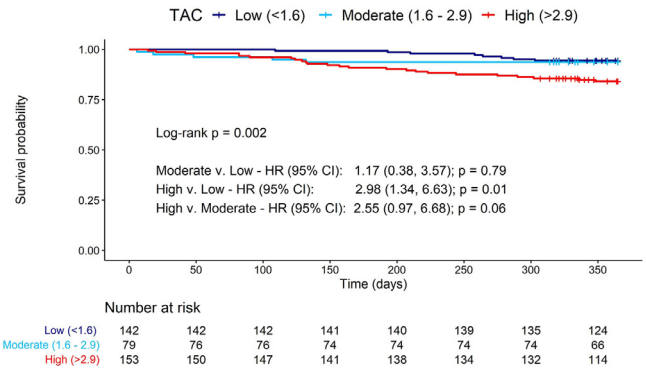

Figure 4. Kaplan-Meier curves with Cox-proportional hazard model estimates of the hazard ratio of moderate and high TAC relative to low TAC, and high TAC relative to moderate TAC. CI, confidence interval; HR, hazard ratio.

various frailty metrics may improve their predictability.[18,19] However, several studies have suggested that these markers may be limited by subjectivity bias.[20,21] TAC measurements can be obtained from CT scans, which are routinely performed before TAVI. Adding TAC to preoperative evaluation may provide an objective, reproducible, and widely available tool that can help identify poor TAVI responders at 1 year. After adjusting for frailty markers, TAC proved to be an independent prognostic factor for mortality. The

Table 3.
Risk of mortality of high TAC (>2.9 cm^3) relative to low TAC (<1.6 cm^3) by univariable and multivariable Cox regression analysis

	HR (95%CI)	p value
Unadjusted		
TAC high vs low	2.98 (1.34 − 6.63)	0.008
TAC high vs moderate	2.55 (0.97 − 6.68)	0.06
TAC moderate vs low	1.17 (0.38 − 3.57)	0.79
Adjusted Model 1		
TAC high vs low	2.73 (1.21 − 6.15)	0.02
TAC high vs moderate	2.02 (0.88 − 4.65)	0.10
TAC moderate vs low	1.14 (0.37 − 3.48)	0.82
Adjusted Model 2		
TAC high vs low	2.78 (1.32 − 5.85)	0.007
TAC high vs moderate	2.66 (1.14 − 6.22)	0.02
TAC moderate vs low	1.04 (0.40 − 2.73)	0.93
Adjusted Model 3		
TAC high vs low	2.38 (1.09 - 5.17)	0.03
TAC high vs moderate	2.10 (0.88 − 4.98)	0.09
TAC moderate vs low	1.13 (0.43 − 3.01)	0.80

Adjusted Model 1: Society of Thoracic Surgeons predicted risk of mortality.

Adjusted Model 2: Age, gender, coronary artery disease, diabetes mellitus, New York Heart Association (NYHA) functional classification > II, peripheral vascular disease, ejection fraction, and transcatheter aortic valve implantation route.

Adjusted Model 3: Age, body mass index, glomerular filtration rate, peripheral vascular disease, coronary artery disease, cerebrovascular disease, postoperative mean aortic gradient, right ventricular pressure, and Society of Thoracic Surgeons predicted risk of mortality.

present study provides additional evidence supporting the importance of vascular calcium load measurements to optimize risk stratification and management of patients with severe aortic stenosis. Larger studies may be needed to evaluate the predictive value of adding a TAC score instead of PAD within the STS-PROM score or TAVI score calculation.

This study is a retrospective analysis of a single-center experience with a limited study cohort, and thus, may not be representative of the broader experience. Technological refinement and inclusion of patients with lower risk profiles may improve future outcomes.

In conclusion, TAC is a predictor of late mortality after TAVI. Adding TAC to preoperative evaluation may provide an objective, reproducible, and potentially widely available tool that can help in decision-making.

Author's Contribution

Mohanad Hamandi: Writing-Original draft preparation. **Pierre Amiens**: Data curation. **Paul A. Grayburn**: Conceptualization, Methodology. **Karim Al-Azizi**, **Ambarish Gopal**, **Molly A. Szerlip**, **Srinivasa Potluri**, and **J. Michael DiMaio**: Data Curation. **Johanna S. van Zyl**: Data analysis, statistics. **Allison T. Lanfear**: Draft preparation. **Muriel Rabilloud** and **Benjamin Riche**: Data analysis and statistics. **Michael J. Mack**: Conceptualization, Methodology. **Brahim Harbaoui**: Conceptualization, Methodology. **Pierre Lantelme**: Conceptualization, Methodology, and Supervision.

Disclosures

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2020.10.045.

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