Changes in left ventricular global longitudinal strain after transcatheter aortic valve implantation according to calcification burden of the thoracic aorta

Gegenava, T.; Vollema, E.M.; Rosendael, A. van; Abou, R.; Goedemans, L.; Kley, F. van der; ... ; Delgado, V.

Changes in Left Ventricular Global Longitudinal Strain after Transcatheter Aortic Valve Implantation according to Calcification Burden of the Thoracic Aorta

Tea Gegenava, MD, E. Mara Vollema, MD, Alexander van Rosendael, MD, Rachid Abou, MD, Laurien Goedemans, MD, Frank van der Kley, MD, Arend de Weger, MD, Nina Ajmone Marsan, MD, PhD, Jeroen J. Bax, MD, PhD, and Victoria Delgado, MD, PhD, *Leiden, The Netherlands*

Background: After transcatheter aortic valve replacement (TAVR), changes in left ventricular (LV) function are partly influenced by the vascular afterload. The burden of thoracic aorta calcification is a component of vascular afterload.

Objective: To assess changes in LV systolic function measured with global longitudinal strain (GLS) in relation to the burden of thoracic aorta calcification in patients with severe aortic stenosis treated with TAVR.

Methods: Calcification of the thoracic aorta was estimated on noncontrast computed tomography in 210 patients (50% male, 80 ± 7 years) undergoing TAVR. Conventional and speckle-tracking echocardiography were performed at baseline (prior to TAVR) and 3-6 months and 12 months after TAVR. Patients were divided according to tertiles of calcification burden of the thoracic aorta.

Results: At baseline, patients within the first tertile of thoracic aorta calcification (0-1,395 Hounsfield Units, HU) had better LV systolic function (LV ejection fraction [LVEF], 47% ± 9%; and LV GLS, −15% ± 5%) as compared with the second tertile (1,396-4,634 HU; LVEF, 46% ± 10%; and LV GLS, −14% ± 4%), and the third tertile (>4,634 HU; LVEF, 44% ± 10%; and LV GLS, −12% ± 4%). During follow-up, patients within tertile 1 of calcification of thoracic aorta achieved significantly better LV systolic function and larger regression of LV mass at 12 months of follow-up than patients within the other tertiles. This pattern was more pronounced in patients with reduced LVEF at baseline.

Conclusions: After TAVR, LVEF and GLS improves and LV mass index is reduced significantly at 3-6 and 12 months of follow-up. Patients within the lowest burden of thoracic aorta calcification achieved the best values of LVEF and LV GLS at 1-year follow-up. (J Am Soc Echocardiogr 2019;32:1058-66.)

Keywords: Transcatheter aortic valve replacement, Global longitudinal strain, Left ventricular mass, Thoracic aorta calcification

In patients with severe aortic stenosis (AS), the left ventricle faces a double load: the valvular load caused by the stenotic valve and the vascular (arterial) load. The calcification of the thoracic aorta is an important determinant of the vascular afterload of the LV. In response to this double afterload, the left ventricle develops concentric hypertrophy to keep the wall stress at minimum and the left ventricular ejection fraction (LVEF) preserved. However, strain echocardiography has shown that LV systolic function can be impaired at early stages of the disease when LVEF is still normal. Various studies have shown that LV global longitudinal strain (GLS) is impaired in patients with severe AS and preserved LVEF, regardless of the symptomatic status.[1,2] After aortic valve replacement, improvement in LV systolic function and regression in LV mass have been reported.[3,4] However, the changes in LV systolic function and regression in LV mass may be influenced by the remaining vascular afterload. Calcification of the thoracic aorta is an important underlying pathophysiological mechanism of vascular afterload and has been associated with poor prognosis.[5-7] In patients with symptomatic severe AS who are referred for transcatheter aortic valve replacement (TAVR), computed tomography (CT) is pivotal for the

From the Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands.

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Reprint requests: Victoria Delgado, MD, PhD, Department of Cardiology, Heart Lung Center, Albinusdreef 2, 2300 RC Leiden, the Netherlands (E-mail: *V.delgado@lumc.nl*).

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Abbreviations

AS = Aortic stenosis

euroSCORE = European System for Cardiac Operative Risk Evaluation

GLS = Global longitudinal strain

LV = Left ventricular

LVEF = Left ventricular ejection fraction

SAC = Systemic arterial compliance

SVR = Systemic vascular resistance

TAVR = Transcatheter aortic valve replacement

Zva = Valvulo-arterial impedance

procedural planning and device size selection. Nonenhanced CT may form part of the CT data acquisition protocol and permits the assessment of calcification burden of the thoracic aorta. The present observational study investigated the influence of thoracic aorta calcification burden on the changes in LV systolic function and LV mass after TAVR. In addition, the effect of thoracic aorta calcification burden was compared between patients with preserved versus reduced LVEF at baseline.

METHODS

Patient Population

A total of 210 patients (50% male, 80 ± 7 years) treated with TAVR who had noncontrast-enhanced CT of the aortic valve and complete echocardiographic follow-up (baseline, 3-6 months and 12 months) were analyzed. Severe AS was defined according to current recommendations: an aortic valve area <1.0 cm^2 or indexed aortic valve area <0.6 cm^2/m^2, peak aortic jet velocity ≥4 m/sec, and a mean transvalvular pressure gradient ≥40 mm Hg.[8]

Clinical Data

Clinical data included demographics, cardiovascular risk factors, clinical symptoms, medications, and operative mortality risk calculated according to the logistic European System for Cardiac Operative Risk Evaluation (euroSCORE). All clinical data were collected from the Cardiology Department Information System (EPD-Vision; Leiden University Medical Center, Leiden, The Netherlands). The institutional review board approved this retrospective analysis of clinically acquired data and waived the need for patient written informed consent.

Echocardiography

Commercially available ultrasound systems equipped with M5S transducers (E9 and E95 systems, General Electric Vingmed, Horten, Norway) were used to acquire two-dimensional, color, continuous-, and pulsed-wave Doppler data from parasternal and apical views with the patient in the left lateral decubitus position. Images were stored digitally on hard disks for offline analysis (EchoPac version BT13; GE Medical Systems). LV end-diastolic and end-systolic volumes were measured on the apical two- and four-chamber views using Simpson's method, and the LVEF was derived.[9] Aortic valve peak jet velocity was estimated from the continuous-wave Doppler recordings obtained on the three- or five-chamber apical views and, if needed, on the right parasternal view using the Pedoff probe. The peak and mean transaortic pressure gradients were calculated according to the Bernoulli equation. The aortic valve area was calculated using the continuity equation.[8]

In addition to standard echocardiographic measurements, components of LV afterload—systemic arterial compliance (SAC), valvulo-arterial impedance (Zva), systemic vascular resistance (SVR)—were calculated according to recommended formulas.[10-12]

Two-Dimensional Speckle-Tracking Echocardiography

LV GLS was measured with two-dimensional speckle-tracking echocardiography with commercially available software (EchoPac version BT13; GE Medical Systems). On the apical three-, four-, and two-chamber views, the LV endocardial border was traced and the software displayed a region of interest automatically encompassing the LV myocardial wall, and if needed, the region of interest was adjusted manually. LV GLS was calculated as the average of longitudinal strain values of each apical view. LV GLS is presented as negative values conventionally; more negative values indicate better LV systolic function.

Multidetector Row CT

Multidetector row CT scans were performed prior to TAVR using a 320-row CT scanner (Aquilion ONE, Toshiba Medical Systems, Otawara, Japan).[13] The multidetector row CT acquisition protocol started with a prospective calcium scan (collimation 4 × 3.0 mm, tube voltage and current of 120 kV and 200 mA). Subsequently, contrast-enhanced CT data were acquired.[13] The noncontrast calcium scans were used to assess the Agatston thoracic aorta calcium score.

Data processing was performed in a remote workstation with dedicated CT analysis software (Vitrea FX 1.0, Vital Images, Minnetonka, MN). Calcium burden of the thoracic aorta was estimated according to the Agatston method from the noncontrast axial images delineating all the calcified plaques from the aortic sinus to the end of the thoracic aorta. The thoracic aorta was divided into the ascending aorta (from the aortic sinus of valsalva to the origin of the left subclavian artery) and the descending aorta (from the origin of the left subclavian artery to the level of the diaphragm).

Follow-Up

Clinical and echocardiographic follow-up was performed at 3 or 6 months and 12 months after TAVR. Complete transthoracic echocardiography was performed to assess prosthetic valve hemodynamics and LV dimensions and function. Patients were followed up for the occurrence of all-cause mortality.

Statistical Analysis

Patients were classified according to tertiles of the thoracic aorta calcium score. Continuous variables are presented as mean ± SD if normally distributed or as median and interquartile range otherwise. Categorical variables are presented as frequencies and percentages. One-way analysis of variance and Mann-Whitney test for normally and nonnormally distributed variables, respectively, were used to compare continuous variables across the tertiles of thoracic aorta calcification, whereas a χ^2-test was used to compare categorical variables. For multiple comparisons, post hoc Bonferroni analyses were performed. General linear repeated measurement models were used to analyze changes in LVEF, LV GLS, LV mass, and other echocardiographic parameters over time for the overall population and compared across the tertiles of thoracic aorta calcification groups.

HIGHLIGHTS

- Thoracic aorta calcification may increase the vascular load in severe AS.
- Low calcification of the thoracic aorta shows more LV mass regression after TAVR.
- Low calcification of the thoracic aorta shows better LV GLS after TAVR.

Cumulative survival rates were analyzed based on Kaplan-Meier survival method and compared across groups with the log-rank test. Statistical analysis was performed on SPSS for Windows version 23.0 (IBM, Armonk, NY). A two-tailed P value $< .05$ was considered statistically significant.

RESULTS

Baseline Clinical and Echocardiographic Characteristics

Patients were divided according to the following tertiles of thoracic aorta calcification: tertile 1 (0-1,395 Hounsfield Units, HU), tertile 2 (1,396-4,634 HU), and tertile 3 (>4,634 HU). The clinical and echocardiographic characteristics of the overall population and the tertiles of thoracic aorta calcification are presented in Tables 1 and 2. The groups were comparable in terms of age and gender. However, patients in the third tertile (i.e., highest values of thoracic aorta calcification) more frequently had hypercholesterolemia, history of coronary artery disease, and peripheral vascular disease. Patients within the highest tertile of thoracic aorta calcification had the highest pulse pressure compared with the other tertiles. In terms of echocardiographic characteristics, patients within the first tertile of thoracic aorta calcification (i.e., lowest calcium load) showed better LV function (based on both conventional LVEF and advanced LV GLS; LVEF: 47% ± 9% for tertile 1 vs 44% ± 10% for tertile 3, $P = .246$; LV GLS: −15% ± 5% for tertile 1 vs −12% ± 4% for tertile 3, $P < .001$; Table 2) and a smaller LV mass index and relative wall thickness (Table 2). Furthermore, patients within the highest tertile of thoracic aorta calcification showed higher SVR and Zva and significantly lower SAC compared with the other tertiles, indicating that those patients faced the highest vascular afterload (Table 2).

Changes in LV Systolic Function and LV Mass Index after TAVR

Table 3 summarizes changes in conventional and speckle-tracking echocardiographic variables after TAVR. After TAVR, a significant decrease in transvalvular gradients and increase in aortic valve area at 3-6 months and at 1 year of follow-up were observed. LVEF increased at 3-6 months and 1 year of follow-up in the overall population (Table 3). Similarly, LV GLS showed significant improvement over time: from −14% ± 4% to −16% ± 4% at 3-6 months, and to −17% ± 4% at 1-year follow-up in overall population. In addition, LV mass index decreased from 114 ± 44 g/m^2 to 111 ± 59 g/m^2 at 3-6 months and to 90 ± 38 g/m^2 at 1-year follow-up (Table 3).

Table 1 Baseline characteristics of total patient population and divided by thoracic aorta calcium burden (per tertile)

Baseline characteristics	Overall population (N = 210)	Thoracic aorta calcium score, mm^3			P value
		Tertile 1 (0-1,395 mm^3) (n = 70)	Tertile 2 (1,396-4,634 mm^3) (n = 70)	Tertile 3 (>4,634 mm^3) (n = 70)	
Age, years	80 ± 7	79 ± 8.5	81 ± 6	80 ± 7	.252
Gender, male n (%)	105 (50)	39 (56)	31 (44)	35 (50)	.400
EuroSCORE ≥20, n (%)	81 (39)	21 (30)	26 (38)*	34 (49)	.073
History of CAD, n (%)	126 (60)	33 (47)	47 (67)*	46 (66)†	.026
Hypertension, n (%)	159 (76)	49 (70)	57 (81)	53 (76)	.288
Hypercholesterolemia, n (%)	139 (66)	38 (54)	47 (67)	54 (77)†	.016
Diabetes mellitus, n (%)	55 (26)	19 (27)	18 (26)	18 (26)	.976
Peripheral vascular disease, n (%)	54 (26)	11 (16)	18 (26)	25 (36)†	.026
Current smoker, n (%)	50 (24)	17 (24)	14 (20)	19 (27)	.607
NYHA class 3-4, n (%)	119 (57)	42 (60)	39 (56)	38 (55)	.833
SBP, mm Hg	139 ± 24	137 ± 24	137 ± 23	142 ± 25	.309
DBP, mm Hg	70 ± 12	71 ± 12	69 ± 12	70 ± 13	.642
PP, mm Hg	69 ± 21	66 ± 22	68 ± 20	72 ± 19	.183

CAD, Coronary artery disease; *DBP*, diastolic blood pressure; *NYHA*, New York Heart Association; *PP*, Pulse pressure; *SBP*, systolic blood pressure.
*$P < .05$, tertile 1 vs tertile 2.
†$P < .05$, tertile 1 vs tertile 3.

Table 2 Preprocedural echocardiographic findings in total TAVR population and divided by thoracic aorta calcium burden (per tertile)

Variable	Total population (*N* = 210)	Thoracic aortic calcium score			*P* value
		Tertile 1 (0-1,395 mm^3) (*n* = 70)	Tertile 2 (1,396-4,634 mm^3) (*n* = 70)	Tertile 3 (>4,634 mm^3) (*n* = 70)	
Aortic valve area, cm^2	0.7 ± 0.2	0.7 ± 0.3	0.7 ± 0.2	0.8 ± 0.3	.737
Mean aortic valve gradient, mm Hg	41 ± 18	44 ± 21	43 ± 16	36 ± 15*	.020
Peak aortic valve gradient, mm Hg	64 ± 26	69 ± 25	67 ± 28	57 ± 23*,†	.015
LVEF, %	46 ± 10	47 ± 9	46 ± 10	44 ± 10	.246
Stroke volume index, mL/m^2	43 ± 16	41 ± 15	44 ± 16	43 ± 16	.665
LVEDV, mL	93 ± 33	89 ± 35	94 ± 28	96 ± 34	.402
LVESV, mL	53 ± 26	52 ± 32	51 ± 20	55 ± 23	.689
LV GLS, %	−14 ± 4	−15 ± 5	−14 ± 4	−12 ± 4*,†	<.001
LV mass index, g/m^2	114 ± 44	100 ± 39	119 ± 49‡	122 ± 40*	.005
RWT	0.5 ± 0.2	0.4 ± 0.2	0.5 ± 0.2	0.5 ± 0.2	.047
SAC, $mL/m^2/mm$ Hg	0.7 ± 0.4	0.72 ± 0.4	0.73 ± 0.4	0.55 ± 0.4*,†	.006
SVR, $dyne.s.cm^{-5}$	2,875 ± 1,346	2,757 ± 1,052	2,748 ± 1,694	3,118 ± 1,207	.192
Zva, $mm Hg/mL/m^2$	4.8 ± 1.9	4.6 ± 1.7	4.8 ± 2.2	5.2 ± 1.8	.246

LV, Left ventricle; *LVEDV*, left ventricular end-diastolic volume; *LVESV*, left ventricular end-systolic volume; *RWT*, relative wall thickness.
*$P < .05$, tertile 1 vs tertile 3.
†$P < .05$, tertile 2 vs tertile 3.
‡$P < .05$, tertile 1 vs tertile 2.

Table 3 Changes in clinical and echocardiographic parameters over time in overall population

Variable	Baseline (*N* = 210)	3-6 months of follow-up (*N* = 210)	1 year of follow-up (*N* = 210)	*P* value
SBP, mm Hg	142 ± 27	146 ± 22	146 ± 26	.115
DBP, mm Hg	71 ± 13	71 ± 12	72 ± 13	.007
PP, mm Hg	71 ± 22	75 ± 19	74 ± 21	.146
Aortic valve area, cm^2	0.7 ± 0.2	1.5 ± 0.5*	1.4 ± 0.5†,‡	.010
Mean aortic valve gradient, mm Hg	41 ± 18	9 ± 5*	9 ± 6†	<.001
Peak aortic valve gradient, mm Hg	64 ± 26	18 ± 10*	18 ± 10†	<.001
LVEDV, mL	93 ± 32	84 ± 32*	76 ± 30†,‡	.072
LVESV, mL	53 ± 26	43 ± 21*	36 ± 20†,‡	<.001
LVEF, %	46 ± 10	51 ± 9.5*	54 ± 10†,‡	<.001
Stroke volume index, mL/m^2	43 ± 16	43 ± 16	41 ± 15	.122
LV GLS, %	−14 ± 4	−16 ± 4*	−17 ± 4†,‡	.001
LV mass index, g/m^2	114 ± 44	111 ± 59	90 ± 38†,‡	<.001
RWT	0.5 ± 0.2	0.4 ± 0.1*	0.4 ± 0.1†	.015

DBP, Diastolic blood pressure; *LV*, left ventricle; *LVEDV*, left ventricular end-diastolic volume; *LVESV*, left ventricular end-systolic volume; *PP*, pulse pressure; *RWT*, relative wall thickness; *SBP*, systolic blood pressure; *SVi*, Stroke volume index.
*$P < .05$, baseline vs 3-6 months of follow-up.
†$P < .05$, baseline vs 1 year of follow-up.
‡$P < .05$, 3-6 months vs 1 year of follow-up.

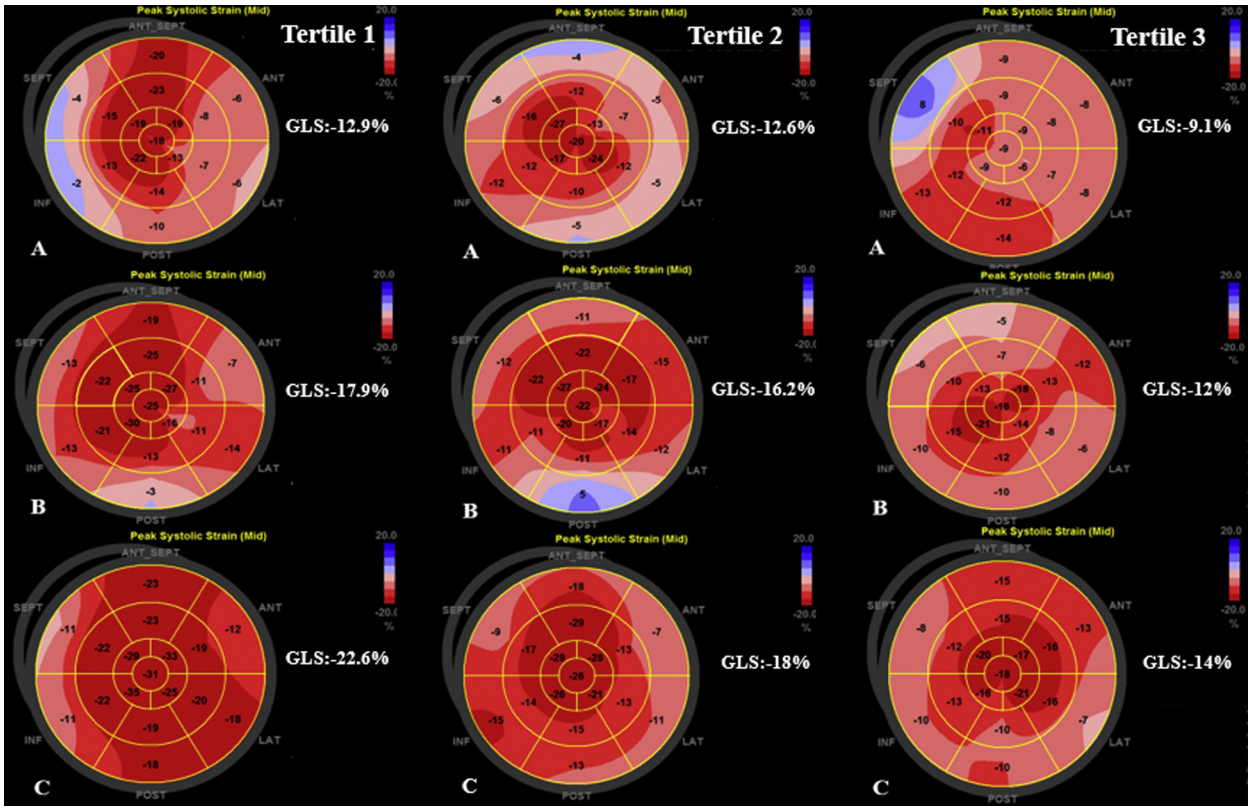

Figure 1 Examples of changes in LV GLS after TAVR: the *left panels* show the bull's-eye plots of a patient within the first tertile of thoracic aorta calcification, the *middle panels* correspond to a patient within the second tertile, and the *right panels* correspond to a patient within the third tertile of thoracic aorta calcification. LV GLS improves from baseline **(A)** to 3-6 months follow-up **(B)** and 1-year follow-up **(C)** for all tertiles.

When dividing the population according to the tertiles of thoracic aorta calcification, all groups showed a significant reduction in mean transaortic gradients and increase in aortic valve area immediately after TAVR. LVEF and LV GLS also increased significantly in all groups (Figures 1 and 2 and Table 4). However, patients within the first tertile of thoracic aorta calcification showed the best values of LVEF and LV GLS at 1-year follow-up compared with the patients of the other groups.

In addition, LV mass index decreased significantly in all groups. However, patients within the first tertile of thoracic aorta calcification showed the lowest value of LV mass index at 1- year follow-up (Figure 2 and Table 4).

Influence of Thoracic Aorta Calcification Burden on Changes in LV Systolic Function and LV Mass in Patients with Reduced versus Preserved LVEF at Baseline

There were 102 patients with preserved LVEF (≥50%) and 108 with reduced LVEF (<50%). Both groups of patients showed significant changes in LV systolic function and LV mass index during follow-up (Supplemental Tables 1 and 2, available at www.onlinejase.com). However, patients with a reduced LVEF at baseline showed a higher magnitude of improvement in LVEF and LV GLS as compared with patients with preserved LVEF at baseline. In addition, patients with reduced LVEF at baseline had the lowest values of LV mass index at 1 year of follow-up. The influence of thoracic aorta calcification on changes in LV systolic function and LV mass index was similar in patients with preserved and reduced LVEF and similar to those observed in the overall population.

Influence of LV GLS and Calcification Burden of Thoracic Aorta on the Outcomes in TAVR Patients

Patients were divided according to a cutoff value of LV GLS −14% based on previous studies.[2,14] LV GLS ≤ −14% was considered as more preserved LV systolic function, whereas > −14% LV GLS was considered as impaired LV systolic function. At baseline, 23 (33%) patients within tertile 1 of thoracic aorta calcification burden had LV GLS > −14% versus 47 (67%) patients within tertile 3; at 1 year of follow-up 14 (20%) patients showed LV GLS > −14% within tertile 1 versus 22 (31%) patients within tertile 3 (Figure 3).

During a median follow-up of 31 months (interquartile range, 17-48 months), 64 patients (31%) died. The Kaplan-Meier analysis shows that patients within tertile 3 had the worst survival and particularly those with LV GLS > −14% had more events than patients with LV GLS ≤ −14%, although the difference is not statistically significant ($\chi^2 = 0.322$, log rank = 0.570; Figure 4). In the tertile 1 group, the cumulative rate of all-cause mortality of patients with LV GLS ≤ −14% was 18% versus 19% for the patients with LV GLS > −14. In the tertile 3 group, the cumulative rate of all-cause mortality for the patients with LV GLS ≤ −14% was 22% versus 27% for the patients with LV GLS > −14% (Figure 4).

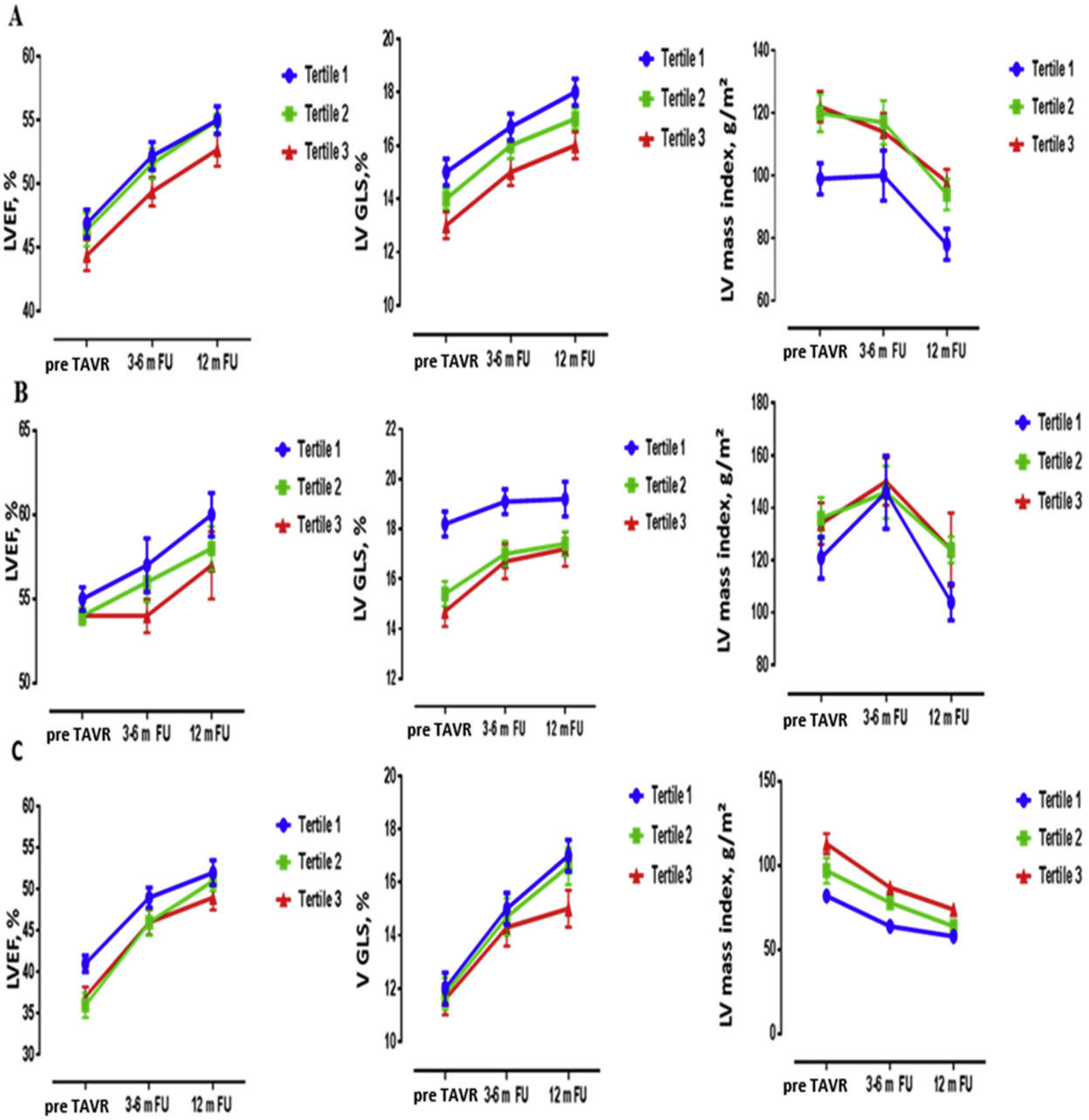

Figure 2 Changes in LVEF, LV GLS, and LV mass index over time according to tertiles of thoracic aorta calcification in the overall population **(A)**, patients with preserved LVEF **(B)**, and patients with reduced LVEF **(C)**. *LV*, Left ventricle.

DISCUSSION

Changes in LVEF, LV GLS, and LV mass index after TAVR are strongly associated with the calcium load in the thoracic aorta. Patients with the lowest burden of thoracic aorta calcification showed the largest improvement in LV systolic function and regression in LV mass, independently of the baseline LVEF.

Influence of Thoracic Aorta Calcification on Changes in LV Systolic Function and LV Mass Regression after TAVR

The excessive pressure overload in AS causes an increase of systolic wall stress with concentric remodeling expressed as myocardial hypertrophy, myocardial fibrosis, and diastolic and systolic dysfunction. Aortic valve replacement reduces the ventricular afterload caused by the valvular component and favors a reverse LV remodeling with LV mass regression and improvement in LV systolic function. However, the vascular component of the LV afterload may remain unchanged after aortic valve replacement. Cho *et al.*[15] demonstrated in 47 patients with severe AS undergoing surgical aortic valve replacement that the patients with the highest values of calcium score of the thoracic aorta had the largest LV mass index. After multivariate regression analysis, calcium score of the thoracic aorta was the only independent variable associated with LV mass index. Interestingly, after aortic valve replacement, LV mass index was reduced significantly and LVEF improved. The change in LV mass index was significantly

Table 4 Changes in vascular afterload and echocardiographic parameters at 3 to 6 and 12 months of follow-up according to thoracic aorta calcification tertiles

	Tertile 1 (n = 70)			Tertile 2 (n = 70)			Tertile 3 n = 70				
Patients (N = 210)	Pre-TAVR	3-6 months of follow-up	1 year of follow-up	Pre-TAVR	3-6 months of follow-up	1 year of follow-up	Pre-TAVR	3-6 months of follow-up	1 year of follow-up	P for time	P between subject effects
SBP, mm Hg	141 ± 28	149 ± 13	143 ± 22	138 ± 27	148 ± 28	155 ± 30	145 ± 27	143 ± 23	143 ± 27	<.001	.821
DPB, mm Hg	73 ± 11	74 ± 12	73 ± 13	69 ± 14	72 ± 11	71 ± 12	71 ± 14	68 ± 11	72 ± 14	<.001	.343
PP, mm Hg	68 ± 23	74 ± 15	69 ± 17	69 ± 26	76 ± 24	83 ± 25	75 ± 19	75 ± 20	72 ± 20	<.001	.421
Aortic valve area, cm^2	0.7 ± 0.3	1.5 ± 0.6	1.4 ± 0.5	0.7 ± 0.2	1.6 ± 0.5	1.4 ± 0.4	0.8 ± 0.2	1.6 ± 0.6	1.4 ± 0.5	<.001	.363
Mean aortic valve gradient, mm Hg	44 ± 21	9.5 ± 6	9.7 ± 5	43 ± 16	9.4. ± 6	9 ± 6	36 ± 15	9 ± 4.5	9 ± 5	<.001	.018
Peak aortic valve gradient, mm Hg	68 ± 25	18 ± 10	19 ± 10	67 ± 28	18 ± 11	18 ± 10	57 ± 23	18 ± 8	17 ± 9	<.001	.025
LVEF, %	47 ± 9	52 ± 9	55 ± 9	46 ± 11	52 ± 10	55 ± 8	44 ± 10	49 ± 10	53 ± 11	<.001	.143
Svi, mL/m^2	42 ± 15	44 ± 17	41 ± 16	44 ± 16	42 ± 15	39 ± 12	42 ± 16	41 ± 16	40 ± 16	.098	.918
LV GLS, %	-15 ± 5	-17 ± 4	-18 ± 4	-14 ± 4	-16 ± 4	-17 ± 4	-12 ± 4	-15 ± 4	-16 ± 5	<.001	.006
LV mass, g	185 ± 68	160 ± 87	145 ± 74	214 ± 74	187 ± 71	171 ± 68	229 ± 83	191 ± 73	180 ± 62	<.001	.002
LV mass index, g/m^2	99 ± 39	100 ± 67	78 ± 38	120 ± 49	117 ± 60	94 ± 38	122 ± 40	115 ± 49	98 ± 36	<.001	.005
LVEDV, mL	89 ± 35	85 ± 34	77 ± 30	95 ± 28	81 ± 27	73 ± 26	96 ± 34	84 ± 34	77 ± 35	<.001	.792
LVESV, mL	52 ± 32	41 ± 20	35 ± 19	51 ± 21	42 ± 21	33 ± 16	54 ± 23	45 ± 22	40 ± 23	<.001	.418
RWT	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.5 ± 0.2	0.4 ± 0.1	0.4 ± 0.2	0.5 ± 0.2	0.4 ± 0.1	0.4 ± 0.1	<.001	.074

DBP, Diastolic blood pressure; *LV*, left ventricle; *LVEDV*, left ventricular end-diastolic volume; *LVESV*, left ventricular end-systolic volume; *PP*, pulse pressure; *RWT*, relative wall thickness; *SBP*, systolic blood pressure; *SVi*, Stroke volume index.

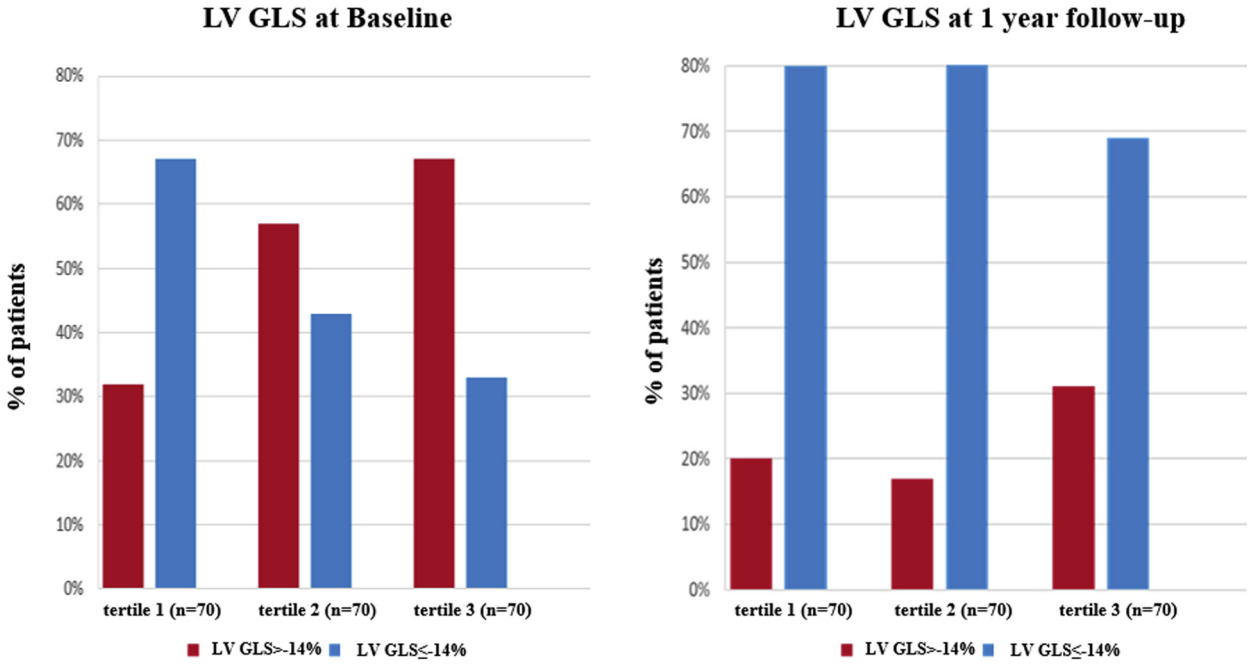

Figure 3 LV GLS at baseline and at 1-year follow-up according to calcification burden of thoracic aorta.

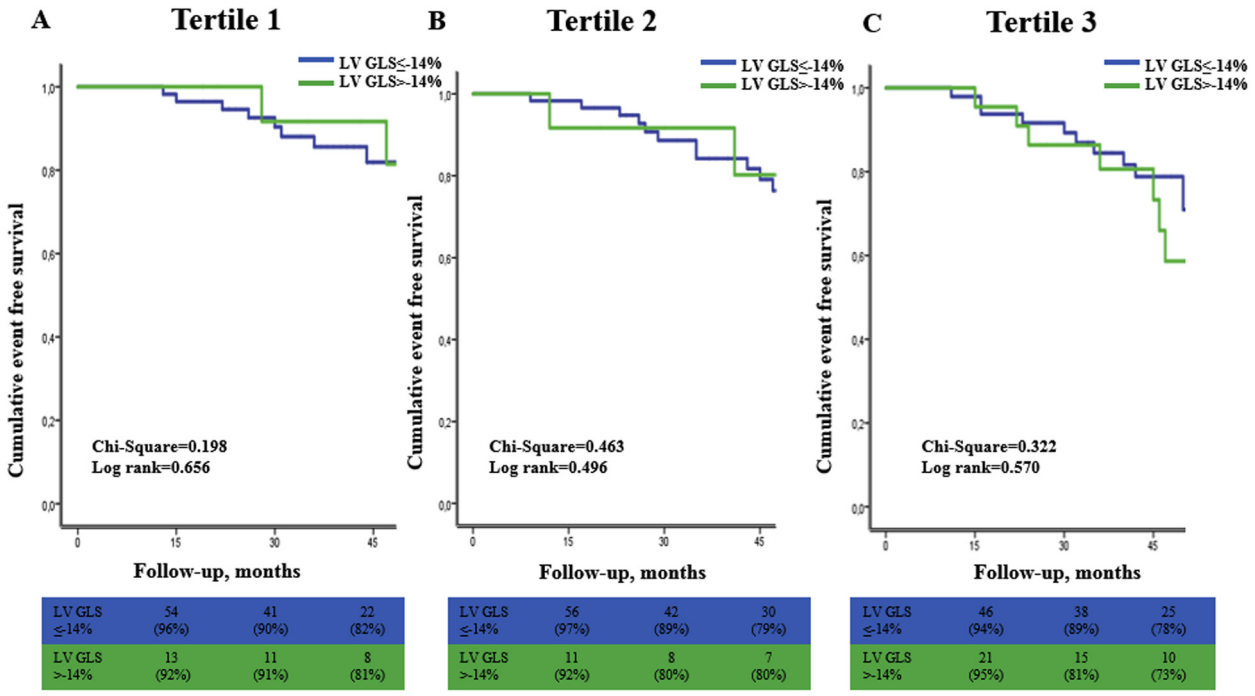

Figure 4 Influence of LV GLS and calcification burden of thoracic aorta on the outcomes in TAVR patients.

correlated with the calcium score of the thoracic aorta: patients with the lowest values of calcium score exhibited the largest LV mass regression. Structural alterations of the media layer of the aortic wall, deposition of collagen, and vascular calcification contribute to the increased stiffness of the thoracic aorta leading to increased LV afterload and LV hypertrophy. The present study confirms these results and shows that patients within the lowest tertile of thoracic aorta calcification had the largest improvement in LV systolic function and regression in LV mass.

In addition, the present study provides further insights into the improvement in LV systolic function by providing data on LV GLS. In 68 patients with low-flow low-gradient severe AS undergoing TAVR, Kamperidis *et al.*[3] showed that LV systolic function as measured by LV GLS improved in patients with reduced LVEF at baseline and in patients with preserved LVEF.[3] In the present study we confirm that LV GLS improves after TAVR in patients with both reduced and preserved LVEF and this improvement is more pronounced in patients within the lowest tertile of thoracic aorta

calcification. Yotti *et al.*[16] demonstrated in 23 patients treated with TAVR a large reduction in transvalvular gradient followed by significant increase in vascular resistance. Vascular resistance and other components of remaining vascular afterload after the TAVR such as calcification burden of thoracic aorta may influence changes in LV systolic function and less regression in LV mass as demonstrated in the present study.

Furthermore, the present manuscript provides additional evidence on the prognostic implications of calcification burden of the thoracic aorta, showing that patients with the highest burden of thoracic aorta calcification have the highest mortality rates regardless of the value of LV GLS.

Study Limitations

Several limitations should be acknowledged. This was a retrospective, single-center study. Patients were selected based upon the availability of noncontrast-enhanced CT scans. In a considerable number of patients, follow-up was not performed at a fixed time point, and, therefore, these patients were excluded from the study.

CONCLUSION

After TAVR, LVEF and GLS improve and LV mass index reduces significantly at 3-6 and 12 months of follow-up. Patients within the lowest burden of thoracic aorta calcification achieved the best values of LVEF and LV GLS at 1-year follow-up.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.echo.2019.05.011.

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APPENDIX

Supplemental Table 1 Changes in echocardiographic parameters and in blood pressure at 3-6 and 12 months of follow-up according to tertiles of thoracic aorta calcium burden in TAVR patients with preserved LVEF

Patients (n = 102)	Tertile 1 (n = 31)			Tertile 2 (n = 41)			Tertile 3 (n = 30)			P for time	P between subject
	Pre-TAVR	3-6 months	1-year follow-up	Pre-TAVR	After 30-90 days	1-year follow-up	Pre-TAVR	After 30-90 days	1-year follow-up		
SBP, mm Hg	147 ± 28	147 ± 14	142 ± 20	135 ± 25	147 ± 27	166 ± 27	158 ± 27	150 ± 27	155 ± 27	<.001	.391
DBP, mm Hg	73 ± 11	71 ± 10	74 ± 10	66 ± 15	69 ± 12	72 ± 13	77 ± 13	69 ± 10	75 ± 14	<.001	.304
PP, mm Hg	74 ± 24	75 ± 15	66 ± 16	69 ± 29	79 ± 23	94 ± 23	81 ± 19	81 ± 23	79 ± 19	<.001	.277
Aortic valve area, cm^2	0.7 ± 0.2	1.42 ± 0.4	1.4 ± 0.5	0.7 ± 0.2	1.6 ± 0.4	1.4 ± 0.3	0.7 ± 0.2	1.5 ± 0.5	1.4 ± 0.4	<.001	.499
Mean aortic valve gradient, mm Hg	51 ± 23	10 ± 5	12 ± 6	45 ± 15	10 ± 4	9 ± 7	39 ± 15	9 ± 4	9 ± 6	<.001	.023
Peak aortic valve gradient, mm Hg	74 ± 18	20 ± 8	23 ± 11	69 ± 29	19 ± 8	19 ± 12	60 ± 23	18 ± 10	19 ± 11	<.001	.064
LVEF, %	55 ± 4	57 ± 9	60 ± 7	54 ± 3	56 ± 8	58 ± 8	54 ± 3	54 ± 8	57 ± 12	<.001	.339
Svi, mL/m^2	48 ± 12	48 ± 16	44 ± 16	51 ± 15	43 ± 15	39 ± 11	51 ± 14	42 ± 12	40 ± 17	<.001	.646
LV GLS, %	−18 ± 3	−19 ± 3	−19 ± 4	−16 ± 3	−17 ± 3	−18 ± 3	−14 ± 3	−16.7 ± 4	−17 ± 4	<.001	.001
LV mass, g	224 ± 77	209 ± 109	195 ± 77	235 ± 60	217 ± 77	207 ± 60	245 ± 85	227 ± 79	220 ± 50	<.001	.371
LV mass index, g/m^2	121 ± 44	147 ± 78	104 ± 39	136 ± 49	146 ± 63	115 ± 35	134 ± 50	151 ± 49	124 ± 30	<.001	.393
LVEDV, mL	87 ± 25	84 ± 27	74 ± 24	94 ± 25	79 ± 27	69 ± 22	95 ± 25	78 ± 22	70 ± 31	<.001	.972
LVESV, mL	42 ± 14	37 ± 16	30 ± 12	43 ± 12	35 ± 15	29 ± 13	44 ± 12	36 ± 12	32 ± 17	<.001	.812
RWT	0.5 ± 0.2	0.5 ± 0.1	0.48 ± 0.1	0.6 ± 0.2	0.5 ± 0.1	0.5 ± 0.2	0.6 ± 0.2	0.5 ± 0.1	0.5 ± 0.2	<.001	.364

DBP, Diastolic blood pressure; *LV*, left ventricle; *LVEDV*, left ventricular end-diastolic volume; *LVESV*, left ventricular end-systolic volume; *PP*, pulse pressure; *RWT*, relative wall thickness; *SBP*, systolic blood pressure; *SVi*, Stroke volume index.

Supplemental Table 2 Changes in echocardiographic parameters and in blood pressure at 3-6 and 12 months of follow-up according to tertiles of thoracic aortic calcium burden in TAVR patients with reduced LVEF

Patients (n = 108)	Tertile 1 (n = 39)			Tertile 2 (n = 29)			Tertile 3 (n = 40)			P for time	P between subjects
	Pre-TAVR	3-6 months	1-year follow-up	Pre-TAVR	After 30-90 days	1-year follow-up	Pre-TAVR	After 30-90	1-year follow-up		
SBP, mm Hg	135 ± 27	150 ± 13	144 ± 25	143 ± 31	148 ± 29	140 ± 30	135 ± 23	137 ± 19	135 ± 24	<.001	.359
DBP, mm Hg	73 ± 12	77 ± 14	72 ± 16	72 ± 13	75 ± 9	69 ± 11	66 ± 13	67 ± 13	69 ± 13	<.001	.133
PP, mm Hg	62 ± 22	74 ± 16	72 ± 18	70 ± 24	73 ± 27	71 ± 22	71 ± 18	71 ± 16	66 ± 18	<.001	.932
Aortic valve area, cm^2	0.7 ± 0.3	1.5 ± 0.7	1.4 ± 0.5	0.7 ± 0.2	1.7 ± 0.7	1.4 ± 0.5	0.8 ± 0.3	1.6 ± 0.7	1.4 ± 0.5	<.001	.510
Mean aortic valve gradient, mm Hg	38 ± 18	9 ± 6	8 ± 4	41 ± 16	9 ± 7	8 ± 4	34 ± 14	9 ± 5	8 ± 5	<.001	.297
Peak aortic valve gradient, mm Hg	64 ± 30	17 ± 11	16 ± 6	65 ± 27	17 ± 14	17 ± 8	55 ± 23	18 ± 8	16 ± 7	<.001	.279
LVEF, %	41 ± 7	49 ± 8	52 ± 9	36 ± 8	46 ± 9	51 ± 7	37 ± 7	46 ± 9	49 ± 9	<.001	.169
SVi, mL/m^2	36 ± 15	42 ± 19	39 ± 16	36 ± 15	41 ± 15	40 ± 15	36 ± 15	41 ± 18	41 ± 16	<.001	.956
LV GLS, %	–13 ± 4	–15 ± 4	–17 ± 4	–12 ± 4	–15 ± 4	–17 ± 4	–11 ± 4	–14 ± 4	–15 ± 5	<.001	.315
LV mass, g	155 ± 40	122 ± 33	106 ± 42	185 ± 83	147 ± 35	121 ± 35	218 ± 81	166 ± 54	150 ± 53	<.001	<.001
LV mass index, g/m^2	82 ± 23	63 ± 18	58 ± 22	97 ± 41	77 ± 16	64 ± 18	113 ± 37	87 ± 26	79 ± 28	<.001	<.001
LVEDV, mL	91 ± 41	86 ± 38	79 ± 34	95 ± 32	85 ± 27	80 ± 30	96 ± 40	89 ± 41	84 ± 37	<.001	.819
LVESV, mL	61 ± 39	44 ± 23	40 ± 22	62 ± 25	52 ± 24	39 ± 17	62 ± 27	51 ± 26	46 ± 26	<.001	.635
RWT	0.4 ± 0.1	0.3 ± 0.08	0.3 ± 0.1	0.4 ± 0.08	0.3 ± 0.09	0.3 ± 0.1	0.4 ± 0.1	0.3 ± 0.1	0.3 ± 0.08	<.001	.590

DBP, Diastolic blood pressure; *LV*, left ventricle; *LVEDV*, left ventricular end-diastolic volume; *LVESV*, left ventricular end-systolic volume; *PP*, pulse pressure; *RWT*, relative wall thickness; *SBP*, systolic blood pressure; *SVi*, Stroke volume index.