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INCREASED CORONARY TORTUOSITY IS ASSOCIATED WITH INCREASED LEFT VENTRICULAR LONGITUDINAL MYOCARDIAL SHORTENING

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Abstract

Background—The mechanistic basis for tortuosity of the coronary arteries (TCA) is unclear. We hypothesized that the relative degree of systolic longitudinal shortening of the LV which deforms co-axially-oriented coronary arteries is associated with TCA.

Methods—Adult subjects undergoing coronary angiography and comprehensive echocardiography within 3 months were classified dichotomously as with (n=32) or without (n=42) TCA defined based on number and severity of coronary angles. Systolic LV longitudinal deformation was determined by mitral annular plane systolic excursion (MAPSE) from both B-mode displacement and tissue Doppler time-velocity integral; data were indexed to LV diastolic long-axis length.

Results—There were no differences between groups with respect to age, gender, hypertension, or coronary artery disease. Patients with TCA had significantly ($p<0.01$) lower LV mass index and a shorter total LV diastolic long-axis length (8.3 ± 1.9 vs 9.1 ± 2.2 cm, $p<0.01$). Despite having a shorter length, those with TCA had a greater MAPSE by both methods. MAPSE normalized to diastolic length was significantly greater ($p<0.01$) in those with TCA, and remained the case after excluding subjects with reduced LV ejection fraction. Multiple linear regression found that lateral annular MAPSE had the largest effect size with a 13-fold increase in likelihood for TCA for every 0.1 of normalized MAPSE.

Conclusions—TCA is not associated with increased LV mass but rather with smaller hearts that have greater relative longitudinal shortening of the LV. This finding suggests that TCA could represent an adaptive response to longitudinal systolic distortion of co-axially-oriented coronary arteries that dynamically produce shear stresses associated with expansive coronary remodeling.

Keywords

Coronary anatomy; Coronary Tortuosity; Longitudinal Shortening

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Excessive tortuosity of the coronary arteries (TCA) is a somewhat common finding in patients referred for coronary angiography, reported in 14–40% of patients referred for angiography.^{1–4} The presence of TCA has been associated with chest pain and myocardial perfusion abnormalities during stress in the absence of obstructive coronary artery disease.^{2,5,6} Fluid dynamic modeling suggests that stress-induced ischemia may be attributable to a reduction in distal coronary artery perfusion pressure from viscous and turbulence energy losses.^{7,8} The physiologic reasons for TCA are unclear. Pre-clinical studies where elastases and collagenases were used to alter arterial morphology together with genetic and pathologic analysis of rare clinical disorders such as arterial tortuosity syndrome have indicated that arterial tortuosity arises from abnormalities in arterial elastin fibers and extracellular matrix.^{9,10} Apart from inherited disorders, some but not all studies have linked TCA with hypertension and female sex,^{1,4,11} and with increased left ventricular (LV) mass from pressure but not volume overload and smaller heart size, suggesting that this form of coronary remodeling is not from increased LV mass alone.¹² Dynamic forces on the coronary arteries have not been studied.

During ventricular systole at rest, there is normally a 15 to 25% longitudinal shortening of the left and right ventricular dimensions. Accordingly, epicardial arteries oriented along the ventricular long-axis, which are those that are most likely to develop TCA, must dynamically deform. Fluid dynamic models predict that systolic hinging of vessels during longitudinal shortening would be expected to produce excessive wall shear stress.^{13,14} High shear stress at coronary bends predisposes to what has been termed “expansive remodeling” which likely involves shear-dependent pathways including regional production of proteases, fragmentation of the elastic laminae, and smooth muscle cell apoptosis.^{15,16} Accordingly, we hypothesized that TCA is associated with the relative degree of longitudinal shortening, particularly in small but hypertrophic hearts which produces a scenario of increase in flow demand at rest yet an economy of epicardial space during systole. To test this hypothesis, echocardiographic measurements of LV geometry and longitudinal shortening was compared for subjects referred for coronary angiography with and without TCA.

METHODS

Subjects

The study was approved by the Investigational Review Board at Oregon Health & Sciences University. The design was a retrospective case-control study. Medical records from 450 consecutive adult patients (>19 years of age) undergoing elective diagnostic coronary angiography during a 6-month time interval were screened to identify 76 subjects who had comprehensive echocardiography within 30 days of angiography. Patients were excluded for acute coronary syndrome at the time of coronary angiography, prior coronary artery bypass surgery, mitral valve prosthesis, connective tissue disease, moderate or greater valvular regurgitation, major cardiovascular event (death, acute coronary syndrome, coronary revascularization, or hospitalization for heart failure) or change in any medical therapy that could influence inotropic status (beta blockers, calcium channel blockers) between the study angiogram and the echocardiogram, or inadequate echocardiographic views to make accurate measurements.

Patient demographics were obtained from review of the electronic medical record documented at the time of the angiogram. Hypertension was defined as a past or current history of hypertension requiring medication. Coronary artery disease was defined as history of myocardial infarction, revascularization, or coronary stenosis >50% on angiography.

Coronary Angiography

Digitized images of selective coronary angiography were analyzed by an experienced reader blinded to echocardiography results. The presence of TCA was defined according to previously suggested criteria as three or more abrupt turns of $>45^\circ$ in at least one major epicardial coronary artery supplying the LV.¹ Because of non-longitudinal orientation, the left circumflex and the right coronary artery were not included in analysis whereas the left anterior descending (LAD), major diagonal, major obtuse marginal arteries and the posterior descending arteries were included. ImageJ (National Institutes of Health, Bethesda, MD) was used to quantify the length and span of each target coronary at end-diastole, as previously described. Length was defined as the true distance each coronary traversed from its origin to the most distal visualized portion of the vessel during diastole. Span was measured as the shortest distance each artery could potentially traverse if linear in geometry. Tortuosity for each artery was calculated using previously published criteria by dividing length by span, and a tortuosity index (TI) for each subject was calculated by combining data for all vessels and weighting according length.^{12,17} Intraobserver variability of TCA measurement was assessed by reanalysis of TI >6 months later in 15 randomly selected subjects from the total population.

Echocardiography

Quantitative two-dimensional and Doppler echocardiography data on LV dimensions, mass, relative wall thickness, and systolic function were made according to American Society of Echocardiography guidelines,¹⁸ except that normal left ventricular ejection fraction was defined as >50%. Previously-published criteria based on LV mass and dimensions were used to characterize LV mass as normal, concentric remodeling, concentric hypertrophy, or eccentric hypertrophy.¹⁸ Stroke volume was calculated by the product of left ventricular outflow tract diameter and time velocity integral (TVI). From the apical 4-chamber view, left ventricular length was defined as the distance from the mitral annular plane to the apical epicardium at end-diastole. Two-dimensional longitudinal excursion of the lateral mitral annulus from end-diastole to the maximal end-systolic descent (MAPSE) was measured using digital video calipers. Doppler-based MAPSE was also calculated by measuring the TVI of the systolic tissue Doppler velocity (S') of the medial and lateral mitral annulus.¹⁹ For all measurements, an average of 5 beats was used for subjects in atrial fibrillation. Reproducibility of MAPSE measurement from Doppler-derived and 2-D methods was assessed by reanalysis of >6 months later in 15 randomly selected subjects from the total population.

Statistical Analysis

Statistical analysis was performed with SPSS (version 23.0, SPSS Inc. Chicago, IL) and R programming language version 3.2.2 (R Core Team 2015). Continuous variables were expressed as mean ($\pm$ SD) except for non-normally distributed data which were expressed as

median and interquartile (IQ) range. Group-wise comparisons were made by a non-paired Student's t-test or a Mann-Whitney U test. For multiple comparisons, a one-way ANOVA with post-hoc Student's t-test and Bonferroni correction were used. Categorical variables were summarized by frequency and percentages and analyzed by a Chi square test. A P value of <0.05 was considered statistically significant. Multivariate prediction models for TI and binary TCA status were built with linear and logistic regressions, respectively. The best predictive subset of associated variables (see Online Supplement) was chosen by the regularized regression method least absolute shrinkage and selection operator (LASSO).^{20,21} LASSO models were fit with tuning parameter chosen by the cross-validation method in the "glmnet" R package.²² Prediction accuracy measures were estimated with 5-fold cross-validation to remove the overfitting bias from prediction accuracy measures estimated on the same data set that was used to train the regression models. The best fitting and most predictive models for TI and TCA status were chosen with cross-validation. Variability of measurements from re-analysis of TI and MAPSE data was assessed by the intra-class correlation coefficient (ICC).

RESULTS

Patient Characteristics and Coronary Angiography

In the study cohort, there were 33 subjects categorized as having TCA and 43 without TCA. Age and sex were not different between the two patient cohorts (Table 1). Those with TCA were characterized by smaller body mass index, and were less likely to have a known past history of CAD, diabetes, or tobacco use (Table 1). A history of hypertension, which in some studies has been correlated with TCA, was not different between the two groups, although the prevalence of hypertension was high in both the TCA and non-TCA groups. There were no significant differences in the use of negative inotropic anti-hypertensive medications at the time of echocardiography that could have influenced measurements of LV systolic function.

Coronary Angiography and Echocardiography Variables in TCA

Reproducibility of TCA measurements was excellent with an ICC of 0.955 for averaged TI and ICC of 1.0 for binary TCA classification. Examples of coronary angiograms with different degrees of TCA, and mean TI for the different cohorts are shown in Figure 1. As anticipated, the numeric TI was higher for those classified as having TCA. On coronary angiography, significant obstructive CAD (>50% stenosis) tended to be less frequent in those with TCA than those without (66.7% vs. 83.7%, $p=0.08$).

Echocardiographic results are provided in Table 2. Those with TCA had a smaller LV mass and LV mass index, while relative wall thickness was not significantly different between the groups. When characterizing according to hypertrophic subtypes, those with TCA tended to be more likely to have normal LV mass and geometry, and less likely to have concentric hypertrophy while the prevalence for concentric remodeling and eccentric hypertrophy was similar (Figure 2). The mean LV diastolic length was on average 10% shorter for those with TCA (Table 2). Despite having a shorter LV length, those with TCA had a greater degree of systolic longitudinal displacement (MAPSE) measured by both 2-D displacement and by

TVI of the lateral and medial annular tissue Doppler profiles (Figure 3A), although borderline statistical significance was found for the latter. The longitudinal displacement for each of these methods normalized to LV diastolic length was significantly greater for those with TCA (Figure 3B). In a related finding, stroke volume index was greater in those with TCA. Diastolic parameters on echocardiography indicated slightly higher early diastolic relaxation velocities of the mitral annulus and lower loading pressures in those with TCA (see Online Supplemental Table 1).

In order to address the confounding feature that those without TCA had a greater proportion of patients with reduced LV systolic function, manifest by lower LVEF and stroke volume index, data were re-analyzed for those with normal LVEF. In this subgroup, there were no major differences between those with and without TCA with respect to age (67.8 vs. 67.8 yrs, $p=0.99$) and hypertension (73% vs 79%, $p=0.46$). The LV mass index and LV diastolic length were still significantly smaller in those with TCA (Table 3). Again, those with TCA had a greater degree of systolic longitudinal displacement of the lateral annulus measured by both 2-D and tissue Doppler methods and greater displacement of the lateral annulus indexed to diastolic length (Figure 4).

The influence of longitudinal shortening on TCA would imply that epicardial vessels residing on myocardial territories with long-standing akinesis would be less prone to TCA or would have had regression of TCA. We identified four TCA-positive subjects with regional wall motion abnormality that involved akinesis of the anterior wall which can reliably be correlated with the location of the LAD. In three of these subjects, anterior akinesis was known to be chronic and angiography demonstrated TCA of the obtuse marginal system but not of the LAD. The one patient who had TCA of the LAD despite akinesis had no CAD and a wall motion abnormality of unknown duration.

Predictive Models for TCA

For the prediction of the continuous measurement of TI, a LASSO model containing diabetes mellitus, LV mass index, and MAPSE indexed to diastolic length had the best predictive value for the degree of TI (see Online Supplement, Table 2) with Spearman's correlation with TI of 0.65. The lateral annulus MAPSE index had the largest effect size. For case-control selection of variables associated with TCA, a model that included DM, tobacco use, stroke volume index, LV mass index, MAPSE index, relative wall thickness, and LV geometry classification fit with LASSO (Table 4) and had the highest area under the receiving-operating characteristic curve with a 5-fold cross validation area-under-the-curve of 90.8%. The lateral annulus MAPSE index by TVI had the largest effect size, with an adjusted coefficient of 26.28, meaning that every increase in MAPSE index by 0.1 is associated with 13-fold increase of odds of TCA. When the LASSO model was performed for only subjects with normal LVEF, the selection of variables associated with TCA (case-control analysis) revealed similar coefficient estimates as the entire group (Supplemental Table 3) with a 5-fold cross validation area-under-the-curve of 85%. Again the lateral annulus MAPSE index had the largest effect size, with an adjusted coefficient of 32.94. For analysis of variables associated with TI, the smaller population size resulted in the lack of

any strong associations, although again MAPSE indexed to diastolic length had the best predictive power (0.788 coefficient with Spearman's correlation of 0.50).

DISCUSSION

The mechanistic basis for coronary tortuosity remains elusive. Proposed explanations for excessive TCA have included genetic, biochemical, or ultrastructural explanations.¹³ In this study we have studied dynamic geometric changes of the heart that influence coronary fluid dynamics and have demonstrated that TCA is associated with the absolute and proportional degree of longitudinal systolic shortening of the heart. These findings support the idea that relative systolic longitudinal shortening of the LV epicardial surface will distort co-axially-oriented coronary arteries sufficiently to produce shear-dependent coronary remodeling.

There are many potential contributors to TCA. It has been suggested that tortuosity in vascular beds comes as a consequence of both inherited abnormalities in vascular connective tissue and hypertension.^{10,12,13} The concept underlying the current study is that dynamic economy of space on the epicardial surface also contributes to TCA, possibly through a similar mechanism. This hypothesis is supported by the observation that women and those with smaller hearts with higher LV mass tend to be associated with greater predisposition to TCA.^{1,4,12} The implication is that the epicardial surface area is small relative to the degree of total LV mass and, perhaps, to coronary flow requirements. Physiologic ventricular hypertrophy is associated with increased coronary diameter, indicating that adaptive change in coronary arteries occurs from higher flow and shear alone.²³ Our results, however, cast doubt on the notion that LV hypertrophy or increased myocardial blood flow requirement, such as in hypertension, *alone* predispose towards TCA. Moreover, a recent large cross-sectional study demonstrated that the prevalence of hypertension was not higher in patients with TCA.¹¹ Instead, our finding of reduced LV diastolic length and smaller LV mass and surface area in those with TCA supports the idea that an economy of space is an important determinant.

Epicardial surface area is dynamic and decreases during systole due primarily to circumferential and longitudinal strain. For the basal to mid epicardial surface, the amount of normal systolic shortening in the longitudinal direction is approximately 20%.²⁴ An "accordion hypothesis" has been suggested which proposes that the diastolic geometry of coronary vessels under basal conditions is tortuous to allow for adaptive straightening in the event of ventricular dilation in response to elevated load.¹² Our study represents a corollary to this idea that is based on a dynamic stress hypothesis over the entire cardiac cycle as opposed to over the spectrum of diastolic dimensions that vary with load. With increased relative longitudinal shortening of the heart during systole, there is greater repetitive deformation of the co-axially oriented coronary arteries. This would be predicted to lead to lower systolic axial arterial strain, which has been shown in other arterial beds to lead to tortuosity.²⁵ In addition, acute bends, or in extreme forms kinking, of linear coronary arteries constrained within their arterial sheath is predicted to produce extremely high periodic wall shear stresses and shear heterogeneity.¹³ These shear stresses have been associated with biochemical and cellular changes that are important in bringing about the modification of the matrix and smooth muscle that occurs with vascular remodeling.¹⁶ Although TCA itself

results in abnormal distribution of shear, this form of arterial remodeling which results in multiple gradual rather than focal sharp bends during systole would more evenly distribute shear forces and reduce the net pressure drop across the epicardial artery.^{7,26} In other words, the gradual bends of TCA may increase shear and heterogeneity of shear during diastole, but it serves as a “shear absorber” to evenly distribute shear during exaggerated shortening along the major axis. This concept implies that tortuosity may not necessarily be a maladaptive process, which could potentially explain the lower incidence of CAD, a disease also influenced by shear heterogeneity, in those with TCA and the neutral effect of TCA on cardiovascular outcomes.^{1,4}

The notion that TCA occurs as an adaptive result of dynamic deformation is supported by our finding that both absolute longitudinal displacement (MAPSE) and displacement indexed to the length of the heart (MAPSE index) was significantly greater in those with TCA. These findings remained largely true when only including those with normal LVEF. When considering the results of the logistic regression models that adjusted for other possible clinical and echocardiographic predictors, MAPSE of the lateral annulus, particularly when indexed to the diastolic LV longitudinal length, had the strongest effect size. It was also quite compelling that the three patients with TCA and known chronic anterior akinesis had left-sided TCA but sparing of the LAD, indicating either prevention or “regression” of TCA in areas where longitudinal shortening was absent. We did not include hypokinetic territories in this analysis since longitudinal strain can still be present in these individuals.

Since we are postulating that TCA is an adaptive response to greater relative longitudinal shortening, a prospective rather than cross-sectional study would provide stronger argument for effect rather than association. Planning such a trial would be difficult since coronary remodeling is likely to occur over many years or decades. However, additional evidence that systolic deformation leads to TCA is provided by post-hoc analysis of angiography from several subjects which revealed a greater degree of change in coronary angle from diastole to systole (Supplemental Figure 2). A caveat to this finding is that if TCA is an adaptive response that minimizes the acute change in coronary angle as a shear absorber, then our analysis of differences in the degree of coronary angle “bending” over the cardiac cycle may be actually be minimized by the TCA process itself.

In this study we did not assess arterial tortuosity in other less “kinetically-active” vascular beds. This analysis could have been useful for evaluating whether patients with TCA also had evidence for genetic susceptibility through abnormalities in elastin and other arterial elastic components that have been associated with tortuosity.^{9,10} This limitation underscores the notion that TCA is likely to have a multifactorial origin involving genetic and biochemical determinants. Our data helps understand how the dynamic nature of coronary deformation also contributes to TCA, probably in combination with compositional variables that influence risk for systemic tortuosity and aneurysmal dilation. Better understanding of the pathophysiology is clinically important since this knowledge could be used to develop therapeutic strategies that are designed to retard TCA or specifically treat TCA-related chest pain through negative inotropy and possibly negative chronotropy which increases relative duration of diastole to systole. It could also be important for predicting likelihood and

treating chest discomfort which can occur after coronary stenting;²⁷ although the relationship of this phenomenon to TCA has not yet been established.

There are several limitations of this study that should be acknowledged. TCA lacks a universal definition. Accordingly, our analysis of associations was performed using accepted categorical definitions based on number of 45° bends which has been frequently used to diagnose or exclude this condition in a binary fashion. Because of this limitation, we have also presented data on the TI which provides a continuous variable. Another consideration is that MAPSE was measured at rest, whereas in active individuals, the degree of MAPSE would be expected to increase substantially during exertion which may have influenced TCA as well. It should also be mentioned that the mean longitudinal displacement in the TCA cohort was at the upper limits of established normal values.²⁸ Accordingly, we have tried not to imply that tortuosity is associated with “hyperdynamic” longitudinal function; only that it is associated with greater longitudinal function as a proportion of the baseline length. Although angiography and echocardiography were not simultaneously performed, we believe that this is a minor limitation since TCA is likely to develop over years to decades. For 2D MAPSE measurements we used a single location rather than multiple locations along the mitral annulus. Finally, only longitudinally-oriented vessels were studied since testing our hypothesis in non-longitudinal coronary segments situated in the atrioventricular groove would have best performed with prospective analysis of circumferential strain of the base of the LV and RV. Accordingly, we cannot say with certainty that associations, or lack of associations, with tortuosity also apply to more circumferentially oriented arterial segments.

In summary, we did not find that TCA was associated with increased LV mass. Instead, TCA was associated with smaller LV mass, shorter longitudinal LV dimension, and especially greater degree of longitudinal systolic displacement despite shorter LV length. These findings suggest that dynamic changes in longitudinal span influences coronary tortuosity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Quantification of Coronary Tortuosity. (A–C) Coronary angiography in the right anterior oblique view illustrating no, mild and severe TCA (TI 1.04, 1.24, and 1.41, respectively).

(D) Mean ($\pm$ SD) tortuosity index and individual data in patients classified as with (+TCA) or without (–TCA) tortuosity.

Figure 2.

Mean ($\pm$ SEM) mitral annular plane systolic excursion (MAPSE) determined by 2-D imaging (lateral annulus only) and by tissue Doppler imaging (TDI) time-velocity integrals of the lateral and medial annulus. Data are shown for (A) MAPSE and (B) MAPSE indexed to the diastolic left ventricular long-axis dimension. Reproducibility of MAPSE measurements was good to excellent (ICC 0.78 and 0.62 for Doppler and 2-D measurements, respectively).

Figure 3.

Mean (±SEM) mitral annular plane systolic excursion (MAPSE) for the normal LVEF subgroups determined by 2-D imaging (lateral annulus only) and by tissue Doppler imaging (TDI) time-velocity integrals of the lateral and medial annulus. Data are shown for (A) MAPSE and (B) MAPSE indexed to the diastolic left ventricular long-axis dimension.

Figure 4.

Percent of patients in each cohort whose cardiac morphology was categorized as normal, concentric hypertrophy, concentric remodeling, and eccentric hypertrophy.

Table 1

Clinical Characteristics and Angiographic Results

	- TCA (n=43)	+ TCA (n=33)
Age (yrs.)	66.9±10.6	67.6±10.0
Sex (% male)	46.5	51.5
BMI (kg/m ²)	32.1±7.2	26.1±4.1 *
Hypertension (%)	86.0	78.8
Diabetes (%)	62.8%	15.2% *
Hyperlipidemia(%)	62.8%	51.5%
Heart Failure (%)	51.2%	15.2% *
History of CAD (%)	41.9%	24.2%
CAD on angiography (%)		
Single vessel (%)	16.3	27.2
Two vessel (%)	20.9	21.2
Three vessel (%)		
Atrial Fibrillation (%)	7%	0%
Tobacco Use (%)	53.5%	24.2% *
Medications (%)		
Beta blocker	46.5%	33.3%
ACE-I or ARB	58.1%	42.4%
Calcium Channel Blocker	18.6%	12.1%
Statin	42.4%	55.8%

ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, Body Mass Index; CAD, coronary artery disease.

*
p<0.05

Table 2**Imaging and Hemodynamic Measurements**

	– TCA (n=43)	+ TCA (n=33)
Average TI	1.06±0.05	1.26±0.12 *
Systolic Blood Pressure (mm Hg)	128±22	128±21
Diastolic Blood Pressure (mm Hg)	72±18	70±12
LVEF (%) (IQR)	49.5 (32.0–60.0)	62.0 (57.0–64.0) *
LVEF >50% (%)	60.4	87.9 *
Stroke Volume (ml)	62±32	73±15
Stroke Volume Index (ml/m ²)	32±16	39±8 *
Septal Wall Thickness (cm)	1.21±0.28	0.95±0.17 *
Posterior Wall Thickness (cm)	1.17±0.25	0.89±0.15 *
Left Ventricular Diastolic Diameter (cm)	5.00±0.85	4.55±0.63 *
Relative Wall Thickness	0.48±0.13	0.40±0.09 *
Left Ventricular Length (cm)	9.2±1.1	8.3±1.0 *
Left Ventricular Mass (g)	235.5±84.3	142.2±38.1 *
Left Ventricular Mass Index (g/m ²)	121.0±41.3	77.6±18.5 *

LVEF, Ejection Fraction; TI, tortuosity index; IQR, interquartile range.

* p<0.05 versus – TCA.

Table 3

Tortuosity Index and Echocardiographic Measurements in the Normal LVEF Subgroups

	– TCA (n=26)	+ TCA (n=29)
Average TI	1.04 (1.03–1.08)	1.26 (1.19–1.32) *
Systolic Blood Pressure (mm Hg)	129±21	128±21
Diastolic Blood Pressure (mm Hg)	69±13	68±12
LVEF (%) (IQR)	60.0 (52.0–62.0)	62.0 (57.0–66.0)
Stroke Volume (ml)	66.4±30.7	70.7±14.9
Stroke Volume Index (ml/BSA)	35.1±16.1	38.4±7.1
Septal Wall Thickness (cm)	1.21±0.30	0.96±0.17 *
Posterior Wall Thickness (cm)	1.15±0.24	0.91±0.15 *
Left Ventricular Internal Diameter (cm)	4.68±0.71	4.56±0.62
Relative Wall Thickness	0.50±0.13	0.41±0.09 *
Left Ventricular Length (cm)	8.9±0.9	8.3±1.0 *
Left Ventricular Mass (g)	209.8±71.8	144.6±36.6 *
Left Ventricular Mass Index (g/m ²)	110.0±37.1	78.5±18.4 *

BSA, body surface area; LVEF, left ventricular ejection fraction; TI, Tortuosity Index;

*
p<0.05

Table 4

LASSO Predictive Model for Differentiating Case-Control (TCA status)

Variable	Coefficient
Diabetes mellitus	-2.679
Tobacco use	-0.378
Stroke Volume Index	0.030
Posterior Wall Thickness	-1.103
LV Mass Index	-0.037
MAPSE Index (TDI - medial)	-7.526
MAPSE Index (TDI - lateral)	26.282
Relative Wall Thickness	-0.023
LV Geometric Category	-0.269
Age	0
Body Mass Index	0
Hypertension	0
Normal LVEF	0
Septal Wall Thickness	0
LV Diastolic Diameter	0
Coronary artery disease	0

LV, left ventricular; MAPSE, mitral annular plane systolic excursion; TDI, tissue Doppler imaging