Original Article

Comparison of two ellipsoidal models for the estimation of left ventricular end-systolic stress in patients with significant coronary artery disease

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Background: The shape of the left ventricle (LV) is an important index to explore cardiac pathophysiology. A comparison was provided to estimate circumferential, longitudinal, and radial wall stress in LV based on the thick-walled ellipsoidal models of Mirsky and Ghista-Sandler for discriminating significant coronary artery disease (CAD) patients from no CAD patients. **Materials and Methods:** According to the angiography findings, 82 patients with CAD were divided into two groups: 25 patients without significant CAD and 57 patients with significant CAD of single vessel and multivessel. An ellipsoidal LV geometry was used to calculate end-systolic passive stress as the mechanical behavior of LV. Echocardiographic views-based measurements of LV diameters used to estimate the end-systolic wall stress. **Results:** Circumferential wall stress between the control group and significant CAD groups was significantly elevated for the Ghista model ($P = 0.008$); also, radial and longitudinal stress of the multi-vessel CAD group was significantly higher than the control group ($P = 0.01$ and $P = 0.005$, respectively). All stress parameters of the multi-vessel CAD group were statistically significant compared to the control group for the Mirsky model. Receiver operating characteristics curve analysis was shown the circumferential stress of multi-vessel CAD with an area under the curve (AUC) of 0.736 for the Ghista model and an AUC of 0.742 for the Mirsky model. **Conclusion:** These results indicated that Ghista and Mirsky model estimates of circumferential passive stress were the potential biomechanical markers to predict patients with multi-vessel CAD. It could be a noninvasive and helpful tool to quantify the contractility of LV.

Key words: Ellipsoidal model, thick walled, wall stress

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INTRODUCTION

Coronary artery disease (CAD) is the most common type of heart disease. Over time, changes in vascular function left ventricular (LV) perfusion decrease and caused the heart muscle's attenuation.[1] Pathophysiological conditions such as ischemia, advanced CAD, and systolic dysfunction cause pressure overload. Alteration of LV mechanical loading and contractility is often associated with the variation shape of the LV and changes in oxygen consumption determined by elevated wall stress. Therefore, end-systolic wall stress as a biomechanical marker could be more applicable.[2]

Mathematical modeling has provided the distribution of passive wall stress *in vivo* indirectly.[3] Heart models with the human *in vivo* data are still a challenge, and wall stress has not developed as a routine diagnostic tool in the clinic.[4] Thick-walled ellipsoidal models of Mirsky and Ghista-Sandler have been proposed and developed by equations to define stress distribution.[4] In this article, two-dimensional (2D) echocardiography images-based LV for Mirsky and Ghista models are

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introduced to quantify LV geometry and investigate systolic wall mechanical stress parameters between the control group and significant CAD patients for each model. This study aims to compare the two models and evaluate the hypothesis that which models, based on longitudinal, radial, and circumferential wall stress of LV at end-systole may have differentiated significant CAD patients, as this has not previously been investigated. A superior model with high sensitivity and specificity to the identification of significant CAD patients for revascularization is found.

MATERIALS AND METHODS

Patient selection

Ninety-six subjects (men; mean age 57.9 ± 9.1 years) with unstable chest pain and suspected acute coronary syndrome who were candidates for angiography and angioplasty participated. They were referred to 2D echocardiography first and then underwent coronary artery angiography (CAG). Patients with left ventricle ejection fraction (LVEF) >50% and obviously normal systolic function were included in the study. Patients with heart failure, ventricular wall motion abnormality or reduced ejection fraction (LVEF ≤50%), valvular heart disease, atrial fibrillation, history of surgery, previous coronary intervention, LV hypertrophy, malignancy, and electrocardiogram (ECG) abnormalities were excluded from the study. According to the current guidelines, medical treatment was prescribed for all patients.[5] The number of enrolled patients due to motion artifact, poor quality imaging, or unsuccessful CAG decreased.

Written informed consent was received from all patients. The ethics review board approved the study of cardiovascular Shaheed Rajaie Hospital and Tarbiat Modares University (ethical code: IR.RHC.REC.1397.070).

Conventional echocardiographic examination

After selection and preparation of patients, brachial blood pressure (Riester 0124, Jungingen, Germany) and transthoracic echocardiography (TTE) Affiniti 50 Ultrasound Machin (Philips, Andover, MA, USA) with an S4–2 transducer (2–4 MHz) were performed. Patients were placed in a quiet room and scanned in the left lateral decubitus position. Standard 2D images included parasternal short-axis views and apical views were taken (frame rate, 50–90 frame/s) at end-expiration. Time phases were monitored with lead ECG on images at three cardiac cycles. Conventional echocardiographic parameters were measured according to the guidelines of the American Society of Echocardiography.[6] Diastolic and systolic diameter of LV was the line that perpendicular to the long axis of LV [Figure 1] and fractional shortening was calculated. The measurement of posterior and interventricular wall thickness was acquired in the basal level of the short axis and averaged. LVEF was calculated by biplane Simpson's method. Color Doppler and tissue Doppler imaging of the velocity of mitral inflow was assessed at the mitral annulus.

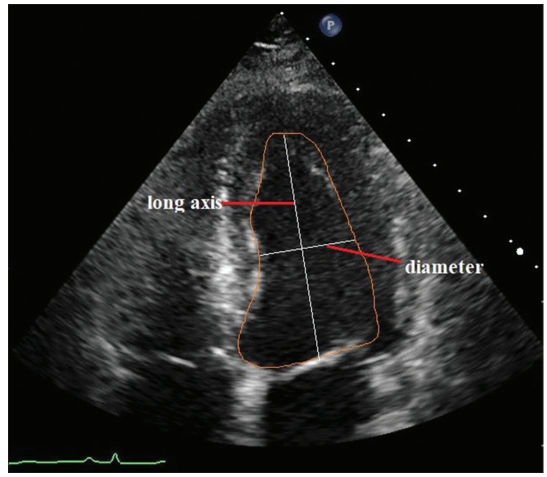

Figure 1: four-chamber view used to measure the length of LV and diameter end-systole

Coronary angiography

During 24 h after TTE, all patients were referred to invasive CAG. Standard technique and visual assessment in two orthogonal planes were performed.[7] Definition for significant stenosis was the reduction of luminal diameter ≥70% in the left main or in the left anterior descending, left circumflex, or right coronary artery or ≥50%.

Thick-walled ellipsoidal model

The wall stress is defined as the forces divided into areas. Currently, mathematical models describe the appropriate shape of LV and estimate passive wall stress due to the values of LV chamber dimensions. Thus, simpler mathematical models have been expanded in the research to eliminate the complex and confusing factors and be appropriate to the realistic anatomy of the heart. In this study, the geometry of LV was approximately simulated by a thick-walled ellipsoid. The components of stress are perpendicular to a surface (normal stresses) and parallel to the surfaces (shear stress). It is conveniently described as a spheroidal or cylindrical coordinate and transformation to Cartesian coordinate (X, Y, and Z), as are shown in Figure 2a and b. Myocardial mechanical properties and wall stress rely on measurements architecture and orientation of myocardial fibers. Hence, in this study, to simplify the formulas and simulation of models, myocardium assumptions were included as isotropic, linearly elastic, and homogeneous.[4]

Mirsky model estimate normal stress (radial stress) and shear stress (longitudinal and circumferential stress). The

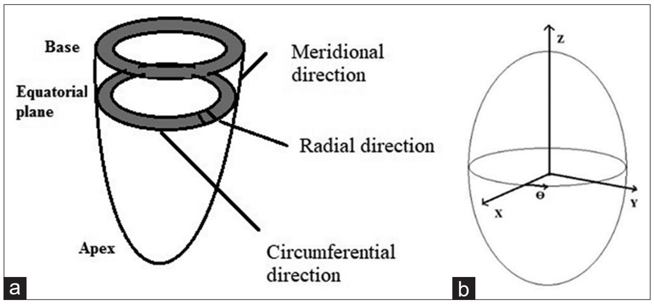

Figure 2: (a) directions of wall stress in the spherical coordinates system, (b) ellipsoidal model for LV is illustrated by Cartesian coordinate (X, Y, Z)

differential equations were solved by numerical integration that equations were taken from the three-dimensional (3D) equations of elasticity. Wall thickness is uniform for the geometry of the LV by a prolate spheroid and the LV cavity does not change during the cardiac cycle. Instantaneous stress estimation was calculated by static analysis.[8]

Ghista and Sandler model is based on a 3D elasticity model. In this model, the geometry of LV is approximated by a quasi-ellipsoidal analysis, and the shape of LV varies during the cardiac cycles. In the systole phase, it is more ellipsoidal, thicker, and the cavity is smaller. The geometry of the Ghista model is not really ellipsoidal, but a very similar one. Therefore, it is so close to the real shape of LV. The required geometrical information for estimating the wall stress to represent the human LV in control and significant CAD patients was provided by 2D echocardiography.[9]

Technical method of calculation

Two ellipsoid thick-walled models were considered for the distribution of wall stress in equatorial (Mirsky and Ghista-Sandler). With a cylindrical coordinate system (r, θ, z), we can show the equatorial surface of the closed elliptical shell with a parametric form.[4]

$r = b \sin \xi,\ z = -a \cos \xi \quad 0 \le \xi \le \pi$

Where a and b are the major semi-axis (mm) and minor semi-axes (mm) of the ellipsoid, respectively. The coordinate ξ represents an eccentric angle of the ellipse [Figure 3]. Hence, in the middle of ellipsoidal: [4]

at the equator $\xi = \frac{\pi}{2}$ $R_\xi = \frac{\alpha^2}{b} R_\theta = b$ that R_ξ and R_θ are the circumferential and meridional radius of the curvature, respectively.

In Mirsky model,[8] wall stress at equatorial (largest transverse diameter) is obtained from the following formula:

$$\sigma_r = (P/2)\,(1 - 3\,h/4b) \qquad (1)$$

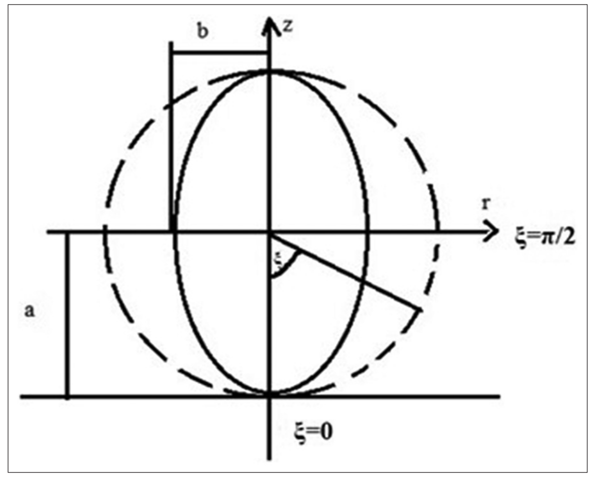

Figure 3: The ellipsoidal thick-shell model is represented by a cylindrical coordinates system (r, Θ, z) of the middle surface of the closed elliptical shell

$$\sigma_\theta = (Pb/2\,h)\,(1 - h/2b)^2 \qquad (2)$$

$$\sigma_\xi = (Pb/h)\,(1 - b^2/2a^2 - h/2b + h^2/8a^2) \qquad (3)$$

σ_r, σ_θ, and σ_ξ are radial, longitudinal, and circumferential stress. P is pressure of cavity and h is wall thickness. It is uniform throughout the cardiac cycle.

Ghista-Sandler model[9] investigated the distribution wall stress of LV. Assumptions were similar to Mirsky model. The geometrical shape of Ghista model is shown in Figure 4. Wall stress at the equator was estimated by the following relations:

$$\sigma_{rr} = -\frac{\frac{4A}{a^2}\left(2d_c^2 + 1\right)}{d_c^2\left(d_c^2 + 1\right)^{\frac{3}{2}}} + B \qquad (4)$$

$$\sigma_{yy} = -\frac{\frac{4A}{a^2}}{d_c^2\left(d_c^2 + 1\right)^{\frac{3}{2}}} + B \qquad (5)$$

$$\sigma_{ww} = -\frac{\frac{4A}{a^2}}{d_c^2\left(d_c^2 + 1\right)^{\frac{1}{2}}} + B \qquad (6)$$

σ_{rr}, σ_{yy}, and σ_{ww} are radial, longitudinal, and circumferential stress, respectively, A and B are intensity parameters[4] and $d_c = (W + H)/2a$ that a is size parameter (half-length of LV), H and W, are wall thickness and half-diameter of LV respectively.

LV blood pressure (mm Hg) was proportional to wall stress. Therefore, the final result was multiplied by a factor of 1.33 to express stress in kdynes/cm^2.

Statistical analysis

The continuous variables were reported as mean ± standard deviation (SD) and categorical variables were presented as frequencies (number of cases) and percentages. Normal distribution of variance was assessed by the Kolmogorov–Smirnov test (K–S). Independent-samples *t*-test was used to compare the mean values between control and significant CAD groups for conventional echocardiographic parameters and stress parameters. $P < 0.05$ was considered statistically significant. Receiver operating characteristics (ROC) curves and area under the curve (AUC) were applied for the stress parameters in two models to identify significant CAD patients. SPSS statistical software package (version 23) was performed for the data analysis (SPSS Inc. Chicago, IL, USA).

RESULTS

Patient characteristics and echocardiographic study

The inclusion criteria were provided for 82 men patients. According to the results of the angiography, patients were classified into two groups. The control group had no significant stenosis (n = 25) and significant stenosis group (n = 57) that stratified into two subgroups were included of single vessel (n = 35) and multivessels (n = 22).

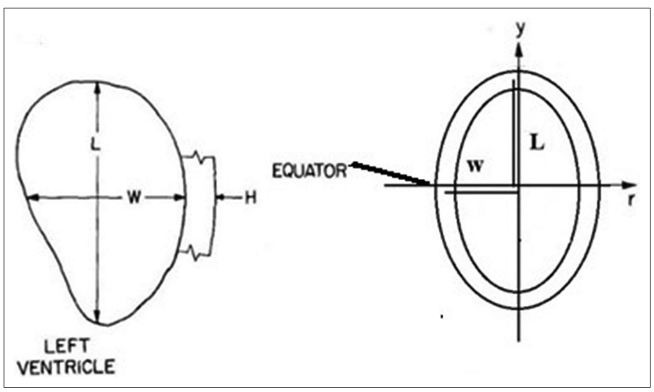

Figure 4: Left ventricular geometry with Ghista and Sandler model in cylindrical coordinates[4]

Demographic and echocardiographic data of the included four groups are revealed in Table 1 as mean ± SD. In comparison between the control group and each of the other three groups, there were no significant differences in clinical data includes of age, body mass index, heart rate, systolic blood pressure (SBP), and diastolic blood pressure. Furthermore, conventional echocardiographic parameters for single-vessel and multi-vessel CAD groups and control group are shown in Table 1 and angiographic results are presented in Table 2.

Comparison of stress parameters for two models

The comparison results of end-systolic mean stress parameters among the three groups for Mirsky and Ghista-Sandler were indicated radial, longitudinal, and circumferential stress in multi-vessel and single-vessel CAD groups had higher absolute values compared to the control group. Radial stress value was negative, longitudinal and circumferential values were positive for the two models. Significant difference was shown in radial stress between the multi-vessel and control group (P = 0.02), but there was not a significant difference in single-vessel CAD compared with the control group (P = 0.26). Multi-vessel CAD group had significantly higher longitudinal stress than the control group (P = 0.03), but longitudinal stress for single-vessel CAD displayed no significant changes compared with the control group (P = 0.44). Circumferential stress value was higher than longitudinal and radial stress for all groups. Circumferential stress was significantly increased in significant CAD, multi-vessel compared with the control group (P = 0.003).

Ghista model demonstrates a higher estimation of wall stress values compared with the Mirsky model. Absolute values of stress components for the control group were lower than the other two groups. Radial stress of significant CAD, those of multi-vessel CAD, was significantly increased

Table 1: Mean±standard deviation of characteristics demographic and echocardiographic parameters of participants in the study groups

Variable	Control group (n=25)	Significant CAD (n=57)	Single-vessel CAD (n=35)	Multi-vessel CAD (n=22)	P
Age (year)	57.5±9.2	57.1±9.0	57.7±9.5	56.1±8.2	0.85
BMI (kg/m^2)	24.9±2.5	24.7±2.6	24.5±2.4	25.1±2.9	0.79
HR (beats/min)	71.1±4.7	72.2±5.4	71.7±4.8	73.0±6.4	0.36
SBP (mmHg)	133.0±8.1	136±9.3	135.3±8.4	137.1±10.6	0.16
DBP (mmHg)	81.0±5.5	84.0±7.7	83.4±7.6	84.0±8.1	0.19
LVESV (mL)	40.4±5.2	43.7±7.6	43.5±8.3	44.1±6.4	0.05
LVEDV (mL)	103.8±13.2	109.6±19.8	109.4±22.3	109.9±15.5	0.18
EF (%)	61.0±2.8	59.9±3.4	59.9±3.8	59.8±2.8	0.14
FS (%)	24.4±5.5	23.1±7.8	23.6±7.6	22.3±8.2	0.45
SI (mL/m^2)	36.6±5.5	35.7±8.3	35.6±9.3	35.8±6.7	0.63
E (cm/s)	69.1±14.1	71.0±16.6	69.4±15.8	73.5±17.9	0.63
e′ lateral (cm/s)	8.9±2.6	7.9±2.0	72.0±5.0	73.0±6.0	0.05
E/e′	8.1±1.9	9.4±2.5	9.2±2.6	9.7±2.3	0.02

P-value shows the comparison of control group and significant CAD. E=Mitral early diastole velocity; e′vPeak mitral annular velocity during early diastole. BMI=Body mass index; HR=Heart rate; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; LVDS=Left ventricle diameter systole; WTS=Wall thickness systole; LVESV=Left ventricle end-systole volume; LVEDV=Left ventricle end-diastole volume; EF=Ejection fraction; FS=Fractional shortening; SI=Stroke index; CAD=Coronary artery disease compared to the control group (P = 0.01). There were significant differences between the longitudinal wall stress of the control group and multi-vessel CAD (P = 0.005). There was a significant difference in circumferential stress of significant CAD, single and multi-vessel CAD compared with the control group (P = 0.008). In general, stress values increased as the number of culprit's vessels was elevated.

Diagnostic accuracy of stress parameters for detecting coronary artery disease

The stress parameters of significant CAD (multi-vessel CAD) compared to the control group were significantly increased for two models. Therefore, ROC curve analysis was depicted in four manners in Table 3, stress parameters (radial, longitudinal, and circumferential) to predict multi-vessel CAD patients for two models. Circumferential stress for the Mirsky model and Ghista model was slightly superior to the longitudinal and radial stress to predict significant CAD. The diagnostic accuracy of the Ghista and Mirsky model was approximately the same for multi-vessel CAD in all stress parameters. For identifying multi-vessel CAD, radial and circumferential stress had similar discriminatory performance, but the AUC of circumferential stress was slightly lower than radial stress in the Ghista model.

DISCUSSION

In the present study, wall stress was calculated by two passive mechanical models. We discussed comparing two mathematical models to estimate circumferential, radial, and longitudinal mean stress at the equator in end-systole as a noninvasive method. The main target of this study was that Ghista-Sandler model and Mirsky model were relatively ideal and simple models for computational mean stress parameters of single-vessel and multi-vessel CAD patients. Our findings represent that stress components of the two models are the sensitive biomechanical markers for identifying multi-vessel CAD patients.

Most referral patients to coronary angiography do not have stenosis in coronary arteries.[10,11] Therefore, the exploration of noninvasive methods to detect significant CAD patients is controversial. In this study, increased wall stress of significant CAD patients indicated that demand for myocardial oxygen is elevated in the endocardial region at systole. Oxygen perfusion status against demand mismatch will be increased due to decreasing myocardial perfusion.

Passive wall stress depends on LV loading conditions (LV pressure) and ventricle geometry (left longitudinal and circumferential curvature, and wall thickness). In previous studies, the relationship between cuff SBP and end-systolic micromanometer LV pressure was proven.[12] Our results indicated increased mean values of wall stress at end-systole for significant CAD patients with normal EF was statistically significant. Also, the study by Zhong *et al.*[13] investigated increased regional stress. In their research, regional wall stress was quantified to evaluate cardiac mechanics by cardiac magnetic resonance imaging. It seems that wall stress only changes when the ventricle is not able to compensate for pressures or volume loading.

In our study, the myocardium of LV is in a passive state and LV have composed of isotropic and homogeneous material. Same basic assumptions have been considered for the thick shell theory (Mirsky) and elasticity model (Ghista-Sandler). These ellipsoidal models are systematically different. The absolute value of circumferential stress obtained from the two models is higher than radial and longitudinal stress because of differences in the longitudinal and circumferential curvature radius. The mechanism of these results is so complicated and related to LV contractility.

Several studies have been published about the various thick-wall ellipsoidal models. There have been few and

Table 2: Number of angiographic results in different groups

Variables	Control (25)	Significant CAD 57	Single vessel CAD 35	Multi vessel CAD 22
Location of stenosis				
LAD	0	43	21	20
LCX	0	14	6	9
RCA	0	17	8	10

RCA=Right coronary artery; LAD=Left anterior descending artery; LCX=Left circumflex artery; CAD=Coronary artery disease

Table 3: Receiver operating characteristic curve result of multi-vessel coronary artery disease for Ghista and Mirsky model

	Parameter (kdyn/cm^2)	Multi-vessel CAD			
		AUC	Cut off point	Sensitivity (%)	Specificity (%)
Ghista model	Radial stress	0.747	59.46	68.2	76.0
	Circumferential stress	0.742	195.01	68.2	64.0
	Longitudinal stress	0.713	160.73	63.6	68.0
Mirsky model	Radial stress	0.708	52.86	59.1	76.0
	Circumferential stress	0.736	175.97	63.6	68.0
	Longitudinal stress	0.660	88.33	59.1	64.0

CAD=Coronary artery disease; AUC=Area under the curve old studies to calculate wall stress by these models and connected them to pathophysiological cases.[14,15] In the study of Murai *et al*.,[16] the correlation between wall stress and myocardial strain or strain rate in normal subjects was discussed. Lee *et al*.[17] revealed that the peak end-systolic myofiber stress significantly decreased after surgery. Although the bulk wall stress can be predicted using Laplace's law, the myofiber stress prediction requires mathematical modeling. Their results indicated more accuracy in predicting LV remodeling and the decline of regional oxygen consumption.

These models have encountered limitations due to simplifying assumptions. However, elimination of restrictions requires complex mathematical calculations and more information of images therefore, geometrical models have not been developed as a diagnostic tool in the clinic[18,19] also wall stress distribution must be validated by experimental measurements that it is not easily feasible. Without experimental confirmation, the comparison of thick-walled models in their accuracy is somewhat difficult. However, in our study, a comparison of stress parameters based on these two ellipsoidal models was reported by their sensitivity and specificity without direct measurement.

The sensitivity of stress components for prediction multi-vessel CAD was superior to single-vessel CAD for two models because of vessel stenosis. However, the usefulness of stress parameters for identifying multi-vessel CAD patients has not been proven clinically so far. According to previous studies,[4] the Ghista model is more close to the actual shape of LV, and the shape of the model dynamically change throughout a cyclic heart according to dynamic geometrical observations of human LV. As the internal cavity becomes larger, the model becomes less oval in shape during diastole. As the cavity becomes smaller, the model becomes a greater ellipse shape at systole. Elasticity is applied to extend this model and provide stress variations along with the wall thickness. The thickness along the wall is assumed to be constant for the Mirsky model. Both models indicated the same results in this study. Therefore, clinical use of the Mirsky model for stress calculations can be easier and faster as a noninvasive method. Results of other researchers about stress have been published. Goldfine *et al*.[20] used a simple mathematical model to estimate systolic stress after surgery. However, accurate quantification of wall stress in a subtle clinical study can be challenged; their findings had significant results in wall stress after mitral valve replacement (with and without chordal preservation). Results for maximum wall stress indicate that anatomical changes may play an important role in determining wall stress. Hemodynamic effects that show a significant increase in Ea may not be sensitive to local stress changes in the wall.

In another study by Huisman *et al*.,[21] stress distribution was compared between several homogeneous, isotropic, and thick-walled ellipsoidal models. Circumferential and longitudinal stress variations along the wall were estimated. In all models, circumferential stress was higher than longitudinal stress. Also, the maximum values of circumferential stress were at the endocardium level and decreased by approximately 50% toward the epicardium. The longitudinal stress decreased by 26% from endocardium to epicardium for the Ghista and Sandler model but increased by 36% for the Mirsky model. At the mid-wall, all the models' stresses vary by about 16%. Another result was that peak stress in the Ghista model is higher than the other three models. Since Ghista and Sandler models do not have any shell theory limitation, it can be considered the best representation of LV shape and stress distribution compared to other models.

Most reports for wall stress are based on two, and three-dimensional models, which are provided by simplified geometry analysis with spheroid, ellipsoid and sphere models; to assessing better LV wall stress, modeling and imaging need to be synchronized. Finally, we can suggest an ellipsoidal model that is simple and suitable for clinical and physiological applications.

Limitations

One of the limitations for these models' estimates of stress parameters was that there were no specific cutoff values for clinical decision-making.

CONCLUSION

Estimation of passive mean stress parameters using mathematical models is a noninvasive method for determining the function of LV. Ghista-Sandler and Mirsky model estimates of wall stress are powerful mathematical models for detecting multi-vessel CAD. This study also demonstrated that stress parameters are inferior to identify the single-vessel CAD patients for two models. Stress parameters can be utilized as an important biomarker in the clinical application for the detection of CAD patients.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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