ORIGINAL ARTICLE

Assessment of Physical and Mechanical Parameters of the Left Ventricle by Speckle Tracking Technique for Prediction Coronary Artery Disease Patients

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Abstract

Purpose: The goal of the study was to identify earlier pathology of the Left Ventricle (LV) using Speckle Tracking Echocardiography (STE) without angiography results for detecting Coronary Artery Disease (CAD) patients who have need invasive coronary reperfusion.

Materials and Methods: A total of seventy-five referral patients to angiography (mean age 57±9 years) with chest pain, underwent Two-Dimensional Echocardiography (2D-ECG). Conventional echocardiographic parameters were calculated for the assessment of LV function. End systole and early diastole longitudinal strain, strain rate, and velocity with 2D-STE were estimated to evaluate myocardial function. Discriminated analysis was performed to detect CAD patients from the healthy group.

Results: According to the angiography results, patients were divided into CAD group (n=55) and healthy group (n=20). There was a significant decrease in longitudinal strain, strain rate, and velocity in patients with CAD compared to the healthy group (systolic longitudinal strain for CAD group -15.9±2.2% vs. -19.6±2.2% for healthy group and early diastolic longitudinal strain for CAD patients -9.5±1.2% vs. -12.0±1.3% for the healthy group) (P-value<0.05). Discriminate analysis of end-systolic and early diastolic longitudinal strain with 81.8% and 89.1% indicated the highest sensitivity, respectively.

Conclusions: End systolic and early diastolic longitudinal strain parameters derived with the STE method are superior predictors for detecting CAD patients referred to angiography for revascularization.

Keywords: Strain; Strain Rate; Speckle Tracking Echocardiography.

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1. Introduction

One of the leading causes of death in the world is cardiovascular disease, of which Coronary Artery Disease (CAD) is one of the most common. The prevalence and death of this disease are increasing every year. CAD is associated with decreased blood flow to the arteries and impaired perfusion of the Left Ventricular (LV) segments [1]. Over time, changes in vascular function and weakening of the heart muscle lead to heart failure and arrhythmias. The only diagnostic method as the gold standard for CAD patients is coronary angiography. Limitations of angiography include the need for hospitalization, ionizing radiation exposure, invasive interventions, time consuming, and high cost [2]. Due to these limitations and the elevated workload of angiography centers, providing a non-invasive and available method for evaluating the mechanical parameters of the LV is useful in diagnosing CAD patients. Studies show that poor perfusion in patients with significant coronary artery stenosis can alter the biomechanical properties of LV and myocardial contractile function. Echocardiography (ECG) is an advanced tool for the identification and quantification of LV function. Also, Two-Dimensional Speckle Tracking Echocardiography (2D-STE) is a non-invasive and angle-independent technique. STE measures motion in all directions, frame by frame, during the cardiac cycle and quantifies myocardial contractility with longitudinal strain, strain rate, and velocity parameters [3]. According to the reports, STE has shown a good correlation with cardiac magnetic resonance and validated [4]. According to research, strain values extracted from the STE technique provided accurate information about LV dysfunction and early signs of ischemia before changes in normal echocardiographic parameters such as Ejection Fraction (EF) and left ventricular wall dysfunction. Sarvari *et al.* [5] Showed that this advanced technology can be used to identify patients with coronary artery stenosis.

Żebrowska *et al.* [6] suggested evaluation of the basal rotation and circumferential strain by STE can be used for prediction cardiac disorders. In other research [7] the structural and functional changes on myocardium were investigated by radial, longitudinal, and circumferential strain using STE.

This study aimed to estimate strain, strain rate, and velocity parameters using STE in patients with the CAD. The present hypothesis shows that early LV dysfunction can be diagnosed and evaluated with longitudinal strain derived using STE. The advantage of this study is to discriminate CAD patients with non-invasive physical and mechanical parameters of LV in end systolic and early diastolic phases. In addition, this study helps decrease the workload of angiography departments for patients who do not have significant stenosis for reperfusion therapy.

2. Materials and Methods

In the present study, 75 male patients with an age range of 40-70 years (mean age 57±9 years) suspected of chest pain were selected. Written consent was received from all patients in this study. The study was approved by the Ethics Review Board of Tarbiat Modares University and Shahid Rajaei Cardiovascular Center (approval No. 1397.095 and 1398.091). They had no previous history of cardiovascular disease. Before angiography, all subjects underwent two-Dimensional Echocardiography (2D-ECG). Echocardiographic images were taken by Philips Affiniti 50 system (Philips N.V., The Netherlands) equipped with a cardiac transducer sector S4-2 (2-4 MHz) and frame rate 60-100 frame/sec.

1.1. Speckle Tracking Method

The speckle echocardiographic pattern is obtained by using gray-scale images as a result of interference between tissue interferences. Each myocardial region is represented by a relatively stable and specific speckle pattern and differentiated from other regions during the cardiac cycle. As a result, after defining an area in a frame, it can be identified in the next frame with equal size and shape to the similar speckle pattern of the previous frame which makes it possible to track a certain area from one frame to another frame (Figure 1). The most common

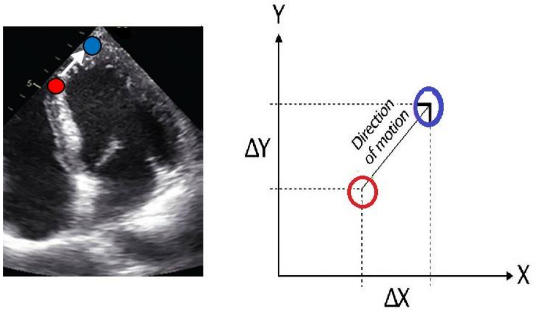


Figure 1. Represented speckles in the gray-scale image. Displacement changes are determined by changing the speckles from one frame to another frame in a different direction [8]

algorithm used for tracking is Sum-Absolute-Difference (SAD) algorithm. The SAD algorithm provides accurate myocardial tissue tracking by minimum absolute distances traveled per pixel and searching for the best matching region (the smallest difference in the average pixel signal intensity).

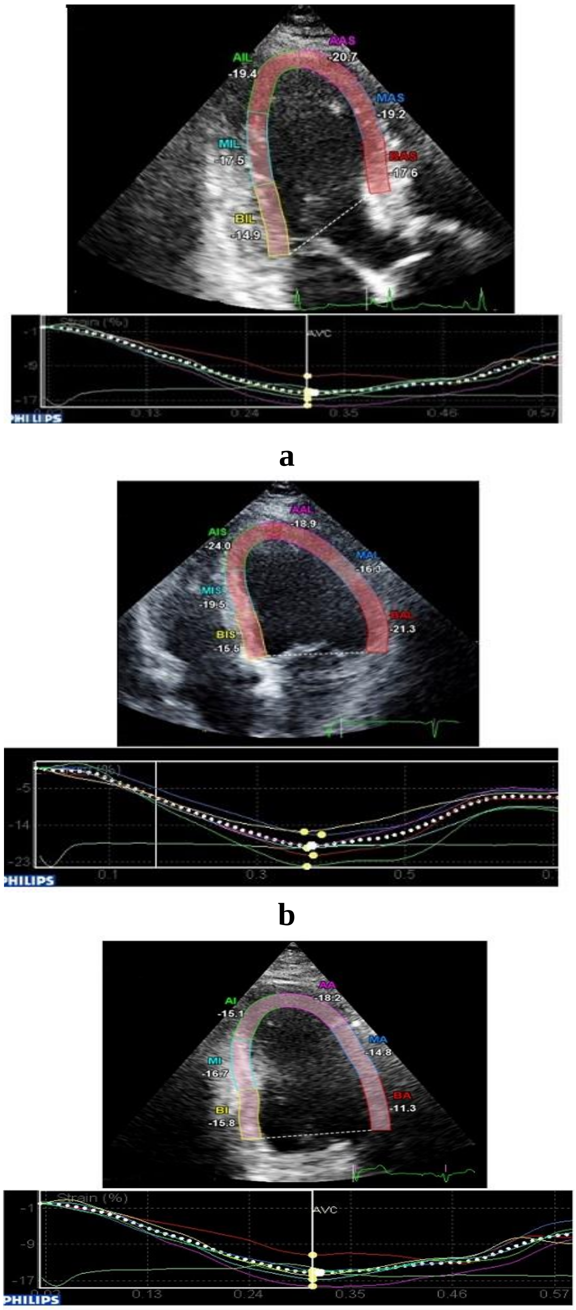
The speckle tracking technique evaluates the myocardial strain (ε) according to the Lagrangian strain formula [9]:

$$\varepsilon = \frac{L - L_0}{L_0} \qquad (1)$$

L_0 is the initial length of the myocardium at the end of diastole and L is the length of the myocardium after deformation. Strain is a dimensionless parameter and is expressed as the percentage of myocardial deformation.

In this study, 2D-STE analysis was performed offline using version 12 (QLAB Philips Healthcare, Andover, the Netherlands) to evaluate and quantify left ventricular function. First, images in apical views (two-chamber, four-chamber, and three-chamber) were transferred to software to measure the longitudinal strain of the LV. In long-axis views, the systolic frame was identified by the Aortic Valve Closure (AVC). The end-systolic frame was automatically selected from the cardiac cycle when the images were opened in the software. If the automatic selection of the desired frame seemed incorrect, we would adjust it manually. The software then created a Region Of Interest (ROI) to cover the entire thickness of the myocardium.

Endocardial borders were traced in all frames of 2D images automatically for each cycle at the end of systole, and poor tracking segments were manually adjusted. QLAB software divided the left ventricular wall into 18-segments for three levels (base, mid, and apex). Every three levels are divided into six segments (anteroseptal, inferoseptal, anterior, anterolateral, inferolateral, and inferior wall). For each view, segmental longitudinal strain curves were created and global longitudinal strain values in apical views were calculated by averaging all 18 segments at peak systole and early diastole. Apical three-chamber view showed inferolateral and antroseptal longitudinal strain in Figure 2a. Apical two-chamber view showed inferoseptal and antrolateral longitudinal strain in Figure 2b. Apical four-chamber view showed inferior and anterior longitudinal strain in Figure 2c.



a

b

c

Figure 2. Longitudinal strain. Strain parametric images of the left ventricle in the upper, with a strain-time curve during a cardiac cycle at the bottom. a) 3-chamber view with the six segments of anteroseptal and inferolateral, b) 2-chamber view with the six segments of anterior and inferior, c) 4-chamber view with the six segments of inferoseptal and anterolateral. The vertical axis represents the strain (%) and the horizontal axis shows the time (S)

1.2. Statistical Analysis

Data were represented as mean ± Standard Deviation (SD). Normally distributed continuous variables were evaluated by the Kolmogorov-Smirnov test (K-S). An independent t-test was used to compare the patient group with the healthy group. A P-value less than 0.05 was considered statistically significant. Discriminate analysis and test statistics were calculated for different parameters. Then, discriminate analysis was used to determine the optimal sensitivity and specificity of the variables to predict significant stenosis.

Univariate and multivariate logistic regression analyzed significant predictors for discriminating CAD patients. PSS statistical software package was performed for data analysis (SPSS Inc. Chicago, IL, USA).

3. Results

Using the results of coronary angiography, subjects were divided into two groups: the patients with significant coronary artery stenosis (n = 55) and the healthy group (n = 20), patients with non-coronary artery stenosis.

Table 1 represents the mean and SD of clinical and conventional echocardiographic parameters of the two groups. Comparison between healthy group and CAD group with independent t-test analysis showed that at a 95% significance level, there were no significant differences between groups in terms of mean age, body mass index, and systolic and diastolic blood pressure. There was a statistically significant difference in EF but clinically had no diagnostic value.

The results of the mean and SD of longitudinal strain, strain rate, and velocity end-systolic and early diastolic in the healthy group and CAD group are presented in Figures 3, 4 and 5, respectively. Comparison of the mean values between the healthy group and CAD group with independent t-test analysis showed that at a significance level of 95%, there was a significant difference in longitudinal strain, strain rate and velocity in end-systole and early diastole between the healthy group and CAD patients. In addition, significantly decreased end-systolic and the early diastolic longitudinal strain was observed in CAD patients compared to the healthy group (-15.9 ± 2.2 % vs. -19.6 ± 2.2 % P-value < 0.05 for end-systole) and (-9.5 ± 1.2 % vs. -12.0 ± 1.3 % P-value < 0.05 for early diastole) shown in Figure 3.

Compared with a healthy group, significantly lower end-systolic and early diastolic longitudinal strain rate of the CAD group were shown in Figure 4 (-1.8 ± 0.2 s-1

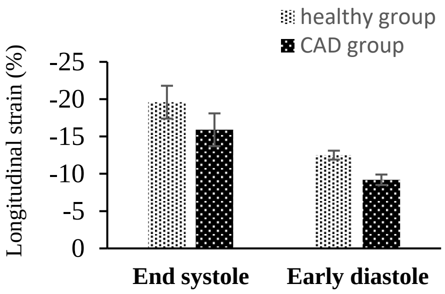


Figure 3. The bar chart shows the longitudinal strain of Left Ventricle (LV), end-systole and early diastole strain were decreased significantly in the Coronary Artery Disease (CAD) group compared to the healthy group. Bars and error bars demonstrate the means and 1 standard deviation of the mean, respectively

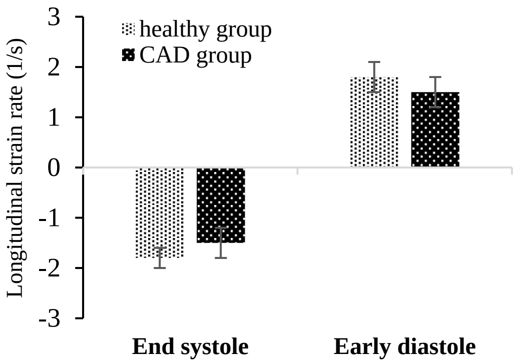


Figure 4. The bar chart shows that the longitudinal strain rate of Left Ventricle (LV), end-systole and early diastole strain rate decreased significantly in the Coronary Artery Disease (CAD) group compared to the healthy group. Bars and error bars demonstrate means and 1 standard deviation of the mean, respectively

Table 1. Baseline clinical characteristics and conventional echocardiographic parameters

Variables	Healthy group	CAD group	P-value
Age (y)	58±10	57±9	0.6
BMI (kg/m^2)	24.6±2.7	24.7±2.6	0.9
SBP (mmHg)	131±7	136±9	0.1
DBP (mmHg)	81±6	84±9	0.1
EF (%)	60.6±2.8	59.3±2.2	0.03
FS (%)	24.3±5.8	23.9±6.6	0.8

Variables are presented as mean ±standard deviation. CAD, Coronary Artery Disease; BMI, Body Mass Index; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; EF, Ejection Fraction; FS, Fractional Shortening for healthy vs. -1.5 ± 0.3 s-1 for CAD group P-value < 0.05 for end-systole) and (1.8 ± 0.3 s-1 for healthy vs. 1.5 ± 0.3 s-1 for CAD group P-value < 0.05 for early diastole). The value of the end-systolic longitudinal strain rate was negative and the value of the early diastolic strain rate was positive.

In the CAD group, significantly decreased end-systolic and early diastolic longitudinal velocity was observed compared to the healthy group (5.5 ± 0.8 cm/s for healthy vs. 4.7 ± 0.9 cm/s for CAD group P-value < 0.05 for end-systole) and (-5.9 ± 0.7 cm/s for healthy vs. -4.9 ± 0.90 cm/s for CAD group P-value < 0.05 for early diastole). The value of end-systolic longitudinal velocity was positive and the value of the early diastolic velocity was negative (Figure 5).

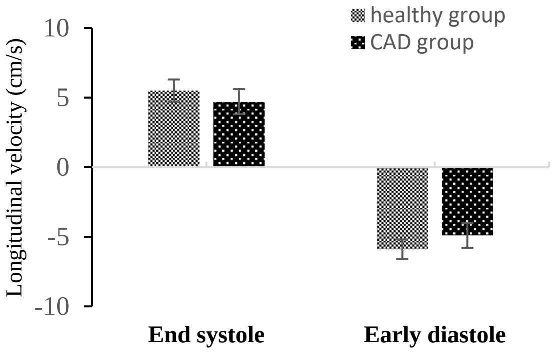


Figure 5. The bar graph shows that the longitudinal velocity of Left Ventricle (LV), end-systole, and early diastole velocity decreased significantly in the Coronary Artery Disease (CAD) group compared to the healthy group. Bars and error bars demonstrate the means and 1 standard deviation of the mean, respectively

Discriminate analysis and test statistics were calculated for strain, strain rate, and velocity parameters in two groups (healthy and CAD patients) and presented in Table 2. The results of the analysis showed that the highest percentage of specificity with values of 80% and 90% are related to the end-systolic longitudinal strain and early diastolic longitudinal strain, respectively. Also, the sensitivity of these parameters was 81.8% and 89.1%, respectively.

Table 2. Results of discriminate analysis and test statistics for strain, strain rate, and velocity

Variable	Sensitivity (%)	Specificity (%)
End systolic LS	81.8	80
Early diastolic LS	89.1	90
End systolic LSR	72.7	80
Early diastolic LSR	69.1	70
End systolic LV	65.5	65
Early diastolic LV	65.5	75

LS; Longitudinal Strain, LSR; Longitudinal Strain Rate, LV; Longitudinal Velocity

3.1 . Univariate and Multivariate Analysis

Univariate logistic regression analysis was performed for age, EF, end-systolic and early diastolic longitudinal strain, strain rate, and velocity. In addition, a multivariate analysis was used for the significant variables in univariate analysis. Multivariate logistic regression analysis displayed that the most predictive parameters for CAD patients were end-systolic longitudinal strain (OR 2.8, P-value < 0.001) and early diastolic longitudinal strain (OR 5.9, P-value < 0.001) (shown in Table 3).

Table 3. Univariate logistic regression and multivariate analysis

Variable	P-value	
	Univariate	Multivariate
EF%	0.034	-
Age	0.643	-
End systolic LS	0.001	0.001 (OR=1.9)
Early diastolic LS	0.001	0.001 (OR=3.2)
End systolic LSR	0.001	-
Early diastolic LSR	0.002	-
End systolic LV	0.003	-
Early diastolic LV	0.001	-

LS; Longitudinal Strain, LSR; Longitudinal Strain Rate, LV; longitudinal Velocity

4. Discussion

CAD is a spectrum of heart disease with the highest mortality rate in the world [10]. There is little information about LV dysfunction in patients with CAD. The results of various studies are controversial [11]. Despite the importance of assessments of LV function by determining the percentage of EF and fractional shortening, novel echocardiographic methods such as ST are used with greater accuracy and precision in estimates of LV myocardial systolic and diastolic function [12].

In this study, STE was used to quantify LV function in patients with coronary artery stenosis who were candidates for revascularization therapy. The main results of the study showed that end-systolic and early diastolic longitudinal strain by 2D-STE with a sensitivity of 81.8% and 89.1%, respectively, are more sensitive parameters than the conventional echocardiographic parameters in the diagnosis of CAD patients. In LV myocardial, the effects of stenosis revealed as impaired blood flow to the LV segments and consequently contractile defects. During the early stages of the disease, the usual functional parameters of LV echocardiography, such as volume and EF, are usually normal. Non-invasive diagnosis of LV dysfunction is not possible with the usual parameters of Transthoracic Echocardiography (TTE) [13]. Evaluation of the results indicated the physical parameters derived using STE in end-systole and early diastole can show a significant difference between the healthy group and the group with stenosis (P-value < 0.05).

Following coronary artery stenosis and decreased myocardial perfusion, the results of this study have shown that strain, strain rate, and velocity parameters derived using STE for the CAD group were lower than the healthy group in all the systolic and diastolic phases. Myocardial muscle movement of LV in the systolic and early diastolic phases is due to LV contraction therefore insufficient blood flow to LV segments affects both systolic and early diastolic function [9, 14].

The longitudinal fibers are mostly located in the subendocardial region near the LV cavity and farther away from the coronary arteries. The movement of longitudinal fibers, including shortening and lengthening creates longitudinal strain. These areas are very susceptible to ischemia and with the onset of ischemia, the longitudinal function of the LV wall is initially affected. Therefore, strain reduction in the endocardial layer is due to damaged fibers in the longitudinal direction. Caspar *et al.* [15] showed in their study that global longitudinal strain values vary in groups with varying degrees of coronary artery stenosis. Left Ventricular Ejection Fraction (LVEF) was 60.7 ± 4.6% in the CAD group and 61.6 ± 5% in the control group (no CAD) and global longitudinal strain in the CAD group compared to no CAD was statistically significant (-16.7 ± 3.4% vs. -22.4 ± 2.9% respectively, P-value < 0.001). Therefore, global longitudinal strain with a sensitivity of 81% and specificity of 88% was an excellent diagnostic value for the prediction of CAD. The longitudinal strain sensitivity of this study was similar to our study (with 82% sensitivity). Rumbinaite *et al.* [16] studied global and segmental longitudinal strain during systole and diastole. Also, the parameters were evaluated for patients with moderate to severe coronary artery stenosis at rest and during dobutamine stress echocardiography. Global longitudinal stress at rest for no CAD was -21.5 ± 2.4% compared to the CAD group -16.2 ± 2.1%, P-value = 0.00. The findings represented that the global longitudinal strain provided a higher Area Under the Curve (AUC), sensitivity, and specificity (0.955, 94% and 92%, respectively) than the strain rate in early and end-diastole and visual assessments for the diagnosis of coronary artery stenosis. The result of this study was in agreement with our research. Our study reported systolic and early diastolic longitudinal strain with high sensitivity (81.8% for systolic longitudinal strain) and (89.1% for early diastolic longitudinal strain) were reported as powerful parameters for predicting CAD patients. With multivariate logistic regression analysis, early diastolic and end-systolic longitudinal strains were identified as useful parameters for detecting CAD patients.

Also, the results of our research were approximately consistent with the study of Radwan *et al.* [17]. Their study showed that global longitudinal strain was significantly reduced in patients with significant coronary artery stenosis compared with those without coronary artery stenosis (-11.86 ± 2.89% vs. -18.65 ± 0.79%, P-value < 0.000). In addition, the sensitivity and specificity for discriminating significant CAD were 93% and 82%, respectively.

Shimoni *et al.* [18] studied patients with CAD. They observed longitudinal strain significantly lower in patients with significant CAD (-17.3%) than patients with non-significant CAD (-20.8%), (P-value < 0.05). Peak systolic global and segmental strain of area under the curve were 0.8 and 0.76, respectively. The result showed that global longitudinal strain could predict significant CAD with 81% sensitivity and 67% specificity.

In the study of Moladoust *et al.* [19], CAD patients were identified with stress parameters. They used tissue Doppler imaging and estimated non-invasive end-diastolic pressure. There were significant differences between patients with 70% stenosis and the healthy group. The results showed that stress with 83% area under the curve was a powerful parameter for discrimination of CAD patients, which is different from our study. Our research showed that the early diastolic longitudinal strain was the strongest parameter for the detection of CAD patients. Since the longitudinal strain shows the contraction between the endocardial and epicardial layer of fibers in the longitudinal direction, with the beginning of ischemia, the longitudinal function of the LV is affected. Therefore, the study of longitudinal dysfunction of the LV segments is important [20].

In general, studies show that ischemic areas in patients with coronary artery stenosis reduce the physical-mechanical parameters of myocardial muscle compared to healthy group. Speckle tracking analysis can be investigated significant reduction in LV function in the systolic and diastolic phases following a reduction of blood flow in the early stages of the disease [21]. STE software is rapidly evolving in both research and technology. It is essential to define the normal value of strain and clinical setting to indicate the benefit of STE to the assessment of LV function. Optimization of strain and strain rate for evaluation of these algorithms will occur, including endocardial and epicardial border detection algorithms with higher flexibility. The current study only measured the strain in a longitudinal direction, which was based on simplifying the contraction pattern of myocardial fibers and did not consider out off-plane movement. These problems are limitations of the study. It is hoped that these barriers will be removed with new methods and advanced algorithms.

5. Conclusion

STE technique was a powerful and non-invasive method for the evaluation of LV function in patients with CAD. In this study, early diastolic longitudinal strain with a sensitivity of 89.1% and end-systolic longitudinal strain with a sensitivity of 81.1% were introduced as independent predictors to detect CAD patients. These results can be helpful for referral patients to the angiography department.

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