

## Evaluation of Left Atrial Strain Parameter in Coronary Artery Stenosis: A New Tool to Predict LCX Stenosis

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### ABSTRACT

**Introduction:** Speckle tracking echocardiography (STE) based on frame-to-frame tracking of acoustic speckles is a novel angle-independent method, used for evaluating myocardial deformation and recently to assess left atrium (LA) function.

To the best of our knowledge, there is no investigation evaluating the predictor role of LA strain parameters in detection of coronary artery stenosis in ischemic heart disease. In this study, we assessed this parameter for predicting the culprit artery in patients underwent selective coronary angiography (SCA) in Mashhad, Iran.

**Materials and Methods:** This was a case-control study, which was performed in Imam Reza and Ghaem Hospitals in Mashhad, Iran between 2017 and 2018 in patients referred for SCA. Subjects with two or three- vessel diseases were excluded. Sixty-five cases were included in the study and divided into four groups according to the vessel involved: Group (1): normal coronary artery subjects (n=36); group (2): patients with left anterior descending (LAD) artery stenosis (n=12); group (3): patients with left circumflex artery (LCX) stenosis (n= 7) and group 4: patients with right coronary artery (RCA) stenosis (n=10). Patients underwent routine TTE and Speckle Tracking Imaging.

**Results:** The mean age of participants was 56.72± 10.69 years old. The male/female ratio was 0.96. Mean absolute value of LA strain was 24.74% in normal subjects, while in groups with stenotic coronary artery disease, less values were defined as 18.63%, 16.03% and 19.05%, respectively (p value=0.05). The amounts of left ventricle end systolic volume (LVESV), LV global longitudinal strain (GLS) and Em of septal annulus were significantly different between normal group and those with LCX stenosis. Among different echocardiographic parameters, LA strain, LVESV and Em of septal annulus were defined as predictors of LCX occlusion with regression analysis.

**Conclusion:** LA strain in subjects with coronary artery stenosis was lower than the strain in normal group and could predict isolated LCX occlusion.

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## Introduction

Nowadays, cardiovascular disorders are the most cause of mortality and complications in all over the world.(1) Dramatic changes have been made in the therapeutic approaches, which caused better outcomes and knowledge on the nature of cardiovascular diseases.(2) In most patients, coming to the emergency department, electrocardiogram (ECG) is non-diagnostic or even the symptoms are atypical; so it is challenging for the physicians to diagnose acute coronary syndrome (ACSs) and identify patients who need admission or interventional procedures.(3) In cases of acute myocardial infarction (MI), blood supply of the three major pericardial coronary arteries could be varied from person-to-person and the predilection of involvement of particular sites of conduction system differ by each coronary artery. The clinical presentation, morbidity, and mortality are also affected by the artery involved. (4) Early identification of the culprit coronary artery gives a best view to the clinicians in managing the life-threatening diseases. (4)

The echocardiographic evaluation is one of the instruments that can be used for prediction of early or late outcomes in ischemic heart disease (IHD). (5) Although the detection of left ventricular (LV) ejection fraction and other parameters are very helpful in this field, exact tracing of the endocardium is needed; it could be operator-dependent, and also it is affected by the heart rate or loading conditions. Therefore, a noninvasive, independent and accurate method is needed for measurement of myocardial contractility and performance with lower inter-operative variability. (6) Measurements of myocardial strain and strain rate (SR) are newer indices, which can overcome the mentioned limitations. They are reflective of the magnitude and rate of

myocardial deformation. Myocardial deformation parameters change in the early stage of myocardial ischemia so could be a sensitive tool for detecting regional myocardial dysfunction. (7)

Previous studies have shown that acute myocardial infarction mortality, heart failure, stroke, new onset atrial fibrillation and severity of diastolic dysfunction could be predicted by LA size. (8-9) LA function is generally determined by its size and volume, (10-11) but nowadays it could be evaluated by speckle tracking echocardiography (STE). (12-13), in both the normal population and those patients with cardiac abnormalities. (14-15)

To best of our knowledge, there is no investigation for evaluating the predicting role of LA strain in detection of coronary artery stenosis in patients. This aim was targeted in those patients who underwent selective coronary angiography (SCA) admitted in tertiary hospitals, Mashhad, Iran.

## Materials and Methods

### Study Population

This was a case-control study, performed in Imam Reza and Quam Hospitals, in Mashhad, Iran between 2017 and 2018, in patients who referred for SCA.

First of all, one hundred patients with suspicious diagnosis of coronary artery disease (CAD) were enrolled in this study who was referred for SCA with isolated artery stenosis. Exclusion criteria were previous history of coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI), significant aortic valve disease, decompensated heart failure, uncontrolled hypertension, arrhythmias such as atrial fibrillation (AF), acute pulmonary embolism, severe LV systolic dysfunction, hypertrophic obstructive cardiopulmonary, history of rheumatic mitral valve disease, moderate or higher

degree of mitral insufficiency, grade II or more diastolic dysfunction.

### Study Groups

Thirty-five subjects were excluded from the study because of two or 3-vessel disease. Finally sixty-five patients with normal sinus rhythm were remained, divided into four groups according to coronary artery stenosis location: group (1): normal coronary artery subjects (n=36); group (2): patients with left anterior descending (LAD) artery stenosis, greater than 75% (n=12); group (3): patients with left circumflex artery (LCX) stenosis, greater than 75% or cut off proximally with LA branch defined separated from the artery (n= 7) and group 4: patients with right coronary artery (RCA) stenosis, greater than 75% (n=10). Informed consent was obtained from each subject. Demographic, electrocardiographic (ECG) and echocardiographic findings of them were recorded in the checklists.

### Transthoracic Echocardiography (TTE)

Echocardiography was done in left lateral decubitus position, using Philips IE33 Scanner (Bothell, WA, USA). Transthoracic images of the left ventricle, including the apical, four, two and three chambers were obtained. LV ejection fraction (LVEF) was calculated according to the biplane Simpson's method. LVEF of >52% for men and >54% for women were defined as normal LV systolic function. (16-17) Regional wall motion analysis was assessed semi quantitatively with a 16-segment model of the left ventricle. (18) LA and RA areas and volumes were measured in four chamber views.

### Speckle Tracking Echocardiography

In four-chamber view, three-beat cine-loop clips were selected. Selected images were exported and analyzed by Qlab software. The process began with manual tracing of LA endocardial surface, in a single frame at end systole by a point-click approach. The epicardial

tracing is then automatically generated. The periodic displacement of the tracing was automatically tracked in subsequent frames. With consideration of the reference point at the beginning of the QRS complex, software automatically calculated strain. The SD of longitudinal strain in six segments was then calculated and defined as "LA strain" in the results. Left ventricle global longitudinal strain was also measured using three apical views.

### Statistical Analysis

Descriptive statistical analyses were used to present mean and standard deviation of quantitative variables. Chi-square test were used with 95% confidence limits. ANOVA was used for comparing echocardiographic variables between four groups, then we used post hoc test of Dunnett to compare each group (with statistically significant difference in ANOVA test) with normal group. For definition of the relationship between independent variables logistic regression analysis was performed. For all analyses, the SPSS (SPSS 21.0 for Windows; SPSS Inc. Chicago, Illinois) software was used. P-values of less than 0.05 were considered significant.

### Ethics

This study was assigned 950044 code and approved by editorial board of Mashhad University of Medical Sciences. The researchers considered all ethical issues for patient's information and procedures based on the ethical committee of Mashhad University of Medical Sciences and ethical statements. Informed consent was filled out by each patient prior to echocardiography.

### Results

The mean age of participants was 56.72±10.69 years old. The male/female ratio was 0.96. Other baseline characteristics of participants was shown in Table 1.

There was no significant difference in the baseline characteristics between the four groups of study population ( $P > 0.05$ ), except to gender ( $p = 0.009$ ).

**Table 1:** Baseline characteristics of the study population and comparison between different groups

Characteristics	Total number= 65	Group (1) n= 36	Group (2) n= 12	Group (3) n= 7	Group (4) n= 10	P value
Age (years)	56.27± 10.69 (35-83)	53.69±10.01	58.42±8.43	61.29±12.50	62.40±11.84	0.6 <sup>a</sup>
Gender (n, %)	Male (32, 49.2) Female (33, 50.8)	11(31%), 25(69%)	8(67%), 4(33%)	5(71%), 2 (29%)	8(80%), 2(20%)	0.009 <sup>b</sup>
Height (cm)	161.93± 7.68 (150-182)	162±7.79	160±0.00	160±0.00	164±11.20	0.58 <sup>a</sup>
Weight (Kg)	71.47± 14.32 (46-112)	75±14.2	68±12.26	61±10.38	68±16.61	0.63 <sup>a</sup>
Body Surface Area (m <sup>2</sup> )	1.71± 0.20 (1-2.26)	1.7±0.22	1.67±0.17	1.61±0.15	1.73±0.23	0.42 <sup>a</sup>
SBP (mmHg)	130.95± 17.09 (100-161)	130±17.01	127±15.16	131±2.35	136±18.67	0.71 <sup>a</sup>
DBP (mmHg)	83.03± 10.04 (67-107)	82±10.09	84±11.31	81±9.53	85±9.48	0.74 <sup>a</sup>
Heart Rate	73.40± 11.03 (57-109)	70±8.34	76±9.40	74±16.01	76±16.58	0.38 <sup>a</sup>
Diabetes Mellitus (n, %)	10, 15.4	6, 60%	1, 10%	2, 20%	1, 10%	0.646 <sup>b</sup>
Hypertension (n, %)	22, 33.8	12, 54.5%	2, 9.2%	3, 13.6%	5, 22.7%	0.391 <sup>b</sup>

SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, Group (1): normal coronary artery subjects; Group (2): patients with left anterior descending (LAD) artery stenosis; Group (3): patients with left circumflex artery (LCX) stenosis; Group (4): patients with right coronary artery (RCA) stenosis. <sup>a</sup>ANOVA test, <sup>b</sup>Chi-square test

Echocardiographic parameters were listed in Table 2. The decrease in LA strain was marginally significant in group 3 with LCX stenosis (mean: 16.03%, p value=0.042) in comparison with the normal cases (group 1). The amount of LVESV, LV GLS, Em-septal were also significantly different between group 1 and 3.

Logistic regression analysis, after data entry of LA strain, LVESV, LVGLS, and Em-septal, showed that only LA strain, LVESV and Em-septal remained significant predictors of LCX stenosis (with p value < 0.1 in previous model). Other data were shown in Table 3.

**Table 2:** Comparison of echocardiographic variables in different groups

Echo parameter	Group (1) n= 36	Group (2) n= 12	Group (3) n= 7	Group (4) n= 10	P- value <sup>a</sup>	P value <sup>b</sup>
LVEF (mean rank)	60.75	45.66	52.42	52.43	<0.001	<0.001 between group 1 and 2
LVEDV (mean± S.D)	83.80 ±19.74	94.08±30.31	85.10±22.37	73.00±1.54	0.27	
LVESV (mean rank)	20.49	34.35	34.13	29.79	<0.001	<0.001 between group 1 and 2, 0.039 between 1 and 3
LV GLS (mean± S.D)	18.94±3.91	13.75±3.01	15.64±3.42	16.64±4.41	<0.001	<0.001 between group 1 and 2, 0.042 between 1 and 3
Em-lateral (mean± S.D)	9.18±2.67	7.40±2.68	7.33±1.70	9.41±3.18	0.83	
Em-septal (mean± S.D)	8.36±2.51	7.21±2.53	6.51±1.84	5.90±1.78	0.022	0.039 between group 1 and 3, 0.024 between 1 and 4
LA volume (mean rank)	22.31	25.14	27.42	27.80	0.628	
LA area (mean rank)	21.82	23.43	23.96	29.55	0.186	
LA strain (mean rank)	24.74	18.63	16.03	19.05	0.05	0.042 between group 1 and 3
RA volume (mean± S.D)	37.30±12.12	35.28±10.40	36.66±9.92	36.30±4.08	0.98	

LVEF: left ventricular ejection failure; LVED: left ventricular end-diastolic; LVESV: left ventricular end-systolic volume; LVGLS: Left ventricular global longitudinal strain; LA: left atrium; RA: right atrium; LA-strain4: left atrial strain with four-chamber view. Group (1): normal coronary artery subjects; Group (2): patients with left anterior descending (LAD) artery stenosis; Group (3): patients with left circumflex artery (LCX) stenosis; Group (4): patients with right coronary artery (RCA) stenosis. <sup>a</sup> Comparison between all groups by ANOVA test, <sup>b</sup> P-value in post hoc test in groups with statistically significant difference (with normal group) in ANOVA test.

**Table 3:** Logistic Regression to define the predictive factors of isolated LCX occlusion

Parameters	95% C.I. for EXP (B)		Exp (B)	p
	lower	Upper		
LA strain	0.814	0.991	0.898	0.032
LVESV	1.007	1.250	1.122	0.037
Em septal	0.240	1.003	0.490	0.051

LA-strain: left atrial strain, LVESV: left ventricular end-systolic volume

## Discussion

Despite the improvements in early outcome in patients with ST-elevation myocardial infarction (STEMI) (19), late results are still not satisfactory. Therefore, defining a predictor for long term mortality is essential. One of these predictors could be the location of the infarction. Inferior wall STEMI has better outcome than anterior STEMI. (20) However, inferior STEMI may be the result of either LCX or RCA stenosis, leading to different long-term prognosis. LCX stenosis even if occluded, does not frequently lead to ECG changes. This might result in delayed diagnosis or intervention, in patients presented with acute coronary syndrome or even stable coronary artery disease. (21)

The LA has an essential role in the overall cardiac function. The LA function includes three parts: a reservoir function during left ventricular (LV) systole, a passive conduit for the passage of blood from the pulmonary veins to LV during early ventricular diastole, and finally a booster pump function with an active LA emptying during late ventricular diastole.(22) After myocardial infarction, LA function could be an important predictor for mortality. (23) Nowadays, strain imaging by two dimensional speckle tracking echocardiography (2d STE) is a novel technique for assessment of LA function.(14, 24) In this study, we evaluated the value of LA strain in predicting coronary artery occlusion in patients who underwent SCA. The amounts of LVESV, LV GLS, Em-septal were significantly different between the normal subjects and patients with LCX stenosis. LA strain was lower in group 3 (16.03%, P value=0.042) in comparison with the normal subjects. The decrease was marginally significant and this might be applicable in the practice. Logistic regression analysis showed that LA strain, LVESV and Em- septal were the predictors of LCX stenosis. To our knowledge, there was no similar study, conducted in human. There was an animal experiment in which LA and diastolic function were assessed in sheep, after induction of ischemia by LCX occlusion. It was demonstrated that LA stroke volume was reduced significantly after LCX occlusion (compared to LAD). (25)

Liu et al. evaluated LA function in patients with CAD by strain and strain rate imaging. In patients with CAD and normal LA size, LA reservoir and passive conduit functions could be impaired. Other traditional parameters such as LA ejection fraction and trans-mitral inflow patterns did not significantly differ between the controls and CAD patients with normal-size LA. They showed that LA strain and strain rate could be more reliable markers for the changes in LA function than traditional parameters. (26)

Left ventricular compliance could affect LA conduit function during early diastole. (27) Left ventricular ischemia induces diastolic abnormalities, reduces LV compliance, resulting in abnormal LA conduit function (28).

Previously published studies showed the left atrial contractility was enhanced in the patients with left ventricular ischemia compared with control groups. (29-30) Liu et al. indicated that strain did not change between patients with CAD and normal LA size and controls. (26) Another study demonstrated that intensification of LA contraction was mostly seen in the patients with LAD occlusion. (29) Several animal and clinical studies, agreed that during LAD occlusion, atrial function could be different from occlusion of proximal part of LCX. (25-31-32) this could be explained by this fact that, LA perfusion is mostly achieved from proximal part of LCX and in smaller amount by RCA whereas LAD does not perfuse LA. (25)

Limitations: Further studies with larger sample size are needed. Long term follow up is suggested to define the outcome of such changes in LA function parameters.

## Conclusion

LA strain could have a specific predictive role for isolated coronary artery occlusion, including LCX lesions. Therefore, in patients presenting with chest pain, reduced LA strain without obvious reason, could be a clue for LCX stenosis. Performing large-scale investigations with higher sample size with mid to long-term follow up could improve the results.

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### Conflict of interest

None.

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