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# Strain Analysis Using Speckle Tracking Echocardiography for Detection of Coronary Artery Disease in Stable Angina Patients with No Regional Wall Motion Abnormality at Rest

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**Abstract** **Original Research Article**

***Background*:** Speckle-tracking imaging is a novel method for assessing left ventricular (LV) function and ischemic changes. The aim of this study was to predict the presence of coronary artery disease by longitudinal 2D strain analysis using speckle tracking echocardiography in patients with stable or unstable angina with no regional wall motion abnormality at rest. ***Objectives*:** Objective of this study is to predict the presence of significant CAD in a patient with no regional wall motion abnormality by longitudinal 2D strain analysis using speckle tracking echocardiography. ***Methods*:** This cross-sectional study included a total 66 patients (mean age, 51.92±8.9 years) with suspected CAD without RWMA on resting echocardiography who underwent coronary angiography. Longitudinal 2D strain analysis by STE was performed in all patients before coronary angiography. Global and segmental peak systolic longitudinal strain (PSLS) were recorded & computed by offline dedicated software semi-automatically on bull's-eye report. The patients were divided into two groups according to the coronary angiographic findings; group- I: significant CAD on coronary angiogram (n=35), group-II: normal coronaries on CAG (n=31).All the baseline characteristics and outcome were then compared between the two groups. ***Results*:** PSLSs of all left ventricular segments were obtained successfully in 66 patients. PSLS (both global and segmental) was significantly decreased in patients with significant CAD on CAG group. Receiver operating characteristic (ROC) curve analysis demonstrated that global PSLSs could effectively detect patients with CAD (area under ROC curve = 0.877, 95% CI=0.749–0.960). According to ROC curve analysis, -18.77% appeared to be a good cutoff value for predicting those with significant CAD (specificity 77.4% and sensitivity 82.9%). ***Conclusion*:** Global and segmental PSLS using speckle tracking echocardiography at rest was significantly lower in patients with CAD without RWMA, and might be useful for identifying patients with a significant CAD with good degree of sensitivity and specificity.

**Keywords:** Speckle tracking echocardiography, Peak systolic longitudinal strain, Coronary artery disease.



## INTRODUCTION

Coronary artery disease (CAD) is a major cause of death and is a global health problem reaching epidemic in both developed as well as in developing countries [1].

Early detection of coronary artery disease is very important to combat cardiovascular morbidity & mortality and may often influence treatments and establish prognosis [2]. The echocardiographic assessment of regional myocardial function plays a critical role in the diagnosis and management of ischemic heart disease [3].

During recent years, velocity imaging, displacement imaging and deformation imaging (strain and strain-rate imaging) have emerged as valuable tools for more comprehensive and reliable echocardiographic assessment of myocardial function [4].

The recently introduced 2D strain modality opens entirely new possibilities for advanced, real-time analysis of myocardial wall motion. The new modality is based on recently developed speckle tracking echocardiography (STE) technique that allows 2D imaging and tracking of natural acoustic markers (reflectors/speckles), and has a clear advantage of providing the possibility for measurements of myocardial velocity, displacement, and strain not only in longitudinal but also in radial and circumferential direction. This is of importance because several studies performed hitherto have indicated that the analysis of circumferential (rotational) myocardial motions may be a useful and sensitive tool for the detection of myocardial ischemia and ischemic myocardial injury [5].

The subendocardium is the area of the left ventricle most vulnerable to the effects of hypoperfusion and ischemia. LV longitudinal mechanics at rest may therefore be attenuated in patients with coronary artery disease [6]. For example, Liang *et al*., (2006) found that a peak longitudinal strain rate of -0.83/sec and an early diastolic strain rate of 0.96/sec obtained from resting echocardiography could predict >70% coronary stenosis with sensitivity of 85% and specificity of 64%. Speckle tracking–derived longitudinal strain is also useful in predicting the extent of coronary artery disease [7]. Choi *et al*., (2009, p.700) reported that a segmental mid and basal peak longitudinal strain cutoff value of -17.9% was capable of discriminating severe 3-vessel or left main coronary artery disease from disease with lesser severity with sensitivity of 78.9% and specificity of 79.3% [8].

With technical improvements in the temporal and spatial resolutions of two-dimensional (2D) echocardiography, LV peak systolic longitudinal strain (PSLS) can now be measured using the 2D speckle tracking Method. This method might provide a useful means of measuring LV long-axis function, and might detect subtle changes in LV systolic function which could be caused by myocardial ischemia. Recently, a semi-automated algorithm for automated function imaging (AFI) has developed that can assist PSLS measurements. This method can provide quantitative measurements of global and segmental PSLS using a simple bull's eye display [8].

As repetitive ischemic insults to LV, which occurs with CAD, would reduce systolic longitudinal function, although resting regional wall motion remains normal. Therefore, in this study my aim is to evaluate whether global and segmental PSLS measurement by the 2D speckle tracking method with AFI is useful for predicting severe CAD. This modality of noninvasive imaging has not been evaluated for coronary artery disease (CAD) in the population of Bangladesh. Hopefully, the findings of longitudinal 2D strain using speckle tracking echocardiography will help us to diagnose CAD noninvasively in an appropriately selected patient for planning further management.

## OBJECTIVES

**General Objective:**

To predict the presence of significant CAD in a patient with no regional wall motion abnormality by longitudinal 2D strain analysis using speckle tracking echocardiography.

**Specific Objective:**

- To analyze myocardial longitudinal 2D strain using speckle tracking echocardiography in patients suspected of CAD without resting regional wall motion abnormality.
- To detect CAD by coronary angiogram in a patient without resting RWMA.
- To compare between parameters of CAG findings and longitudinal 2D strain.

## METHODOLOGY

**Type of study:** This was cross-sectional type of study.

**Place of Study:** This study was carried out at the Department of Cardiology and the Department of Echocardiography of the National Heart Foundation Hospital and Research Institute, Mirpur, Dhaka.

**Study period:** October, 2013 to September, 2014

**Study population:** Patients with suspected Coronary artery disease (stable angina, Effort angina, unstable angina) with no regional wall motion abnormality at rest on 2D echocardiography & scheduled for CAG at National Heart Foundation Hospital and Research Institute.

**Sampling technique:** Non Random sampling

**Sample Size:** 66 Paitients

**Sample Selection criteria**

**Inclusion Criteria:**

1. Evaluation of angina in patients with suspected CAD who were admitted for Scheduled CAG,
2. Patients without RWMA at rest by conventional echocardiography.
3. Normal sinus rhythm without left bundle branch Block
4. Adequate echo window for analysis of myocardial strain using STE.

**Exclusion Criteria:**

1. Patients with acute myocardial infarction & history of previous myocardial infarction,
2. NYHA class-III / IV Heart failure or haemodynamically unstable patients,
3. Past History of PTCA or CABG,
4. Associated valvular (moderate to severe) and congenital heart disease,

5. Patients with extremely severe concomitant disease (Severe dementia, chronic kidney disease, advanced malignancy),
6. Suboptimal two dimensional Echo images to analyze myocardial strain by using STE.
7. Patient who don't give consent for coronary angiography.

**Data Collection & Statistical Analysis:**

Data was collected in a predesigned data collection form, After processing of all available data, statistical analysis of their significance was done. Obtained data was expressed in frequency, percentage, mean and standard deviation as applicable. Comparison between groups was done by Student's T-test for continuous variables. Categorical data was analyzed by chi-square test.

Logistic regression was performed in order to adjust for baseline characteristics (age, gender, diabetes, hypertension, smoking and BMI) for the assessment of the independency of strain parameters associated with CAD. Analysis of variance (ANOVA) was performed to test if the Global PSLS varied with increasing severity of CAD defined by increased number of stenotic coronary vessels. Receiver Operating Characteristics (ROC) curves were constructed and Area under curve (AUC) was calculated. From the ROC curves constructed for global and segmental PLS the optimal cut-off value with highest sensitivity and specificity for diagnosing CAD were identified. Statistical programme for social science programme (SPSS) version 16.0 for windows was used to analyze the data. Statistical significance was defined as P-value of <0.05.

# RESULT

**Table I: Distribution of the study patients according to age (n=66)**

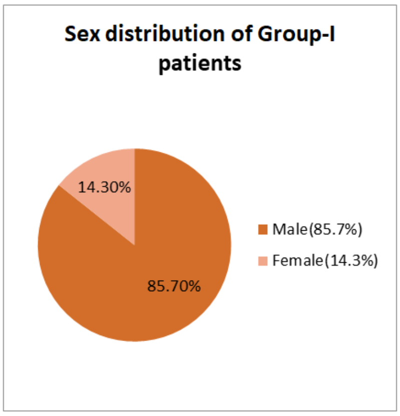
| Age | Group I (n=35) Significant CAD on CAG | | Group II (n=31) Normal CAG or no significant CAD on CAG | | p value |
|---|---|---|---|---|---|
| | n | % | n | % | |
| 31-40 | 4 | 11.4 | 6 | 19.4 | * 0.722 NS |
| 41-50 | 12 | 34.3 | 12 | 38.7 | |
| 51-60 | 11 | 31.4 | 8 | 25.8 | |
| 61-70 | 8 | 22.9 | 5 | 16.1 | |
| Mean ± SD | 53.43 ± 8.6 | | 50.23 ± 9.1 | | ** 0.149NS |

S = Significant; NS= Non significant

* p value reached from $X^2$ test, p value significant < 0.05

** p value reached from unpaired t – test, p value significant < 0.05

The above table shows the age distribution of the patients and found that most of the patients belonged to 41-50 years in both groups, which were 12(34.3%) and 12 (38.7%) in group I (significant CAD on CAG) & group II (normal CAG or no significant CAD on CAG) respectively. No statistically significant age difference was found between two groups (p=0.722). The mean age of group I patients was 53.43 ± 8.6 years and 50.23 ± 9.1 years for group II patients .But the mean age difference was not statistically significant (p>0.05).



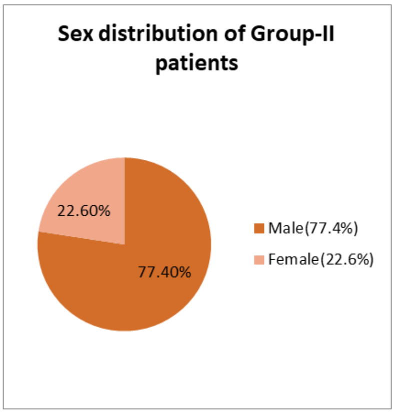




**Figure 1: Distribution of the study patients according to sex (n=66)**

Among group- I patients 85.7 percent was male and 14.3 percent was female, where as in group- II patients 77.4 percent was male and 22.6 percent was female. Analysis revealed that there was no statistically significant difference regarding sex between two groups of patients p= 0.0383.

**Table II: Clinical diagnosis of the study patients by group (n = 66)**

| Clinical diagnosis | Group I (n=35) With Significant CAD on CAG | | Group II (n=31) With normal CAG | | P value |
|---|---|---|---|---|---|
| | **n** | **%** | **n** | **%** | |
| Chronic stable Angina | 28 | 80 | 29 | 93.5 | $0.109^{NS}$ |
| Unstable Angina | 7 | 20 | 2 | 6.5 | |

NS = Not significant

p value reached from $X^2$ test, p value significant < 0.05

Table II shows that most of the patients in both groups presented with chronic stable angina (80% in group I and 93.5% in group II) & rest of the patients presented with unstable angina (20% in group I and 6.5% in group II). But analysis found no statistically significant (p=0.109) difference considering clinical diagnosis between two groups.

**Table III: Summary of risk factors distribution of the study patients (n=66)**

| Risk factors | | Group I (n=35) with significant CAD on CAG | | Group II (n=31) with normal CAG | | p value |
|---|---|---|---|---|---|---|
| | | **n** | **%** | **n** | **%** | |
| Smoking | Current | 11 | 31.4 | 5 | 16.1 | $*0.333^{NS}$ |
| | Former | 10 | 28.6 | 12 | 38.7 | |
| | Never | 14 | 40 | 14 | 45.2 | |
| Hypertension | | | | | | |
| Yes | | 23 | 65.7 | 16 | 51.7 | $*0.245^{NS}$ |
| No | | 12 | 34.3 | 15 | 48.4 | |
| Diabetes | | | | | | |
| Yes | | 23 | 65.7 | 9 | 29 | |
| No | | 12 | 34.3 | 22 | 71 | $*0.003^{S}$ |
| Dyslipidemia | | | | | | |
| Yes | | 18 | 51.4 | 7 | 22.6 | |
| No | | 17 | 48.6 | 24 | 77.4 | $*0.016^{S}$ |
| Family history of IHD | | | | | | |
| Yes | | 5 | 14.3 | 2 | 6.5 | |
| No | | 30 | 85.7 | 29 | 93.5 | $*0.302^{NS}$ |
| Obesity | | | | | | |
| Obese | | 0 | 0 | 2 | 6.5 | |
| Over weight | | 19 | 54.3 | 12 | 38.7 | |
| Normal | | 16 | 45.7 | 16 | 51.6 | $*0.226^{NS}$ |
| Under weight | | 0 | 0 | 1 | 3.2 | |

S = Significant, NS = Not Significant

* p value reached from $X^2$ test, p value significant < 0.05

Diabetes and dyslipidaemia were significant risk factors in group I (p <0.05). No statistically significant difference were observed between two groups of patients (p >0.05) regarding the other risk factors – smoking, hypertension, family history of IHD and obesity.

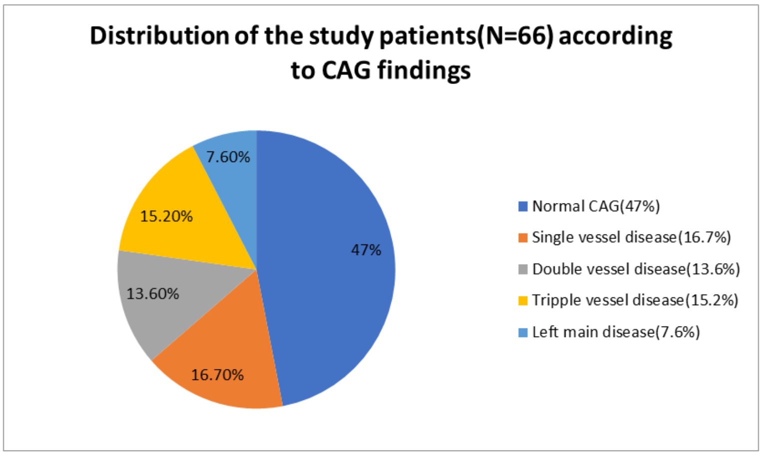



**Figure 2: Coronary angiogram findings of the study patients (n=66)**

Above figure shows that in group- I (n=35) patients CAG revealed SVD was 16.7%, DVD was 13.6%, TVD was 15.2% and left main disease was 7.6 %. In group-II patients (n=31) CAG revealed normal coronaries (47%).

**Table IV: Distribution of groups by 2-D strain parameters using Speckle tracking echocardiography (n=66)**

| Strain Parameters | Group I (n=35) with significant CAD on CAG (Mean ± SD) | Group II (n=31) With normal CAG (Mean ± SD) | p value |
|---|---|---|---|
| Global PSLS (%) | -16.88±2.2 | -20.60±2.8 | < 0.001^S |
| Segmental PSLS | | | |
| Basal PSLS (%) | -15.25±2.7 | -18.05±2.4 | < 0.001^S |
| Mid- PSLS (%) | -16.79±2.3 | -20.07±2.9 | < 0.001^S |
| Apical PSLS (%) | -18.74±3.4 | -23.83±4.3 | < 0.001^S |
| Mid & Basal PSLS (%) | -16.01±2.3 | -19.12±2.6 | < 0.001^S |

PSLS, Peak systolic longitudinal strain. S = Significant,
p value reached from unpaired t – test, p value significant < 0.05

Table shows that Global and segmental PSLS were lower in significant CAD group than no significant / normal CAG group & also statistically significant p <0.001. Segmental PSLS analysis also shows that Basal PSLS, Mid-PSLS, Apical PSLS, Mid & basal PSLS (%) values were lower in group-I than group-II. And analysis showed statistically significant (p<0.001) difference considering segmental PSLS between two groups.

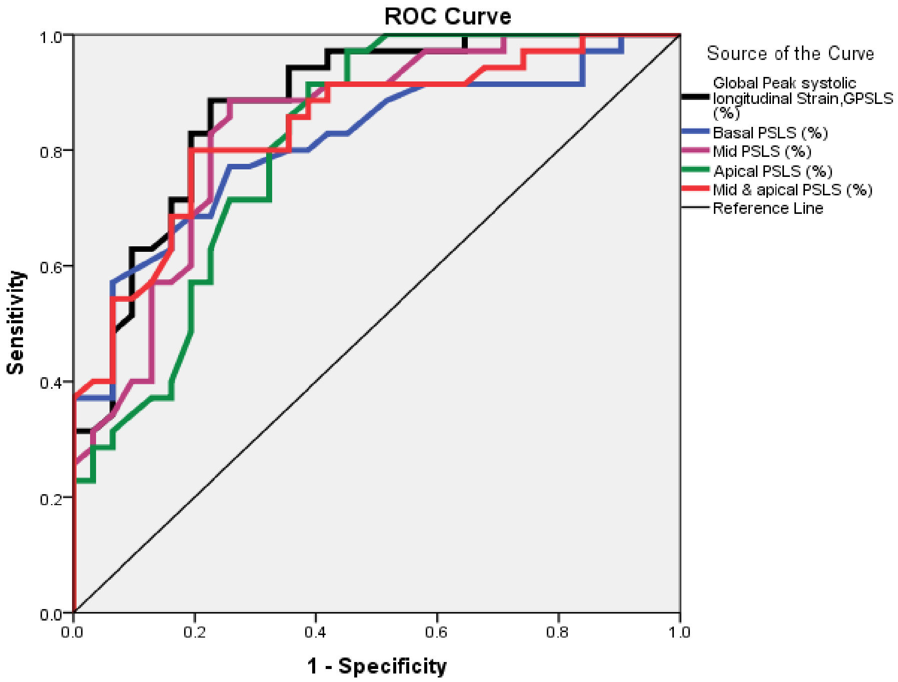



**Figure 3: Receiver operating characteristic (ROC) curve analysis for prediction of significant coronary artery disease defined as >70% stenosis in any of 3 main coronaries (LAD/LCX/RCA) or their major branch vessels or >50% stenosis in left main coronary artery**

Receiver Operator Characteristic (ROC) curve for Global Peak systolic Longitudinal Strain, GPSLS, Basal PSLS, Mid PSLS, Apical PSLS and Mid & Apical PSLS as predictors of significant CAD on CAG (area under the curve [AUC] for GPSLS: 0.877 (0.794 – 0.960), Std. Error 0.043; P<0.001 as compared to AUC for Basal PSLS: 0.812 (0.708 – 0.916), Std. Error 0.053; P<0.001, compared to AUC for Mid PSLS: 0.840 (0.743 – 0.936), Std. Error 0.049; P<0.001, compared to AUC for Apical PSLS: 0.812 (0.706 – 0.917), Std. Error 0.054; P<0.001, compared to AUC for Mid & Apical PSLS: 0.840 (0.745 – 0.935), Std. Error 0.048; P<0.001).

**Table V: Sensitivity and specificity of strain echocardiographic variables for the detection of significant coronary artery disease**

| 2D strain Variables | Cut-off value | Sensitivity | Specificity | AUC ( 95% CI ) | P - value |
|---|---|---|---|---|---|
| Basal PSLS (%) | -16.81 | 77.1 % | 71.0 % | 0.812(0.708-0.916) | < 0.001$^s$ |
| Mid PSLS (%) | -18.58 | 82.9 % | 77.4 % | 0.840(0.743-0.936) | < 0.001$^s$ |
| Apical PSLS (%) | -21.12 | 74.3 % | 67.7 % | 0.812(0.706-0.917) | < 0.001$^s$ |
| Mid and basal PSLS (%) | -17.45 | 80 % | 77.4 % | 0.840(0.745-0.935) | < 0.001$^s$ |

PSLS, Peak systolic longitudinal strain; AUC, area under curve; CI, Confidence interval.
S = Significant

Table shows the result of ROC analysis for the prediction of significant CAD and operational cutoff values with corresponding predictive characteristics are presented. For the detection of significant CAD, the optimal cutoff value for Global peak systolic strain was -18.77% (sensitivity = 82.9% & specificity= 77.4%), Basal PSLS was -16.81% (sensitivity=77.1% & specificity= 71.0%), Mid-PSLS was -18.58% (sensitivity =82.9 % & specificity = 77.4%), Apical PSLS was -21.12% (sensitivity=74.3% and specificity=67.7%) and Mid &basal PSLS was -17.45% (sensitivity =80.0% & specificity =77.4%). Result was statistically significant p<0.001.

# DISCUSSION

In this study, using a newly developed AFI technique for measuring longitudinal 2D strain by speckle tracking echocardiography, i found that the systolic function, as determined by peak systolic longitudinal strain (PSLS) values, of patients with significant CAD was significantly lower than in patients with normal CAG or no significant CAD.

In the present study mean age of patients were 51.92±8.9 years. The commonest age group of study patients was 41-50 years in both the groups (34.3% and 38.7% in group I and group II respectively). Mean age difference was not statistically significant (p=0.149). Nearly similar pattern of age distribution was reported by Akanda *et al*., in their study in Bangladesh [9]. But there was difference in mean age with different studies done in abroad Choi, et al.(2009) 59±9 years, Shimoni *et al*., (2011) 59.93±12 years, Montgomery, et al.(2011) 60±2 years, Tsai *et al*., (2010) 63±12 years and Sorensen, et al.(2013) 61.45±9.9 years [8, 10, 13]. Most probably this was due to the late onset of atherosclerotic coronary artery disease in developed countries than that of a third world country population.

Most of the patients; 81.8 % were male and 18.2% patients were female in this study. Male & female ratio was 4.4:1 in the whole study population, which indicates that male patients were predominant in this study. In Bangladesh & abroad, the various studies showed, the female patients formed a small percentage. Choi *et al*., (2009) found 29.2 percent, Shimoni *et al*., (2011) 21.7 percent, Montgomery, et al.(2011) 40.7 percent and Sorensen *et al*., (2013) found 45 percent female patients in their respective studies [8, 10, 11, 13].

Group I and Group II patients had no significant difference regarding the occupation and clinical presentation.

There were similar type of risk factors like hypertension, diabetes, smoking, dyslipidaemia, obesity and family history of IHD in both groups. But statistically significant difference (p value <0.05) was observed between two groups in diabetes and dyslipidaemia (diabetes 65.7% vs. 29% and dyslipidaemia 51.4% vs. 22.6%). Smoking history (current smoker 31.4% vs. 16.1%, former smoker 16.7% vs. 16.1% and never smoked 40% vs. 45.2% in group I and group II respectively), hypertension (65.7% vs. 51.7% in group I and group II respectively), obesity (BMI was 25.26±2.6 $kg/m^2$ in group I and 24.56±3.5 $kg/m^2$ in group II) and family history of CAD (14.3 % in group I and 6.5 % in group II ) was similar for both groups and no statistically significant differences (p>0.05) were found. Nucifora *et al*., (2010) showed statistically significant difference (p<0.05) in smoking and dyslipidaemia (smoker 43% vs. 22% and dyslipidaemia 59% vs. 19% between obstructive CAD & no CAD group respectively) [14]. Montgomery *et al*., (2011) showed that diabetes and dyslipidaemia were the commonest risk factor in CAD group [11]. Choi *et al*., (2009) also observed in their study that dyslipidemia as a commonest risk factor in high risk CAD group [8].

This present study demonstrated the usefulness of longitudinal strain for the diagnosis of CAD without stress echocardiography with acceptable sensitivity and specificity. A few recent 2D strain studies have shown that in patients with CAD, strain or strain rate parameters can detect impaired function at rest. However, the populations tested and the strain parameters analyzed were different in each study. Liang *et al*., (2006) assessed the usefulness of segmental longitudinal 2D strain and strain rate for evaluation of LV deformation in patients with stable angina referred to coronary angiography [7]. They reported that strain rate was the most specific and sensitive parameter for the prediction of CAD at rest. Choi *et al*., (2009) assessed PSS in patients with stable and unstable angina [8]. They showed that resting GS and SPSS were significantly reduced in patients with severe CAD, even when resting wall motion and LV ejection fraction were normal. They reported better accuracy of SPSS in the mid and basal segments in the detection of high-risk CAD compared with SPSS in the apical segments and compared with Global strain. Nucifora *et al*., (2010) studied 182 patients with suspected CAD referred to 64 slice computed tomography for coronary evaluation, because of increased risk profile and/or stable chest pain [14]. The pretest likelihood of obstructive CAD was assessed using the Duke clinical score. Conventional echocardiographic parameters of LV systolic and diastolic function, GS, and strain rate were obtained. The investigators found that only GS provided significant incremental value over the Duke clinical score for the identification of patients with obstructive CAD on multi slice computed tomography. The cutoff for GS was -17.4%, with sensitivity and specificity of 83% and 77%, respectively. Tsai *et al*., (2010) showed in their study that peak systolic global longitudinal strain (GLS), peak segmental longitudinal strain difference (LSD) and its ratio to peak systolic GLS were significant higher in patients with CAD. Using 1.0 as a cutoff point for the ratio of peak segmental LSD to peak systolic GLS, sensitivity was 77.3% and specificity 79.2%.

My study supports these observations and adds new information on the accuracy of strain analysis in detecting CAD in patients with chronic stable and unstable angina. Global PSLS (%) in group- I was -16.88±2.2 and in group- II was -20.60±2.8, which was statistically significant ($p<0.001$). There was also statistically significant difference ($p<0.001$) considering segmental PSLS between two groups. Thus analysis showed that global and segmental PSLS were significantly lower in group- I than group- II. Receiver operating characteristic (ROC) curve analysis showed that for the detection of significant CAD , the optimal cutoff value for global peak systolic strain was -18.77 % (sensitivity = 82.9% & specificity= 77.4%) , basal PSLS was -16.81% (sensitivity=77.1% & specificity= 71.0%), mid-PSLS was -18.58% (sensitivity =82.9 % & specificity = 77.4%), apical PSLS was -21.12% (sensitivity=74.3% and specificity=67.7%) and mid &basal PSLS was -17.45% (sensitivity =80.0% & specificity =77.4%) which was statistically significant $p < 0.001$. In this study, global peak systolic longitudinal strain (GPSLS) showed the higher sensitivity & specificity of 82.9% and 77.4% respectively with the optimal cutoff value was -18.77% to detect the significant CAD.

Strain parameters (Global & segmental PSLS) were still remained significantly different & independent predictors of CAD after multivariate analysis.

## CONCLUSIONS

The present study showed that resting PSLS (Global & segmental) is significantly reduced and highly sensitive to detect significant CAD in patients with stable & unstable angina, even when resting wall motion and LV ejection fraction were normal. It is also observed that 2DSTE seems capable in identifying high risk patients with left main & triple vessel disease. Therefore, PSLS measured by 2D strain using speckle tracking echocardiography with AFI technique may be a more sensitive marker than wall motion abnormality for ischemic heart disease.

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