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DETECTION OF SIGNIFICANT CORONARY ARTERY DISEASE IN PATIENTS WITH EFFORT ANGINA USING GLOBAL LONGITUDINAL STRAIN DERIVED FROM TWO-DIMENSIONAL SPECKLE TRACKING ECHOCARDIOGRAPHY: AN ANGIOGRAPHIC CORRELATION

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Abstract:

Aims: Coronary artery disease is a global concern at the present scenario with changing life style and irrespective of the socioeconomic condition. Conventional treadmill test or invasive coronary angiogram are often not very acceptable from the patient's perspective. Conventional echocardiography also does not help much in detecting the coronary vessel condition. The present study was conducted to determine the relationship between coronary artery disease (CAD) severity and resting 2-dimensional-speckle tracking echocardiography (2D-STE) in stable angina patient and whether there is any diagnostic value when added to routine treadmill testing (TMT), in identifying the presence of coronary artery disease in patients presenting with stable angina.

Methods: A descriptive, cross sectional, single-centre study was conducted on n=92 stable angina patients based on inclusion /exclusion criteria. 2D Speckle-tracking echocardiography (STE) were done to quantify global longitudinal strain (GLS) by GE for each patient. All the patient then underwent angiography performed by percutaneous femoral or radial approach and was obtained for each coronary vessel in ≥ two projections. Stenosis ≥70% reduction of

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the arterial lumen area was considered significant. Angiographic severity will be calculated using the SYNTAX scoring. Then correlation with GLS and angiographic severity was done.
Result: 51.1% patients had significant LAD involvement, 48.9% patients had significant LCX involvement, 46.7% patients had significant RCA involvement and 13.0% patients had significant LMCA involvement in coronary angiogram. As per Coronary Angiogram Syntax Score, majority of patients had intermediate syntax score (42.9%), 19.0% patients had high syntax score and 38.1% patients had low syntax score. Patient who have high syntax score having mean GLS [-12.8833±0.9229] and GLS value of [14.0200±1.0084] and [-16.2167±1.0184] for intermediate and low syntax score group respectively all were low when we compared with minor CAD or normal CAG group mean GLS was -20.0690±0.7960 and this is statistically significant ($p<0.0001$) .
Conclusion: Global Longitudinal Strain by 2-D speckle tracking echocardiography well correlate with significant coronary artery disease and can be used as a noninvasive screening test in predicting significant coronary artery stenosis and can complement TMT in risk stratification and in selecting patients for coronary angiogram.

Running Title: 2D-speckle tracking echocardiography in chronic stable angina patients
Key Words: 2-D speckle tracking echocardiography, myocardial strain, stable angina, SYNTAX scoring

Introduction:

Coronary artery disease (CAD) is the leading cause of death globally of all income groups, accounting more than 9 million deaths in 2016. [1] Treadmill test (TMT) or exercise stress test is the primary screening test for detecting coronary artery disease. TMT has an average sensitivity and specificity of 68% and 77%, respectively especially in single and double-vessel disease, which leads to unnecessary referral to invasive coronary angiogram.[2,3] American college of cardiology national data registry showed only 38% of patients without known cardiac disease had obstructive coronary artery disease in elective coronary angiogram.[4] Conventional echocardiography does not provide much information about the presence of coronary artery disease (CAD) in suspected stable angina patients.

The need for a more quantitative and less invasive method for evaluation of CAD in the stable angina patients has provoked the introduction of several imaging methods, of which strain is showing great promises. Longitudinally orientated myocardial fibers are located sub-endocardially, the area most susceptible to ischemia. So the measurement of longitudinal motion and deformation may be the most sensitive markers of CAD using tissue Doppler imaging (TDI) (4) or 2-dimensional strain echocardiography (2DSE).[5,6] Even though newer non-invasive modalities with good predictive values, such as CT coronary angiography and myocardial perfusion imaging, are available, they are not widely used in a developing country like India because they are expensive and can be accessed only in urban advanced medical centers.[7] In patient with coronary artery disease, speckle tracking echocardiography (STE) can detect the presence of coronary artery occlusions. Myocardial strain shows regional dysfunction in systole and diastole in patients with chest pain and normal ECG. Left ventricular (LV) longitudinal mechanics at rest may be impaired in patients with CAD and can be determined by two-dimensional speckle tracking echocardiography

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(2DSTE). Moustafa S et al (2018) found that there was a statistically significant difference in the mean of global longitudinal peak systolic strain between normal coronaries and different degrees of coronary artery disease.[4] Madhavan S et al and Kaushik Biswas et al also showed GLS by 2DSTE can be used as a non-invasive screening test in predicting significant coronary artery stenosis and can complement TMT in risk stratification and in selecting patients for coronary angiogram. [1,8]

In this scenario, an echocardiography based imaging modality for diagnosis of CAD would be of significant value. Similar study using longitudinal strain have been previously conducted in other parts of the world [9], but so far, there are limited research work in developing country like India on these aspects. Therefore this study was conducted in a tertiary multi speciality hospital with the primary objective to determine the relationship between coronary artery disease (CAD) severity and resting 2-dimensional-speckle tracking echocardiography (2D-STE) in stable angina patient and secondarily to identify the diagnostic value of 2DSTE when added to routine treadmill testing (TMT), in identifying the presence of coronary artery disease in patients presenting with stable angina.

Materials & Methods:

A descriptive, cross sectional, single-centre study was conducted in the Department of Cardiology including IPD & OPD of IPGMER and SSKM Hospital, Kolkata for a period of 18 months (February 2020 to October 2021) with prior approval from the institutional ethics committee. A total of (n= 92) patients of ages ≤ 75years and either sex were recruited based on having a positive exercise stress test, either suspected or proven to have stable CAD with normal ejection fraction who was referred for coronary angiography (CAG) after TMT . Patients with history of acute symptoms, past history of acute coronary syndrome (ACS), co existent valvular heart disease, pericardial disease, cardiomyopathies ,pacemaker therapy, bundle branch block and extreme of age (>75yr) were excluded. After taking the informed consent of the study participants a detailed history, physical examination and 2D Speckle-tracking echocardiography (STE) were done to quantify global longitudinal strain (GLS) by GE for each patient. They underwent 2-D speckle tracking echocardiography for measurement of myocardial strain using automated function imaging (AFI). It was performed from the apical four chamber, two-chamber, and apical long-axis view planes. By speckle tracking, endocardial border was traced in end systole. All the patient then underwent angiography performed by percutaneous femoral or radial approach and was obtained for each coronary vessel in ≥ two projections. Stenosis ≥70% reduction of the arterial lumen area was considered significant. Angiographic severity will be calculated using the SYNTAX scoring. The SYNTAX score was derived from the summation of the individual scores for each separate lesion defined as ≥ 50% luminal obstruction in vessels ≥ 1.5 mm. The SYNTAX scores were calculated for all patients using dedicated software (available at http://www. syntaxscore.com/calc/start.htm).Then correlation with GLS and angiographic severity was done. All data were collected in a pre –designed proforma. The study plan is depicted in the flow chart Figure 1.

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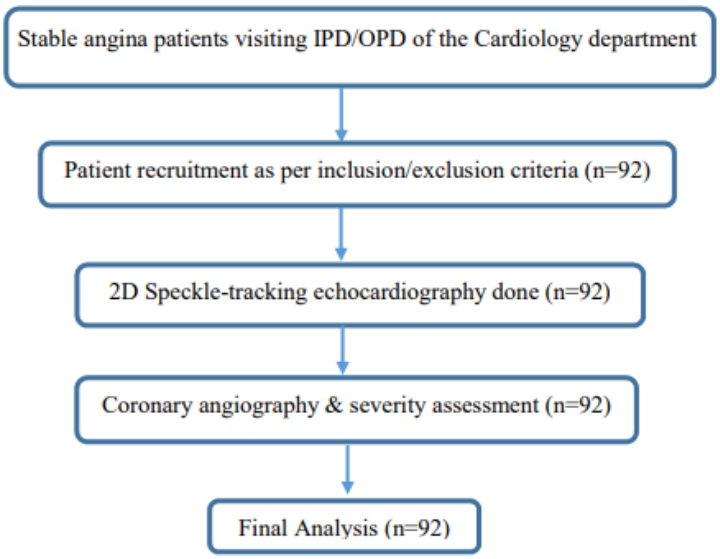

Figure 1: Flow chart of the study

Statistical analysis: The collected data were organized, tabulated, and statistically analyzed using SPSS software statistical computer package version 18 (SPSS Inc., USA). For quantitative data, the mean and standard deviation (SD) were calculated. Other parameters were presented as bar diagram and pie chart.

Results:

In our study, all the recruited patients' were analyzed at the end of the study and there was not a single drop out case. The demographic and other parameters of the study participants was depicted in **Table 1**. Most of the patients were between 51-60 years with a mean age of patients was 57.85± 7.28 years. Male patients were predominant (66%) as compared to female population.

Table 1: Demographic and other parametric findings of the study population (n=92)

Parameters	Value
Age (years), mean (SD)	57.9 (7.3)
Male, n (%)	66 (71.7)
Religion, n (%) Hindu Muslim	 59 (64.1) 33 (35.9)

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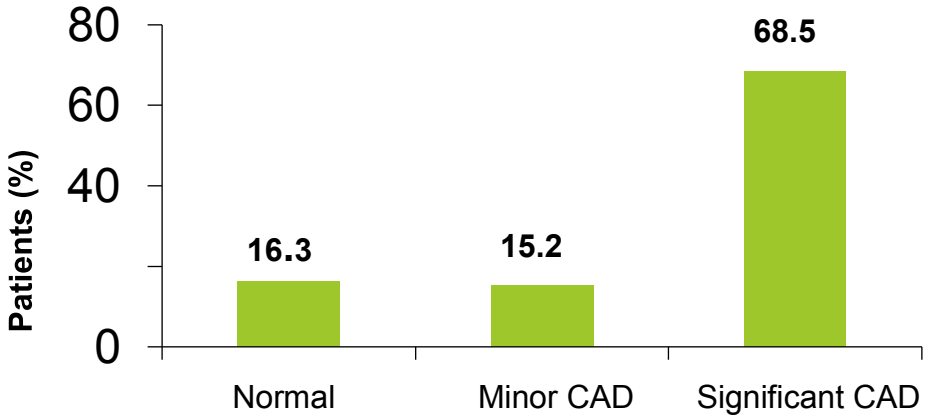
Geographic areas, n (%) Urban Rural	 61 (66.3) 31 (33.7)
Diabetes, n (%)	42 (45.7)
Hypertension, n (%)	62 (67.4)
Smoking, n (%)	49 (53.3)
Alcohol, n (%)	18 (19.6)
Family history of CAD, n (%)	11 (12.0)
Dyslipidemia, n (%)	29 (31.5)
BMI, mean (SD)	25.3 (1.4)

The distribution of the pattern of CAD among study participants is described in **Figure 2** below.

Figure 2: Distribution of the pattern of severity of Coronary artery disease (CAD)



In the present study as depicted in **Figure 3**, 51.1% patients had significant LAD involvement, 48.9% patients had significant LCX involvement, 46.7% patients had significant RCA involvement and 13.0% patients had significant LMCA involvement in coronary angiogram.

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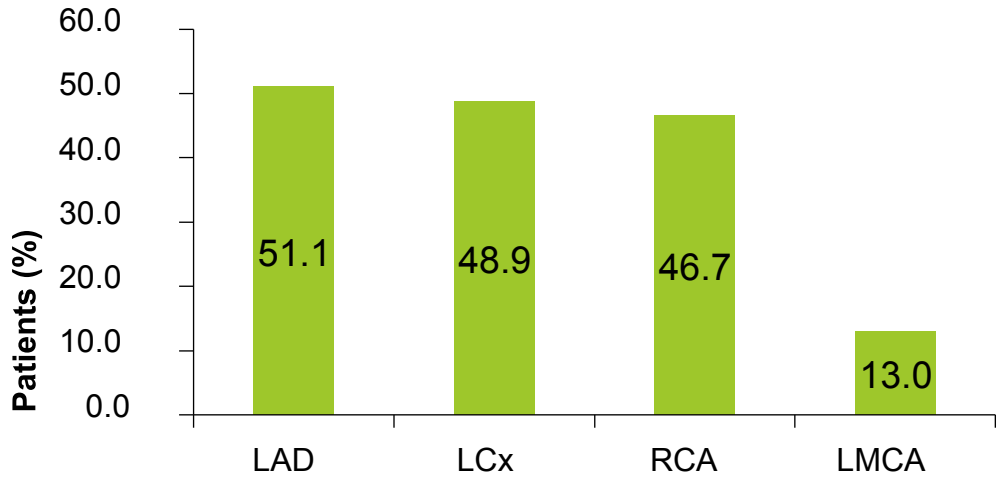
Figure 3: Distribution of the pattern of vessel involved in Coronary artery disease (CAD)

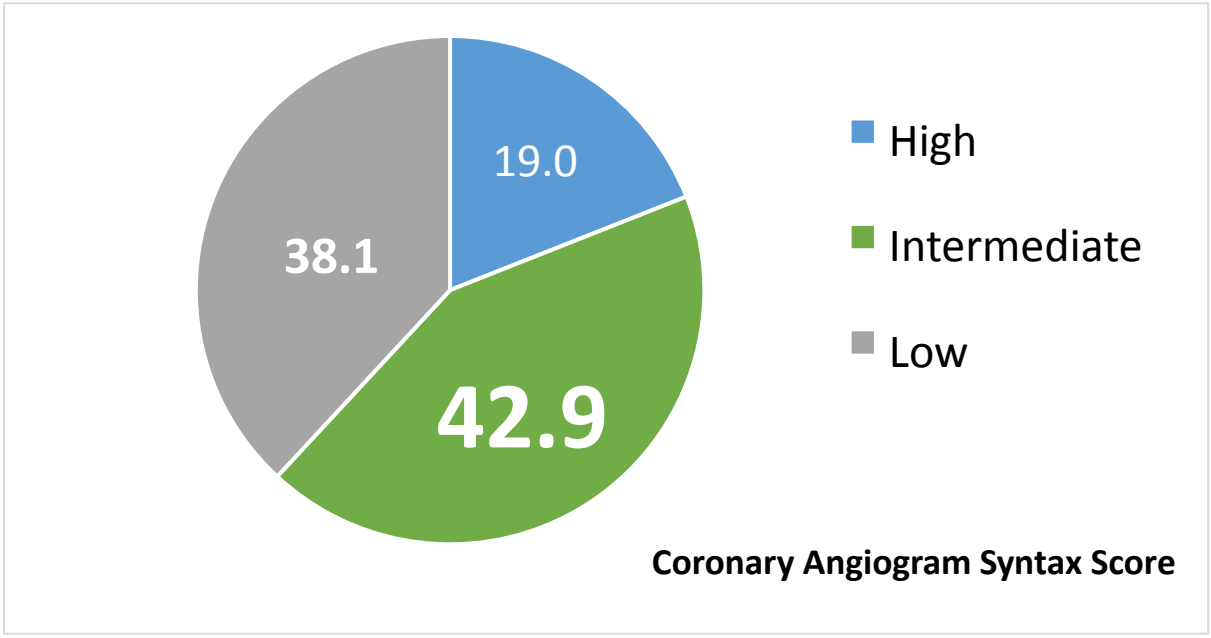


LAD: Left anterior descending, LCx: Left circumflex, RCA: Right coronary artery, LMCA: Left main coronary artery

It was observed that out of (n = 63) patients who had significant coronary artery disease 33(52.38%) had a multi vessel disease without LMCA involvement,12 (19.04%) patients had multi vessel disease with left main coronary artery involvement, 8 (12.69%) patients had isolated LAD involvement, 5 (7.93%) patients had isolated LCX and (7.93%)] patients had isolated RCA involvement.

Present study also showed that, as per Coronary Angiogram Syntax Score, majority of patients had intermediate syntax score (42.9%), 19.0% patients had high syntax score and 38.1% patients had low syntax score. [**Figure 4]**

Figure 4: Distribution of Coronary Angiogram Syntax Score among study patients



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This study also showed that BMI was slightly elevated in high syntax score group compared to intermediate and low syntax score group and normal and minor CAD but this was not statistically significant. ($p>0.05$)

From this study, it was observed that echocardiography ejection fraction was normal in all but slightly less in high syntax score group compared to Intermediate syntax score group, Low syntax score group and Normal and minor CAD group but this was also not statistically significant.

In the present study the group with normal coronary angiography and the group with minor CAD had the mean echocardiographic GLS [-20.0689 ± .7960] and in significant coronary artery disease group had low the mean echocardiographic GLS [-14.6809 ± 1.6555]. Difference between mean echocardiographic GLS of this two group is statistically significant ($p < 0.0001$)

Patient who have high syntax score having mean GLS [-12.8833±0.9229] and GLS value of [14.0200±1.0084] and [-16.2167±1.0184] for intermediate and low syntax score group respectively all were low when we compared with minor CAD or normal CAG group mean GLS was -20.0690±0.7960 and this is statistically significant ($p<0.0001$)

It was also found that GLS was significantly low in multi vessel with LMCA group and also in multi vessel without LMCA involvement, LAD, LCX and RCA involvement and when we compared with minor CAD or normal CAG group GLS value this is statistically significant ($p<0.0001$). Table 2

Table 2: Distribution of mean global longitudinal strain in the different coronary vessels

Vessel (n)	Mean (SD)	P value
MV without LMCA (n=33)	-14.4 (1.2)	<0.0001
MV with LMCA (n=12)	-12.9 (1.2)	
LAD (n=8)	-15.6 (0.5)	
LCx (n=5)	-16.8 (0.7)	
RCA (n=5)	-17.0 (1.2)	

MV: Multi vessel, LAD: Left anterior descending, LCx: Left circumflex, RCA: Right coronary artery, LMCA: Left main coronary artery

Discussion:

The quest for diagnosis of CAD before the development of debilitating endpoints like myocardial infarction is the subject of interest in nowadays world of early diagnosis and management. [10] I Echocardiography is an important cardiac imaging tool in patients with suspected cardiac disease. However, conventional echocardiography has a limited value in the diagnosis and risk stratification of suspected CAD patients as most of these patients with no

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previous myocardial infarction or myocardial stunning have no wall motion abnormalities at rest. [2] In the current study LAD was the most affected artery (51.1%) which was close to the findings of the study of Madhavan S et al having 57% involvement. [1]

In the current study the global longitudinal strain was significantly lower in patients with significant CAD than those with non-significant CAD ($p<0.001$). Various studies have found different cut-off values for GLS for predicting the presence of significant CAD. Shimoni et al (11) found that the cut-off value for GLS predicted significant CAD at -19.7% (sensitivity 81% and specificity 67%). Montgomery et al (12) showed that GLS -17.8% might predict significant obstruction of CAD with 66% sensitivity and 76% specificity. Smedsrud et al (13) found a low sensitivity (51%) but optimum specificity (81%) of GLS at a cut-off value of -17.4% for prediction of significant CAD.

In this study BMI was found to be slightly elevated in high syntax score group compared to intermediate and low syntax score group and normal and minor CAD but this was not statistically significant. In other studies of Srinivasan et al. [14] where they observed that patients with 5–10 years of diabetes mellitus have a significant increase in the mean SYNTAX score ($p = 0.019$) when compared to those with less diabetes duration. In the study of El Kersh et al. [15] they found positive correlation was present between SYNTAX score and smoking ($p = 0.001$) although such findings were not evident from the present study.

There were certain limitations in this study. Although the patients were enrolled consecutively, selection bias may have occurred as selecting effort angina patients only. Relatively low number of patients were studied in a single-center study. Strain and strain rate are influenced by left ventricular mass, various hemodynamic variables, and software platform type, in addition to myocardial ischemia. All these factors could be potential confounders and may influence study outcome.

Conclusion:

Global Longitudinal Strain by 2-D speckle tracking echocardiography well correlate with significant coronary artery disease and can be used as a noninvasive screening test in predicting significant coronary artery stenosis and can complement TMT in risk stratification and in selecting patients for coronary angiogram. GLS by 2DSTE can be used as a noninvasive screening test in predicting significant coronary artery stenosis and can complement TMT in risk stratification and in selecting patients for CAG.

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