

# Correlation between Myocardial Strain by 2-D Speckle-Tracking Echocardiography and Angiographic findings by Coronary Angiogram in Stable Angina

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## ABSTRACT

**Background and aims:** Identification of coronary artery disease by non-invasive means is a subject of interest for all. Myocardial strain has shown some promising results. This study intends to see if change in strain value correlates with the angiographic findings in patients with stable angina. It is also assessing whether myocardial strain can predict the presence of coronary artery disease (CAD) in stable angina patients.

**Methods:** This cross-sectional study was carried out on 84 stable angina patients with no previous cardiac history and normal LV function undergoing coronary angiogram for guideline-based indication. After careful history, clinical examination and investigations, including conventional echocardiography, selected participants underwent 2-D speckle tracking echocardiography for measurement of myocardial strain by automated functional imaging. All participants underwent coronary angiogram and stenosis >70% was considered significant. Gensini score was calculated. The myocardial strain value and Gensini score were correlated.

**Results:** Global longitudinal strain (GLS) was significantly lower in patients with significant CAD than those with non-significant CAD ( $-16.1 \pm 2.6\%$  vs  $-19.4 \pm 2.2\%$ ;  $p < 0.001$ ). The optimal cut-off value of GLS, which discriminated between patients with and without significant coronary artery disease, was  $-18.05\%$  (sensitivity=81.8% and specificity=85%). Also, GLS declined incrementally with the increasing

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severity of CAD defined by increasing number of stenotic vessels. There was an inverse correlation between GLS and severity of CAD (expressed in Gensini score) in this study ( $r = 0.669$ ,  $p < 0.001$ ), meaning that GLS decreased with increasing severity of CAD. GLS remained an independent predictor for the presence of significant CAD after multivariate adjustment for other significant baseline characteristics and echocardiographic parameters.

**Conclusion:** The myocardial strain by 2DSE correlates with the angiographic severity by coronary angiogram in patients with stable angina. It is an independent predictor of significant coronary artery disease, which it can detect with good sensitivity and specificity.

**Keywords:** 2-D speckle tracking echocardiography, myocardial strain, global longitudinal strain, coronary artery disease, stable angina, Gensini score.

## INTRODUCTION

Chronic stable angina from coronary artery atherosclerosis remains a chief public health concern in most industrialized nations and has become a leading cause of death and disability in developing countries (1). The ability to predict the presence of significant coronary stenosis can help to decrease morbidity and mortality due to ischemic heart disease.

Conventional echocardiography does not provide much information about the presence of coronary artery disease (CAD) in suspected stable angina patients. Exercise testing has been recommended as a first-line diagnostic test in patients with suspected stable angina (2), although its limited sensitivity and specificity have been criticized (3). Dobutamine stress echocardiography (DSE) is widely used for assessing the presence, location, and extent of CAD, but it remains limited by its subjective interpretation and dependence on both image quality and experience (4). Invasive coronary angiography, though the gold standard for diagnosis of CAD, consideration of this approach should be weighed against the risks of the invasive procedure (5).

The need for a more quantitative and less invasive method for evaluation of CAD in stable angina patients has provoked the introduction of several imaging methods, of which strain is showing great promises. Longitudinally orientated myocardial fibers are located subendocardially, 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) (6, 7).

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 Bangladesh because they are expensive and can be accessed only in urban advanced medical centers. In this scenario, an echocardiography based imaging modality for diagnosis of CAD would be of significant value. Similar studies using longitudinal strain have been previously conducted in other parts of the world (11), but so far, none was performed in our geographical area.

The aim of this study is to evaluate the correlation between myocardial strain value by 2-D speckle-tracking echocardiography and angiographic findings by coronary angiogram in patient with stable angina. □

## METHODS

### Study population

From November 2016 to December 2017, 84 patients with stable angina coming for evaluation to UCC, BSMMU, were included. Stable angina was defined as chest pain or discomfort (angina) suspected to be caused by myocardial ischemia. Anginal symptoms were considered stable if they were present for several weeks without deterioration and were typically induced by activity or stress. All patients, including the young population, were considered for coronary angiogram based upon guideline-based indication (5) (positive exercise tolerance test). Patients with known ischemic heart disease, except stable angina, congestive heart failure, heart valve disease, congenital heart disease, left ventricular ejection fraction (LVEF)  $< 50\%$ , intraventricular conduction disturbances, pathological Q waves

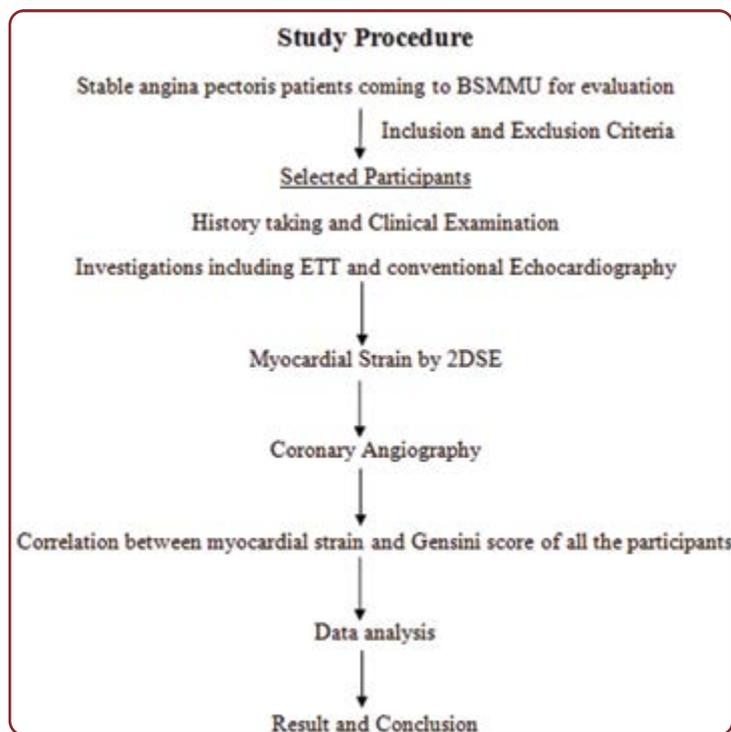


FIGURE 1. Study procedure flow chart

and arrhythmias, were excluded. Detailed history-taking, clinical examination and investigations including ETT, conventional echocardiography and 2DSE were done. All participants underwent CAG (Figure 1).

### Echocardiography

Echocardiography (conventional and 2DSE) was done using Vivid E9 (GE Healthcare) with a 3.5 Mhz transducer. Conventional echocardiography was done to assess left ventricular wall thickness, internal dimensions, wall motion abnormality, systolic and diastolic function by 2D, M-mode and Color Doppler echocardiography.

Participants 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. In case of poor tracking, ROI was readjusted. The results of all three planes were combined in a single bull's eye summary (agreeing with the standard 17-segment model), which presented the analysis of each segment along with a global peak systolic strain value for the LV (Figure 3).

### Coronary angiogram

All participants underwent coronary angiogram. Coronary angiography (CAG) was performed by percutaneous femoral or radial approach and was obtained for each coronary vessel in  $\geq$ two projections. Stenosis  $\geq$ 70% reduction of the arterial lumen area was considered significant. Participants' Gensini score was calculated for correlation with the myocardial strain value. Coronary angiography has been visually analyzed by an experienced operator who was blinded to the results of the echocardiographic examinations.

### Statistical analysis

Analysis was conducted with SPSS 16 (Statistical Package for Social Sciences version 16) for Windows software. Continuous parameters were expressed as mean  $\pm$  SD (SD=statistical deviation) and categorical parameters as percentage. Comparison between groups (continuous parameters) was done by unpaired t test. Correlation analysis was done by Pearson's correlation coefficient. ANOVA (analysis of variance) was used to test whether GLS varied with increasing severity of CAD defined by increasing number of stenotic coronary vessels. A p-value of  $<0.05$  was considered as significant. Intra-observer and inter-observer reproducibility was assessed in ten randomly selected patients using the intra-class correlation coefficient.

### Ethics

Informed consent was taken from all patients and the study was approved by the Ethical Review Committee of BSMMU.  $\square$

### RESULTS

Eighty four patients were enrolled in the study based on established inclusion and exclusion criteria.

Subjects' age ranged from 28 to 66 years, with mean age of  $50 \pm 9.5$  years (Table 1). Most patients were in their fourth (38.1%) and fifth (31%) decade of life. Three patients (3.6%) were under the age of 30.

Fifty one (60.7%) patients were males, with a male to female ratio of about 3:2. The baseline characteristics and frequency of various risk factors are shown in Table 1.

TABLE 1. Baseline characteristics and risk factors

		Patients (N=84)
Mean age (mean±SD)		50.1 ± 9.5 years
	Range	28–66 years
Sex	Male	51 (60.7%)
	Female	33 (39.3%)
Family history of CAD		26 (31%)
Hypertension		47 (56%)
Diabetes mellitus		28 (33.3%)
Dyslipidemia		16 (19%)
Smoker		33 (39.3%)
Overweight & obese		38 (45.2%)

Continuous data are expressed as mean±SD and categorical parameters as percentage.

TABLE 2. CAG findings

	Patients (N=84)
Non-significant CAD	40 (47.6%)
SVD	14 (16.6%)
DVD	13 (15.4%)
TVD	17 (20.2%)

CAG=coronary angiogram;  
CAD=coronary artery disease;  
SVD=single vessel disease;  
DVD=double vessel disease and  
TVD=triple vessel disease.

Coronary angiography revealed that non-significant CAD was the most common finding (47.6%), followed by triple vessel disease-TVD (20.2%), as shown in Table 2.

Conventional echocardiography showed a mean LVEF of 66.7±4.2% and a mean LVIDD of 47.1±4.2 mm in the study population. GLS calculated by 2DSE revealed that mean GLS was significantly lower in patients with significant CAD than those with non-significant CAD (-16.1±2.6% vs -19.4±2.2%; p < 0.001). The

TABLE 3. Association between GLS and severity of CAD

Severity of CAD	GLS (%)	P-value
No or non-significant CAD (n =44)	-19.4 ± 2.2	< 0.001
SVD (n = 14)	-16.7 ± 2.0	
DVD (n = 13)	-15.8 ± 2.6	
TVD (n = 17)	-15.8 ± 3.0	

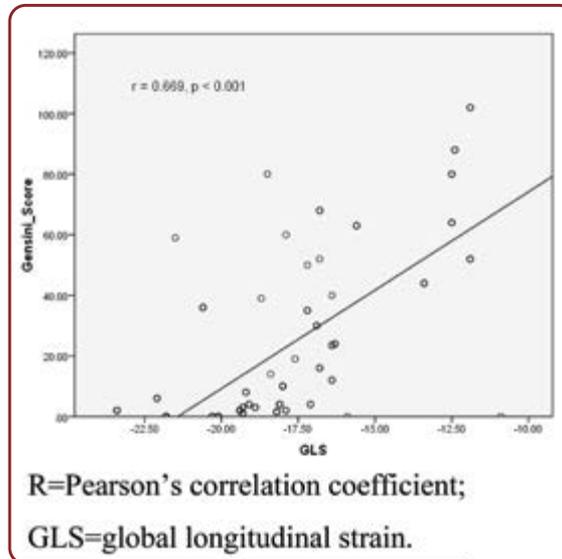
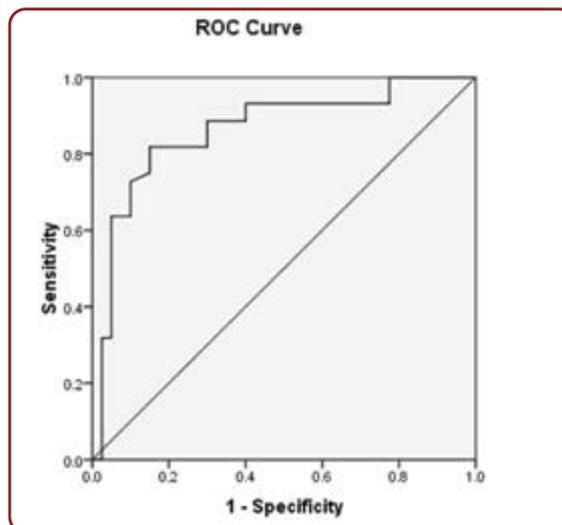


FIGURE 2. Scatter diagram showing correlation between GLS and Gensini score



Parameter	Cut-off value	AUC	95% CI	P-value
GLS score	-18.05 %	0.86	0.78–0.95	<0.001

FIGURE 3. Receiver operating characteristic (ROC) curve analysis for determination of cut-off value to differentiate significant from non-significant coronary artery disease

GLS values according to the involved number of vessels are summarised in Table 3.

There was an inverse relationship between GLS and Gensini score of the patients in the study population. The Pearson's correlation coefficient was 0.669 (p < 0.001) (Figure 2).

The optimal cut-off value of the GLS score, which discriminated between patients with or without significant coronary artery disease, was

	Univariate analysis		Multivariate analysis			
			Baseline characteristics (sex and angina type) + one of each echocardiographic parameter listed below		Baseline characteristics (sex and angina type) + all echocardiographic parameters listed below	
	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value
<b>E</b>	.038 (.004-.380)	0.005 <sup>S</sup>	.016 (.001-.258)	0.004 <sup>S</sup>	.038 (.001-1.738)	0.094 <sup>NS</sup>
<b>e'</b>	0.66 (0.50-0.88)	0.005 <sup>S</sup>	0.55 (0.37-0.82)	0.003 <sup>S</sup>	0.71 (0.40-1.26)	0.245 <sup>NS</sup>
<b>GLS</b>	1.89 (1.39-2.56)	<0.001 <sup>S</sup>	1.77 (1.29-2.43)	<0.001 <sup>S</sup>	1.51 (1.06-2.17)	0.023 <sup>S</sup>

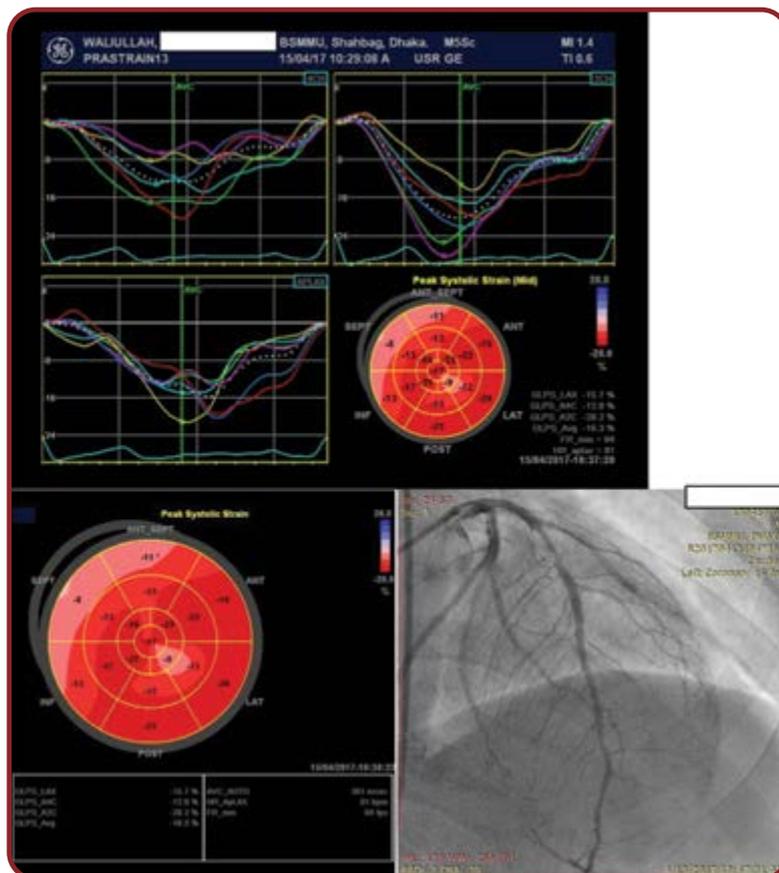
**TABLE 4.** Independent echocardiographic predictors of coronary artery disease

E=peak transmitral early diastolic inflow velocity; e'=average peak early diastolic longitudinal mitral annular velocity obtained from septal and lateral myocardial segment

-18.05% (sensitivity 81.8% and specificity 85%; p<0.001) (Figure 3).

After multivariate adjustment for baseline characteristics (sex and angina type) and conventional echocardiographic parameters (E and e'), GLS was the only measure that remained an independent predictor of coronary artery disease, with an odds ratio of 1.51 (95% CI 1.06–2.17; p=0,023) (Table 4).

Intra- and inter-observer variability was assessed for ten randomly selected patients by intra-class correlation coefficient (R). R value was 0.983 (95% CI 0.935–0.996; p<0.001) for intra-observer variability and 0.980 (95% CI 0.918–0.995; p<0.001) for inter-observer variability, which showed excellent reproducibility of GLS measurements for both identical and different operators. □



**FIGURE 4.** Global longitudinal strain of a patient with mid LAD lesion. GLS was reduced (-16.3%) and Gensini score was 24

## 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. Considering the invasive approaches over-enthusiastic for patients with normal systolic function, the non-invasive approaches with low cost and good sensitivity and specificity are important researchers' targets. This is where the myocardial strain stands out. In the present study, the myocardial strain by 2-D speckle tracking echocardiography has been evaluated for its correlation with the angiographic findings in stable angina patients.

Global longitudinal strain was significantly lower in patients with significant CAD than those with non-significant CAD ( $-16.1 \pm 2.6\%$  vs  $-19.4 \pm 2.2\%$ ;  $p < 0.001$ ), which is in agreement with findings of previous studies on CAD patients. In the study of Ng *et al*, conducted on 177 patients with stable CAD, the mean value of resting GLS was  $-16.3 \pm 2.4\%$  in subjects with significant CAD and  $-19.1 \pm 2.9\%$  in those with non-significant CAD ( $p < 0.001$ ) (8). Shimoni *et al* (6) studied 97 patients with suspected CAD and found that GLS was significantly lower among those with significant CAD than those with non-significant CAD ( $-17.3 \pm 2.4\%$  vs  $-20.8 \pm 2.3\%$ ,  $p < 0.001$ ). Montgomery *et al* (9) found that GLS was significantly lower among patients with significant CAD than those with non-significant CAD, with mean values of GLS being  $-16.8 \pm 3.2\%$  and  $-19.1 \pm 3.4\%$ ,  $p < 0.001$ . In a study on 86 patients with stable chest pain, Smedsrud *et al* (10) found a GLS value of  $-17.9 \pm 3.5\%$  in subjects with significant CAD and  $-20.1 \pm 2.9\%$  in those with non-significant CAD. In the study conducted by Biering-Sørensen *et al* (11) on 296 stable angina patients, there was significantly lower GLS in those with CAD compared to subjects without CAD ( $-17.1 \pm 2.5\%$  vs  $-18.8 \pm 2.6\%$ ;  $p < 0.001$ ). Norum *et al* (12) performed a meta-analysis of six studies (781 patients with suspected CAD) and found that GLS was significantly lower among those with significant CAD, with mean values of GLS ( $-17.2 \pm 2.6\%$  vs  $-19.2 \pm 2.8\%$ ,  $p < 0.001$ ). However, these studies included patients who presented to the emergency department with various types of CAD, ranging from acute coronary syndrome to

non-specific chest pain; so, our population is more homogenous, as it included only patients with stable angina.

Also, GLS declined incrementally with the increasing severity of CAD defined by increasing number of stenotic vessels (GLS for non-significant CAD:  $-19.4 \pm 2.2\%$ ; SVD:  $-16.7 \pm 2.0\%$ ; DVD:  $-15.8 \pm 2.6\%$ ; TVD:  $-15.8 \pm 3.0\%$ ), which was statistically significant ( $p < 0.001$ ). So, decreasing GLS marked the chances of multivessel disease and/or higher degree of stenosis. Biering-Sørensen *et al* (11) agreed that GLS declined incrementally with the increasing number of stenotic vessels (GLS for no CAD  $-18.8 \pm 2.6\%$  vs SVD  $-18.0 \pm 2.4\%$  vs DVD  $-16.7 \pm 2.7\%$  vs TVD  $-16.3 \pm 2.3\%$ ,  $p < 0.001$ ). Radwan and Hussein (13) and Moustafa *et al* (14) have also reported similar decrease in GLS values with increasing number of stenotic vessels. In the study of Biering-Sørensen *et al* (11), regional longitudinal strain (RLS) has been also calculated, which helped to provide information about how significant the stenosis was in the vascular territory, *i.e.*, LAD, RCA or LCX. However, RLS was not done in our study, so we could not quantify the functional significance of different vessel stenosis. Neither radial and circumferential strain was performed in the present study. Subendocardial region, the most susceptible area to ischemia, has longitudinally orientated myocardial fibers. So, the measurements of longitudinal motion and deformation may be the most sensitive markers of CAD (6, 7).

In this study, there was an inverse correlation between GLS and severity of CAD (expressed in Gensini score) ( $r = 0.669$ ,  $p < 0.001$ ). This finding is in agreement with the report of Al-Zaky *et al* (15), who conducted a study on 141 patients with acute coronary syndrome ( $r = 0.60$ ,  $p < 0.001$ ). Other angiographic scoring systems have also been used to study the correlation between GLS and severity of CAD. Vrettos *et al* (16) correlated GLS and Syntax score in 71 stable angina patients and found a significant inverse correlation ( $r = 0.3869$ ,  $p < 0.001$ ). Similarly, Moustafa *et al* (14) performed a study on 200 stable angina patients and found an inverse correlation between GLS and Syntax score which was significant for intermediate and high score ( $p < 0.001$ ) but insignificant for low score ( $p = 0.05$ ). However, Gensini score has been shown to strongly correlate with the atheroscle-

rotic plaque burden assessed by IVUS (17), so the use of Gensini score in this study for quantification of CAD severity is justified.

The optimal cut-off value of GLS score, which discriminated between patients with and without significant coronary artery disease, was -18.05% (81.8% sensitivity and 85% specificity, AUC 0.86, 95% CI 0.78–0.95,  $p < 0.001$ ); also, it was an independent predictor for the presence of significant CAD. Various studies have found different cut-off values for GLS for predicting the presence of significant CAD. Shimoni *et al* (6) found that the cut-off value for GLS predicted significant CAD at -19.7% (sensitivity 81% and specificity 67%). Montgomery *et al* (9) showed that GLS -17.8% might predict significant obstruction of CAD with 66% sensitivity and 76% specificity. Smedsrud *et al* (10) found a low sensitivity (51%) but optimum specificity (81%) of GLS at a cut-off value of -17.4% for prediction of significant CAD. Biering-Sørensen *et al* (11) found the optimal cut-off value for GLS to be -18.4%, with 74% sensitivity and 58% specificity. In the Hunt Study (18), the GLS value of normal individuals was -17.4% ( $\pm 2.3$ ) in women and -15.9% ( $\pm 2.3$ ) in men. In previous studies, the variation in optimal cut-off value of GLS could be explained by the clinical characteristics of selected patients, effect of diastolic function and their hemodynamic parameters (i.e., blood pressure) during image acquisition (19), by using different equipment, different design, vendor dependent 2DSE software and operator skills (9, 10, 20). 2DSE software is the most important factor responsible for the variation in GLS measurement, so EACVI/ASE/Industry Task Force has advised for standardization of deformation imaging to reduce intervendor variability of strain measurement (21). The determination of a fixed diagnostic GLS cut-off value to diagnose obstructive CAD, independent of the ultrasound equipment or software used for image acquisition, would be required to increase the clinical usefulness of strain imaging.

Though both 2DSE (GLS) and conventional echocardiographic (E and e') parameters are affected in patients with CAD, only GLS remained an independent predictor of CAD (Table 4). It supports GLS as a diagnostic parameter in prediction of CAD.

The reproducibility of GLS for same and different operators was found to be excellent (intra-

class correlation coefficient for intra-observer variability 0.983 and inter-observer variability 0.980,  $p < 0.001$ ). So, provided good image quality, GLS can be consistently determined by the same operator or different operators, which is very important for it to be established as a diagnostic tool. This is supported by Biering-Sørensen *et al* (11), who proved a good intra-observer and inter-observer agreement for GLS in 25 randomly selected patients.

### Limitations

This was a single-centered study with a relatively small sample size, which makes it difficult to generalize its results to all patients with stable angina. So, further studies on larger populations are needed.

A potential selection bias can be noted because only stable angina patients going for coronary angiogram were included; a significant number of patients were left out. This study followed a cross-sectional design, so subjects were not followed up. The clinical and prognostic value of GLS could not be determined.

The segmental strain was not assessed, so the significance of different vessel stenosis could not be evaluated. We did not get left main disease patient in our study population, so the effect of left main disease on strain value could not be assessed.

Radial and circumferential strains were not assessed, so these strain value changes in stable angina could not be evaluated. However, longitudinally oriented fibers located sub endocardially are the most susceptible to ischemia, which makes GLS the most sensitive marker of CAD (6, 20, 22).

On comparison of the diastolic parameters between patients with and without significant CAD, E and e' were found to be significantly lower. However, a proper diastolic profiling of the patients included was not done. So, its confounding effect on the GLS value could not be evaluated. Given that GLS is lower in patients with diastolic dysfunction (23), further research is required to differentiate whether lowering of GLS is due to diastolic dysfunction or CAD.

The study was conducted in November 2016 to December 2017 when the term "chronic coronary syndrome" (CCS) was not well established and hence, the terminology is not used in the manuscript. □

CONCLUSION

The myocardial strain by 2-D speckle tracking echocardiography correlates with the angiographic severity by coronary angiogram in patients with stable angina. Global longitudinal strain is an independent predictor of significant coronary artery disease, which it can with good sensitivity and specificity. Thus, this study has

helped to open the gateway to further research in myocardial strain, which promises to be an efficient, non-invasive diagnostic tool in stable angina patients at an affordable cost. □

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