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ORIGINAL ARTICLE

Global Longitudinal Strain Value and its Association with Coronary Artery Disease Severity

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Abstract

Background: Coronary Artery Disease (CAD) is one of the commonest non communicable cause of mortality and morbidity in the world today. Global Longitudinal Strain (GLS) Assessment can be an important tool inassessing severity of CAD. **Aim:** To assess role of GLS in predicting severity of CAD. **Material and Methods:** 160 patients, aged 18 to 75, suspected of CAD, underwent transthoracic echocardiograms before coronary angiography. Simpson's method was used to measure LVEF. Depth-adjusted 2D images of the LV were taken in various views for offline measurement of 2D speckle-tracking myocardial strain. Global peak systolic strain was calculated by averaging six regional values from different views to measure longitudinal strain. **Results:** In this study, patients with significant CAD exhibited significantly lower GLS compared to those with non-significant CAD (-15.89 ± 2.84% vs -18.36 ±2.60%, p = 0.0001). As CAD severity increased, GLS values decreased significantly (-17.14 ± 2.57% vs -16.27±2.42% vs -14.74±2.78%). A decremental trend in GLS with increasing CAD severity was observed, indicating a higher risk of multi-vessel disease with lower GLS values (p<0.0001). **Conclusion:** Reduced GLS indicates early LV systolic dysfunction in significant CAD patients. Thus, GLS measurement serves as an important diagnostic tool for predicting severe CAD.

Key Words

Global Longitudinal Strain, Coronary Artery Disease, LV systolic dysfunction

Introduction

Coronary artery disease (CAD) is a leading global cause of mortality among adults, often diagnosed invasively via coronary angiography, revealing no significant stenosis in a notable subset of patients with chest pain[1,2]. Left ventricular function, assessed by LVEF on echocardiography, remains normal in early CAD stages[3]. Global longitudinal strain (GLS), assessed non-invasively through 2D speckle tracking echocardiography, serves as a sensitive indicator of to detect early subtle derangement of cardiac function in patients with significant coronary artery disease[4,5].

Subendocardium is the furthest layer from epicardial coronary flow[6]. It undergoes extreme fluctuations in pressure and compression in both systole and diastole, and also appears prone to early structural, microvascular and architectural change, making it the earliest affected myocardial layer[7]. In ischemic heart disease, subendocardial fibers suffer ischemia early, impacting

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longitudinal contraction and correlates with CAD severity [8,9].

Aim: To assess role of Global Longitudinal Strain in predicting severity of Coronary Artery Disease.

Objectives

- To compare Global Longitudinal Strain by 2D - speckled tracking imaging with coronary angiography for assessing coronary artery disease severity.
- To evaluate diagnostic accuracy of Global Longitudinal Strain in predicting severity of underlying coronary artery disease.

Material and Methods

Study design: Cross sectional, observational study

Study Population: 160 patients between the age of 18 to 75 years with suspected coronary artery disease referred for coronary angiography at Department of Cardiology, P.D. Hinduja Hospital and Research Centre, Mahim, Mumbai, India.

Inclusion criteria

1. Patients $\geq$ 18 yrs of age and $\leq$ 75 years of age
2. LVEF > 55%

Exclusion criteria

1. Prior coronary artery bypass graft surgery and coronary PCI
2. Prior history of myocardial infarction
3. Prior history of hospitalization for heart failure
4. History of pre-existent LV dysfunction
5. Acute Coronary Syndrome
6. Chronic Kidney Disease

The study was approved by Institutional Ethics Committee (IRB/1294/AL/19/39). Period of study was of 2 years (2020-2021), and written informed consent was obtained from all patients enrolled in the study. A detailed cardiac history was obtained at recruitment including clinical risk factors for heart disease along with demographic data. All echocardiograms were performed at a single site by either of the two experienced sonographers blinded to patients Angiography results, using a Vivid E9 digital ultrasound system (GE Medical Systems, Mumbai) with a 3.5 MHz variable frequency transducer. A comprehensive transthoracic echocardiogram was done on patients in the left lateral position. Parasternal, apical, and subcostal views images were taken. LVEF of 55% and above were considered normal.

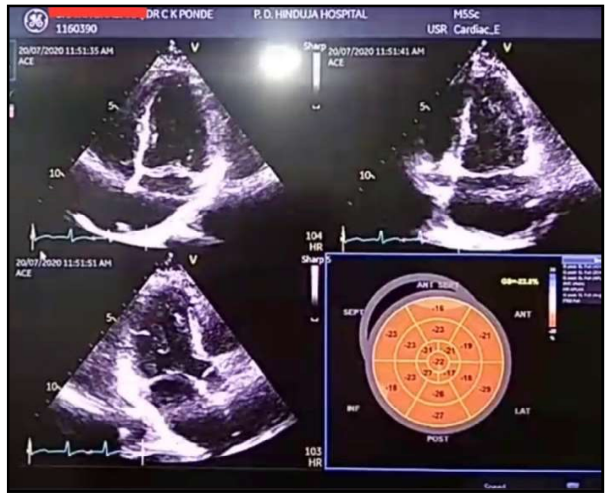

Fig 1: Calculation of Global Longitudinal Strain (Bulls eye)

Depthadjusted 2D images of the LV in the apical four-chamber, two-chamber, and long- axis views were acquired and stored for off-line measurement of 2D speckle-tracking myocardial strain. Frame rates were optimized between 50 and 70 fps during acquisition. Systole was defined as the interval from aortic valve opening to closure, measured using pulsed-wave Doppler sampling in LV outflow tract. Strain measurements from three consecutive cardiac cycles were averaged to obtain peak systolic regional strain. Global peak systolic strain was calculated by averaging six regional values from apical four-chamber, two-chamber, and APLAX views for longitudinal strain. Normal range was -17 to -22%. (*Fig-1*)

All patients with suspected CAD with Normal LVEF underwent coronary angiography by all aseptic precautions via percutaneous radial or femoral approach. Patients were divided in to two groups. Group 1 consisted of patients with significant coronary artery disease (CAD) which was defined as the stenosis more than 70% of the lumen diameter, depending on number of vessels involved it was further divided into Single vessel, Double Vessel, LM/ Triple vessel CAD. The Group 2, Non-Significant CAD group which was defined as no stenosis or the stenosis less than 70% of the lumen diameter.

Statistical Analysis

Results for Quantitative Variables were expressed as mean (±SD), median [range], IQR. Results for Qualitative Variables were expressed as frequency and percentages. Shapiro-Wilks Test was used to determine whether data sets differed from a normal distribution. For continuous variables, between groups means was compared using unpaired T test or Mann – Whitney U test based on normality testing.For categorized variables, Pearson's chi square test or Fisher's exact test was used. Results were considered significant at $P < 0.05$. Software "R software version 3.5.1" was used.

Results

In this study mean age of patients with significant CAD was 59.39 ± 8.83 years and mean age of patients without significant CAD was 57.13 ± 10.26 years.

Out of the 160 patients included in the present study, 71 (44.4%) patients had non-significant CAD and 89 (55.6%) had significant CAD. Severity of coronary artery disease was taken as ≥ 70% reduction in arterial luminal diameter in vessel size of ≥ 2.5 mm in diameter (epicardial coronary artery). Out of 89 significant CAD patients, 29 (32.6%) patients had single-vessel disease, 22 (24.7%) patients had double vessel diseases and 38 (42.7%) patients had triple vessel disease. Out of the 89 patients with significant CAD 57(64.04%) were male and 32 (35.96%) were female and out of 71 patients with non-significant CAD 46 (64.79%) were male and 25 (35.21%) were female.

Global Longitudinal Strain

GLS was significantly lower among patients with significant CAD than those with non-significant CAD (Table 1)

Correlation between GLS and CAD Severity

GLS declined incrementally with increasing severity of CAD as defined by increasing number of stenotic coronary vessels. The GLS of patients with SVD was

Table 1: Global Longitudinal Strain in Significant vs Non-significant CAD Patients

CAG	GLS(%)			
	Mean ± SD	Median (IQR)	Range	P value Mann Whitney
Significant	-15.89±2.84	-16(-18 to -14)	-21 to -10	P < 0.0001
Non-significant	-18.36±2.60	-19(-20 to -17)	-22 to -12	

Table 2: Correlation between GLS and CAD Severity

CAG	GLS (%)				
	N	Mean ± SD	Median (IQR)	Range	P value One-way ANOVA
SVD	29	-17.14 ±2.57	-16(-20 to -15)	-21 to -13	P < 0.0001
DVD	22	-16.27±2.42	-16(-18 to -15)	-21 to -13	
TVD	38	-14.74±2.78	-15(-16 to -13)	-21 to -10	
Non-significant	71	-18.36±2.60	-19(-20 to -17)	-22 to -12	

Table 3: Diagnostic Performance of GLS for Detection of Significant CAD

	Associated criterion	Sensitivity	Specificity	AUC	P value
GLS	< -17	69.66	80.28	0.742	<0.0001

greater than the GLS of patients with DVD which was in turn greater than those with TVD (p value being significant) (Table 2)

Diagnostic Performance of GLS in Predicting Significant CAD

The optimal cut off value of GLS was less than -17% to diagnose significant coronary artery disease [AUC 0.74, $p < 0.0001$]. The sensitivity and specificity of GLS for predicting significant CAD were 69.66%, 80.28% respectively. (Table 3)

Discussion

Roughly one-third of patients referred for coronary angiography experience chest pain without regional wall motion abnormalities on echocardiography and are considered at intermediate risk for CAD without significant coronary artery stenosis. The inner layer of LV, the sub-endocardium, is highly vulnerable to hypoperfusion and ischemia, potentially leading to decreased LV longitudinal mechanics in significant CAD cases. GLS, a non-invasive test, can detect subtle changes in LV function and is underused in CAD evaluation despite its effectiveness in identifying early systolic function decline in significant CAD cases. Furthermore, GLS serves as an independent predictor of significant coronary artery disease, assisting in the identification of high-risk patients[10].

The principal finding in this study suggested that GLS can detect early subtle changes in LV function in significant coronary artery disease before decrease in LVEF and thus, GLS is accurate diagnostic tool to predict underlying severe coronary artery disease[11,12].

In the present study, a statistically significant lower GLS in patients with significant CAD was seen as compared to those with non-significant CAD and as the severity of coronary artery increased there was significant decrease in GLS value. We found that GLS declined incrementally with increasing severity of CAD defined by increasing number of stenotic coronary vessels. So, the risk of multivessel disease increases with decreasing GLS. Present study found that cut-off GLS score of less than -17% had a sensitivity of 69.66% and specificity of 80.28% in predicting significant CAD (stenosis >70%) [AUC 0.74, $p < 0.0001$].

Radwan *et al*.[13] studied 80 patients with suspected stable angina pectoris and no regional wall motion abnormalities with normal Left Ventricular Ejection Fraction. There was a significant decrease in GLS in patients with significant CAD compared to patients without CAD (“11.86 ± 2.89% vs. “18.65 ± 0.79%, $P < 0.0001$). The sensitivity, specificity, and accuracy of GLS for detecting significant CAD were 93.1%, 81.8%, and 90%, respectively. There was incremental significant decrease in GLS with increasing number of coronary vessels involved. Based on these observations, the study concluded that assessment of GLS using 2D Speckle tracking echocardiography is sensitive and accurate tool in the prediction of severe CAD. These findings were in corroboration with the present study.

Gopinath *et al*[14] in their study, using global strain as a measure to predict obstructive coronary artery disease showed that patients with obstructive CAD had a lower mean peak global strain value (-18.37 ± 4.13) as compared to patients who did not have obstructive CAD (-21.18 ± 3.81); p value <0.01, they also showed that GLS progressively decreased as severity of CAD increases which was similar to our study.

Moustafa *et al*.[15] studied 200 patients with stable angina and normal conventional echocardiography. There was a statistically significant difference in the GLS between normal coronaries and different degrees of CAD

(–20.11 ± 0.8 for normal, –18.34 ± 2.52 for single vessel, –16.14 ± 2.85 for two vessels, –14.81 ± 2.12 for three vessels, and "13.01 ± 2.92 for left main disease) (p=0.001). They concluded that 2D STE has good sensitivity and specificity to predict the presence, extent, and severity of CAD. The present study findings were consistent with this study, and showed that with significant fall in GLS, the severity of CAD increases.

Bakhoum *et al*[16] studied 82 patients and found that GLS were significantly lower in patients with significant CAD compared to normal coronary arteries group (-16.55 ± 2.77% vs 21.11 ± 0.8 %*P*=0.000). The study concluded that myocardial deformation analysis by 2D-STE was not only useful to diagnose CAD, but also predicts the extent of CAD affection in patients with suspected CAD. This study was consistent with our study.

Montgomery *et al*[4] studied 123 patient which found that GLS was significantly lower among patients with significant CAD than those with non-significant CAD with mean values of (GLS) were (-16.8 ± 3.2% vs -19.1 ± 3.4%, p < 0.0001) with sensitivity 66% and specificity 76%. These findings are consistent with present study.

Smedsrud *et al*[6] included 86 patients with stable chest pain. They found that GLS value was (-17.9% ± 3.5%) in patients with significant CAD and (-20.1 ± 2.9) in patients without CAD. There was statistically significant difference between these patients (p = 0.003), with sensitivity (66%) and specificity (81%) at cut off value of GLS < -17.4. Similar results were found in our study.

Gaibazzi *et al*[17] showed that patients with CAD group had significantly reduced rest GLS (-19 + 2.4% vs -22.7 + 2.4%, P = 0.001) compared with patients with non-significant CAD. They showed that GLS -20.7 may predict significant CAD, with sensitivity 81.6% and specificity 84.9%. This study was consistent with present study.

Bala *et al*[18] studied a total of 150 subjects of stable angina with normal LVEF showed that GLS was reduced in participants with significant CAD than those without CAD (–18.3% ± 2.4% vs. 15.1% ± 2.5%, *P* < 0.001). Study also showed that GLS values were lower as the severity of CAD increased, as measured by the number of vessels with significant CAD on invasive CAG. This observation was consistent with the present study stating that there was a fall in GLS as severity of CAD increases.

Billehaug *et al* [19] used 6 studies (778 patients with suspected CAD), which aimed to assess the diagnostic accuracy of GLS to predict significant coronary artery disease. They found that GLS was significantly lower among patients with significant CAD, with mean values of GLS were (-17.2 ± 2.6% vs -19.2 ± 2.8, p < 0.000). They concluded that GLS measurements at rest have modest diagnostic accuracy in predicting CAD among patients presenting with chest pain which was in corroboration with the current study. Our study further underlines the value of GLS in patients with stable angina to detect the severity of underlying CAD.

Conclusion

- Reduction of GLS signifies early subtle derangement of LV systolic function in patients with significant coronary artery disease.
- Measurement of GLS, therefore, is a sensitive, specific and accurate diagnostic tool in the prediction of severe CAD in patient referred for coronary angiography for suspected coronary artery disease.

Limitations

1. Only GLS values were evaluated and other parameters e.g., radial and circumferential strain were not measured.

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