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Global Longitudinal Strain (GLS) by 2D speckle tracking echocardiography to predict and diagnose coronary artery disease

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ABSTRACT

Background: Non-invasive cardiac imaging is increasingly used nowadays to predict and diagnose structural and functional diseases of coronary arteries with improved efficacy, safety and cost.

Objective: To evaluate the ability of two-dimensional (2D) global longitudinal strain (GLS) by speckle echocardiography to predict the presence of significant coronary artery disease (CAD), disease severity and its' reproducibility in the stratification of coronary disease risk in suspected patients.

Patients and methods: An observational study that was conducted at Al Nasiriya Cardiac Hospital and included 75 patients with suspected CAD who were admitted for elective diagnostic coronary angiography. They divided into 3 groups according to presence of coronary artery stenosis and the degree of significance. 2D speckle tracking echocardiography was performed for all and its' ability in the prediction and diagnosis of CAD was studied.

Results: Study showed that 60% of patients had significant stenosis, while 30.67% had no stenosis and 9.33% had a non- significant stenosis by coronary angiography. There was a significant variance regarding gender preference and hypertension with no significant variance regarding age, diabetes and smoking status. GLS had significant associations with the degree of coronary stenosis and culprit vessels, having a cut of value of -16.5% for discrimination of significant, non-significant and no stenosis with 83% sensitivity and 84% specificity. GLS had a significant positive correlation with the ejection fraction, $r = 0.511$ at a p-value <0.001.

Conclusions: 2D speckle tracking echocardiogram GLS has the potential to improve the value of echocardiography in identifying high-risk patients, detecting CAD and CAD severity (degree of stenosis) which provides more information for the clinical physician.

Keywords: Coronary artery disease, Global longitudinal strain, Speckle tracking echocardiography, Coronary angiography, Left ventricular function.

1. Introduction

Echocardiography is a non-invasive cardiac imaging that can be used to obtain sufficient information for morphological and functional assessment of the heart. Non-invasive tests are easy to perform, safe, costless with no need of surgical intervention as in invasive coronary angiography, which requires a catheter to be entered into the heart through the vascular system that carry a high risk of complications. Together, more than 50% of coronary angiography procedures demonstrated normal or non-obstructive coronary artery disease [1].

Two-dimensional (2D) echocardiography and speckle tracking is one of non-invasive imaging modality that can be used for assessing heart and coronary artery problems. 2D speckle tracking provides measurement of global longitudinal strain (GLS) that can be used in the estimation of functional changes of the coronary vessels and the distal layer of coronary arteries (endocardial wall deformities) [2] , which is highly susceptible for ischemia and infarction [3]. During the measurement of longitudinal strain, only the longitudinal fibers of myocardium are found to be correlated and could represent myocardial ischemia or infarction extent and size [4].The prognostic utility of GLS has been studied widely in last recent years in different clinical states; acute myocardial infarction (MI), aortic stenosis (AS) and heart failure (HF) management [6-8].Several echocardiographic studies made a strong recommendation for routine GLS use for making a clinical decision [9].

Starin means the fractional or percentage change in shortening or lengthening of myocardium, shortening occur when myocardium contracted and lengthening occur with myocardium stretch out or relax, this deformation can be measure by echocardiogram which is must be equal in each cardiac cycle, formula for strain: Strain = (L-L0)/L0 100 L0: initial myocardium length, L: final length. The constant 100 to transform strain to percentage. As demonstrated in clinical practice, left ventricular (LV) dysfunction commonly complicates severe CAD without significant impairment of LV ejection fraction which always remain normal in the early stage of the disease.

Thus, an establishment of a more sensitive index for detecting early stage left ventricle dysfunction is very necessary [10]. It had been suggested that abnormal GLS patterns are well recognized in the presence of CAD [9]. Studies that had been performed on healthy individuals suggested that GLS LV values > -18% are considered normal and values between -16-18 % are considered borderline [12], an intra- and inter- individual variations of normal GLS value are not uncommon [13].

A study that was done by Yang and his group concluded that a longitudinal peak strain cutoff value of -14.08 % is sufficient for the detection of myocardial ischemia and -6.65% for the detection of MI [14]. Despite of being operator-independent, GLS is easily measured and more reproducible than LV ejection fraction by echocardiography. It is a myocardial deformation analysis representing the function of sub-endocardial longitudinal fibers that are more sensitive to stress and ischemic damage and can show abnormal contraction patterns in spite of apparently normal left ventricular ejection fraction [15]. Thus, this study was designed to evaluate the ability of non- invasive 2D speckle echocardiography in the prediction and diagnosis of CAD and whether can replace diagnostic coronary angiography in the future or not.

2. Patients and Methods:

An observational study that was conducted throughout the period from May, 2023 to February, 2024 at Al-Nasiriya Cardiac Hospital and included 75 patients who were suspected of having CAD and admitted for elective diagnostic coronary angiography. The study was approved by the Local Ethical Committee of Iraqi board for medical specializations and a written informed consent was taken from the patient before the start of the study. A questionnaire included the demographic characteristics was followed; patients' age, gender, address, occupation, level of education, smoking state, medical history of hypertension, diabetes and previous CAD.

Echocardiography scan was done using Vivid E9, GE Health Care, a semi-automated algorithm at a framerate of 60–80 frames/s using the 2D speckle tracking was done demonstrating three apical views (long-axis, 4CH and 2CH) (Echo Pac, GE Healthcare) at least 3 cardiac cycles per specified recording. The involved areas were illustrated in such a way that the whole myocardium from base to apex was imaged excluding pericardium, papillary muscles and their trabeculations. The closure of the aortic valve was also identified together with the 17 segments covering the entire left ventricle, Figure 1. Automatic calculation of GLS was done as the mean of the global peak systolic strain from each of the three views, Figure 2 and Figure 3.

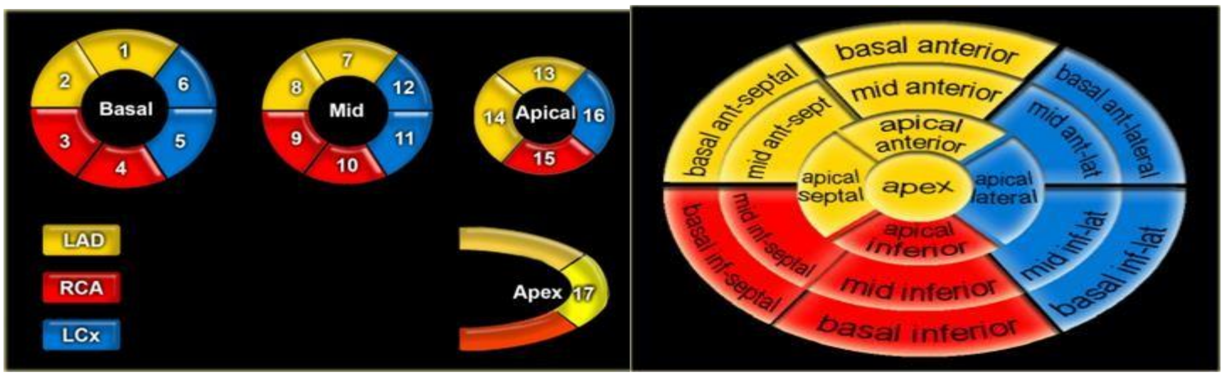

Figure 1. The American Heart Association 17 segments assigned to the 3 major coronary arteries.

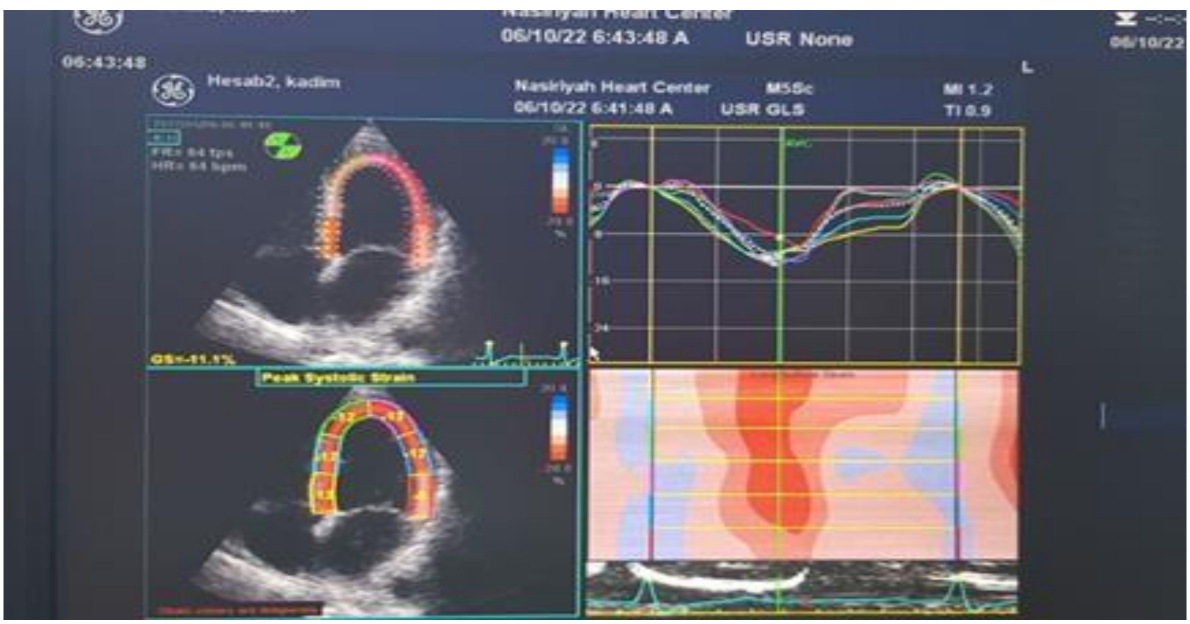

Figure 2 . A longitudinal strain by speckle-tracking echocardiography.

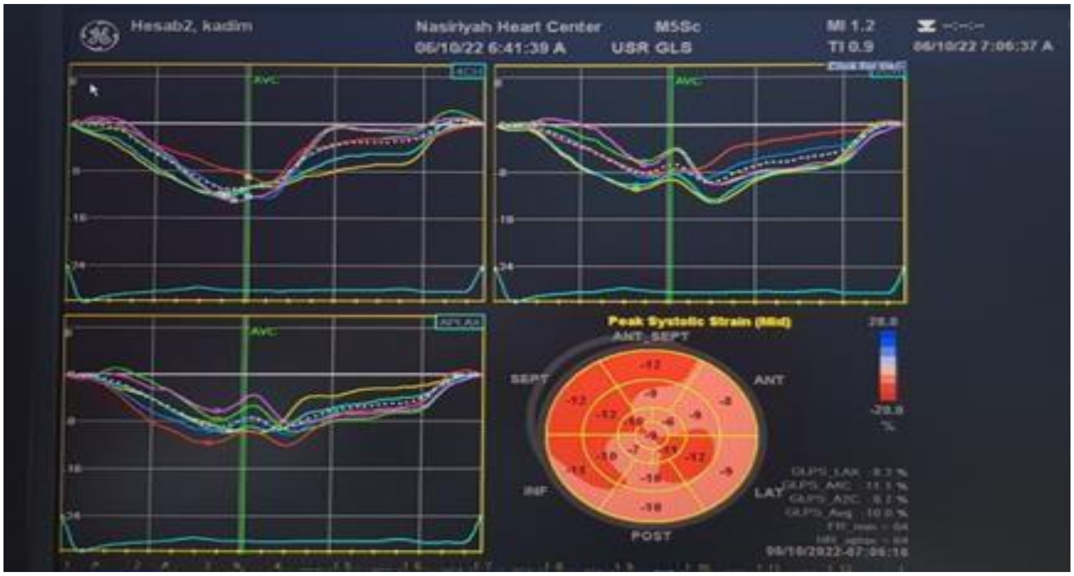

Figure 3. A peak systolic strain demonstrating the Bull's eye map.

The strain velocity curves of the individual myocardial segments in three views used to generate the bull's eye image on the fourth quadrant (the apical four-chamber, two-chamber, and three-chamber views). Elective coronary angiography was performed using the percutaneous femoral & radial approach for each coronary vessel in ≥ 2 projections. Patients with a stenosis of ≥ 70% of arterial lumen area reduction were classified as significant stenosis group (n= 45), those with a stenosis < 70% (n=7) were classified as non-significant stenosis group, while normal group were those with no stenosis (n=23). Coronary angiograms results were assessed visually blinded to echocardiographic examination results. Data were analyzed statistically using SPSS software version 25.0 (SPSS, Chicago).

Mean and standard deviation was used for expressing the continuous variables and the degree of significance was analyzed. using ANOVA test, while number and percentage was used for expressing the categorical variables and the degree of significance was analyzed with Chi-square test. The predictive value of GLS was evaluated using the receiver operating characteristic curve (ROC) in the context of discrimination of the three groups; significant, non-significant and no stenosis. The possible correlation between EF and GLS was assessed by Pearson’s correlation test. A p-value ≤ 0.05 indicated a statistically significant variance among the studied parameters in the groups.

Ethical considerations: Approval was taken from Cardiac Imaging Scientific Committee of Iraqi Board. An agreement for research was taken from hospitals' authorities.

3. Results:

The demographic characteristics of the patients are best illustrated in table 1. The mean age of the patients was 58.56 ± 10.1 years. Males represent about three-fourths (73.33%) of the patients. Hypertension and type 2 diabetes were common past medical history accounting for 70.67% and 41.33% of the patients respectively. Smoking habit was reported in 44% of the patients.

Table 1. Patients' characteristics and demographic data

Values	Variables (n=75)
Age (years) Mean±SD Range	58.56± 10.1 24-75
Gender Male Female	55(73.33%) 20(26.67%)
Past medical history Hypertension Type 2 diabetes mellitus	53(70.67%) 31(41.33%)
Smoking status Never Ex/current	42(56%) 33(44%)

While figure 4 demonstrates patients' categorization according to degree of stenosis during elective diagnostic coronary angiography, patients were categorized into three groups: those with significant stenosis ≥ 70%, those with non-significant stenosis < 70% and those without stenosis.

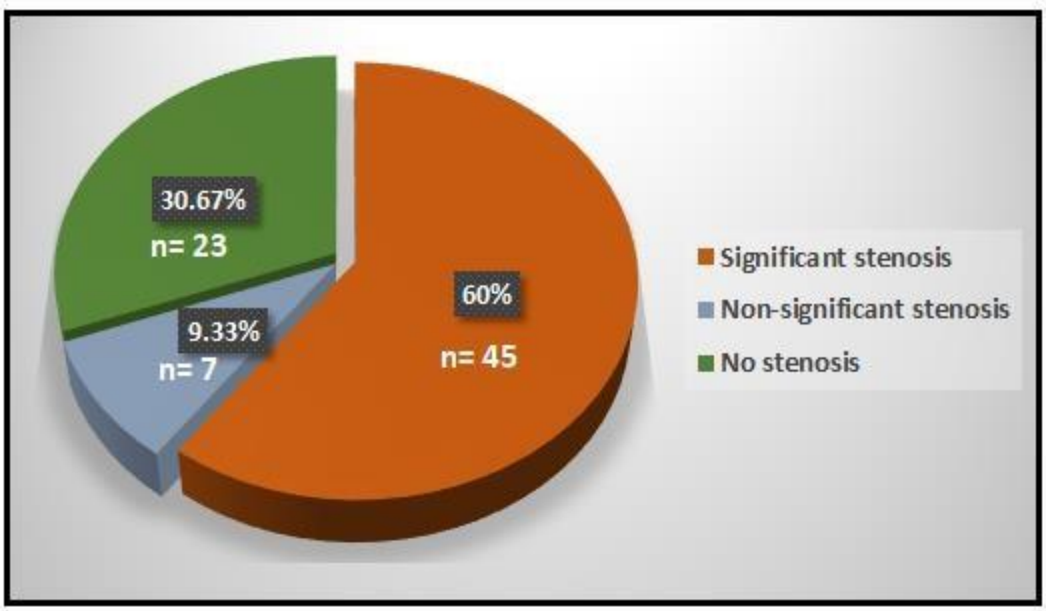

Figure 4. Patients categorization according to degree of stenosis

Table 2 represents the association of demographic characteristics with stenosis. Males were more frequent in significant stenosis (86.67%) than females (13.33%) while the reverse was true for non-significant stenosis. Furthermore, hypertension was reported in 80% and 100% of patients with significant and non-significant stenosis, respectively compared with 26.09% in those without stenosis with a high significant variance.

Table 2. The association of demographic characteristics with coronary artery stenosis.

Variables	Significant stenosis (n=45)	Nonsignificant stenosis (n=7)	No stenosis (n=23)	p-value
Age (years) Mean±SD Range	59.78±8.92 28-73	60.86±9.0 51-75	55.48±12. 1 24-74	0.207
Gender Male Female	39(86.67%) 6(13.33%)	3(42.86%) 4(57.14%)	13(56.52%) 10(43.48%)	0.005
PMH Hypertension T2DM	36(80%) 22(48.87%)	7(100%) 3(42.86%)	10(43.48%) 6(26.09%)	0.002 0.195
Smoking Never Ex/current	24(53.33%) 21(46.67%)	5(71.43%) 2(28.57%)	13(56.52%) 10(43.48%)	0.667

SD: standard deviation, PMA: past medical history

While table 3 demonstrates the association of GLS, LV ejection fraction and coronary artery stenosis. The mean GLS in patients with significant stenosis was -13.77% ± 3.88 which was lower than that of patients with non-significant stenosis (-17.59% ± 2.75) or those with no stenosis (-18.78% ± 2.48) with significant variance.

There was no significant difference between patients with non-significant stenosis and patients with no stenosis in GLS. Although, the GLS for those with no stenosis was higher as compared with non-significant stenosis.

Table 3. The association of left ventricle ejection fraction and GLS with stenosis

Variables	Significant stenosis (n=45)	Nonsignificant stenosis (n=7)	No stenosis (n=23)	p-value
GLS % Mean±SD Range	-13.77±3.88[a] -21 to -4	-17.59±2.75[b] -22 to -15	- 18.78±2.48 b -22 to -13	<0.00 1

Although left anterior descending (LAD) associated with higher mean GLS -13.41% ± 3.88 than either left circumflex (LCX) -11.52% ± 4.55 or right coronary artery (RCA) -10.9% ± 4.57, the variance were not significant.

In contrast, involvement of multiple vessels associated with lower GLS -10.22% ± 3.96 compared with single vessel -15.7% ± 2.12 with a highly significant variance as illustrated in table 4.

Table 4. The association of culprit vessels with GLS.

Vessels	Global-longitudinal strain	p-value
LAD **Mean±SD Range**	-13.41±3.88 -18 to -4	0.112
LCX **Mean±SD Range**	-11.52±4.55 -21 to -4	
RCA **Mean±SD Range**	-10.9±4.57 -17 to -4	
Single vessel **Mean±SD Range**	-15.7±2.12 -21 to -11	<0.001
Multiple vessels **Mean±SD Range**	-10.22±3.96 -16 to -4	

The GLS predictive value for coronary arteries stenosis was evaluated using the receiver operating characteristic (ROC) curve in the context of discrimination between significant, non-significant and stenosis groups. The area under the curve (AUC) was 0.924, at 95% CI= 0.858-991 and p value < 0.001. The sensitivity and specificity of the test at cut off value of GLS -16.5% was 83% and 84%, respectively, Figure 5.

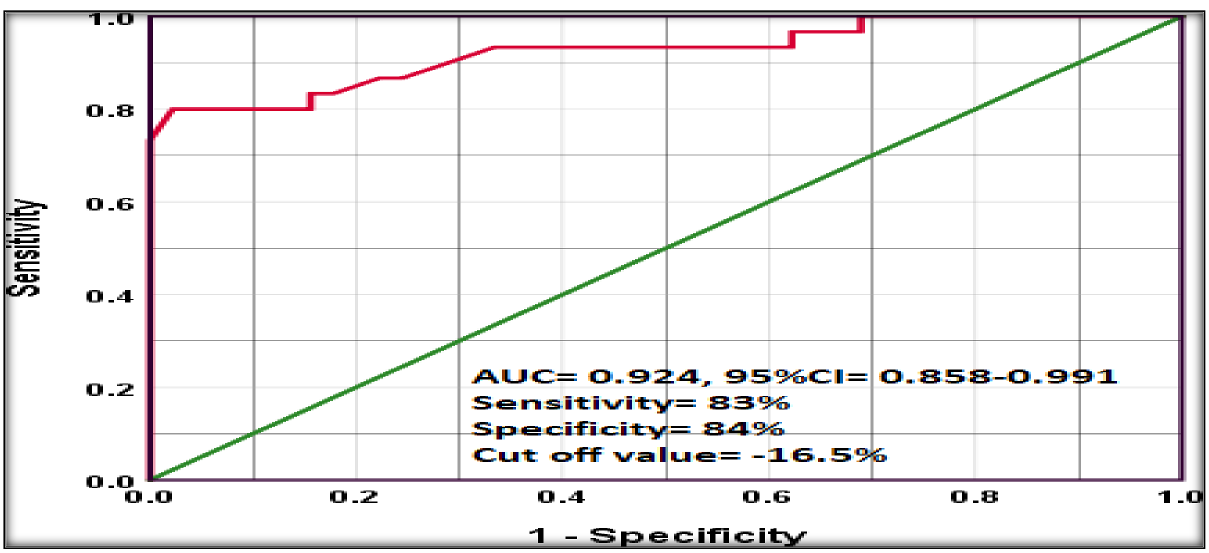

Figure 5. Receiver operating characteristic curve for GLS in the context of discrimination between significant stenosis and non- significant/no stenosis groups.

While figure 6 demonstrates the correlation between EF and GLS which was explored by Pearson's correlation. There was a significant positive correlation, $r = 0.511$, $p < 0.001$ as shown in figure below.

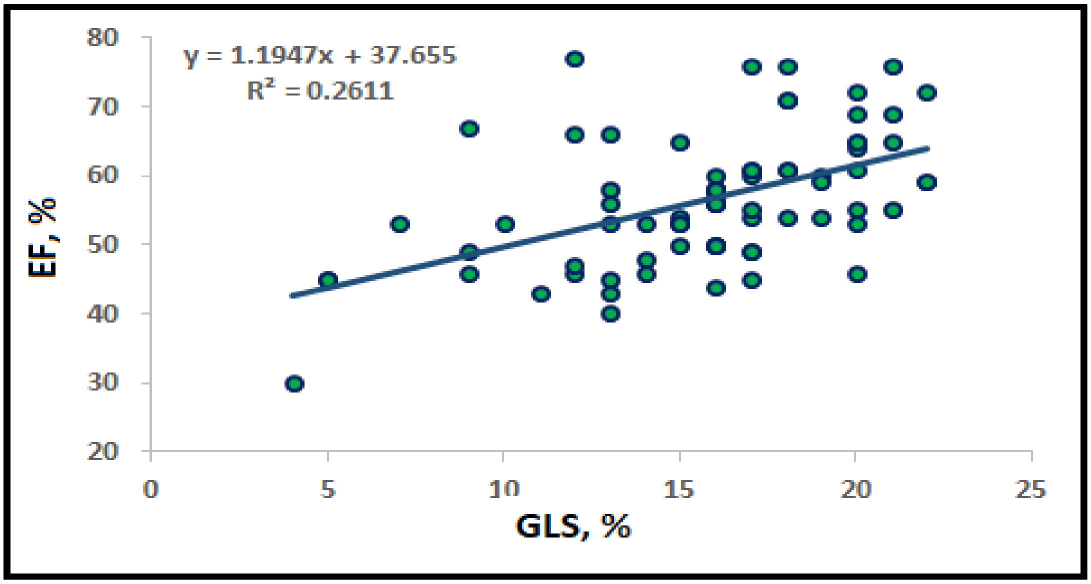

Figure 6 .Scatter plot and regression line between GLS and EF.

4. Discussion:

For every invasive diagnostic test, there is a trends toward replacing it with a non-invasive one providing better or at least same efficacy and reproducibility to avoid complications and improve cost. Current study showed that patients with significant CAD exhibited significantly less GLS value -13.77 ± 3.88 than those with non- significant CAD -17.59 ± 2.75, p < 0.001. A GLS < -16.5% might have a predictive ability of >70% stenosis (significant obstruction) in 60 % of patients with 83% sensitivity and 84% specificity, thus, GLS assessment might have a high diagnostic accuracy in the prediction of significant CAD among CAD suspected patients.

Similar results had been believed by several studies that assessed patients with CAD and tried to evaluate GLS predictive power in diagnosis of obstructive CAD following elective angiography which suggested a significant reduction in GLS in patients with significant compared to non-significant CAD [16-22].

Meanwhile, they showed that measurement of CAD has a modest diagnostic accuracy in the prediction of obstructive CAD which is in disagreement with current study results. This could be explained by GLS cut off value -16.4% in this study which is lower than previous studies cut off value - 17.1% and small sample size. A study which was performed on 182 patients showed cut off GLS value -17.4, with a prediction power of >50% of coronary artery obstruction that was proved by multi-slice computed tomography coronary angiography, with 83% sensitivity and 77% specificity [16].

While a study which was performed on 97 patients with suspected CAD, showed that GLS cut off value -17.7 was significantly less among significant CAD patients than those with non-significant disease, predicting >50% of obstruction with 81% sensitivity and 67% specificity [17]. Another one had found that mean value of GLS in significant group - 16.8 ± 3.2 in contrast to 19.1 ± 3.4 in non-significant ones, $p < 0.000$, and a cut off value of -17.8 may predict significant obstruction, with 66% sensitivity and 76% specificity [18].

A study that was performed on 86 patients with stable angina exhibited that significant CAD group had a GLS cut off value -17.9 ± 3.5, while non-significant group had a cut off value -20.1 ± 2.9, and the cut off value of for prediction of >50% stenosis (significant coronary artery disease) was -17.4% with 51% sensitivity and 81% specificity [19]. Together, a study that enrolled 296 patients with stable chest pain showed similar results with a GLS cut off value -17.1 ± 2.5 in significant stenosis vs -18.8 ± 2.6 in non-significant stenosis, $p < 0.000$ and a GLS of -18.4% may predict >70% stenosis (significant obstruction) with 74% sensitivity and 58% specificity [20].

From previous studies results, one could conclude that GLS measurements at rest has a modest diagnostic accuracy in the prediction of significant CAD among patients complaining of chest pain (suspected CAD) which could be possibly explained by the effect of diastolic function and afterload on GLS, and the overlap in distribution of GLS values between the significant and non-significant CAD groups. The variance of cut off value among previous studies could be explained that GLS depends on the clinical characteristics of patients, their hemodynamic state (blood pressure) during imaging, diastolic function, operator skills and using equipment with different design, vendor-dependent 2D-STE software [17].

In the current study, left anterior descending (LAD) vessel was more commonly involved than other vessels, followed by left circumflex (LCX) and then right coronary artery (RCA), with no significant variance between significant, non-significant stenosis and GLS in the detection rate of all the three vessels. Together, the study showed that the GLS reduced with increasing severity of CAD and there was an increased risk of multi-vessels diseases with decreasing GLS. This study also found that GLS exhibited a significant positive correlation with ejection fraction which is in agreement with results of studied that were done by Biering-Soerensen et al., Evensen et al., and Delgado et al., [20-22].

5. Conclusions:

2D spickle tracking echocardiogram GLS has the potential to improve the value of echocardiography in identifying high-risk patients, detecting CAD and CAD severity (degree of stenosis) which provides more information for clinical physician.

Recommendations: Future studies are required for further evaluation of the role of GLS as a recent available non-invasive test to assess and stratify patient with suspected CAD in the sitting of Chronic Coronary Syndrome & Acute Coronary Syndrome which could be very helpful for categorizing patient risk.

Conflict of interest: The authors have no conflict of interest.

The manuscript has been agreed upon by all authors to be submitted.

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