

## Speckle Tracking as Predictor of Coronary Artery Disease in Diabetic Female with Acute Chest Pain

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### Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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## ABSTRACT

**Background:** Cardiovascular disease is the most common reason of mortality and morbidity all over the world and is the major complication of diabetes. Diabetes mellitus (DM) has reached epidemic proportions worldwide and the consequences of its diagnosis are as severe as a diagnosis of coronary artery disease (CAD). Females are more likely to develop atypical symptoms of coronary CAD than males later in life. Imaging of deformation by two-dimensional speckle-tracking echocardiography (2DSTE) has developed as a highly effective method for quantification of the function of myocardium.

This research aimed to evaluate the accuracy of diagnosis using speckle tracking for prediction of the existence or absence of severe CAD in diabetic female with acute chest pain by using two-dimensional echocardiography.

**Methods:** This study is a cohort prospective research which was carried out at the department of cardiology, Tanta University Hospitals and National Heart Institute from the duration of October 2019 to September 2020 on 60 diabetic female patients above 18 years old with acute chest pain may be prolonged for > 20 minutes or transient, changes in ECG in the form of depression of ST segment and/or inversion of T wave (ECG may be normal) and cardiac biomarkers (troponin and CKMB) may be elevated or normal.

**Results:** 2D speckle tracking was good predictor for multi-vessels disease with 95% total accuracy, then for single vessels disease with 85% total accuracy and finally for double vessel disease stenosis with 80% accuracy as shown in table. Among Non-STEMI group, 2D speckle tracking was

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good predictor for multi-vessels disease with 95% total accuracy, then for single vessels disease with 80% total accuracy and finally for double vessel disease stenosis with 75% accuracy as shown in table.

**Conclusions:** We found that speckle tracking is effective in predicting presence of CAD in diabetic female patients had acute chest pain and in prediction of affected vessels depending on the distribution of affected segments in longitudinal strain by GLS. In addition, it can be used as non-invasive test for patients with acute coronary syndrome.

*Keywords: Acute chest pain; coronary artery disease; diabetes mellitus; speckle tracking.*

## 1. INTRODUCTION

Cardiovascular disease is the first reason of mortality and morbidity all-over the world, comprising 31% of all deaths. Coronary artery disease (CAD) is defined by atherosclerosis in the epicardial coronary arteries. The reduction in the flow of coronary may be asymptomatic or symptomatic, happens with exertion or at rest, and result in angina or myocardial infarction (MI) , based on the severity of obstruction and the development rapidity [1].

The principle complication of diabetes is cardiovascular disease, representing 50% of all mortality of diabetes. This is not only because of CAD and associated hypertension, but also because of diabetes's direct adverse effect on the heart, regardless of other cardiovascular risk factors, a condition known as diabetic cardiomyopathy [2].

Diabetes mellitus (DM) has reached epidemic proportions worldwide, and its prevalence is increasing. The diagnosis of DM is just as serious as the diagnosis of CAD. Cardiovascular mortality in all age groups and for both sexes increases equivalently with a history of MI or DM and both are profoundly synergistic [2].

Despite the increasing use of provocative testing and imaging, non-invasive diagnosis of patients with CAD still a clinical challenge; more than half of patients referred for coronary angiography currently have non-obstructive coronary artery disease (CAD) [3].

Over the last years, imaging of deformation by two-dimensional speckle-tracking echocardiography (2DSTE) has developed as a highly effective method for quantification of the function of myocardium. Supporting evidence of the role of 2DSTE-derived strain in daily clinical practice has gathered rapidly in a variety of clinical settings. Additionally, attempts to establish reference values for 2D strain

parameters have risen, allowing for the construction of rigorous abnormality criteria and their incorporation into recent guidelines [4].

Women are more exposed than men to acquire atypical CAD symptoms later in life. Additionally, they have a higher mortality and morbidity rate when CAD occurs, including sudden death and MI . Women also have a distinct atherosclerotic profile than men, with microvascular disease predominating in the absence of significant obstructive CAD on imaging [5].

The aim of this research to evaluate the accuracy of diagnosis using speckle tracking to detect the existence or absence of significant CAD in diabetic female with acute chest pain by using two-dimensional echocardiography.

## 2. PATIENTS AND METHODS

This study is a cohort prospective research which was conducted at cardiology department, Tanta University Hospitals and National Heart Institute from the duration of October 2019 to September 2020 on 60 diabetic female patients above 18 years old with acute chest pain may be prolonged for > 20 minutes or transient, changes in ECG in the form of depression of ST segment and/or inversion of T wave (ECG may be normal) and cardiac biomarkers (troponin and CKMB) may be elevated or normal.

Patients with poor echocardiographic window, any rhythm other than sinus rhythm severe valvular lesions except functional mitral incompetence, atrial fibrillation, previous CABG or PCI, bundle branch block and previous MI were excluded.

All patients underwent routine history and physical examination, electrocardiogram, laboratory work-up, transthoracic echocardiography, conventional echocardiography.

## 2.1 Speckle Tracking Echocardiography (STE)

### 2.1.1 Image acquisition

Longitudinal strain imaging was performed using 2DSTE with ECG gated images of high quality from the apical four-chamber, two-chamber and three-chamber views, all of these measurements were taken at very equal heart rates. Improvement of to the gain settings have been made. The depth was reduced to ensure that the LV took up the majority of the image sector. To avoid LV foreshortening, effort was taken to keep the gray-scale framerate between 50 and 90 frames/s and to ensure that each loop acquired a minimum of three cardiac cycles.

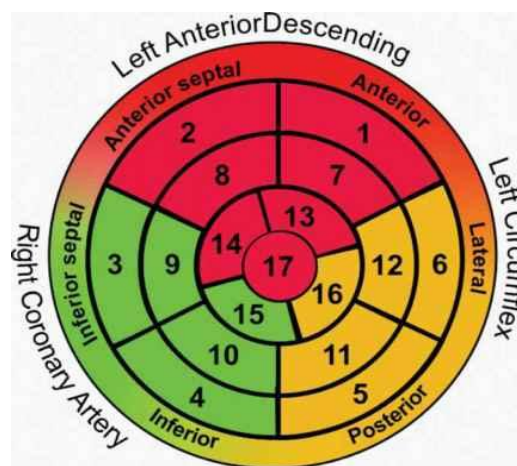
### 2.2 Strain Analysis

We analyzed the digitally stored clips offline using commercial imaging analysis software on a Philips “epic 7” machine. The operator manually identified three spots for each of the three apical views: two on either side of the mitral valve and one at the apex of the left ventricle. At the end of systole, the software detected the endocardium automatically, tracking myocardial motion throughout the cardiac cycle, and forming inverted U-shaped zones of interest that included the apical, middle and basal regions of two opposing LV walls. The operator evaluated the quality of tracking, which was then scored by the software. If the operator determines that the tracking was insufficient, the operator may repeat the imaging by changing the endocardial tracing or adjusting software settings such as the region

of interest's width and smoothing until a better score is obtained. Segments that were not effectively tracked were excluded from the study automatically. In the apical long-axis perspective, systole duration was defined as the time interval between the ECG's peak R and the first frame in which the aortic valve closed.

The software automatically determined the peak longitudinal strain in each segment of a 17-segment LV model, which is expressed as bull's eye. For each major coronary artery (left circumflex artery (LCX), right coronary artery (RCA), and left anterior descending artery (LAD)) the territorial longitudinal strain (TLS) was defined as the average peak systolic longitudinal strain in segments inside the theoretical perfusion area of the artery.

We utilized a standardized model of myocardial perfusion territories to calculate the following variables in each of the perfusion territories supplied by LAD, LCX, and RCA. Each of the 3 perfusion territories was then named culprit or non-culprit depending on the results of coronary angiography. We utilized the standardized 17 segment model of myocardial perfusion territories recommended by the American Heart Association adapted from assigning one coronary artery for each segment to be able to perform the statistical analysis, for identification of significant coronary stenosis, the lowest absolute territorial strain value for each patient was used as a marker, then the results of bull's eye strain analyses were correlated with the results of coronary angiography.



**Fig. 1. Assignment of the 17 myocardial segments to the territories of the left anterior descending (LAD), right coronary artery (RCA), and the left circumflex coronary artery (LCX) [6]**

## 2.3 V-Coronary Angiography and Revascularization

By using the standard (Judkins) approach, coronary angiography was conducted, including the acquisition and preservation of digital images. All analyses were conducted offline using a single experienced invasive cardiologist who was unaware of the outcome of the other imaging trials. The infarcted vessel was identified as the culprit in cases with single vessel illness. CAD was visually assessed in each individual stenosis using several projections to avoid overlapping side branches and foreshortening severe coronary stenoses. Coronary occlusion was known as a TIMI (Thrombolysis in Myocardial Infarction) flow grade of 0 or 1, whereas severe coronary artery stenosis was defined as a vascular diameter decrease of more than 70% in peripheral arteries or more than 50% in the left main artery.

## 2.4 Statistical Analysis

SPSS v27 (IBM, Chicago, IL, USA) was used to conduct statistical analysis. The Shapiro-Wilks test and histograms were used to determine the distribution of the data. The ANOVA (F) test and a post hoc test (Tukey) were used to determine the mean and standard deviation (SD) of quantitative parametric data. The Chi-square test was used to examine qualitative variables that were represented in terms of frequency and percentage (percent). Correlations were found using the linear correlation coefficient between two quantitative variables ( $r$ ). ROC curve analysis was used to evaluate the diagnostic performance of each test. When two tailed tests were used, a P value of 0.05 was considered statistically significant.

## 3. RESULTS

Demographic data and risk factors for studied groups were shown in (Table 1).

Regarding LV strain data by 2D speckle tracking Echo, the septal wall was significantly affected in non-STEMI group at basal segment  $-12.38 \pm 5.04$  as compared to  $-16.13 \pm 4.11$  in control group. Mid segment was statistically affected in non-STEMI group  $-14.40 \pm 3.80$  as compared to  $-16.85 \pm 3.00$ ,  $-18.40 \pm 3.56$  in unstable angina and control groups respectively. Apical segment was lower in non-STEMI and unstable angina  $-19.75 \pm 9.03$ ,  $-22.40 \pm 7.51$  as compared to  $-30.65 \pm 12.2$  in control group. Cumulative strain was statistically

affected in non-STEMI group  $-16.07 \pm 3.93$  as compared to  $-18.35 \pm 2.94$ ,  $-19.94 \pm 3.41$  in unstable angina and control groups respectively. The lateral wall was significantly affected in non-STEMI group at apical segment  $-17.95 \pm 6.78$  as compared to  $-22.40 \pm 6.92$  in unstable angina group. The anterior wall was significantly affected in non-STEMI group at basal segment  $-15.70 \pm 6.83$  as compared to  $-22.88 \pm 9.78$  in control group. The inferior wall was significantly affected in unstable angina group at mid segment  $-17.54 \pm 4.77$  as compared to  $-20.72 \pm 4.06$  in control group while apical segment was lower in unstable angina ( $-20.73 \pm 8.02$ ) and non-STEMI group ( $-21.35 \pm 7.47$ ) as compared to  $-29.98 \pm 11.7$  in control group. Cumulative strain was statistically affected in unstable angina ( $-18.36 \pm 4.57$ ) and non-STEMI group ( $-18.83 \pm 4.48$ ) as compared to  $-21.57 \pm 3.87$  in control group. The Anteroseptal wall was significantly affected in non-STEMI group at mid segment  $-14.40 \pm 3.89$  as compared to  $-19.92 \pm 4.80$ ,  $-18.02 \pm 4.24$  in unstable angina and control groups respectively. Apical segment was affected in non-STEMI group  $-14.65 \pm 5.17$  as compared to  $-19.44 \pm 4.19$ ,  $-19.22 \pm 4.92$  in unstable angina and control groups. Cumulative strain was statistically affected in non-STEMI group  $-14.11 \pm 3.68$  as compared to  $-18.13 \pm 3.47$ ,  $-18.05 \pm 3.05$  in unstable angina and control groups respectively. Finally, the global longitudinal strain of the LV was significantly affected in non-STEMI group  $-15.81 \pm 1.92$  and unstable angina group  $-16.86 \pm 0.99$  as compared to  $-18.17 \pm 0.79$  in control group p value  $\leq 0.05$  (Table 2).

Regarding the vessel affected as suspected by 2DSTE, LAD was affected in 75% of unstable angina and 80% in non STEMI group as compared to 30% in control group with statistically significant difference. Two vessels and three vessels affection were higher in both unstable angina and non STEMI group 45%, 20% as compared to 15% and 0% in control group (Table 3).

Regarding the 2DSTE validity in detection of stenosis of LAD in unstable angina group, it was good predictor for stenosis of LAD with 75% specificity and 87.5% sensitivity, 93.3% PPV, 60% NPV and 85% accuracy. Among Non STEMI group, 2DSTE was good predictor for stenosis of LAD with 100% specificity and 88.9% sensitivity, 100% PPV, 50% NPV and 90% accuracy Regarding 2DSTE validity in identification of LCX stenosis in unstable angina group, it was good predictor for LCX stenosis

with 100% specificity and 75% sensitivity, 100% PPV, 85.7% NPV and 90% accuracy. Among Non-STEMI group, 2D speckle tracking was good predictor for LCX stenosis with 100% specificity and 72.7% sensitivity, 100% PPV, 75% NPV and 85% accuracy (Table 4).

**Table 1. Sociodemographic data and risk factors among studied groups**

Demographic data	Unstable angina (n=20)	Non STEMI group (n=20)	Control group (n=20)	Test of significance		
				P1	P2	P3
<b>Age (years)</b> Mean ± SD	50.25±8.34	51.00±7.61	54.65±8.39	t=1.66 p=0.105	t=1.44 p=0.158	t=0.297 p=0.768
<b>Smoking</b>				FET	FET	FET
Yes	3 (15.0%)	2 (10.0%)	4 (20.0%)	P=1.0	P=0.661	P=1.0
No	17 (85.0%)	18 (90.0%)	16 (80.0%)			
<b>HTN</b>				χ <sup>2</sup> =0.1 P=0.752	χ <sup>2</sup> =0 P=1.0	χ <sup>2</sup> =0.1 P=0.752
Yes	10 (50.0%)	11 (55.0%)	11 (55.0%)			
No	10 (50.0%)	9 (45.0%)	9 (45.0%)			
<b>Dyslipidemia</b>				χ <sup>2</sup> =0.102 P=0.749	χ <sup>2</sup> =0.10 P=0.752	χ <sup>2</sup> =0.404 P=0.525
Yes	12 (60.0%)	10 (50.0%)	11 (55.0%)			
No	8 (40.0%)	10 (50.0%)	9 (45.0%)			
<b>Hx of ACS</b>				χ <sup>2</sup> =2.56 P=0.11	χ <sup>2</sup> =1.67 P=0.197	χ <sup>2</sup> =0.1 P=0.752
Yes	11 (55.0%)	10 (50.0%)	6 (30.0%)			
No	9 (45.0%)	10 (50.0%)	14 (70.0%)			
<b>BMI</b> Mean ± SD	33.10±4.50	32.24±4.56	27.97±4.63	t=3.55 p=0.001*	t=2.93 p=0.006*	t=0.604 p=0.549

t: student t- test, χ<sup>2</sup>: Chi square test, FET: Fischer exact test, P1: Comparison between Unstable angina and control groups, P2: Comparison between Non-STEMI and control groups, P3: Comparison between Unstable angina and non-STEMI groups

**Table 2. Speckle tracking Echo (LV strain) among studied groups**

Speckle tracking ECHO	Unstable angina (n=20)	Non-STEMI group (n=20)	Control group (n=20)	Test of significance		
				P1	P2	P3
<b>Septal wall</b>						
Basal	-14.05±5.30	-12.38±5.04	-16.13±4.11	t=1.38 p=0.174	t=2.57 p=0.014*	t=1.02 p=0.314
Mid	-16.85±3.00	-14.40±3.80	-18.40±3.56	t=1.49 p=0.145	t=3.43 p=0.001*	t=2.26 p=0.03*
Apical	-22.40±7.51	-19.75±9.03	-30.65±12.2	t=2.57 p=0.014*	t=3.20 p=0.003*	t=1.01 p=0.319
Cum.	-18.35±2.94	-16.07±3.93	-19.94±3.41	t=1.57 p=0.124	t=3.33 p=0.002*	t=2.08 p=0.044*
<b>Lateral wall</b>						
Basal	-16.68±4.81	-18.00±5.02	-16.35±3.95	t=0.233 p=0.817	t=1.15 p=0.257	t=0.848 p=0.402
Mid	-19.12±6.30	-16.45±5.56	-17.12±3.29	t=1.26 p=0.216	t=0.464 p=0.646	t=1.42 p=0.163
Apical	-22.40±6.92	-17.95±6.78	-18.62±5.34	t=1.93 p=0.061	t=0.350 p=0.729	t=2.05 p=0.047*
Cum.	-17.34±3.28	-17.47±5.21	-19.22±5.18	t=1.37 p=0.178	t=0.095 p=0.925	t=1.07 p=0.292
<b>Anterior wall</b>						
Basal	-18.43±5.78	-15.70±6.83	-22.88±9.78	t=1.75 p=0.088	t=2.69 p=0.01*	t=1.36 p=0.180
Mid	-15.32±5.72	-16.70±6.96	-15.99±4.37	t=0.419 p=0.677	t=0.384 p=0.703	t=0.685 p=0.498

Speckle tracking ECHO	Unstable angina (n=20)	Non-STEMI group (n=20)	Control group (n=20)	Test of significance		
				P1	P2	P3
Apical	-17.96±5.49	-19.55±6.59	-17.23±6.15	t=0.393 p=0.696	t=1.15 p=0.258	t=0.829 p=0.413
Cum.	-17.38±3.67	-17.32±6.17	-18.72±4.46	t=1.03 p=0.308	t=0.043 p=0.966	t=0.824 p=0.415
<b>Inferior wall</b>						
Basal	-15.08±5.94	-16.85±5.94	-17.08±6.10	t=1.05 p=0.30	t=0.121 p=0.905	t=0.942 p=0.352
Mid	-17.54±4.77	-18.30±4.85	-20.72±4.06	t=2.26 <b>p=0.029*</b>	t=1.71 p=0.095	t=0.496 p=0.622
Apical	-20.73±8.02	-21.35±7.47	-29.98±11.7	t=2.90 <b>p=0.006*</b>	t=2.77 <b>p=0.009*</b>	t=0.253 p=0.802
Cum.	-18.36±4.57	-18.83±4.48	-21.57±3.87	t=2.39 <b>p=0.022*</b>	t=2.07 <b>p=0.046*</b>	t=0.332 p=0.742
<b>Posterior wall</b>						
Basal	-14.95±7.52	-13.62±8.26	-16.22±5.67	t=0.603 p=0.550	t=1.16 p=0.253	t=0.532 p=0.598
Mid	-13.65±5.86	-11.04±7.75	-14.92±5.28	t=0.717 p=0.478	t=1.84 p=0.073	t=1.20 p=0.237
Apical	-13.65±3.99	-11.72±8.52	-15.82±5.23	t=1.47 p=0.149	t=1.83 p=0.075	t=0.237 p=0.365
Cum.	-14.19±5.05	-12.13±7.04	-15.65±4.12	t=0.996 p=0.326	t=1.93 p=0.061	t=1.07 p=0.292
<b>Anteroseptal wall</b>						
Basal	-14.59±3.04	-13.30±3.77	-15.46±3.58	t=0.832 p=0.410	t=1.86 p=0.071	t=1.19 p=0.241
Mid	-19.92±4.80	-14.40±3.89	-18.02±4.24	t=1.32 p=0.193	t=2.81 <b>p=0.008*</b>	t=3.99 <b>p≤0.001*</b>
Apical	-19.44±4.19	-14.65±5.17	-19.22±4.92	t=0.156 p=0.877	t=2.86 <b>p=0.007*</b>	t=3.21 <b>p=0.003*</b>
Cum.	-18.13±3.47	-14.11±3.68	-18.05±3.05	t=0.078 p=0.939	t=3.68 <b>p=0.001*</b>	t=3.55 <b>p=0.001*</b>
<b>GLS</b>	-16.86±0.99	-15.81±1.92	-18.17±0.79	t=4.58 <b>p≤0.001*</b>	t=5.06 <b>p≤0.001*</b>	t=2.18 <b>p=0.036*</b>

GLS: global longitudinal strain

**Table 3. Vessels affection as suspected by speckle tracking**

Coronary ECHO	Unstable angina (n=20)	Non stemi group (n=20)	Control group (n=20)	Test of significance		
				P1	P2	P3
<b>LAD</b>	15 (75.0%)	16 (80.0%)	6 (30.0%)	$\chi^2=8.12$ P=0.004*	$\chi^2=10.1$ P≤0.001*	FET P=1.0
<b>LCX</b>	6 (30.0%)	8 (40.0%)	3 (15.0%)	FET P=0.451	$\chi^2=3.13$ P=0.077	$\chi^2=0.44$ P=0.741
<b>RCA</b>	12 (60.0%)	12 (60.0%)	9 (45.0%)	$\chi^2=0.902$ P=0.342	$\chi^2=0.902$ P=0.342	$\chi^2=0$ P=1
<b>No. of vessels</b>				MC P=0.007*	MC P=0.002*	MC P=0.467
No	0 (0%)	0 (0%)	5 (25.0%)			
One	9 (45.0%)	7 (35.0%)	12 (60.0%)			
Two	9 (45.0%)	9 (45.0%)	3 (15.0%)			
Three	2 (20.0%)	4 (20.0%)	0 (0.0%)			

Concerning 2DSTE validity of in evaluation of stenosis of RCA in unstable angina group, it was good predictor for stenosis of RCA with 100% specificity and 85.7% sensitivity, 100% PPV, 75% NPV and 90% accuracy. Among non-STEMI group, 2D speckle tracking was good predictor for stenosis of RCA with 100% specificity and 85.7% sensitivity, 100% PPV, 75% NPV and 90% accuracy (Table 4).

Concerning 2DSTE validity in detection of stenosis of RCA in unstable angina group, it was good predictor for RCA stenosis with 100% specificity and 85.7% sensitivity, 100% PPV, 75% NPV and 90% accuracy. Among Non STEMI group, 2DSTE was good predictor for RCA stenosis with 100% specificity and 85.7% sensitivity, 100% PPV, 75% NPV and 90% accuracy (Table 4).

Concerning 2DSTE validity in detection of LCX stenosis in unstable angina group, it was good predictor for LCX stenosis with 100% specificity and 75% sensitivity, 100% PPV, 85.7% NPV and 90% accuracy. Among Non STEMI group, 2DSTE was good predictor for LCX stenosis with 100% specificity and 72.7% sensitivity, 100% PPV, 75% NPV and 85% accuracy (Table 4).

Concerning the validity of 2DSTE in identification of number of coronary arteries with stenosis in unstable angina group as compared to coronary angiography, it was good predictor for multivessels disease with 95% total accuracy, then for single vessels disease with 85% total accuracy and finally for double vessel disease stenosis with 80% accuracy as shown in table.

**Table 4. Validity of speckle tracking in detection of LAD, LCX and RCA compared to coronary angiography**

Speckle tracking (LAD)	Unstable angina			Non-STEMI		
	Coronary angiography Positive	Coronary angiography Negative	Total	Coronary angiography Positive	Coronary angiography Negative	Total
Positive	14	1	15	16	0	16
Negative	2	3	5	2	2	4
Total	16	4	20	18	2	20
Validity tests						
Sensitivity	87.5%			88.9%		
Specificity	75%			100%		
PPV	93.3%			100%		
NPV	60%			50%		
Accuracy	85%			90%		
Speckle tracking (LCX)						
	Coronary angiography	Total		Coronary angiography	Total	
Positive	6	0	6	8	0	8
Negative	2	12	14	3	9	12
Total	8	12	20	11	9	20
Validity tests						
Sensitivity	75%			72.7%		
Specificity	100%			100%		
PPV	100%			100%		
NPV	85.7%			75%		
Accuracy	90%			85%		
Speckle tracking (RCA)						
	Coronary angiography	Total		Coronary angiography	Total	
Positive	12	0	12	12	0	12
Negative	2	6	8	2	6	8
Total	14	6	20	14	6	20
Validity tests						
Sensitivity	85.7%			85.7%		
Specificity	100%			100%		
PPV	100%			100%		
NPV	75%			75%		
Accuracy	90%			90%		

PPV: positive predictive value, NPV: Negative predictive value

Among non-STEMI group, 2D speckle tracking was good predictor for multivessels disease with 95% total accuracy, then for single vessels disease with 80% total accuracy and finally for double vessel disease stenosis with 75% accuracy as shown in table (Table 5).

The best cut-off value considering GLS in in prediction of unstable angina severity was -16.69 with 85% sensitivity and 70% specificity, 73.9% PPV, 82.3% NPV and 77.5% accuracy Fig. 2. The best cut-off value considering GLS in in evaluation of severity of Non STEMI was -15.7

with 90% sensitivity and 70% specificity, 75% PPV, 87.5% NPV and 80% accuracy Fig. 3.

#### 4. DISCUSSION

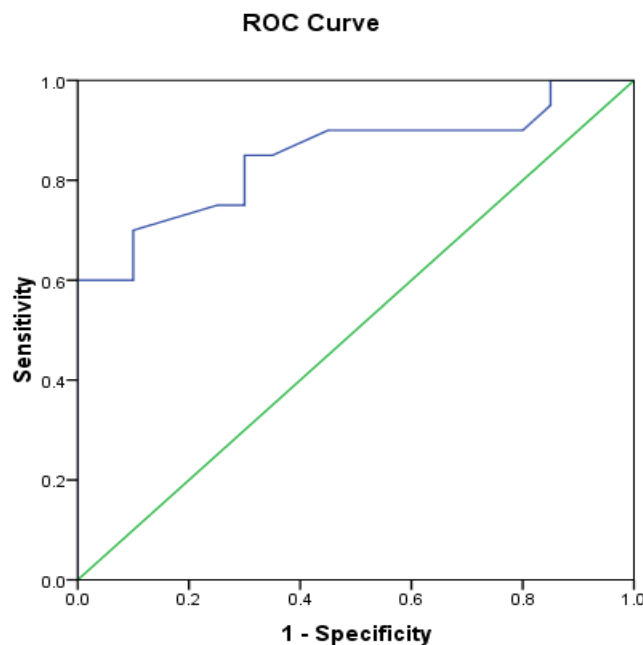
##### 4.1 Demographic Data and Risk Factors

Mean age in unstable angina group was 50.25±8.34 as compared to 54.65±8.39 in control group and 51.00±7.61 in non-STEMI with no statistically significant difference p value >0.05.

**Table 5. Validity of speckle tracking in detection of number of stenosis vessels compared to coronary angiography**

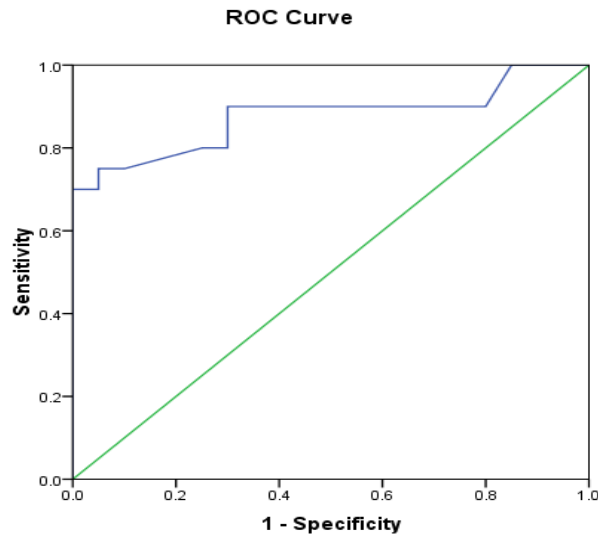
Speckle tracking (No of vessels)	Unstable angina			Non STEMI		
	Coronary angiography			Coronary angiography		
	Single	Double	Three	Single	Double	Three
Single	6	3	0	3	4	0
Double	0	8	1	0	8	1
Three	0	0	2	0	0	4
Validity tests						
Sensitivity	100%	72.7%	66.7%	100%	66.7%	80%
Specificity	78.6%	88.9%	100%	76.5%	87.5%	100%
PPV	66.7%	88.9%	100%	42.8%	88.9%	100%
NPV	100%	72.7%	94.4%	100%	63.6%	93.7%
Accuracy	85%	80%	95%	80%	75%	95%

PPV: positive predictive value, NPV: Negative predictive value



**Fig. 2. ROC curve for prediction of unstable angina by GLS**





**Fig. 3. ROC curve for prediction of Non-STEMI by GLS**

Smokers represent (15 %, 10%, 20%), HTN (50%, 55%, 50%), dyslipidemia presented in (60%, 50% 55%) and history of ACS (55%, 50%, 30%) in unstable angina, non-STEMI and control groups, respectively with no statistically significant difference.

Mean BMI was statistically significantly higher in unstable angina and non-STEMI groups  $33.10 \pm 4.50$ ,  $32.24 \pm 4.56$  as compared to  $27.97 \pm 4.63$  in control group

In concordance to our results *Liszka et al.*, founded that there is no significant correlation between the studied population as regarding demographic data, hypertension, smoking and dyslipidemias [7].

In contrary to our results, Conte et al. [8] who assessed the degree of dysfunction of longitudinal fibers using STE in obese and diabetic cases and reported decrease in GLS in those cases.

Also, *Rostamzadeh et al.*, reported that of conventional risk factors, hypertension (67%) and DM (55%) were more common in the studied population. There was a trend toward the ACS group to have more patients with dyslipidemia when compared with the normal and low-risk groups ( $P=0.063$ ) [9].

#### 4.2 Conventional Echo Parameters

Our study showed that the mean LVESD was  $3.41 \pm 0.51$ ,  $3.43 \pm 0.47$ , mean LVEDD was

$5.06 \pm 0.62$ ,  $5.00 \pm 0.64$ , mean LVEF was  $60.47 \pm 4.71$ ,  $59.00 \pm 4.23$ , mean PWD was  $1.11 \pm 0.13$ ,  $1.13 \pm 0.12$ , mean IVS was  $0.99 \pm 0.15$ ,  $1.02 \pm 0.17$  in unstable angina and non-STEMI groups.

*Şahin et al* indicated a significant difference in EF percent between the study population with preserved coronary flow and the study group with impaired coronary flow in 880 consecutive patients receiving coronary intervention [10].

In a trial by *Liszka et al*, they informed that the baseline examination revealed significantly larger LVEDD and lower LVEF in ACS group (high risk group) compared to stable angina group (low risk group) [7].

#### 4.3 2D Speckle Tracking Parameters

A statistically significant correlation between presence of obstructive CAD and decreased values of the GLS by coronary angiography with a cutoff value of  $-16.69$ ,  $-15.7$  in unstable angina and non-STEMI group lower than those non-diabetics, it could be explained by the prevalence of diabetes in 100% of the population of our study and the fact that diabetes is an independent risk factor for decreased LV GLS. Due to the presence of DM, the strain's projected cut-off point would be thrown off. That is why, in the current investigation, GLS was compared at rest in two identical groups with no statistically significant difference in DM prevalence or duration.

H.ZUO et al. [8] previously discovered that CAD patients with DM had significantly lower global and segmental longitudinal strains than patients without DM, as well as a decreased specificity and sensitivity across the study, but particularly in those with DM (sensitivity and specificity (61.1 percent and 52.9 percent, respectively) with a cutoff point of GLS at rest of 17.15 percent vs. 18.35 percent in patients without DM. GLS at rest had an AUC of 0.67 and a P value of 0.048 in patients with diabetes mellitus. Later that year, H.ZUO et al. revealed that the cutoff for serious CAD in non-DM patients was 19.05 percent (higher than previously) with a higher accuracy in diagnosis.

In agreement with our findings, J. Schroeder et al. reported that cutoff values of LVGLS > -18.8 percent had a high sensitivity and specificity (86 and 73%, respectively) for evaluating patients with chest pain and inconclusive electrocardiographic (ECG) and blood test results for significant coronary stenosis [11].

In concordance to our results, Maria Concetta Pastore et al. showed that ability of LVGLS to detect CAD, showing satisfactory results for this noninvasive marker. The mean values of LVGLS for those with and without CAD were -16.5% [95% confidence interval (CI): -15.8% to -17.3%] and -19.7% [95% CI: -18.8% and -20.7%]. Moreover, abnormal LVGLS detected moderate-to-severe CAD with a pooled 74.4% sensitivity, 72.1% specificity [12].

*Madhavan et al.*, stated that in female patients with effort angina, GLS by 2DSTE strongly correlates with severity of CAD angiography and can evaluate substantial coronary lesions with a sensitivity of 94% and specificity of 76%. Thus, GLS by 2DSTE can be utilised as a noninvasive screening test for substantial coronary artery stenosis and can be used in conjunction with TMT for risk stratification and patient selection for coronary angiography [13].

This finding was in line with *Deep Chandh et al* hypothesis who reported that longitudinal myocardial deformation is of a good predictive value for diagnosis of obstructive CAD [14].

Radwan and Hussein [15] also informed that measurements of GLS by 2DSTE is a sensitive & specific technique for evaluation of severity and presence of obstructive CAD in diabetic patients.

Moustafa et al. [16] and Hubbard et al. [17] also reports that cases with normal LV function on 2D echocardiography at rest but significant CAD angiographically could be identified by lower GLS values in STE.

Also, Farokhnejad's et al. [18] opinions were favourable to our findings about the role of STE-derived deformation parameters in diagnosing coronary artery stenosis in diabetic individuals with chronic stable angina. .

Also, in agreement with us Huang et al. [19] informed that GLS changes of LV aid in early diagnosis coronary atherosclerotic disease in high-risk patients.

Additionally, we discovered a positive connection between global longitudinal strain of the LV as determined by speckle tracking and HBA1C with a p value of 0.042.

Findings of *Rostamzadeh et al.*, concurred with our findings and indicated that left ventricle GLS had a significant correlation with CAD severity [9].

This was also described by Motgomery, *et al* who correlated values of AGS with coronary angiography and discovered that they can help in identification of patients with normal coronary arteries [20].

Radwan and Hussein, et al disagreed with our findings and reported that global strain is not a good negative test to exclude existence of obstructive CAD [15].

We found that LV longitudinal strain showed a high specificity and sensitivity for the single vessel CAD diagnosis (100% and 86%, respectively) in unstable angina group and (100%, 76.5%, respectively) in non-STEMI group two vessels disease (72.7%, and 88.9%, respectively) in unstable angina group and (66.7% and 87.5%, respectively) in non-STEMI group. For three vessels CAD (66.7%, and 100%, respectively) in unstable angina group and (80%, and 100%, respectively) in non-STEMI group, which similar to other studies [21].

According to the angiographic findings, left circumflex coronary artery (LCX) stenosis was reported in (43.3%) of patients, and RCA stenosis was reported in (66.6%) of patients and left anterior descending coronary artery (LAD) stenosis was reported in (86%) of patients

whereas Montgomery et al. found stenosis in the LAD only (21%), LCX only (9%) and (7 %) [22].

While in Moustafa et al, (43%) had LCX, (61.7%) had LAD , and (40.5%) had the RCA disease [15].

The longitudinal strain revealed that there was a good performance in evaluation of LAD stenosis with high sensitivity, fair specificity and high accuracy (87.5%, 75%, and 85%; respectively) in unstable angina group and high sensitivity, high specificity and high accuracy (88.9%, 100%, and 90%; respectively). Regarding RCA stenosis, 2-D LV longitudinal strain had a sensitivity of (85.7%), specificity of (100%) and accuracy of (90 %). LCX artery stenosis (sensitivity 75%, specificity 100%, and accuracy 90%) in unstable angina group and (sensitivity 72.7%, specificity 100%, and accuracy 85%) in non-STEMI group. Additionally, this trial showed the longitudinal strain validity in the identification of stenosis in different number of coronary arteries.

This relationship between the reduction of segmental longitudinal strain values by STE and the location of coronary artery lesion as determined by coronary angiography is also declared [16].

While Vrettos et al. found that the systolic strain had the highest specificity for detecting obstructive CAD in the LAD, it is followed by the RCA and LCX strains [23].

*Fang et al*, using tissue Doppler imaging reported that augmentation of radial function in diabetic patients was used to compensate the reduced longitudinal function [24].

According to Nakai et al., univariate analysis demonstrated that a decrease in GLS was significantly linked with the duration of diabetic disease ( $P = 0.0006$ ). There was no correlation between the decrease in GS and either fasting blood glucose ( $P = 0.7489$ ) or glycosylated hemoglobin ( $P = 0.7524$ ). A multivariate linear regression analysis revealed that the duration of diabetes was the sole significant predictor of LS decrease ( $t = 2.22$ ,  $P = 0.0313$ ) [25].

The findings contribute to our understanding of the connection between CAD and GSL and support the clinical utility of STE in coronary angiography assessment.

## 5. CONCLUSIONS

In conclusion, we found that speckle tracking is effective in predicting presence of CAD in diabetic female patients with acute chest pain and in prediction of vessels' affected based on the affected segments distribution in longitudinal strain by GLS. In addition, it can be used for patients with acute coronary syndrome as non-invasive test..

## DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

## CONSENT AND ETHICAL APPROVAL

Written informed consent was obtained from all participants. The trial was approved by ethics committee of faculty of medicine Tanta University.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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