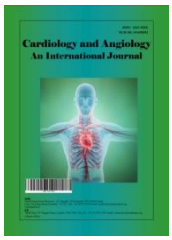

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Speckle Tracking in Acute Non-St Elevation Acute Coronary Syndromes Patients as a Factor of Risk Stratification

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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: Coronary artery disease (CAD) early diagnosis remains a clinical problem in patients with non-ST elevation acute coronary syndrome (NSTE-ACS), especially in the regional wall motion abnormalities' absence on presentation by Echo. This study assessed the relationship between ECG changes and speckle Tracking in subjects with acute NSTE-ACS.
Methods: This prospective trial was performed on 100 subjects with NSTE-ACS. All subjects were subjected to laboratory tests [complete blood picture, renal function test, liver test profile, lipid profile, RBS and cardiac biomarkers (cardiac troponin, creatinine kinase and CK-MB)], 12 lead ECG, Echocardiography (TTE, speckle tracking), Image analysis and coronary angiography.
Results: regarding IVRT, TDI e`, TDI a`**,** a considerable difference between the two groups were found**.** DBP was considerably lower in STD group in comparison with TWI group (P value= 0.047). IVRT, TDI a` and GLS were considerably higher in STD group in comparison with TWI group (P value= 0.024, 0.031, 0.003 respectively).
Conclusions: Speckle tracking could be used as part of standard echo for the examination of individuals suffering from NSTE-ACS.

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Keywords: Speckle tracking echocardiography; non-St elevation; acute coronary syndromes; risk stratification.

1. INTRODUCTION

Worldwide, Ischemic heart disease is the main cause of death. According to the World Health Organization (WHO), more than 1 in 7 fatalities in 2015 were caused by ischemic heart disease [1,2].

Patients with coronary artery disease (CAD) are at risk for nonfatal ischemic episodes that may result in morbidity. In the first year of follow-up, 6.4% of CAD patients were hospitalised for unstable angina (UA) and 4.6% for congestive heart failure in the REACH registry [1,2].

By 2030, it is expected that approximately 20% of the population will be 65 years old and CAD will be contributing to 40% of mortalities. Over the next few decades, With an aging population, the health burden of ischaemic heart disease is expected to grow [1,2].

Acute coronary syndrome (ACS) describes patients with a suspected or confirmed diagnosis of acute myocardial ischemia or infarction. There are three forms of ACS, Non-ST elevation myocardial infarction (NSTEMI), ST-elevation myocardial infarction (STEMI) and UA [3].

The clinical presentation of UA and NSTEMI are comparable, except that by definition the latter is associated with necrosis in the myocardium and has a worse outcome. A marker of necrosis in the myocardium, the apparent incidence of NSTEMI is increasing while that of UA is decreasing as a result of the widespread use of increasingly sensitive troponin assays [3].

Acute myocardial infarction diagnosis and risk stratification mainly rely on echocardiography. In patients with ACS, tools such as tissue Doppler imaging (TDI) and speckle tracking echocardiography (STE), have emerged as newer useful diagnostic and prognostic methods. Their functions in the clinical assessment of NSTEACS patients are now under investigation [4,5].

Speckle tracking is a method that permits for an accurate myocardial motion quantification throughout the cardiac cycle. It identifies distinguishable regions of the myocardium in order to track motion over time, tracing the extent of "myocardial deformation.". Therefore, it may be utilised to diagnose several pathologies. Identifying localised wall motion anomalies due by coronary ischemia is one of the uses. At face value, this appears to be an excellent answer to a challenge we have. Electrocardiograms (ECGs) do not detect all instances of coronary obstruction unfortunately. Also, relying just on the naked eye to detect wall motion anomalies is not very precise. So, when acute coronary syndrome is suspected, STE may be useful as a point-of-care scan to assist identification of individuals who require more urgent revascularization [4,5]. The aim of this work was to assess the relationship between ECG changes and speckle Tracking in patients with acute NSTE-ACS.

2. PATIENTS AND METHODS

This prospective trial was performed on 100 patients aged from 30-70 years old, with acute NSTE-ACS. This trial was done in Cardiology Department.

Exclusion criteria were patient refusal, valvular heart diseases, congenital heart diseases, previous MI, presence of a pacemaker, non-sinus rhythm, severe lung disease, wide QRS complex, pericardial effusion and severe infection.

All subjects underwent: Complete history taking, clinical assessment, tests [complete blood picture, renal function test, liver test profile, lipid profile, RBS and cardiac biomarkers (cardiac troponin, creatinine kinase and CK-MB)], 12 lead ECG, Echocardiography (TTE, speckle tracking), Image analysis and coronary angiography.

2.1 12 lead ECG

With the use of a typical ECG instrument (Hewlett Packard, Page-writer, USA), standard 12-lead resting ECGs were acquired with a paper speed of 25 mm/s.

Transthoracic echocardiography: 2D-speckle tracking imaging, and conventional echocardiographic Doppler study were conducted on all subjects after stabilization, pre coronary intervention and within the first 24 h of the chest pain onset, with the use of Vivid 7, General Electric Healthcare (GE Vingmed, Norway) equipped with harmonic M4S variable frequency phased array transducer and echo Pac software for offline analysis. According to the

guidelines of the American Society of Echocardiography, images were acquired from patients in the left lateral position at end-expiration and a single lead ECG was attached. In the parasternal long- and short-axis views, all standard measurements were obtained; apical 4-chamber, 2-chamber, and apical long axis views. Using M-mode echocardiography, and then using the biplane (modified Simpson method), quantification of the LV dimensions was done. With the use of a 16-segment model, ventricular regional wall motion anomalies' assessment was performed. An experienced cardiologist interpreted the segmental wall motion as normal 1; hypokinetic 2; akinetic 3; and dyskinetic.

2D-speckle tracking echocardiography: at heart rates that were roughly comparable, longitudinal strain imaging by 2D-STE was performed with high quality ECG gated images from the apical four-chamber, two-chamber and three-chamber views. The gain settings were adjusted. For the LV image to occupy most of the image sector, the depth was reduced. Care was taken to prevent LV foreshortening., the gray-scale framerate was kept between 50 and 90 frames/s; each loop had a minimum of three cardiac cycles. To prevent any breathing artifacts, all photos were captured without breathing. In cine-loop format, all images were stored and using the Echopac Software (Echo-Pac version 7.0.0 (GE Vingmed)), data were transferred to a workstation for further offline analysis. Using Pulsed wave Doppler, LV inflow (mitral) and outflow (aortic) velocities were measured for measuring cardiac events' timing.

Coronary angiography was conducted on clinical indication with the use of digital imaging acquisition and storage by standard (Judkins) technique. Revascularization was conducted on clinical indication but was not part of the trial protocol. Complete revascularization was attempted in accordance with current recommendations. Cine loops in multiple angles were stored, and by a single experienced invasive cardiologist, all analyses were conducted retrospectively, blinded to the echocardiographic analyses' results. Thrombolysis in Myocardial Infarction flow (TIMI flow) was noted, and acute occlusion was defined as TIMI flow 0 or 1. Angiographic appearance was used to distinguish between acute and chronic complete occlusions (thrombus, collaterals, and calcification), and the ease of crossing a guide wire.

2.2 Statistical Analysis

A statistical application called SPSS version 22 was used to collect, tabulate, and analyse all of the information (SPSS Inc. Chicago, IL, U.S.A). The Shapiro-test Wilk's was performed to evaluate whether the data were in the normal distribution or not. Mean and standard deviation (SD) were recorded, and paired Student's T-tests were used to compare data from the same group. Use frequency and percentages to express qualitative aspects of the data (percent). Chi square test and Fisher exact tests were used to compare the differences between qualitative variables. Statically significant was considered at P value < 0.05.

3. RESULTS

DBP was considerably lower in STD group in comparison with TWI group (P value= 0.047). IVRT, TDI a` and GLS were considerably higher in STD group in comparison with TWI group (P value= 0.024, 0.031, 0.003 respectively). TDI e` was considerably lower in STD group in comparison with TWI group (P value= 0.039).

High-risk group had significantly higher subtotal occlusion occurrence compared to low-risk group (P value <0.001). The occurrence of non-significant lesion was considerably lower in high-risk group in comparison with low-risk group (P value <0.001).

Single and multivessel were considerably different between both groups (P value <0.001). High-risk group has significantly higher STD and TWI, GLS values than low-risk group (P value= 0.025 and <0.001 respectively. GLS was considerably higher in STD group than TWI group in both high and low risk groups. SBP, DBP, smoking, hypertension (HTN), dyslipidaemia, and familial predisposition for CAD were considerably higher in high-risk group in comparison with low-risk group (P value <0.05). LVEDD and LVEF were considerably lower in high-risk group in comparison with low-risk group (P value = 0.009, 0.042 respectively). LVEDS and GLS were considerably higher in high-risk group in comparison with low-risk group (P value= 0.047, <0.001 respectively).

Table 1. Demographic data, comorbidities distribution, laboratory parameters, structure characteristics, systolic and diastolic functions of the studied patients (n = 100)

Variable		Patients (n=100)
Age (years)		46.87 ± 7.75
Sex	**Male**	75 (75%)
	Female	25 (25%)
BMI (kg/m^2)		26.33 ± 4.54
SBP (mmHg)		126.7 ± 9.49
DBP (mmHg)		72.6 ± 7.64
Smoking		46 (46%)
Current smoker		37 (37%)
Previous smoker		9 (9%)
Hypertension		35 (35%)
Diabetes mellitus		23 (23%)
Dyslipidemia		30 (30%)
Familial predisposition for CAD		57 (57%)
Hemoglobin (g/dL)		13.25 ± 1.42
RBS (mg/dL)		107.96 ± 31.52
TC (mg/dL)		188.97 ± 39.68
LDL (mg/dL)		108.59 ± 27.56
Troponin T (ng/L)		393.88 ± 195.26
LVEDD (cm)		49.59 ± 4.02
LVEDS (cm)		33.6 ± 4.32
IVS (cm)		11.27 ± 0.299
PW (cm)		11.54 ± 0.516
Mitral E-wave (cm/s)		72.01 ± 21.1
Mitral ea-ratio		1.15 ± 0.157
IVRT (cm/s)		127.05 ± 26.14
TDI e` (cm/s)		1.01 ± 0.079
TDI a` (cm/s)		1.11 ± 0.135
LVEF (%)		59.04 ± 8.02
TDI s` (cm/s)		-1.1 ± 0.067
GLS (cm/s)		-15.41 ± 2.41

BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CAD: Coronary artery disease, RBS: Random blood sugar, TC: Total cholesterol., LDL: Low density lipoprotein, LVEDD: Left ventricular end diastolic diameter, IVS: Interventricular septum, PW: Pulsed wave, IVRT: Isovolumic relaxation time, TDI: Tissue doppler imaging, LVEF: Left ventricular ejection fraction, GLS: Global longitudinal strain

Table 2. Demographic data, systolic and diastolic parameters between the two studied groups

Variable	STD (n=40)	TWI (n=60)	p
Age (years)	46.5 ± 7.73	47.12 ± 7.83	0.699
BMI (kg/m^2)	26.73 ± 4.64	26.07 ± 4.49	0.476
SBP (mmHg)	126.25 ± 9.66	127.12 ± 9.44	0.701
DBP (mmHg)	70.75 ± 7.29	73.83 ± 7.67	0.047
Mitral E-wave (cm/s)	68.93 ± 21.39	74.07 ± 20.83	0.234
Mitral ea-ratio	1.13 ± 0.163	1.17 ± 0.153	0.213
IVRT (cm/s)	131.72 ± 25.68	123.05 ± 26.64	0.024
TDI e` (cm/s)	0.831 ± 0.658	1.01 ± 0.078	0.039
TDI a` (cm/s)	1.15 ± 0.138	1.09 ± 0.132	0.031
LVEF (%)	57.85 ± 8.37	59.83 ± 7.75	0.228
STE global s` (cm/s)	-1.11 ± 0.069	-1.09 ± 0.066	0.183
GLS (cm/s)	-13.89 ± 3.13	-15.63 ± 2.52	0.003*

BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, IVRT: Isovolumic relaxation time, TDI: Tissue doppler imaging, LVEF: Left ventricular ejection fraction, STE: Speckle tracking echocardiography, GLS: Global longitudinal strain

Table 3. Relationship between ECG findings and risk stratifications regarding coronary angiography results, GLS, comparison and Echocardiographic parameters of the studied groups according to risk assessment

		High risk (n=64)		Low risk (n=36)		p
		STD	TWI	STD	TWI	
C.A	**Total**	3 (4.7%)	3 (4.7%)	1 (2.8%)	1 (2.8%)	0.921
	Subtotal	26 (40.6%)	30 (46.9%)	4 (11.1%)	5 (13.9%)	<0.001*
	Non-significant lesion	1 (1.6%)	1 (1.6%)	12 (33.3%)	13 (36.1%)	<0.001*
Single vessel		10 (15.6%)	14 (21.9%)	12 (33.3%)	14 (38.9%)	<0.001*
Multi vessel		20 (31.3%)	20 (31.3%)	5 (13.9%)	5 (13.9%)	
GLS						
STD		-10.03 ± 2.95		-14.68 ± 3.08		0.025*
TWI		-12.47 ± 3.33		-15.96 ± 2.14		<0.001*
Age (years)		48.17 ± 7.86		46.13 ± 7.69		0.212
BMI (kg/m^2)		27.2 ± 4.78		26.43 ± 3.41		0.397
SBP (mmHg)		132.51 ± 6.04		119.45 ± 4.39		0.000
DBP (mmHg)		73.85 ± 7.65		70.8 ± 6.93		0.045
Smoking		35 (54.7%)		11 (30.6%)		0.020
Hypertension		28 (43.8%)		7 (19.4%)		0.014
Diabetes mellitus		18 (28.1%)		5 (13.9%)		0.105
Dyslipidemia		27 (42.2%)		3 (8.3%)		0.000
Familial predisposition for CAD		51 (79.7%)		6 (16.7%)		0.000
LVEDD (cm)		46.91 ± 5.03		49.44 ± 3.69		0.009
LVEDS (cm)		29.49 ± 4.62		27.87 ± 3.35		0.047
IVS (cm)		11.28 ± 0.453		11.27 ± 0.454		0.916
PW (cm)		11.55 ± .502		11.53 ± 0.506		0.849
Mitral E-wave (cm/s)		69.47 ± 19.75		71.19 ± 23.59		0.698
Mitral ea-ratio		1.12 ± 0.151		1.15 ± 0.169		0.363
IVRT (cm/s)		129.77 ± 23.07		125.78 ± 31.19		0.468
TDI e` (cm/s)		1.004 ± 0.077		0.999 ± 0.085		0.765
TDI a` (cm/s)		1.14 ± 0.132		1.1 ± 0.142		0.160
LVEF (%)		58.72 ± 8.65		62.25 ± 7.38		0.042
STE global s` (cm/s)		-1.097 ± 0.066		-1.099 ± 0.071		0.888
GLS (cm/s)		-11.09 ± 0.83		-15.69 ± 1.72		<0.001

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CAD: Coronary artery disease, LDL: Low density lipoprotein, LVEDD: Left ventricular end diastolic diameter, IVS: Interventricular septum, PW: Pulsed wave, IVRT: Isovolumic relaxation time, TDI: Tissue doppler imaging, LVEF: Left ventricular ejection fraction, GLS: Global longitudinal strain, CA: Coronary angiography, STD: ST-segment depression, TWI: T-wave inversion

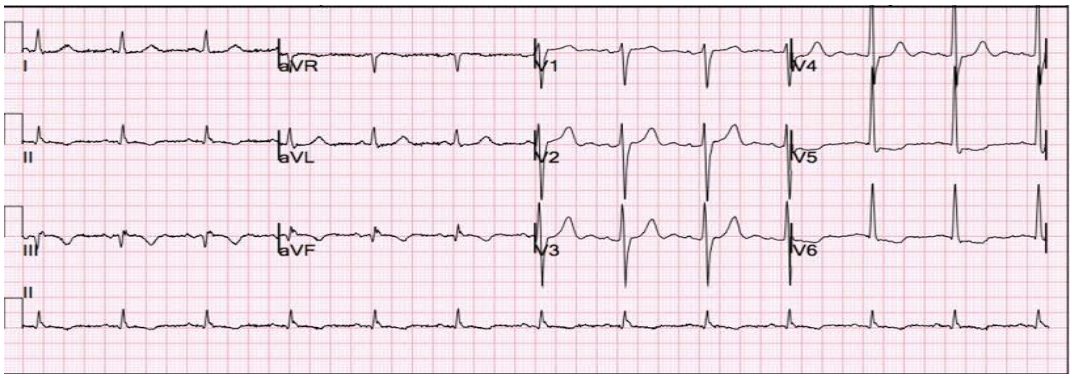


Fig. 1. ECG: T wave inversion II, III, AVF, V5, V6

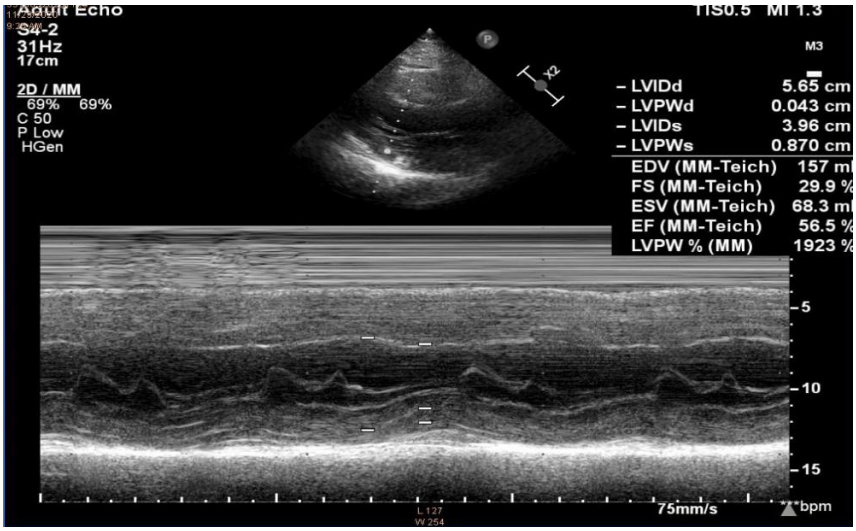
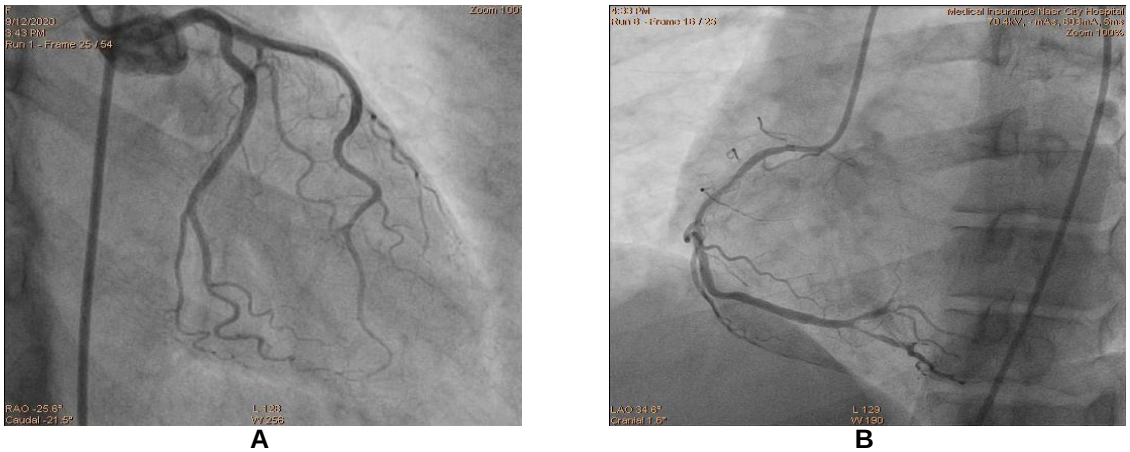


Fig. 2. Echocardiography: EF56%. MILD MR, diastolic dysfunction grade, no SWMA at rest.



A **B**

Fig. 3(A-B):2D. speckle tracking: Showing inferior wall hypokinesia, infero septal hypokinesia

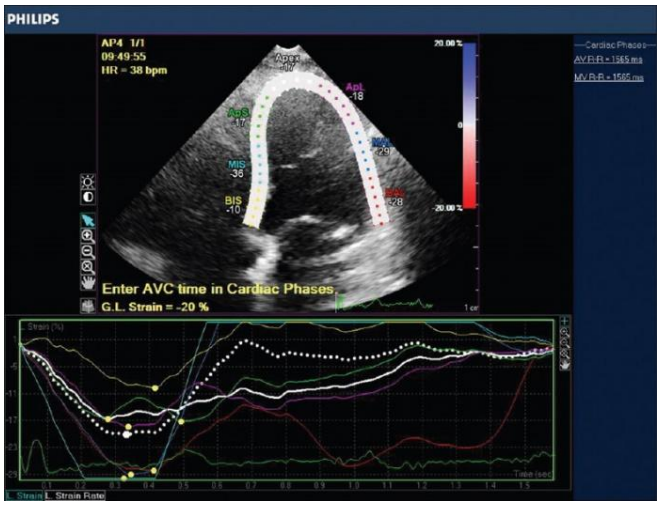


Fig. 4. Coronary angiography: significant lesion in PDA

The patient medical history started 3 months ago with exertional chest pain then the patient was quite well on medical treatment, one hour ago she suffered acute chest pain not relieved by medical treatment and more than she used to experience before, then ECG was done, cardiac enzymes was done, 2D echocardiography speckle tracking was done, angiography was done which approved the diagnosis by 2D speckle tracking.

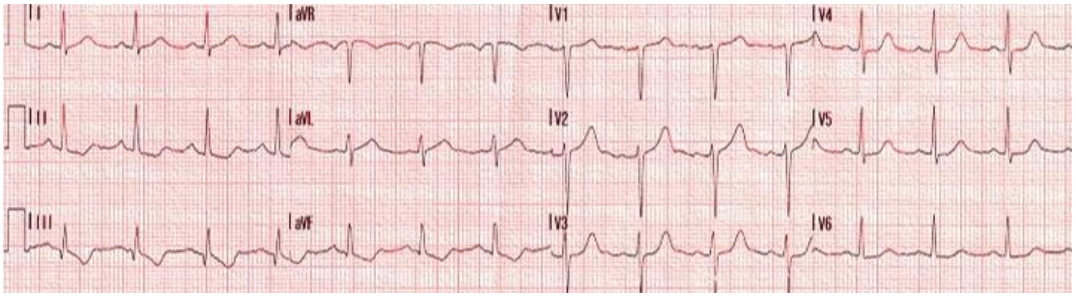


Fig. 5. ECG

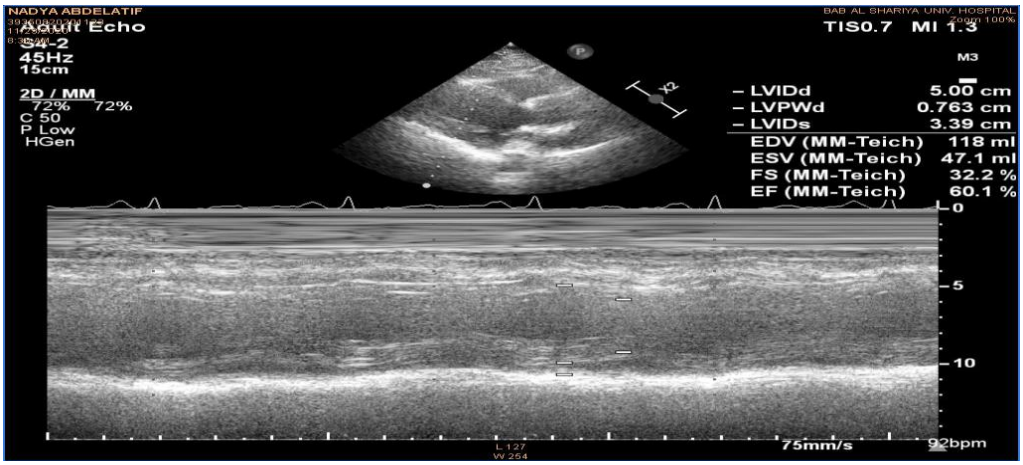
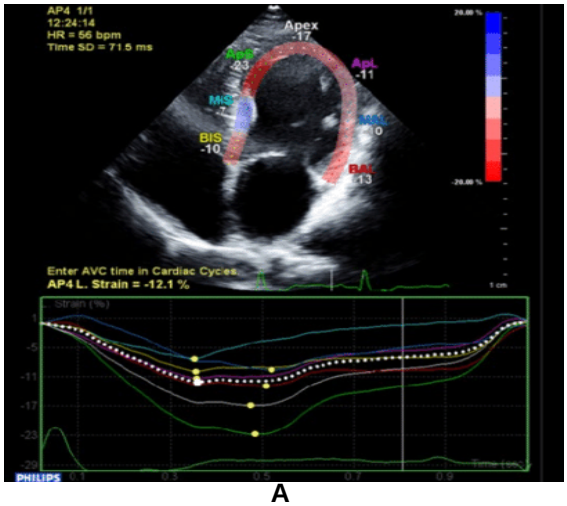
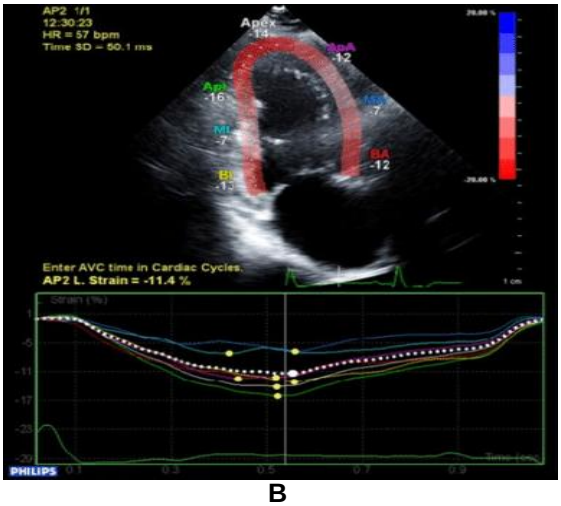


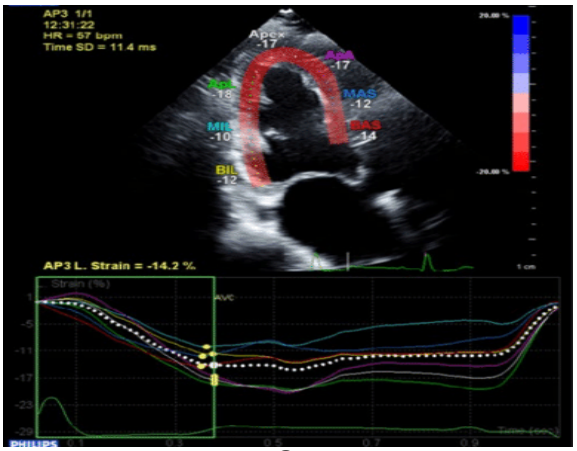
Fig. 6. 2D- Echocardiography



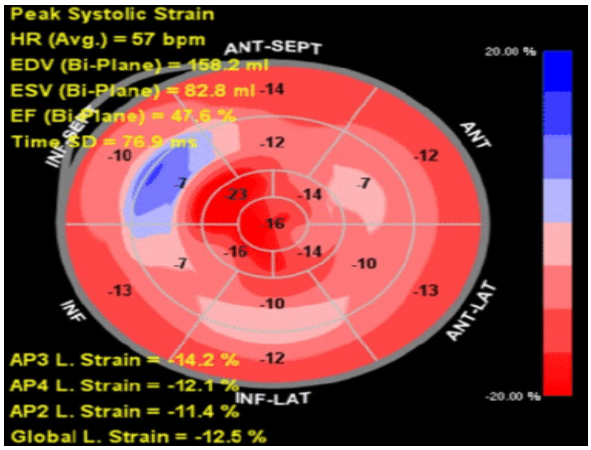
A



B

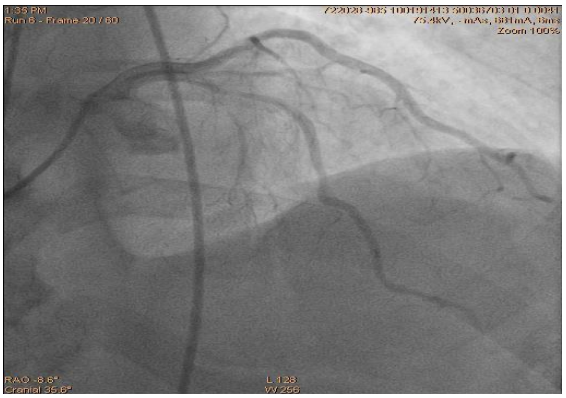


C

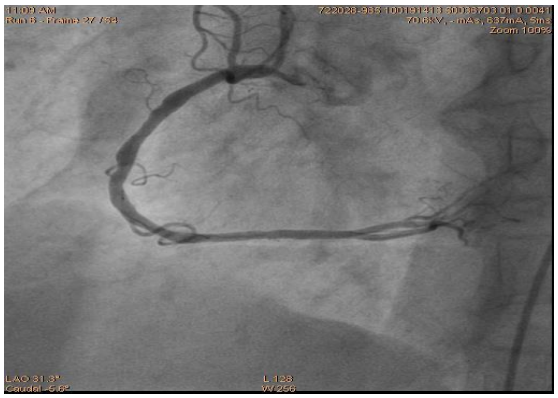


D

Fig. 7(A-D). 2D speckle tracking



A



B

Fig. 8(A-B). Coronary angiography: significant proximal LAD lesion and non significant mid RCA lesion

A 65-year-old female presented to the emergency department with a complaint of chest painon the left side radiating to her left arm. No relieving factors were found. Her previous medical history included HTN, hyperlipidemia, and uncontrolled diabetes mellitus. Any bad habits were denied. 2 city blocks were her baseline exercise tolerance due to fatigue. She had stable vital signs and not impressive physical examination upon presentation. With the use of sublingual nitroglycerin, chest pain was partially relieved. The 12-lead ECG revealed ST depression in the inferior leads. Subsequently, for further evaluation and observation, she was admitted. Her serial cardiac biomarkers were negative.2D speckle tracking and coronary angiography were conducted.

4. DISCUSSION

Our trial agreed with trial of Helmy et al. [6] as they reported that of 133 patients included, 113 (85%) were males and 20 (15%) females. The mean age (+ SD) was 48.8 (+ 12.1) years for both males and females.

In the trial of Keddeas et al. [7], the mean age of the studied subjects was 56.3 ± 9.66 years, and with a range of 31 - 80 years. 21.7% were females and 78.3% of them were males.

Our results were supported with study of Helmy et al. [6] as they reported that 39% of their studied group were hypertensive, 50% of them were diabetics and 47% of them were smokers.

In the study of Tuohinen et al. [8], among their studied cases 45% were hypertensive, 20% of them were diabetics and 30% of them were smokers.

The current study showed that the mean of LVEDD was 49.59 ± 4.02 cm. The mean of

LVEDS was 33.6 ± 4.32 cm. The mean of IVS was 11.27 ± 0.299 cm. No considerable variation between the two groups regarding any of structure parameters was found.

Our results were supported by study of Keddeas et al. [7], as they demonstrated that no considerable variation between the two groups regarding LV dimensions was found. However, in the study of Tuohinen et al. [8], in comparison with subjects without TWI, subjects with TWI had lower left ventricular ejection fraction (LVEF), (57 ± 6% vs 71 ± 4%, p = 0.008).

In the present study, as regard Diastolic function parameters; the mean Mitral E-wave (cm/s) was 72.01 ± 21.1. The mean TDI e` (cm/s) was 1.01 ± 0.079. The mean TDI a` (cm/s) was 1.11 ± 0.135. As regard Systolic function parameters, the mean LVEF (%) was 59.04 ± 8.02. The mean STE global s` (cm/s) was -1.1 ± 0.067. The mean GLS (cm/s) was -15.41 ± 2.41. Considerable variation between the two groups regarding IVRT, TDI e`, TDI a` and GLS was found.

Our results were supported by Tuohinen et al. [8], as they stated that in the STE analysis, when compared with subjects without STD, subjects with STD had prolonged IVRT, lower global early diastolic velocity (e′). STD revealed association with diabetes (r = −0.452, p = 0.045), smoking, and with IVRT. IVRT and e′ had independent correlation with STD presence worldwide. Regional differences revealed independent correlations with e′ and STD.

Information featuring the clinical roles of the novel echo modalities in CAD are emerging. STE-derived strain is correlated with global left ventricular (LV) function and has predictive significance in subjects with acute STEMI, according to many studies including a recent meta-analysis [9]. However, scarce data on NSTACS patients are found. They are unaware of any prior research that has examined ECG and echo parameters using more recent imaging techniques. Due to the significant proportion of NSTEMI subjects with a completely obstructed culprit artery and the ECG's inadequacies in identifying this subgroup, it is crucial to detect these patients with alternative techniques used for diagnosis such as echocardiography [10]. For LV dyssynchrony, STE may be a more sensitive discriminator than TDI, according to research including 40 NSTEMI subject with maintained LV function [11].

Grenne et al. [12] performed a trial including 111 subjects with suspected NSTEMI who had an echocardiogram within 1 h (median value; IQR 0.5–4 h) of admittance, 23% had non-coronary chest pain, , 16% diagnosed with unstable angina, and 61% diagnosed with NSTEMI. Territorial systolic strain, calculated by averaging all segmental peak systolic strain values in each territory in the 16-segment LV model, showed to be the most accurate approach for detecting acute complete obstruction. A territorial circumferential strain value N-10% demonstrated a 90 % sensitivity and an 88 % specificity for identifying a completely blocked culprit artery.33% of patients with an obstructed culprit artery and 31% of individuals with non-occluded culprit artery had symmetrical TWI.

Eek et al. [13] found that NSTE-ACS subjects with coronary artery obstruction, compared to patients without, had reduced GLS. subjects with acute coronary obstruction might be identified by an area of 4 alongside segments with a LS > -14%. They found that speckle tracking derived global strain had a highly considerable correlation in presence of complete obstruction prediction, its sensitivity in coronary artery obstruction detection in NSTE- ACS was 67% and specificity was 71%, the NPV was 0.87 and PPV was 0.38 at cutoff −16.3%. They also stated that functional risk area (number of segments with reduced strain) can anticipate complete obstruction presence, the sensitivity and specificity of number of segments with reduced strain in coronary artery obstruction detection in NSTEACS were 85% and 70% respectively, and the NPV and PPV were 0.44, and 0.38 respectively at cut off 4 segments.

According to ElRabaat et al. [14], there was high considerable variation between cases with cardiac event and those without as regard GLS.

Kuznetsova et al. [15], observed that GLS was considerable predictor of cardiovascular - fatal and nonfatal - events. D'Andrea et al. [16], concluded that the mean strain obtained in all LV segments (global longitudinal strain) is a credible predictor of LVR (≥ 15% increase in LV EDV at 6 months after AMI) with a specificity of 87.8% and sensitivity of 84.8%. LVR was correlated to 4-chamber and 2- chamber global peak longitudinal strain and parasternal short-axis global circumferential strain at 20- month follow-up trial by Hung et al. [17].

Furthermore, Helmy et al. [6], demonstrated that global longitudinal strain was considerably less in the control group (-20.4%), in comparison with CAD (-15.31%), P < 0.001. It was also lower in subjects with nonsignificant CAD, compared to those with CAD (P < 0.05). GS was comparable in the control group and those with non-significant CAD. Correlation between GLS and significant CAD was done in all patients. Using ROC curve; the most useful cutoff value of the global strain (GLS) to detect a lesion was -18.7%, with a sensitivity of 83.5% and a specificity of 69.4%. Correlation between GLS and significant CAD was done in subjects with single-vessel disease (SVD) and multi-vessel disease (MVD). Using a cutoff value of -18.7% for the GLS, the sensitivity and specificity were 80% and 81.5% for SVD, respectively. By contrast, these were 87% and 82% for MVD, respectively.

Multiple factors are possibly the cause of TWI, STD in NSTEMI. TWI has been related to positive prognosis in STEMI patients due to an open infarct-related artery and restored blood flow. However, in late-presenting patients, STD has also been coupled with obstructed culprit artery and worse outcome in the short-term. Interestingly, 20% of subjects presenting with NSTEMI and single-vessel illness had a completely blocked culprit artery, according to the findings of a recent research with a large sample size. Additionally, 25% of NSTEMI patients experienced transmural infarction, according to cardiac magnetic resonance imaging (CMR) data [10].

Therefore, it can be possible that MI patients admitted late may have passed the first stage that shows ST elevation and only show “post-ischemic” STD on the ECG. It is probable that, with therapeutic interventions, quick restoration of normal function of the myocardium is not accomplished in these patients, and different degrees of myocardial edema and stunning may develop instead. Indeed, in a small trial conducted on a sub-type of NSTEMI with TWI – “Wellens' syndrome” – the subjects showed the presence of myocardial edema on cardiac CMR [18].

5. CONCLUSIONS

Speckle tracking can be considered as part of standard echo routine for the examination of individuals with acute non-St elevation ACS. Also, it is a non-invasive technique to detect complete obstruction early in order to identify patients who may benefit from early reperfusion.

CONSENT AND ETHICAL APPROVAL

The patients' informed written consent was acquired. The trial was done following approval from the Ethical Committee from Faculty of Medicine, Tanta University and Institutional Research Board (IRB).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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