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Usefulness of Layer Specific Speckle Tracking 2-Dimensional Echocardiography as A Risk Stratifying Tool in Non St Elevation-Acute Coronary Syndrome

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ABSTRACT

Background: Individual risk stratification should influence the scheduling of invasive coronary angiography and revascularization in NSTE-ACS patients; the importance of risk scores as prognostic evaluation tools in NSTE-ACS patients is obvious. **Aim of the work:** To investigate the hypothesis that layer specific speckle tracking echocardiography (LS-STE) can be a useful risk stratifying tool in NSTE-ACS. **methods:** All patients were subjected to a thorough medical history, a thorough clinical examination, a 12-lead ECG, and a high-sensitivity troponin T test (hs-TnT). On admission, the TIMI risk score for UA/NSTMI was assessed and all patients suspected of NSTE-ACS underwent transthoracic echocardiography, which included 2-dimensional speckle tracking echocardiography (2D-STE). The LS-STE and GLS (global longitudinal strain) were determined. The SYNTAX Score (Synergy Between PCI with Taxus and Cardiac Surgery) was estimated. **Results:** There was a positive correlation between longitudinal strain endomyocardiam (LSEN) with both TIMI score and SYNTAX score**,** Patients were divided into two groups based on their syntax scores: group I with SYNTAX score more than or equal one and group II with SYNTAX score zero. The mean LVEF was higher in group II while the mean GLS and the mean LSEN were higher in group I, and both the mean MAX. hs-TnT/24hrs and the percentage of patients with positive hs-TnT were higher in group I. **Conclusions:** In NSTE-ACS patients, LS-STE and GLS might be employed as a risk stratification to ol.

Keywords: Non ST elevation MI, layer specific longitudinal strain, SYNTAX score, risk stratification

INTRODUCTION

Acute coronary syndromes (ACS) and mortality are among the clinical manifestations of CAD, which range from silent ischemia to stable angina pectoris. There are two forms of ACSs: NSTE-ACS and ST–segment elevation myocardial infarction (STEMI). Individual risk stratification should influence the scheduling of invasive coronary angiography and revascularization in NSTE-ACS patients; the importance of risk scores as prognostic evaluation tools in NSTE-ACS patients is obvious. **[1]**

In the NSTE-ACS, the quantitative assessment of the ischemia using scores is superior to the clinical assessment alone. The TIMI Risk Score for UA/NSTEMI is a risk assessment tool made up of 7 independent risk indicators evaluated at presentation clinically: "age more than sixty-five years, three or more risk factors for coronary artery disease, recognized coronary stenosis, ST deviation 0-5 mm, raised cardiac marker, serious angina manifestations (2 episodes in the previous day), usage aspirin in the previous seven days.". The score is calculated as the simple arithmetic sum of the number of risk indicators present (range 0–7) for each patient. When utilized in this manner, the TIMI Risk Score shows a rising risk of death and recurrent ischemia events as the risk score increases. **[2]**

Clinical risk and the severity of CAD are, in fact, closely related. The SYNTAX score is an angiographic grading system that emphasizes coronary shape and lesion features. It objectively measures the degree of coronary artery disease, identifies individuals who are at higher risk, and assists in the decision among CABG and percutaneous coronary intervention (PCI). **[3]**

Transthoracic echocardiography should be routinely given in emergency departments and chest pain units during NSTE-ACS hospitalization and performed/interpreted by trained clinicians in all patients. This imaging approach is effective for finding abnormalities that might suggest ischemia or necrosis of the myocardium. In the absence of substantial wall motion abnormalities, strain and strain rate imaging might enhance the diagnostic and prognostic value of traditional echocardiography by detecting impaired myocardial perfusion or decreased regional function. **[1]**

Strain echocardiography was presented as an accurate tool for assessing global and regional LV myocardial function, and it had been found to be more sensitive than traditional echocardiographic metrics of systolic LV function in identifying coronary artery occlusion in patients with NSTE-ACS. Anatomic and functional differences among layers of the left ventricular (LV) wall can be found even in normal myocardium. Any method that enables researchers to examine myocardial function at the layer level should aid their understanding of the morphology and pathophysiology of myocardial diseases, notably ischemic heart disease. With new software, endocardial, mid-myocardial, and epicardial myocardial deformations may now be analyzed independently. **[4]**

The aim of this study is to investigate the hypothesis that layer specific STE can be a useful risk stratifying tool in NSTE-ACS.

METHODS

Technical design: This cross-sectional study was planned, supervised, and reviewed in cardiology department at Zagazig University. The practical part was conducted in the period between July 2018 to September 2020 at Salalah heart center in sultanate Oman on ninety patients diagnosed with NSTE-ACS based on ESC 2015 guidelines **[1]** (and agreed for invasive strategy). These cases were classified into two groups according to syntax score; "which is an angiographic tool used to determine the severity of (CAD) in patients undergoing coronary angiography" to Group I: with syntax score ≥ 1 (that included 70 patients) with significant CAD (obstructive CAD) and Group II; with syntax score zero (that included 20 patients) with no significant CAD (non-obstructive CAD). Patients with age < 18 years, ST elevation on admission electrocardiogram (ECG) or new left bundle branch block or hemodynamic instability were excluded from the study. We also excluded patients with history of recent (within three months) acute coronary syndrome, ECG evidence of old myocardial infarction, previous percutaneous coronary intervention, previous coronary artery bypass graft, significant valve disease, atrial fibrillation with heart rate > 100 beats/min or sustained severe arrhythmia, pacing, pre-excitation syndrome or bundle branch block or ejection fraction of left ventricle less than 50%. Patient with poor echocardiographic images or who refused to undergo invasive strategy or to give written informed consent for the research were also excluded.

Methods: All patients were subjected to complete history taking (including current smoking status) as current state of smoking included current smokers who smoke every day or some days during the past 30 days or quit less than 30 days before. Full clinical examination, 12-Lead ECG and hs-TnT were done. The TIMI risk score for UA/NSTMI was calculated on patient's admission, using the TIMI risk score calculator **[2]**. Transthoracic echocardiography including 2D-STE. using Vivid E9 System (GE Vingmed Ultrasound AS, Horten, Norway) equipped with a 2.5-MHz transducer was performed for all patients suspected of NSTE/ACS on admission. 2D speckle tracking strain analysis was performed with the aid of echo Pac software Version 201 (GE Vingmed Ultrasound AS, Horten, Norway) for offline analysis. Global longitudinal strain was recorded from the recorded 2D grayscale images as shown in figures (1), (2). Then layer specific strain was calculated automatically by the software for all layers LSEN , longitudinal strain midmyocardial and longitudinal strain epicardial (LSEP) as demonstrated in figures (3), (4). The SYNTAX Score1 was calculated by two experienced interventional cardiologists, using the online SYNTAX score calculator version 2.28 (http://www.syntaxscore.com/ calculator/ syntax score /frameset.htm) figures (5) **[5]**.

Administrative considerations: Written informed consent was obtained from all participants after clear explanation of the study and the study was approved by both the Institutional Review Board-Zagazig University (IRB-ZU) and the study and research committee in directorate general of health services governorate of Dhofar in sultanate Oman. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

STATISTICAL ANALYSIS

For statistical analysis of the obtained data, IBM's SPSS statistics (Statistical Package for the Social Sciences) for Windows (version 25, 2017) was utilized. The Shapiro-Wilk test was done to ensure that the data distribution was normal. All tests were carried out using a 95% confidence interval. Statistical significance was defined as a P (probability) value of less than 0.05. SPSS' chart builder and Microsoft Excel for Windows 2019 for Windows were used to create the charts. The mean and standard deviation were used to convey quantitative values, whereas frequency and percentage were used to express categorical data. The T and Mann Whitney tests were used to compare parametric and non-parametric continuous data with no follow-up measurements between groups. The crosstabs function was used to compare nominal data between groups using Fisher exact and Chi square tests. Depending on the type of data, Pearson's or Spearman's correlation coefficients were used to examine bivariate correlations.

RESULTS

We recruited 90 patients diagnosed with NSTE-ACS based on ESC 2015 guidelines diagnostic criteria (and agreed for invasive strategy), another 63 patients were excluded from the study (44 patient were excluded because of refusal of invasive strategy, 18 patients were excluded because of poor echo window and non-optimal imaging, one patient was excluded because an alternative diagnosis was settled later on by CMR). The demographic data of the studied groups **[Table 1]** showed that group I was statistically significantly older compared with group II (p= 0.002), the mean age of the cases in group I was 56.10 ± 11.633 years while the mean age in group II was 46.60 ± 11.704 years. On the other hand, regarding gender there were more males in group I vs group II but with no statistically significant difference between the two groups (p=0.269) as in group I, there were 81.4% males while in group II, there were 70% males. Regarding the associated risk factors and comorbidities, There was no statistically significant difference in the associated risk factors and comorbidities between the patients in the two study groups as group I had 35.7% smokers, 41.4% with HTN, 35.7% with DM 62.9% with dyslipidemia and there were 21.4% of the cases with positive family history of premature CAD and Group II had 35% smokers, 20% with HTN, 25% with DM 55% with dyslipidemia and there were 30% of the cases with positive family history of premature CAD. The clinical data in the studied groups **[Table 2]** showed that there was no statistically significant difference between the two groups regarding the HTN (p=0.194) as the mean SBP in group I and group II was 147.04 ± 31.358 and 137.05 ± 25.076 mmHg, respectively. Regarding ST deviation > 0.5 there was no statistically significant difference between the two groups as well (p=0.355) as it was detected in 41.4% and 30% in group I and group II, respectively. But regarding the mean MAX. hs-TnT /24hrs it was statistically significantly higher in group I. rather than group II (p < 0.001) as the mean MAX. hs-TnT /24hrs in group I and group II was 0.50 ± 0.554ng/ml 0.09 ± 0.189, respectively. Group I showed also a statistically significant higher percentage of cases with positive hs-TnT as compared with Group II, it was detected in 80% in group I and 30% in group II with (p < 0.001). The mean serum creatinine in group I and group II were 84.49 ± 22.824 and 80.40 ± 22.338 µmol/L respectively, with no statistically significant difference between the two groups (p=0.480). Angina within 24 hours was detected in 45.7% and 30% in Group I and group II respectively, with no statistically significant difference between the two groups (p=0.210). There were ten cases (14.3%) with aspirin use within 7 days in group I. No cases showed cardiac arrest on admission in the two groups. Regarding LV function parameters **[Table 3]**, we found the mean LVEF was statistically significantly higher in cases of group II (p = 0.011) as the mean LVEF was 53.87 ± 8.787 % and 59.55 ± 7.837 % in group I and group II, respectively. The mean GLS had a high statistically significant difference between the two groups as well (p < 0.001) as the mean GLS of cases in group I was -15.35 ± 3.335 while the mean GLS in cases of group II was -18.99 ± 3.487. The mean GLS was statistically significantly higher in group I. The mean LSEN showed high statistically significant difference between the two groups (p < 0.001), as the mean LSEN was -17.39 ± 3.888 and -22.07 ±

5.722 in group I and group II respectively the mean LSEN was statistically significantly higher in group I. The correlation between LSEN and clinical, angiographic scores in the current study was statistically significant. There was a highly statistically significant positive correlation between LSEN with TIMI score and SYNTAX score as shown in figures (6).

Table (1): Demographic data of the studied groups.

SYNTAX score	Group I (n= 70)	Group II (n= 20)	P
Age (years)	56.10 ± 11.633	46.60 ± 11.704	**0.002**
Female gender	18.6% (13)	30.0% (6)	0.269
Smoking	35.7% (25)	35.0% (7)	0.953
HTN	41.4% (29)	20.0% (4)	0.079
DM	35.7% (25)	25.0% (5)	0.370
DL	62.9% (44)	55.0% (11)	0.525
Family history	21.4% (15)	30.0% (6)	0.424

Age is the only factor shows statistical significance difference between the 2 groups

Table (2): Clinical data in the studied groups.

SYNTAX score	Group I (n= 70)	Group II (n= 20)	P
SBP (mmHg)	147.04 ± 31.358	137.05 ± 25.076	0.194
ST deviation > 0.5	41.4% (29)	30.0% (6)	0.355
MAX. hs-TnT /24hrs(ng/ml)	0.50 ± 0.554	0.09 ± 0.189	**0.002**
Positive hs-TnT	80.0% (56)	30.0% (6)	< **0.001**
Creatinine (μmol/L)	84.49 ± 22.824	80.40 ± 22.338	0.480
Angina within 24 hours	45.7% (32)	30.0% (6)	0.210
Aspirin use within 7 days	14.3% (10)	0.0% (0)	0.073

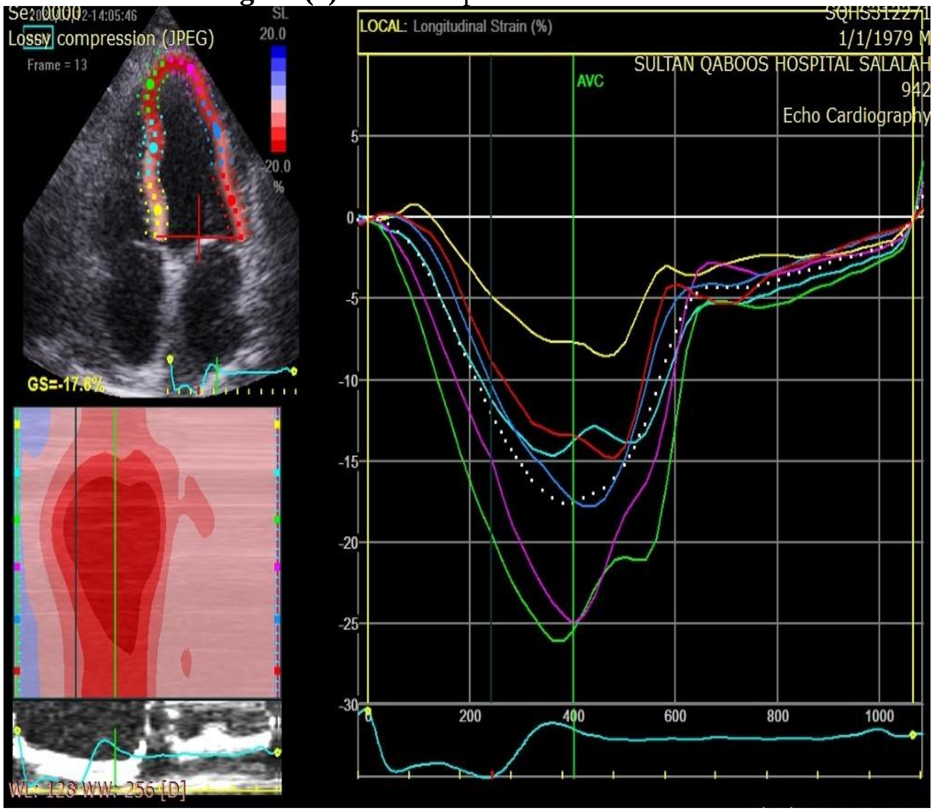
Hs-TNT only shows statistical significant difference between the two groups

Table 3: Ejection fraction and Speckle assessment of the studied groups:

SYNTAX score	Group I	Group II	P
LVEF (%)	53.87 ± 8.787	59.55 ± 7.837	0.011
GLS	-15.35 ± 3.335	-18.99 ± 3.487	< 0.001
LSEN	-17.39 ± 3.888	-22.07 ± 5.722	< 0.001

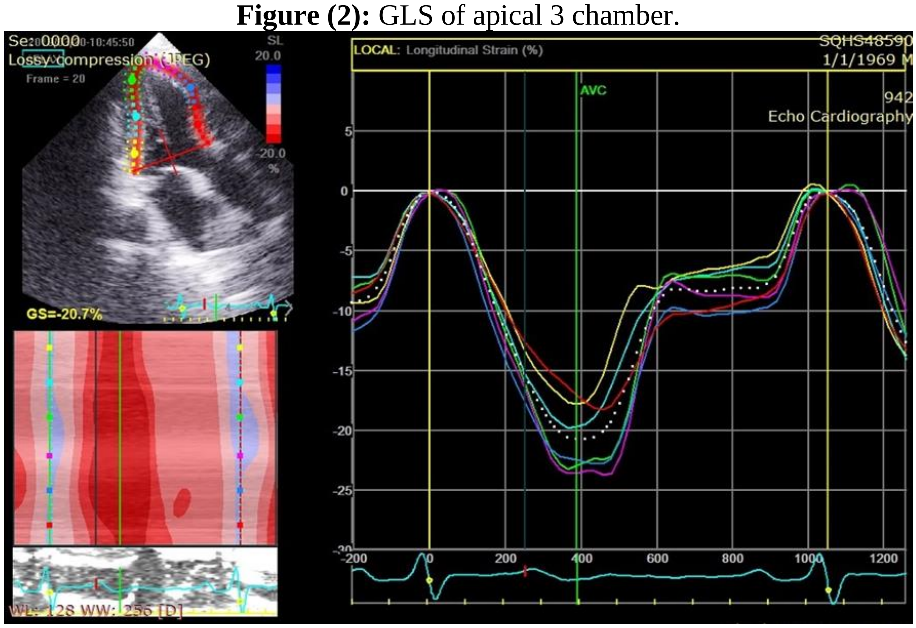
Different LV function parameters show statistically significant difference between the two groups

Figure (1): GLS of apical 4 chamber view.



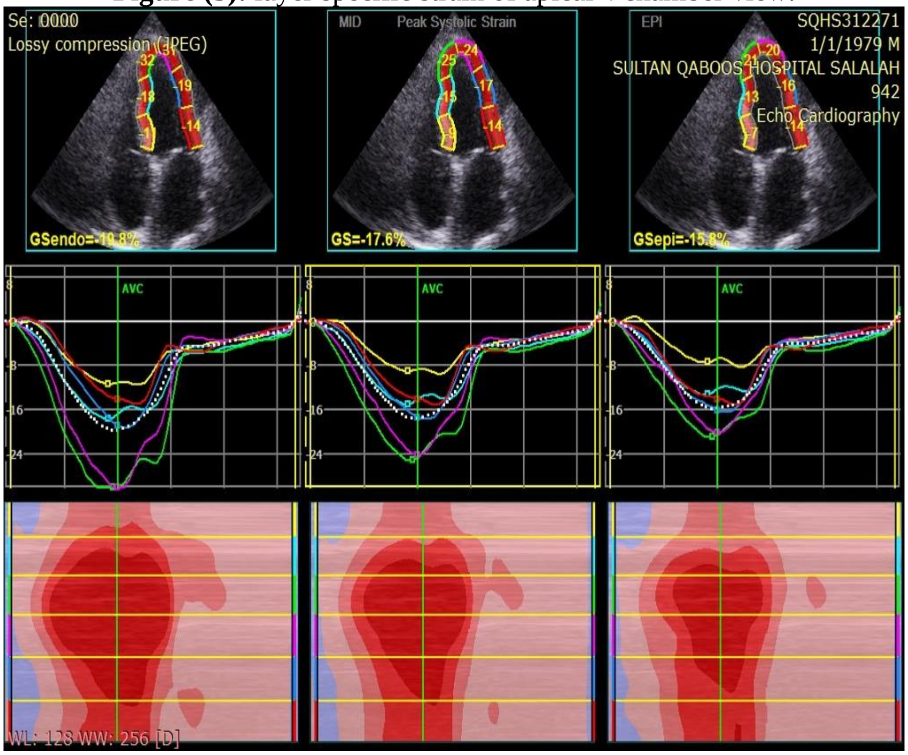
Normal GLS of apical 4 chamber view.

Figure (2): GLS of apical 3 chamber.



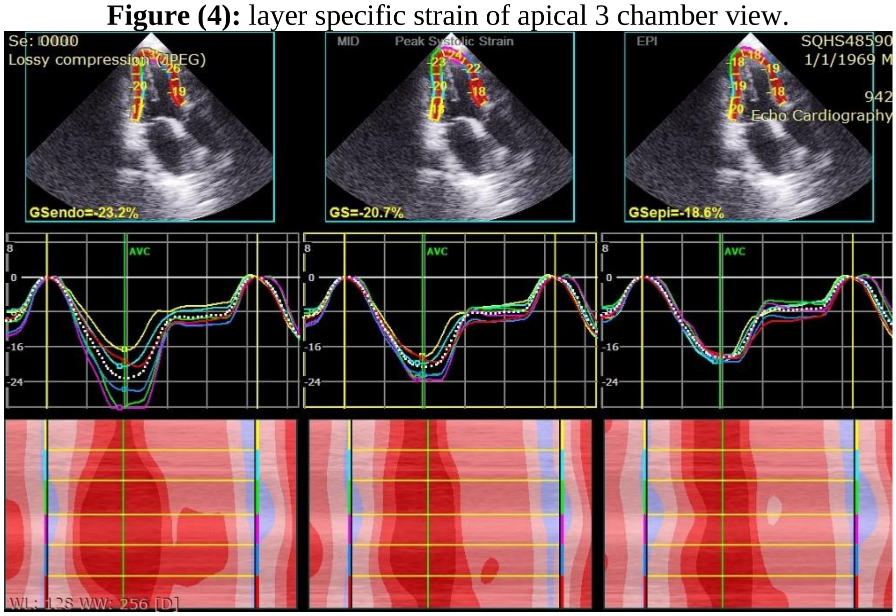
Normal GLS of apical 3 chamber view.

Figure (3): layer specific strain of apical 4 chamber view.



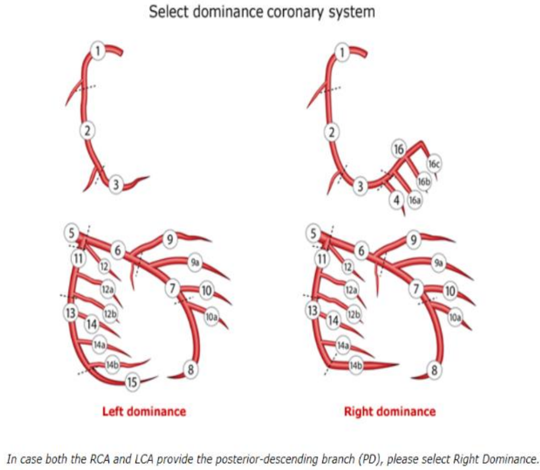
Normal endocardial, midmyocardial and epicardial global strain in apical 4 chamber view.

Figure (4): layer specific strain of apical 3 chamber view.



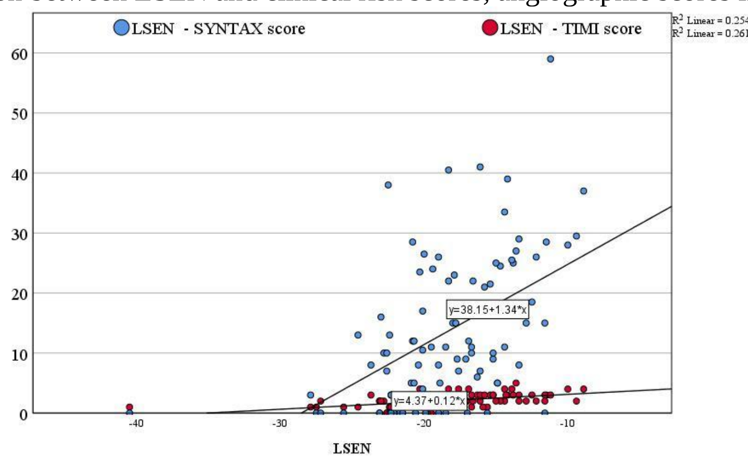
Normal endocardial, midmyocardial and epicardial global strain in apical 3 chamber view.

Figure (5): online SYNTAX score calculator



1st step in calculating online syntax score is selecting the dominance

Figure (6): Correlation between LSEN and clinical risk scores, angiographic scores in the current study.



High statistically significant positive correlation between LSEN with both TIMI score and SYNTAX score

DISCUSSION

A multitude of clinical variables are used to estimate the patient's risk in traditional risk evaluation measures for probable adverse cardiovascular events following NSTE-ACS. Even this, determining patient risk properly remains a difficulty. Many risk ratings, for example, fail to detect a substantial number of fatalities in specific patient categories. As a result, it is critical to use a reliable and highly predictive classification technique to choose the most appropriate therapy or intervention at the most opportune time. **[6]**

Speckle tracking echocardiography (STE) is a two-dimensional (2D) angle-independent quantitative approach for measuring LV global and regional function using grayscale images to follow speckle motion. Layer-specific STE (LS-STE) is a new intramural three-layer speckle tracking and simultaneous assessment of endocardial, midwall, and epicardial strain instrument. LS-STE may be a promising technique for diagnosing difficult CAD and predicting the complexity of coronary artery lesions in people with NSTE-ACS. **[7]**

In the current study we aimed to investigate the hypothesis that layer specific STE can be a useful risk stratifying tool in NSTE-ACS; by assessing the correlation between STE and different risk scores. The age was statistically significantly higher in the cases of Group I. as the mean age of the cases in group I was 56.10 ± 11.633 years while the mean age in group II was 46.60 ± 11.704 years. In line with our study Myers reported that as compared with Obstructive CAD subjects, non-obstructive CAD patients were significantly younger (−6.2 years on average). **[8]**

In a recent cohort analysis, the baseline characteristics revealed an equal prevalence of male and female patients with non-obstructive CAD, which is comparable to our findings. **[9]**

In the present study we found no statistically significant difference between the two groups regarding the conventional CHD risk factors as group I, had 35.7% smokers, 41.4% with HTN, 35.7% with DM, 62.9% with dyslipidemia and there were 21.4% of the cases with positive family history. group II, had 35% smokers, 20% with HTN, 25% with DM 55% with dyslipidemia and there were 30% of the cases with positive family history. In line with our findings, Al-Assaf and colleagues observed no significant differences in confounding factors such as smoking status, history of hypertension, LDL value, creatinine, hemoglobin, and CPK between NSTE patients with non-obstructive CAD and NSTE patients with obstructive CAD. **[10]**

The good standard CHD risk profile of non-obstructive CAD subjects compared to obstructive CAD patients was well-known and recorded in recent research, which mentioned so many possible explanations for the development of the atherosclerotic plaque and hypothesized a major role of non classical risk factors (inflammation, insulin resistance, psychosocial factors, physical inactivity) in ACS etiology for non-obstructive CAD subjects. **[11]**

This difference between our study and the former studies may be attributed to the fact that our study was performed only for NSTE-ACS patients and the number of patients with non-obstructive CAD is only twenty, but the former studies was larger and comprised both NSTE and STEMI patients.

In the present study, we found the mean maximum hs-TnT /24hrs was statistically significantly higher in group I 0.50 ± 0.554 while the mean MAX. hs-TnT /24hrs of the cases in group II was 0.09 ± 0.189, and the percentage of cases with positive hs-TnT was 80% in group I ,this was statistically significantly higher as compared with Group II (30%). In accordance with Lanza et al. as the peak troponin values, were lower in non-obstructive CAD patients. **[12]**

On the other hand, Al-Assaf and colleagues discovered that patients in the obstructive group had a higher median Hs-Troponin value, indicating a higher risk of acute coronary syndrome and the possibility of underlying obstructive coronary artery disease due to increased myocardial damage. **[10]**

In individuals with suspected heart illness, echocardiography is an essential cardiac imaging technique. However, in the diagnosis and risk classification of suspected CAD patients, traditional echocardiography has little use. **[13]** GLS is an innovative approach for identifying and measuring slight changes in LV systolic function utilising automated speckle tracking echocardiography (STE). **[14]** In the present study we found the mean LVEF significantly lower in group I 53.87 ± 8.787 % compared to group II 59.55 ± 7.837 that agrees with a current study that indicated that patients with high SYNTAX scores had lower LVEF than those with low scores. **[15]**

In the present study, we found the mean GLS was highly statistically significant lower in group I ($p < 0.001$) as the mean GLS was -15.35 ± 3.335 and -18.99 ± 3.487 in group I and group II respectively. These finding are in line with different studies ; Alam found that GLS value was significantly lower in patients with significant CAD than those who were free from this condition (-13.5±3.4 vs -19.01±2.3) ($p < 0.001$). **[16]**

The Thrombolysis in Myocardial Infarction (TIMI) risk score for UA/NSTEMI is a comprehensive technique that integrates baseline features from regular medical checkups to identify patients who are at elevated risk of death or other major cardiac ischemia events. Multiple trials have produced a risk score for UA/NSTEMI. In addition to global longitudinal strain (GLS), layer-specific strain (LSS) testing evaluates each heart layer separately. In the current study we assessed LSEN, and LSEP as the used echopac software (v 201) considered the mid layer has the same value of GLS. **[2]** LSEN was found to have high statistically significant difference between the two groups ($p < 0.001$). with the mean LSEN in group I and group II were -17.39 ± 3.888 and -22.07 ± 5.722, respectively.

We also discovered a modest link between LSEN and various risk and angiographic scores (TIMI score and SYNTAX score). Zhang and colleagues discovered a positive relationship between the SYNTAX score and layer-specific longitudinal strain parameters of all three myocardial layers, notably endocardial GLS and endocardial TLS. This data revealed that LS-STE might be used to separate difficult CAD patients from the rest of the population and measure the severity of their coronary artery lesions. **[7]**

CONCLUSION

In NSTE-ACS patients, two-dimensional layer specific strain and global longitudinal strain might be employed as a risk stratification tool. It may give more relevant information for physicians to design an effective management approach because it is a non-invasive procedure.

Conflict of interest: None.

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