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Efficacy of Cardiac Strain Imaging in predicting ischemic heart disease in patients presenting with non specific chest pain and normal LV ejection fraction.

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Abstract:

Objective: The objectives of this study were to evaluate the performance of LVGLS in the detection of severe coronary disease in patients with chest pain suggestive of NSTE-ACS as well as the associations between LVGLS reduction and elevation of ultrasensitive Troponin T (UsTnT), changes in electrocardiography suggestive of ischemia, and the number of severely occluded vessels.

Methodology : Inpatients with suspected coronary artery disease and chest discomfort were evaluated in this prospective, observational investigation. All patients had electrocardiography (ECG), usTnT measurement, Doppler echocardiography, LVGLS measurement, and coronary angiography within 48 hours of being admitted to the hospital (CA).

Results: There were a total of 75 patients, with a mean age of 58 17 years. Of these, 63 patients (or 84% of the total patient population) were men. Significant coronary blockages (lesions >70%) were found to be easier to spot when the Youden index LVGLS score was -16.5. Their values were 96%, 88%, 92%, and 92% for sensitivity, specificity, positive, and negative predictive values, respectively. The number of coronary arteries damaged was directly linked (P 0.001) with the extent of LVGLS reduction.Patients with lower LVGLS were more likely to have elevated UsTnT levels (83% vs. 17%, P 0.0001) than those with normal LVGLS. Abnormal strain was not associated with electrocardiographic anomalies that would have indicated ischemia.

Conclusion: In individuals with suspected NSTE-ACS, LVGLS testing is successful in identifying the presence of severe coronary disease. The quantity of coronary arteries damaged

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directly correlates with the magnitude of LVGLS reduction. Increases in UsTnT are associated with aberrant strain but not with changes brought on by electrocardiographic ischemia.

Keywords:

Cardiac strain imaging, Ischemic heart disease, Chest pain, Normal LV ejection fraction

Introduction:

Non-ST-segment elevation acute coronary syndrome is diagnosed using the clinical presentation, electrocardiographic changes, and cardiac enzyme curves (NSTE-ACS). Diagnosis is frequently difficult because the symptoms are unusual, the electrocardiogram (ECG) findings are normal or nonspecific, and cardiac enzymes are not elevated[1]. On the coronary angiogram, approximately 30% of patients admitted to the hospital with a presumptive diagnosis of NSTE-ACS do not have significant angiographic lesions (CA)[2]. A noninvasive diagnostic method capable of more precisely distinguishing between patients who will benefit from early CA and coronary revascularization and those who do not require an invasive procedure would be appreciated. In patients with NSTE-ACS, myocardial ischemia causes segmental wall motion abnormalities. The severity of ventricular dysfunction is determined by the number of coronary arteries involved, the severity of the obstructions, and the extent of the myocardial territory involved.A validated technique for measuring the strain (deformation) of the left ventricular wall is two-dimensional echocardiography with speckle tracking[3,4,5]. It allows for a more accurate assessment of left ventricular segmental and global systolic function than traditional echocardiographic methods[3,6].

Evaluation of left ventricular global longitudinal strain (LVGLS) in patients hospitalised with precordial pain may distinguish those with severe coronary obstructions who could benefit from an early CA (reduced LVGLS) from those who should undergo a noninvasive functional test (normal LVGLS)[7].As a result, the primary goal of this study was to determine the efficacy of LVGLS in detecting severe obstructive coronary disease in patients hospitalised with suspected NSTE-ACS. The secondary goal was to investigate the links between LVGLS reduction and increases in ultrasensitive troponin T (UsTnT), electrocardiographic changes suggestive of ischemia, and the number of vessels with severe lesions.

Methodology:

Between January 2023 and May 2023, this prospective, observational study was carried out in a tertiary hospital. Patients over the age of 18 who were admitted to the coronary care unit with a presumptive diagnosis of NSTE-ACS based on clinical presentation were included in the study. Before undergoing a CA within 48 hours of hospitalisation, all patients were evaluated with ECG and UsTnT curves, as well as Doppler echocardiography at rest and LVGLS measurement with speckle tracking.Patients were ruled out if they had a history of previous coronary disease (clinical history of infarction or electrocardiographic evidence of previous infarction, aortocoronary bypass, or percutaneous procedures), complete left bundle branch block, an ECG

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with ST-segment elevation, ventricular arrhythmia, pacemaker rhythm, preexcitation, or atrial fibrillation with more than 100 beats per minute. Patients with cardiomyopathy or severe valvular disease, a suboptimal acoustic window, or severe comorbidities with a life expectancy of one year were also excluded.

Methods of diagnosis

The ECG was performed at the time of admission and was repeated after 3, 12, and 24 hours, or whenever there was a change in the symptoms. The digital system ECG View TM version 2.12.0 with 12 simultaneous derivations was used. The European guidelines for NSTE-ACS were used to develop the ECG criteria used to diagnose ST-segment changes suggestive of ischemia[8].

UsTnT levels were measured at admission and three hours later, and values above the 99th percentile of normality (14 ng/dL in our laboratory) were considered abnormal. Before CA, transthoracic echocardiograms were performed under electrocardiographic control. VividTM E9 and E9.5 echocardiograms (GE Vingmed, Horten, Norway) were used, and post processing was completed with the GE EchoPacTM version 110 software. Images were captured in the parasternal views of 4, 3, and 2 cameras along the long, short, and apical axes. In each projection, three consecutive cycles were recorded. To determine the presence of valvular heart disease, colour Doppler images of the mitral, aortic, tricuspid, and pulmonary valves were obtained, as well as flows with continuous and pulsed Doppler. Ejection fraction (EF) was calculated in 4 and 2 cameras at the end of systole and diastole using the modified Simpson formula and the automatic edge detection method.The LVGLS was measured using the speckle tracking technique in four apical chamber views (four, three, and two) and a 16-segment model (six segments in each view) using the automated function imaging method[9]. The endocardial edge of the left ventricle was manually drawn, and the region of interest's width was adjusted to include only the walls of the left ventricle. The software automatically monitored deformation. 72 (±) 15 frames per second was used as the frame rate. The maximum negative systolic value of strain representing the maximum contractility of this segment was measured for each segment. The global longitudinal strain was calculated by averaging the values of each segment. [9] The LVGLS value considered within the normal limits of the software was >-17. To avoid confusion, the values were expressed in absolute numbers, indicating that they indicated an increase or decrease in strain. Shortening and elongation of the myocardial fibres are expressed in negative and positive values, respectively[10]. The echocardiographic images and LVGLS processing were performed by a single experienced sonographer who was unaware of the patients' clinical information.

Diagnostic CA were carried out with a Siemens Artis One or a Phillips Allura FD10 angiographer (Omaha, NE, USA) using the Judkins technique within 48 h of the patient's admission. The decision to revascularize and the method of revascularization, was left to the discretion of the treating cardiologist. A severe coronary lesion was defined as an obstruction of more than 70% of one or more epicardial arteries or more than 50% of the left main coronary

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artery. An experienced cardiologist who was not aware of the LVGLS outcome performed the image analysis. This method has 0%-5% interobserver and 0%-1.3% intraobserver variability[11].

Statistical analysis:

The mean and standard deviation of continuous variables were calculated and compared using the Student's t-test or the Mann-Whitney U-test, as appropriate. Categorical variables were expressed as percentages and compared using the Chi-square test or Fisher's test, depending on the situation. The area under the curve receiver operating characteristic that established the sensitivity and specificity through different values of myocardial deformation was used to evaluate LVGLS's prediction of severe coronary obstruction. The relationship between three or more variables was evaluated using analysis of variance, and the relationship between two variables was evaluated using the Student's t-test. P 0.05 was regarded as significant.

Results

Table 1 shows the baseline characteristics of 75 patients. The echocardiographic evaluation revealed a mean EF of 60% and a mean LVGLS of -15 3, both of which were normal in 32% and reduced in 68%. Cardiac catheterization revealed that 33% of patients lacked angiographically significant lesions. Severe obstructions affected 27% of those with one vessel, 24% of those with two vessels, and 16% of those with three vessels. 44 patients were revascularized in total. Aortocoronary bypass and percutaneous coronary intervention were performed in 4 (6%) and 40 (64%), respectively, patients. Table 1 also includes laboratory values as well as electrocardiographic, echocardiographic, and angiographic findings.

Table 1: Baseline characteristics [12]

Parameters	Total (%)
Age (years)	57 ± (17)
Gender	
Male	63 (84%)
Female	12 (16%)
Risk Factors	
Renal dysfunction	8 (11%)
Hypertension	51(68%)
Diabetes	19 (26%)

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Smoker	28 (37%)
Dyslipidemia	28 (37%)
Medication	
Statins	20 (27%)
Diuretics	5 (7%)
Antiplatelets	19 (25%)
Beta-blockers	18 (24%)
Angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers,	32 (43%)
Others	7 (11)
Electrocardiogram,	
Negative T waves	28 (37%)
ST depression	11 (15%)
Normal	19 (25%)
Others	17 (23%)
Doppler echocardiogram	
Left ventricular global longitudinal strain	−15±3
Ejection fraction,	60±11
Left ventricle mass	163.9±53
Coronary angiogram	
Three-vessel disease	12 (16%)
Two-vessel disease	18 (24%)
One-vessel disease	20 (27%)
No significant lesions	25 (33%)

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Positive Ultrasensitive troponin T	58 (77%)
Angiogram <48 h	75 (100%)
Treatment	
Bypass	4 (6%)
Percutaneous coronary intervention	40 (64%)
Medical	19 (30%)

Patients with severe obstructions in at least one vessel had a higher prevalence of male sex, were smokers, and had higher UsTnT levels, lower EF, and lower LVGLS compared to patients without significant coronary lesions. Patients with decreased LVGLS had no differences in the presence of traditional risk factors when compared to patients with normal LVGLS, with the exception of smoking, which was more prevalent in patients with altered strain [Table 2]. Elevated UsTnT levels were found in patients with abnormal LVGLS more frequently than in those with normal LVGLS (17% vs. 83%, P.0001). There was no correlation between abnormal strain and electrocardiographic changes [Table 2].

Table 2: Comparitive analysis of Normal vs reduced strain[12]

Characteristics	Reduced strain, (n=51)	Normal strain, (n=24)	P
Chronic renal insufficiency	6 (75%)	2 (25%)	0.65
Hypertension	37(73%)	14 (27%)	0.21
Smoker	23 (82%)	5 (18%)	<0.05
Diabetes	13 (63%)	6 (32%)	0.96
Dyslipidemia	20 (71%)	8 (29%)	0.62
Antiplatelets	15 (79%)	4 (21%)	0.23
Angiotensin-converting enzyme inhibitors and angiotensin-receptor	21 (66%)	11 (34%)	0.70

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blockers,			
Beta-blockers	15 (83%)	3 (17%)	0.12
Statins	14 (70%)	6 (30%)	0.90
Diuretics	3 (60%)	2 (40%)	0.69
Others	5 (71%)	2 (29%)	0.73
Electrocardiogram			
ST Depression	9 (82%)	2 (18%)	0
Negative T wave	20 (71%)	8 (29%)	0
Normal	12 (63%)	7 (37%)	0
Coronary angiogram			
Two-vessel disease	18 (100%)	0 (0%)	<0.001
One-vessel disease	18 (90%)	2 (10%)	<0.05
No coronary lesions	3 (12%)	22 (88%)	<0.0001
positive Ultrasensitive troponin T	48 (83%)	10 (17%)	<0.0001
Left main disease	12 (100%)	0 (0%)	<0.01

The Youden index determined that an LVGLS value of -16.5 was useful for detecting severe coronary occlusion (sensitivity, 96%; specificity, 88%; positive predictive value, 92%; negative predictive value, 92%). The value for the area under the curve was 0.91. Abnormal UsTnT levels and electrocardiographic changes had a lower predictive value for the presence of severe lesions in the CA. [Table:3]

Table 3: Sensitivity and specificity analysis[12]

	Positive Ultrasensitive troponin T (%)	Reduced strain (%)	Abnormal Electrocardiogram (%)
Specificity	60%	88%	32%

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Sensitivity	96%	96%	78%
Negative predictive value,	88%	92%	42%
Positive predictive value	83%	92%	70 %

Discussion:

The findings of this study show that measuring LVGLS in patients admitted with suspected NSTE-ACS is effective in distinguishing between patients with severe obstructive disease and those without significant lesions. LVGLS had excellent sensitivity, specificity, positive predictive value, and negative predictive value compared to UsTnT elevation and electrocardiographic changes suggestive of ischemia. Furthermore, there was a direct correlation between LVGLS reduction and the number of coronary arteries with severe obstructions. Although reduced strain was linked to elevated UsTnT, it was not linked to electrocardiographic changes that suggested ischemia. The algorithms available for stratifying the cardiovascular risk of patients presenting with chest pain are time-consuming and imprecise, which explains why approximately one-third of cases undergoing cardiac catheterization show no evidence of significant lesions[10]. Beyond the information provided by clinical presentation, ECG changes, and enzymatic markers, a rapid and simple noninvasive diagnostic method to rule out severe coronary disease is required.

LVGLS assessment is non-invasive and can be completed in a few minutes without subjecting patients to physical exercise.It is more sensitive than traditional echocardiographic methods in detecting global and segmental wall motion abnormalities caused by ischemia.[3] The reason for this is that EF is primarily measured by assessing changes in ventricular volumes, whereas visual evaluation of segmental wall motion abnormalities is dependent on myocardial thickening. Because of the preserved circumferential function in the nonischemic midwall, and the subepicardium opposes a sufficient decrease in EF and inward motion, both parameters are insensitive markers of ischemia[13]. The LVGLS, on the other hand, measures actual deformation in the subendocardial myocardium, which is highly susceptible to early ischemic changes and can distinguish between patients with and without significant coronary disease[13,14].

The LVGLS with a cutoff value of -16.5 was found to be useful in distinguishing patients with severe coronary disease, with 92% positive and negative predictive values. The LVGLS measurement predicted moderate and severe coronary disease with a sensitivity of 74.4%, a specificity of 72.1%, and an area under the curve of 0.80, according to a meta-analysis of 10 studies involving 1385 patients[10]. These figures are lower than those found in the current study, which has a sensitivity of 96%, specificity of 84%, and area under the curve of 0.91. The

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disparity is most likely due to differences in the populations studied as well as the criteria used to define significant coronary disease. The trials included in the meta-analysis looked at people who had an intermediate pre-test probability of having significant coronary artery disease, including people with presumed NSTE-ACS and those with stable angina. Moderate- and severe-degree (>50%) obstructions were defined as angiographically significant lesions. Meanwhile, the evaluated population in the current study had a high pretest probability because only patients with presumed NSTE-ACS were evaluated, excluding those with chronic symptoms. Another distinction was that only severe obstructions (>70%) were considered angiographically significant, while moderate lesions (50%-70% were not). The current study found a link between the number of coronary arteries with severe lesions and the degree of LVGLS reduction, implying that the extent of ischemic territory influences the degree of LVGLS reduction, which is consistent with previous research findings[14,15,16]. The observation that patients with elevated UsTnT levels had abnormal LVGLS more frequently than patients with normal cardiac enzyme levels supports this idea.

Given the low specificity of repolarization abnormalities in diagnosing ischemia, the lack of association between reduced LVGLS and electrocardiographic changes suggestive of ischemia in this study was not surprising[17].Acute processes like myocarditis and Takotsubo syndrome, as well as chronic conditions like arterial hypertension and valvulopathies, can cause ECG repolarization abnormalities that are similar to ischemic ones. False-positive results in patients with reduced LVGLS are possible in conditions such as Takotsubo syndrome, myocarditis, and coronary spasms, where CA is the only way to determine the differential diagnosis. In patients with normal LVGLS, false-negative results may occur when acute ischemic events involve myocardial territories small enough not to induce segmental wall motion abnormalities or when collateral circulation limits the magnitude of ischemia. LVGLS is a practical and novel diagnostic method that could be integrated with ECG and cardiac enzymes as part of routine evaluation in patients with chest pain, according to the clinical implications of this study. Unlike the UsTnT, which rises 1-3 hours after the onset of symptoms, delaying the confirmation of NSTE-ACS in many cases, the LVGLS mutation allows for immediate confirmation of ischemia because myocardial contractile dysfunction occurs only seconds after tissue perfusion is reduced[18]. LVGLS is an ideal tool for evaluating patients with chest pain in the emergency room and identifying those patients who will benefit from an early CA because of this capability and its high positive predictive value. Alternatively, the LVGLS's high negative predictive value may reduce the number of unnecessary CA, which is costly and not without risk. Until studies show that using a "negative strain" as a marker for patients who do not require CA and can undergo noninvasive functional testing is safe, LVGLS should be considered a supplement to existing risk stratification methods. There are some limitations to this study. First, the number of patients included was insufficient to be categorical in our conclusions. Second, while the LVGLS was performed prior to the CA as per protocol, it was often performed after the chest pain had subsided. It would have been preferable to assess LVGLS at the time of arrival in the emergency room or shortly afterwards, when abnormalities in wall motion caused by ischemia are more

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likely to be detected. Some of the false-negative results observed in this study could have been caused by patients with NSTE-ACS whose ischemia had subsided at the time the echocardiography was performed. Unfortunately, no data was collected on the relationship between chest pain, electrocardiographic changes, and echo by LVGLS. Third, the LVGLS cannot be used on all patients because it may provide misleading information in patients with a history of coronary disease and those with preexisting wall motion abnormalities due to its inability to distinguish chronic wall motion abnormalities from those caused by acute ischemia. We excluded patients with a prior history of CAD in this study to reduce the possibility of including subjects with preexisting wall motion abnormalities. Even though we cannot rule out the possibility, it should be minimal given the study population's normal baseline EF. Fourth, assessing only the global longitudinal strain and ignoring the radial and circumferential strains may be considered a limitation. Longitudinal strain was the only one studied because it has been shown to be more sensitive as an indicator of ischemia than the other strain types, which are not currently supported by cardiac imaging societies[19]. Fifth, because the echocardiographic parietal motility index is operator dependent, we chose to investigate a semiautomatic technique with lower interobserver variability. Finally, due to the small number of patients included, we chose not to differentiate between the coronaries involved, instead reporting only the number of arteries compromised.

Conclusions

LVGLS measurement in patients with suspected NSTE-ACS is effective in predicting the presence of severe coronary disease. The degree of LVGLS reduction and the number of coronary arteries involved have a direct relationship. The strain was linked to increases in UsTnT but not to electrocardiographic changes suggestive of ischemia.

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