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Original article

Correlation between Myocardial Strain and Angiographic Severity of Coronary Artery Disease in Non-ST-Elevation Myocardial Infarction Patient

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Abstract

Background and objectives: Noninvasive assessment of coronary artery disease severity remains a clinical challenge. Myocardium subtended by obstructive coronary artery disease may show reduced left ventricular strain. The present study was intended to investigate whether this reduction of strain value correlates with increasing severity of coronary artery disease in Non-ST-Elevation Myocardial Infarction (NSTEMI) patients. ***Methods:*** This cross sectional study included 86 patients of NSTEMI. We assessed myocardial strain in global longitudinal strain (GLS) value using two dimensional speckle tracking echocardiography (2DSE). We performed coronary angiogram of the same patients and documented presence or absence of significant disease, number of affected vessels and Gensini score. Significant coronary artery was defined as ≥70% stenosis in any major coronary artery and or ≥50% stenosis in left main coronary artery. ***Results:*** Global longitudinal strain value was significantly lower in the significant coronary artery disease group (-13.5±3.4% vs. -19.01±2.3%) ($p < 0.001$). GLS declined proportionately with increasing severity of coronary artery disease defined by number of affected vessels ($p < 0.001$). Spearman's rank correlation coefficient test between GLS value and Gensini score showed that the two variables maintained a linear but inverse relationship ($\rho = 0.816$, $p < 0.001$) that implies decreasing GLS is associated with increasing Gensini score. Multivariate logistic regression analysis found global longitudinal strain as an independent predictor of coronary artery disease. ***Conclusion:*** Myocardial strain assessed in global longitudinal strain value correlates with angiographic severity of coronary artery disease in patients with Non-ST-Elevation Myocardial Infarction.

Keywords: ***2D Speckle Tracking Echocardiography, Myocardial Strain, Global Longitudinal Strain, Coronary Artery Disease, Non-ST-Elevation Myocardial Infarction.***

Introduction

Coronary artery disease (CAD) is an overburdened health problem, and is the leading cause of mortality in Bangladesh as well as other parts of the world. Like other South Asians, Bangladeshis are unduly prone to develop CAD, which is often premature in onset, follows a rapidly progressive course and angiographically more severe.[1]

Goals of noninvasive testing in patients with suspected NSTE-ACS include (1) determining the presence or absence of coronary artery disease; (2) establishing CAD as the cause of the elevated cardiac troponin in patients with other possible explanation; (3) evaluating the extent of residual ischemia after medical therapy has been initiated thus guiding further therapy; (4) localizing the ischemia before a planned PCI in patient with multivessel disease; (5) assessment of left ventricular function.[2]

Although conventional echocardiography is considered to be reliable for ventricular wall motion analysis and assessment of regional myocardial function, there is high inter-observer and intra-observer variability and allows only limited evaluation of radial displacement and deformation, without the possibility of assessing myocardial shortening and twisting.[3] In addition, poor temporal resolution of the human eye creates limitations for the accurate visual assessment of the longitudinal myocardial motion in full detail.[4]

During recent years, velocity imaging, displacement imaging and deformation imaging (strain and strain-rate imaging) have emerged as valuable tools for more comprehensive and reliable echocardiographic assessment of myocardial function.[3] Myocardial strain by speckle-tracking echocardiography is a technique based on widely available two-dimensional gray scale echocardiography, enabling the accurate evaluation of global and regional myocardial function, and it has been shown to be sensitive to abnormalities caused by ischemia and necrosis.[5]

Left ventricular (LV) evaluation is the most important use of echocardiography. Speckle tracking strain echocardiography provides a quantitative regional and global LV assessment, is an independent supplement to wall motion analysis and has been validated over the past 10 years. Myocardial strain is three dimensional. The heart shortens and lengthens in the longitudinal direction and circumferential direction. On the contrary it thickens and thins in the radial direction. So, strain can be longitudinal, radial and circumferential. Longitudinal strain is the most sensitive and reproducible of the various strain measurements, so it is the only strain we record.[6] So, in this study we chose global longitudinal strain (GLS) to record.

Global Longitudinal Strain (GLS) assessed using automated speckle tracking echocardiography (STE) is an emerging technique for detecting and quantifying subtle disturbances in LV systolic function. GLS reflects the longitudinal contraction of the myocardium and its accuracy has been validated against tagged magnetic resonance imaging.[7]

To facilitate clinical application, speckle tracking has been integrated into the most recent echocardiographic systems for quick, automated evaluation of left ventricular (LV) function by means of Automated Function Imaging (AFI). AFI is clinically applicable and an effective means of assessing LV function due to its short acquisition time, feasibility and accuracy, whatever the experience of the operator is.[8]

The AFI algorithm tracks the percent of wall lengthening and shortening in a set of three longitudinal 2D-image planes (apical long, two chambers and four chambers) and displays the results for each plane. It then combines the results of all three planes in a single bull's-eye summary (agreeing with the standard 17-segment model), which presents the analysis for each segment along with a global peak systolic value for the LV.[9]

Strain echocardiography can be performed bedside at low cost and has been demonstrated to identify high-risk patients with non–ST-segment elevation acute coronary syndrome (NSTE-ACS) setting.[10] However, even low-grade ischemia might cause deterioration of myocardial function and can be detected by myocardial strain imaging.[11] (Liang, et al., 2006). Symptoms suggestive of acute coronary syndrome account for up to a quarter of acute hospital admissions in the Western world.[12] However, most patients presenting with chest pain and suspected acute coronary syndrome do not have significant coronary artery disease.[13]

The clinical presentation of coronary artery disease (CAD) varies from silent ischemia, stable angina pectoris to acute coronary syndromes (ACS) and death. ACS comprises of Unstable Angina, non-ST–segment elevation-acute coronary syndrome (NSTE-ACS) and ST-segment elevation myocardial infarction (STEMI). The presence of ST-segment elevation typically represents total coronary occlusion requiring acute reperfusion therapy. On the other hand, patients with suspected NSTE-ACS are a more heterogeneous group. Coronary occlusion and/or significant stenosis may or may not be present, and coronary angiography and revascularization therapy might not be necessary. Therefore, a better selection of patients with real need for coronary angiography and revascularization therapy could reduce both complication rates and healthcare costs associated with this procedure.

Approximately 85% patients with a clinical diagnosis of NSTE-ACS have significant coronary obstruction (i.e.,>50% stenosis of the luminal diameter) in at least one major coronary artery. The remaining 15% have no evidence of significant coronary obstruction on angiography.[14]

There are several ways of quantification of CAD severity. In daily clinical practice, number of stenosed vessel or vessel scoring is most commonly used. In this way, CAD is divided into Left Main disease, Single Vessel Disease (SVD), Double Vessel Disease (DVD) and Triple Vessel Disease (TVD). Along the advent of coronary angiography multiple scoring systems have been devised for the quantification of CAD burden. These scores quantify CAD severity more objectively and accurately. Previous study demonstrated that regardless of the degree of heterogeneity among systems, scores are highly and consistently correlated with each other. Among them Gensini score had strongest correlation with IVUS assessed intracoronary plaque burden ($\rho = .90$) ($p < 0.001$).[15] Previous study revealed correlation between Global Longitudinal Strain (GLS) and SYNTAX Score in Stable Angina patient.[16] But to the best of our knowledge none has compared this 2D speckled myocardial strain to Gensini score for angiographic severity of CAD in NSTEMI patient.

Research Question

Does global longitudinal strain value correlate with angiographic severity of coronary artery disease in Non-ST-Elevation Myocardial Infarction (NSTEMI) patient?

Methods

A cross-sectional study was carried out in the University Cardiac Centre, Department of cardiology, BSMMU, Dhaka over a period of 12 months from August 2016 to July 2017 among patients admitted with Non-ST-elevation myocardial infarction. For enrollment in this study patients with NSTEMI who had normal sinus rhythm, had adequate echo window for analysis of myocardial strain using 2 D (Two dimensional) speckle tracking echocardiography (STE) and eligible for Coronary angiography were counted.

Patients with left ventricular ejection fraction (LVEF) <50%, significant valvular or congenital heart disease, prior history of CABG, MI or Coronary intervention were excluded from the study. For feasibility of the study haemodynamically unstable patient and or with severe co-morbid illness were also closed out.

By doing purposive sampling, who full filled the inclusion and exclusion criteria, 96 patients were selected and out of them 10 patients were dropped out due to poor echo window or due to not having both echo and angiogram done. Finally 86 patients were analyzed in the study.

After detailed history-taking, examination and proper investigations conventional echocardiography was done. Of the selected patients who were eligible for coronary angiography according to current clinical practice guideline were included for the study. Speckle tracking echocardiography was performed of all selected patient within 7 days of NSTEMI event and within 2 days before coronary angiography. Approval of the study was obtained by the local ethical committee. All subjects included in the study had signed informed consent with careful explanation of the study procedures.

Two dimensional speckle tracking echocardiography

Two dimensional speckle tracking echocardiography was performed using a Vivid E9 (GE Healthcare) Echocardiography machine with a 3.5MHz Transducer. It was performed from the apical 4-chamber, 2-chamber, and apical long-axis view. By speckle tracking, endocardial border was tracked in end systole. In case of poor tracking, Region of Interest (ROI) was readjusted. In case of persistent inadequate tracking, the participant was excluded. The results of all three planes were combined in a single bull’s eye summary (agreeing with the standard 17-segment model), which presented the analysis of each segment along with a global longitudinal strain value for the left ventricle. All images were obtained at a frame rate of 60-100 frames/sec.

Coronary angiography

Angiographic findings were assessed by interventional cardiologists working in catheterization laboratory of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. Coronary angiogram was visually assessed for all coronary lesions in two orthogonal planes. Lesion locations were assessed and percent diameter stenosis was measured for each coronary lesion. Significant coronary artery disease was defined by presence 70% or more stenosis in any major coronoaryartery, 50% or more stenosis in left main coronary artery.[17] Gensini Score was calculated using pre-designed standard format of all patients.

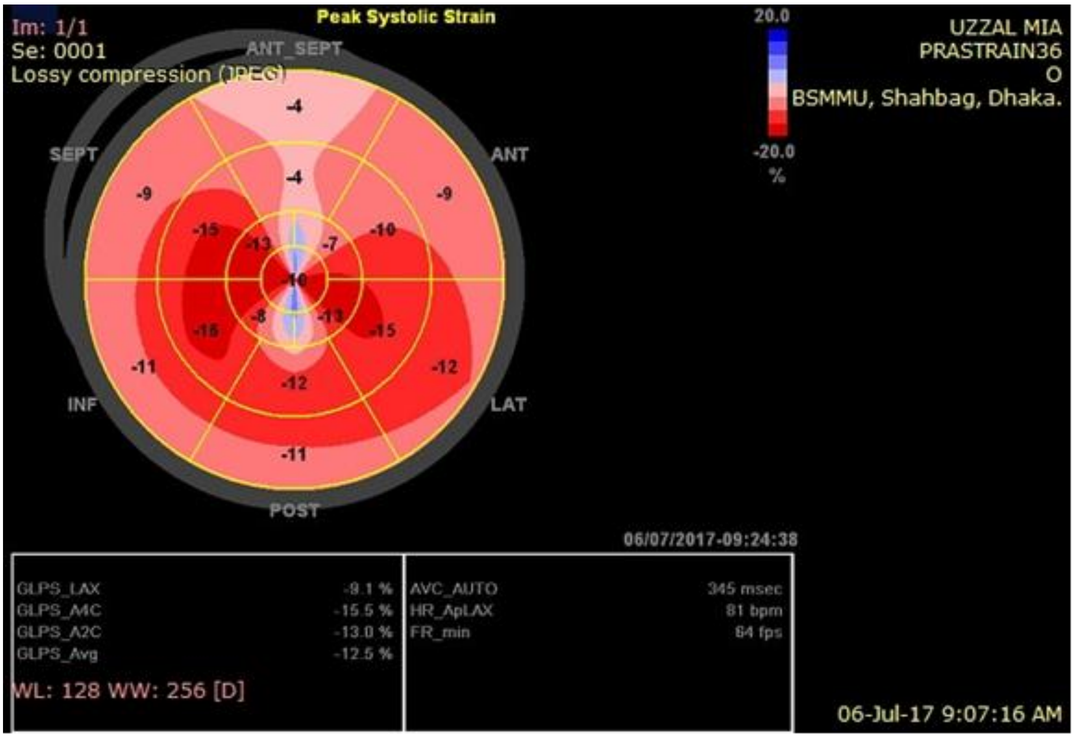

Figure 1: Bull’s Eye display of Segmental and Global Longitudinal Strain.

Statistical Procedure

Data were processed and analysed using computer software SPSS (Statistical Package for Social Sciences) version 16 (SPSS Inc., Chicago, IL, USA). Continuous data were presented as mean ± SD and categorical data as frequency and percentage. Data presented on continuous scale were compared between groups using Student’s t-Test and among groups using one way ANOVA test. Correlation between GLS and Gensini score was analysed by Spearman’s Rank Correlation Coefficient Test. Binary logistic regression analysis was done to adjust for confounding variables (age, diabetes mellitus, hypertension and GLS). Level of significance was set at 5% and p-value <0.05 was considered as significant.

Results

The present study was intended to investigate the correlation between global longitudinal strain (GLS) value measured by 2D speckle tracking echocardiography (2DSTE) and angiographic severity of coronary artery disease (CAD) in patients with Non-ST-Elevation Myocardial Infarction (NSTEMI).

The study findings are summarized in Table I. The mean age of the patients was 55. 5 ± 10.6 years (range: 32 – 74) years. Majority (74.4%) of the patients were male with male to female ratio being roughly 3:1. The predominant risk factor was diabetes (59.3%) followed by smoking (58.1%), dyslipidaemia (55.8%) and hypertension (53.5%). Over 30% of the patients had family history of CAD and 22.1% were overweight and obese. (Table I)

Majority (82.6%) of the patients had significant CAD. Over one-third (36.6%) of those who were suffering significant CAD, had SVD, another one-third (36.6%) DVD and the rest 26.8% had TVD. The mean Gensini score was computed to be 47.2. (Table I)

Table I: Summary of findings.

Trait		
Age	Range (32-74 years)	Mean- 55 ± 10.6 years
Male to Female ratio	3:1	
Risk factors*	Overweight & Obese	19 (22.1%)
	FH of CAD	26 (30.2%)
	Hypertension	46 (53.5%)
	Diabetes	51 (59.3%)
	Dyslipidemia	48 (55.8%)
	Smoker	50 (58.1%)
LVEF (%)	Mean 60.7	SD 3.5
GLS (%)	Mean –14.5	SD -3.8
CAD*	Significant	71 (82.6%)
	Non-significant	15 (17.4%)
Gensini Score	Mean 47.2	SD 33.9

*Number of population with certain character with their percentage in bracket given. FH- Family History, CAD- Coronary Artery Disease, LVEF- Left Ventricular Ejection Fraction, GLS- Global Longitudinal Strain, SD- Standard Deviation

Global longitudinal peak systolic strain was significantly lower in patients with significant CAD than those who were free from this condition ($p < 0.001$). (Table II)

Table II: Comparison of GLS between patients with and without significant CAD (N=86)

Echocardio graphic variable	CAD		P-value
	Significant (n = 71)	No or non-significant (n = 15)	
GLS	-13.5 ± 3.4	-19.01 ±2.3	<0.001^S

Data were analyzed using Unpaired t-Test and were presented as mean ± SD;

N- Number of study population, n- Number in each group, s- Significant, SD- Standard deviation

LVEF- Left ventricular ejection fraction, GLS- Global longitudinal strain

Severity of CAD (based on number of major coronary arteries involved) also demonstrates that more the number of vessels affected, the lower is the GLS ($p < 0.001$). (Table III)

Table III: Association between GLS and severity of CAD by number of diseased vessel (N=86)

Severity of CAD	GLS (Mean ± SD)	P-value
No or non-significant CAD (n = 15)	-19.01 ± 2.32	
SVD (n = 26)	-15.5 ± 2.37	< 0.001^S
DVD (n = 26)	-13.9 ± 2.9	
TVD (n = 19)	-10.23 ± 2.73	

*Data were analyzed using One-way ANOVA statistics and were presented as mean ± SD.

N- Number of study population, n- Number in each group, s- Significant, CAD- Coronary artery disease, GLS- Global longitudinal strain, SVD- Single vessel disease, DVD- Double vessel disease, TVD- Triple vessel disease

Spearman's rank correlation coefficient test between GLS and Gensini score shows that the two variables bear a linear inverse relationship (ρ= 0.816, $p < 0.001$). This means that Gensini score increases while GLS value decreases. (Figure 2)

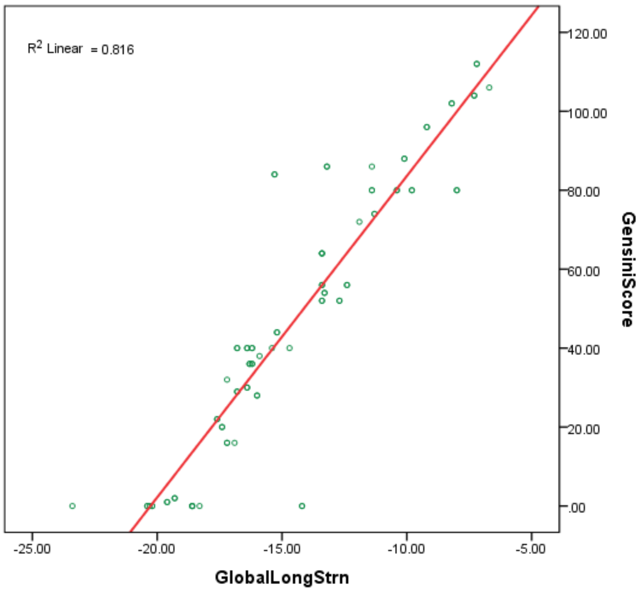

Figure 2: Scatter diagram showing correlation between GLS and Gensini score.

Table IV demonstrates the binary logistic regression analysis of Odds Ratios for characteristics/factors of the patients likely to develop CAD. The variables revealed to be significantly associated with significant CAD at 10% level of significance (that is $p < 0.1$) in univariate analyses were all entered into the model directly. Of the 4 variables (significantly associated with CAD in univariate analysis), age of the patients and GLS emerged as independent predictors of CAD in multivariate analyses. The older patients and lower GLS value were 1.2(95% CI = 0.9 – 1.4) and 3.60(95% CI = 1.53 – 8.49) times more likely to have CAD than then younger patients and patients with lower GLS (p =0.052 and p = 0.003 respectively).

Table IV: Regression analysis showing predictors of coronary artery disease (N=86)

Variables of interest	Univariate analysis (p-value)	Multivariate analysis	
		Odds Ratio (95% CI of OR)	p-value
Age (years)	<0.001	1.2(0.9 – 1.4)	0.052^S
Diabetes	0.001	0.29(0.03 – 2.71)	0.283^{NS}
Hypertension	0.085	0.28(0.03 – 2.41)	0.249^{NS}
GLS	<0.001	3.60(1.53 – 8.49)	0.003^S

N- Number of study population, GLS- Global longitudinal strain, CI- Confidence interval, OR- Odds ratio, S- Significant, NS- Non-significant

Discussion

The present study was intended to investigate correlation between myocardial strain assessed in global longitudinal strain (GLS) value and angiographic severity of coronary artery disease (CAD) in Non-ST-Elevation Myocardial Infarction patient.

In the present study mean age of patients were 51.56 ± 10.62 years. The commonest age group of study patients was 50-60 years. Nearly similar pattern of age distribution was reported by Akanda, et al. in their study in Bangladesh.[18] But there was difference in mean age in different studies done in abroad namely, Choi, et al. 59±9 years and Montgomery, et al. 60±2 years.[19,20] Most probably this was due to the late onset of atherosclerotic coronary artery disease in developed countries than that of a third world country people like Bangladesh.

Most of the patients were male (74.4%) and 25.6% patients were female in this study. Male & female ratio was almost 3:1 in the whole study population. In Bangladesh & abroad the various studies showed the female patients form a small portion of total study. Choi, et al. found 29.2 percent, Shimoni, et al. 21.7 percent, Montgomery, et al. 40.7 percent and Sorensen, et al. found 45 percent female patients in their respective studies.[19-22]

In our study ejection fraction was preserved in most of the cases where global longitudinal strain was impaired. However, this impairment in longitudinal systolic function is known to be compensated by augmentation of circumferential deformation, which might explain why the left ventricular ejection fraction was preserved in most cases, despite impaired longitudinal systolic function.[23] The advantage of global longitudinal peak systolic strain is that it provides incremental value compared with conventional echocardiography.

We have found global longitudinal strain 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) ($p < 0.001$). Similar to our study, an Egyptian study conducted on 80 patients with suspected CAD (by history of angina) demonstrated GLS to be significantly lower among patients with significant CAD than those with non-significant CAD (−11.8 ± 2.9 vs. −18.6 ± 0.8, $p < 0.0001$). Patients with CAD group had significantly reduced rest GLS (−19.0 ± 2.4 vs. −22.7 ± 2.4, $p = 0.001$) compared with patients with non-significant CAD. Variation in strain value between patient with presence or absence of significant CAD in different studies could be explained by various factors.

The variation in value of GLS in previous studies could be explained by clinical characteristics of patients, the effect of diastolic function and their hemodynamic parameters (i.e., blood pressure) during image acquisition[24], by using different equipment, different design, vendor-dependent 2DSE software and operator skills.[19,20,25,26] Another data have indicated that GLS is more dependent on the 2DSE software used, rather than ultrasound equipment used to acquire images[27-29], which makes the use of vendor-independent software particularly attractive to standardize GLS for widespread use. The possibility of using a fixed diagnostic GLS cut-off value to diagnose obstructive CAD, independent of the ultrasound equipment used for images acquisition, would be required to increase the clinical usefulness of strain imaging.

Most of the studies used 50% coronary artery stenosis in any major coronary artery to define significant CAD. This study used 70% stenosis as cut-off value to define significant CAD. This might be one of the reasons of variation in strain value. However, consideration of this clinically useful cut-off value will give more pragmatic information in clinical decision making.

In the present study, we found that GLS declined proportionately with increasing severity of CAD defined by increasing number of stenosed coronary vessels (GLS -19.01 ± 2.32 for no CAD, -15.5 ± 2.37 for SVD, -13.9 ± 2.9 for DVD and -10.23 ± 2.73 for TVD). So the chance of multi-vessel disease and or higher degree of stenosis increases with decreasing GLS. This finding compares well with Sorensen, et al.[22] who showed GLS value to be −18.8 ± 2.6 versus –18.0 ± 2.4 versus –16.7 ± 2.7 versus −16.3 ± 2.3 for patients with non-significant CAD, 1-vessel disease, 2-vessel disease, and 3-vessel disease, respectively. Gaibazzi, et al.[30] and Choi, et al.[19] also reported similar GLS values through increasing severity of CAD, patients with normal coronary arteries had a mean GLS of −22 ± 1.5%, single or double vessel disease −19.4 ± 2.4%, and triple-vessel or left main disease −18.0 ± 2.3%.

Our study found strong, linear inverse correlation with Gensini score ($\rho=0.816$, $p<0.001$). This implies in more than 80% of cases GLS decreases while Gensini score increases. In 2016 Vrettos, et al.[16] on a study investigated the correlation between GLS and SYNTAX score. They found significant but lesser degree of correlation than that of us. This might be due to fact that, SYNTAX score does not consider functional significance of lesion. SYNTAX score is based on anatomical complexity of lesion, primarily designed for guiding decision-making between different revascularisation strategies. Whereas Gensini score considers functional significance of lesion, reflects anatomy as well as physiology of coronary circulation. Therefore, Gensini score can better correlate with GLS which is also a functional parameter.

The higher rates of diabetes and hypertension are closer to a real-world situation, because diabetes and hypertension are major risk factors for CAD. In 2000 Ng, et al.[31] showed that hypertension and diabetes might affect longitudinal strain values. But in present study, GLS still remained significantly different & independent predictors of CAD after multivariate analysis.

Most of the studies in the literature were conducted on suspected Stable Angina patient. Our study was conducted on NSTEMI patient. However, findings of our study are consistent with findings of previous studies though study group was different. So, from our study this may be concluded that GLS changes similarly in different spectrum of coronary artery disease. This area may need more active research.

Conclusion

In conclusion myocardial strain assessed in global longitudinal strain value correlated with angiographic severity of coronary artery disease in patients with Non-ST-Elevation Myocardial Infarction. This gives us a new insight about noninvasive assessment of myocardial strain before invasive coronary angiogram, which may give us idea about the presence and severity of coronary artery disease in Non-ST-Elevation Myocardial Infarction patients.

Limitations

There might be potential selection bias because of large number of exclusion criteria for selection of patients. We assessed myocardial strain in global longitudinal strain value. Global radial strain and circumferential strain was not measured. So, how these strain changes in obstructive coronary artery disease could not be delineated from here.

We could not sample any left main coronary artery disease patient. So, how strain value changes in left main disease could not be deciphered from this study.

Recommendations

Global longitudinal strain can be used with other testing strategy in suspected acute coronary syndrome patient. Further large-scale, multicenter study is recommended to validate the findings of the present study before its inclusion into regular clinical practice.

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