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A study to observe the association of left ventricular ejection fraction and wall motion score index with duration of early systolic lengthening in patients with non-ST-elevation acute coronary syndrome

Dayanand Paswan[1], Lipika Adhikari[2], Sandip Sarkar[3]

[1]Senior Resident, [2]Associate Professor, Department of Cardiology, [3]Assistant Professor, Department of Gynaecology and Obstetrics, RG Kar Medical College, Kolkata, West Bengal, India

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ABSTRACT

Background: Management of non-ST elevation myocardial infarction acute coronary syndrome (NSTEMI ACS) patients is not well defined as that of ST elevation myocardial infarction. The accuracy of results of conventional echocardiography is significantly compromised when imaging is suboptimal, myocardial damage is in small areas, and compensatory hyperkinesias of healthy segment. **Aims and Objectives:** Duration of early systolic lengthening (DESL) may be employed to identify early myocardial ischemia and thus, may help to prepare treatment strategies for NSTEMI patients. **Materials and Methods:** A total of 57 patients with NSTEMI ACS attending the cardiology department were included in the study group. **Results:** More than 80% of patients of NSTEMI have normal or near normal ejection fraction and wall motion score index. In our study, the DESL is prolonged in a significant number of non-ST-elevation acute coronary syndrome patients. **Conclusion:** As DESL is afterload independent, it is superior to global longitudinal strain in assessing myocardial damage. Several studies including ourselves show that DESL of <50 ms may be the cutoff value to reveal minimal myocardial damage.

Key words: Coronary artery disease (CAD); Non-ST-elevation myocardial infarction (NSTEMI); Wall motion score index (WMSI); Left ventricular ejection fraction (LVEF); Global longitudinal strain (GLS); Duration of early systolic lengthening (DESL); Post-systolic shortening (PSS)

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INTRODUCTION

Coronary artery disease is the leading cause of disability-adjusted life year.[1-3] More than one-fourth of the deaths occurring in India can be attributed to cardiovascular diseases (CVD). The age-standardized CVD death rate in India is much higher than the global average (272 vs. 235 per 100,000 population).[4]

Conventional echocardiography is an important predictor of cardiovascular outcomes as it can analyze and assess the regional myocardial function. However, the visual estimation of wall motion is very subjective and operator-dependent. It has 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. Non-ST-elevation acute coronary syndrome (NSTE-ACS) patients can have both stenotic and occluded coronary arteries[5] and varying infarct sizes.[6] The changes in myocardial function caused by coronary occlusion in NSTE-ACS patients were detectable by the duration of early systolic lengthening (DESL), global longitudinal strain (GLS), and wall motion score index (WMSI). DESL is defined

Address for Correspondence:
Dr. Lipika Adhikari, Associate Professor, Department of Cardiology, RG Kar Medical College, Kolkata, West Bengal, India.
Mobile: +91-9434830964. **E-mail:** lipika.adhikari@gmail.com

as the time from onset of Q-wave on electrocardiogram (ECG) to peak positive systolic strain on Speckle-tracking Echocardiography. Recent studies have suggested that DESL may be employed to identify early myocardial ischemia.

Several studies have shown that the extent of damage correlates with clinical outcomes.[7] Significant changes in left ventricle ejection fraction (LVEF) and WMSI require decreased function in several left ventricle (LV) segments, which might not be present in patients with relatively limited myocardial scar. Both these indices have a weak ability to identify patients with minimal myocardial damage.[8] The ischemic myocardium tends to lengthen before the onset of systolic shortening, probably due to its reduced ability to generate adequate active force as the LV pressure rises steeply during the isovolumic contraction phase (IVC).[9] The DESL has been shown to be proportional to the infarct size in STEMI patients.[10] DESL could identify patients with minimal myocardial damage, differentiate between occlusion and non-occlusion, and may be helpful in the risk stratification of patients with NSTE-ACS.

In this study, we evaluated the clinical profile and DESL of patients with NSTE-ACS admitted to cardiology ward and individuals without risk factors. Further, we compared DESL with other indices of LV function including LVEF, WMSI, and GLS.

Aims and objectives

Duration of early systolic lengthening (DESL) may be employed to identify early myocardial ischemia and thus may help to prepare treatment strategy of NSTEMI patients.

MATERIALS AND METHODS

A cross-sectional analytical study was conducted during May 2020–April 2021 in 114 patients at a tertiary health-care center. A total of 57 patients had NSTEMI-ACS and 57 healthy individuals with normal ECG and normal echocardiography, without any cardiac risk factors were included as the control group. The sample size was determined by using Cochran's formula $n=(Z1-\alpha/2)2 \times p \times q/L2$ Where the value of $Z1-\alpha/2=1.96$ considering 95% confidence level Where P=0.14 L=precision in absolute term it is considered here as 7. It gives a sample size of 94.

Patients diagnosed with NSTE-ACS were included in the study. Patients presented with NSTE ACS and heart failure or previous history of STEMI, unstable angina, NSTEMI, coronary artery bypass grafting, left bundle branch block, dilated cardiomyopathy, hypertrophic cardiomyopathy, restrictive cardiomyopathy, stress cardiomyopathy, arrhythmia, heart failure, and valvular heart disease were excluded from the study. A written informed consent was obtained from all study individuals.

Signs and symptoms of NSTE-ACS (chest pain, dyspnea, perspiration, new systolic murmur, pericardial rub) were recorded. Clinical characteristics (age, gender, systemic hypertension [HTN], diabetes mellitus [DM], dyslipidemia, obesity, current smoker) were documented.

Study technology

ECG gated three images in apical view were taken (a4c, a3c, and a2c). The region of interest was adjusted to cover the thickness of the myocardium. Aortic valve closure was identified on continuous-wave Doppler recording through the aortic valve. The LV was subsequently divided into 17 segments covering the entire myocardium. Careful inspection of tracking and manual correction, if needed, was performed, and in case of unsatisfactory tracking, the segment was excluded from the analysis. The Automated Function Imaging algorithm allowed GLS calculated for each of the three apical projections if at least five of six segments were sufficiently tracked. The algorithm then calculated overall GLS as the mean value of all three projections. For each segment, peak negative systolic strain (which represents the maximum segmental systolic shortening) and DESL (≥50 ms) and post-systolic shortening (PSS) (≥20%) were recorded.

Statistical analysis

The clinical as well as 2D echocardiography with strain imaging correlation with other echocardiography variables (DESL, GLS, WMSI, LVEF, PSS) were done with SPSS version 27.0, Inc, Chicago, IL, USA) and Graph Pad Prism version 5. P≤0.05 was considered statistically significant.

Ethical issues

Ethical clearance was taken from the Ethical and Research Committee of R G Kar Medical College.

RESULTS

In our study, 57 (50.0%) patients were in the NSTE ACS Group and 57 (50.0%) patients were in the control group. The male-to-female ratio was 2.3 in the NSTE ACS group.

DISCUSSION

Our study population was matched regarding age, sex, DM, HTN, positive family history, and positive SM. In our study, the mean±SD age of the participants was found to be 55.69±9.87 years. The age range was from 41 to 80 years. Nearly, two-thirds (40, 70.2%) of patients with ACS were

Table 1: Demographics

Parameters	NSTE ACS Group Mean±SD/ n (%) n=57	Control group Mean±SD/ n (%) n=57
Age		
41–50	4 (7)	4 (7)
51–60	16 (28.1)	15 (26.3)
61–70	24 (42)	27 (47.4)
71–80	13 (22)	11 (21.1)
Gender		
Male	40 (70.2)	14 (24.6)
Female	17 (29.8)	43 (74.4)
Smoking status	24 (42.1%)	23 (41%)
Hyperlipidemia	26 (45.6%)	23 (41%)
T2DM	25 (43.9%)	24 (42%)
BMI (kg/m^2)	25.6±2.4	24.2±2.2
Heart rate in BPM	72.2±5.4	70±2.0

*T2DM: Type 2 diabetes mellitus, BMI: Body mass index, NSTE ACS: Non-ST-elevation acute coronary syndrome

male gender, 24 (42.1%) NSTE-ACS patients were current smokers and almost all were male. 24 (45.6%) NSTE -ACS patients were hyperlipidemic, and 43.9 % had diabetes (Table 1). In our study, HTN was the most common risk factor with 33 (57.9%) patients being hypertensive in the NSTE-ACS case. DESL in NSTE- ACS patients was 69.28±4.4 and in the control group 25.6±2.1 which is statistically highly significant (P<0.0001), WMSI 1±0.02 in the control group and 1.2±0.1 (P<0.0001), GLS −19.4±0.9 in control group and −16.1±1.3 in study group (P<0.0148). LVEF 67.3±1.8 in the control group and 57.7±4.1 in the study population (P<57.7±4.1), PSS 0.5±0.2 in the control and −0.7±0.4349 in the study group (P<0.0001) (Table 2). Table 3 shows that DESL has no statistically significant relation with Diabetes, Dyslipidemia HTN Smoking, or Obesity in NSTEMI patients. The present study showed that DESL demonstrated a good correlation with infarct size with the other echocardiography parameters (GLS, WMSI, LVEF) and a short DESL could accurately identify patients with minimal myocardial damage. Table 4 shows that WMSI, GLS, LVEF, and PSS have a positive correlation with DESL in the control group. In the NSTE-ACS group, WMSI and GLS have a positive correlation (P=0.087 and 0.076), and LVEF and PSS have a negative correlation with DESL (P=0.081 and 0.089).

Association of DESL among study subjects with NSTE-ACS: measurement of DESL in NSTE-ACS patients is a novel study. In our study, DESL in NSTE-ACS patients was 69.28±4.4, and in the control group 25.6±2.1 which has a significant correlation and statistically highly significant (P<0.0001).

The measurement of GLS and DESL using speckle tracking echocardiography (STE) has emerged as a new modality for assessing earlier detection of left ventricular myocardial damage the strengths of 2D DELS including better reproducibility and ability to detect minor changes in myocardial function. It is relatively operator-independent.

Table 2: Comparison of parameters between NSTE ACS patients and control group

Parameter	Control (Mean±SD)	NSTE ACS patients (Mean±SD)	P-value
DESL	25.6±2.1	69.2±4.4	<0.0001****
WMSI	1±0.02	1.2±0.1	<0.0001****
GLS	−19.4±0.9	−16.1±1.3	0.0148***
LVEF	67.3±1.8	57.7±4.1	<0.0001****
PSS	0.5±0.2	−0.7±0.4349	<0.0001****

DESL: Duration of early systolic lengthening, NSTE-ACS: Non-ST-elevation acute coronary syndrome, LVEF: Left ventricular ejection fraction, WMSI: Wall motion score index, GLS: Global longitudinal strain, PSS: Post-systolic shortening, P < 0.05 is statistically significant

Table 3: Difference of mean DESL in different parameters among NSTE ACS patients

Parameters	n (%)	Mean	P-value
Obesity			
No	21 (36.8)	69.5±4.7	0.7555
Yes	36 (63.2)	69.1±4.3	
Smoking			
No	33 (57.9)	69.5±4.4	0.7324
Yes	24 (42.1)	69.0±4.6	
Hyperlipidemia			
No	31 (54.4)	69.6±4.3	0.5825
Yes	26 (45.6)	68.9±4.6	
HTN			
No	24 (42.1)	69.2±4.1	0.9176
Yes	33 (57.9)	69.3±4.7	
T2DM			
No	32 (56.1)	68.8±4.6	0.0482
Yes	25 (43.9)	69.8±4.3	

*T2DM: Type 2 diabetes mellitus, HTN: Hypertension, DESL: Duration of early systolic lengthening, NSTE ACS: Non-ST-elevation acute coronary syndrome, P < 0.05 is statistically significant

The present study showed that DESL demonstrated a good correlation between infarct size with the other echocardiography parameters (GLS, WMSI, LVEF) and a short DESL could accurately identify patients with minimal myocardial damage. In NSTEMI-ACS, the ability of DESL to identify patients with coronary occlusion was moderate, and the accuracy in doing so was not significantly different from that of GLS, WMSI, and LVEF. The results imply that short, or lack of, DESL is associated with minimal myocardial damage, while prolonged DESL is associated with larger infarct and occluded arteries and hence, higher risk in patients with NSTE-ACS. When assessing the associations between the number of segments with the presence of DESL and outcome this yielded no significant associations. One of the explanations for this is as demonstrated

Table 4: Correlation between mentioned parameters versus DESL in control and NSTE ACS patients

Parameters	Control group		NSTE ACS Group	
	Pearson correlation coefficient (r)	P-value	Pearson correlation coefficient (r)	P-value
WMSI	0.122	0.309	0.137	0.087
GLS	0.119	0.289	0.143	0.076
LVEF	0.123	0.139	−0.198	0.081
PSS	0.118	0.98	−0.003	0.089

DESL: Duration of early systolic lengthening, NSTE-ACS: Non-ST-elevation acute coronary syndrome, LVEF: Left ventricular ejection fraction, WMSI: Wall motion score index, GLS: Global longitudinal strain, PSS: Post-systolic shortening

by Montalescot[11] the reproducibility of regional DESL is considerably lower compared with global DESL. Secondly, normal versus pathological values of DESL remain to be determined in future studies; hence, our cutoff may not have been the most appropriate value for the general population without risk factors.

Considering this, a part of DESL could potentially be caused by a natural reshaping process of the LV in the general population without risk factors, like what has been described for post-systolic shortening in healthy individuals.

Based on our findings, we may conclude that DESL is a novel phenomenon that should be explored in future studies for the general population. Tragardh et al[12] (Copenhagen, DK) et al., 91 in their study "Early systolic lengthening in patients with STEMI: A Novel predictor of cardiovascular events" showed that assessment of DESL in patients with STEMI yields independent and significant prognostic information on the future risk of cardiovascular events.

Zahid et al.,[16] in their study, showed that ischemic myocardial segments tend to stretch as the intraventricular pressure rises steeply during the IVC before they contract during ejection. DESL was significantly better than GLS, WMSI, and LVEF (P=0.016, 0.008, and 0.001, respectively). A cut-off value of 50 ms could identify patients with minimal myocardial damage with a sensitivity of 77% and a specificity of 92%. The results imply that short, or lack of, DESL is associated with minimal myocardial damage, while prolonged DESL is associated with larger infarcts and occluded arteries, and hence higher risk in patients with NSTE-ACS.

Association of PSS with DESL among study subjects with NSTE-ACS:

Our study almost correlated with other studies, which were published by Christian et al., patients with at least one akinetic segment within the culprit territory (n=21, 60%) demonstrated more PSS (−2.2+1.6 vs. −1.3+1.1%, P ¼ 0.05), than patients with merely hypokinetic segments. our PSS value −2.1–−7.2 in NSTE-ACS patients DESL showed a good correlation with PSS but statistically not significant.

Association of LVEF and WMSI with DESL among study subjects with NSTE-ACS: In our study, more than 80% of NSTE-ACS patients have normal LVEF and WMSI. Our study is almost similar to other studies. For patients with ACS and preserved or mildly reduced LV function at the time of their events, this has important implications as more than two-thirds of patients with NSTEMI and nearly one-half of patients with STEMI have relatively preserved LV function.[6,8] In this study, DESL showed a positive correlation with WMSI and a negative correlation with LVEF.

The accuracy of the results declines significantly when imaging is suboptimal (in the study by Hundley et al.,[17] when ≥2 endocardial segments could not be seen). When quantification of LVEF is necessary, a visual estimate may not always be accurate. Quantification with a Simpson's rule reconstruction improves the estimate, but its accuracy deteriorates rapidly when even two endocardial segments cannot be seen.

Echocardiographic WMSI is a relatively easily obtained marker of global LV dysfunction after myocardial infarction (MI).[12,13] It is derived by grading the wall motion of individual myocardial segments and dividing the total score by the number of analyzable segments. Echocardiographic WMSI found producing an overestimation of low EFs and an underestimation of high EFs. Our data suggest that a greater degree of wall motion abnormality must take place before a lower LVEF occurs. WMSI is more discriminatory for cardiac events than LVEF, the numbers were too small to show definitively at what level of LV dysfunction this difference is most apparent. Echocardiographic WSMI[8,9] is a marker for LV dysfunction.

WMSI is better than LVEF, a commonly observed phenomenon of compensatory hyperkinesia of the healthy segments occurring in the early phase after an AMI.[9] These hypercontractile segments may limit the reduction in systolic function measured by LVEF without limiting it when measured with WMSI since it is based on the contractility of each segment and scores equal to the hypercontractile and normal segments. In large MIs, there is less room for compensatory hyperkinesia, with a higher correlation between WMSI and LVEF, giving both of them similar prognostic information. The WMSI might be a more accurate prognostic marker, especially with smaller myocardial damage, and therefore be particularly useful, in addition to LVEF, in the prognostic stratification of these subgroups.

The superiority of WMSI was observed mainly in patients with NSTEMI.[14] In addition, mortality was higher in patients with major disturbances of WMSI but with relatively preserved LVEF. As the main limitation for LVEF, Mullar[18] measured the WMSI and LVEF on the 1st day of admission, when the compensatory hyperkinesia is maximal and may suppose a bias in the measurement of LVEF, which should become lower with the passage of time as the hyper contractile segments regain normal function. Thus, performing an echocardiogram after the hyperacute phase, as has been done in our work, increases the validity of the comparison of LVEF and WMSI. Although compensatory hyperkinesia is minimal as time goes by the WMSI still has a prognostic value added to LVEF.

It is possible that the superiority of the WMSI over LVEF in predicting readmission for heart failure is due to its higher sensitivity in the detection of myocardial damage, especially in earlier stages.[13] The WMSI can detect incipient damage to systolic function, even in patients with preserved LVEF. In a study of 110 patients by Christian et al.,[14] comparing echocardiographic LVEF derived from the WMSI, echocardiographic Simpson's biplane method and LVEF obtained by CMR, WMSI-derived LVEF had a stronger correlation with CMR than Simpson's biplane method and was more accurate. In a systematic review by Mohanan[5] WMSI-LVEF has proven to be a valid method to LVEF,[14] potentially superior to Simpson's biplane method. Similarly, in a CMR study involving 203 patients, Gjesdal et al.,[15] have demonstrated that the WMSI is an accurate method to measure LVEF[12] and is a useful complement to automatic. WMSI method takes advantage of the multiple incidences of the LV to complete a polar map as opposed to only two sagittal views used for the classical Simpson's biplane method. The Simpson formula is also less precise in patients with very abnormal ventricular geometry (dyskinesia or aneurysm). DESL is better than WMSI and LVEF reason is wall motion score is not designed for the evaluation of hyperkinetic states, because the maximal score by our semi-quantitative model is 65%. This model should be reserved for patients with LV dysfunction and used cautiously in patients with localized hyperkinetic wall motion since it will result in an underestimation of LVEF. Significant changes in LVEF and WMSI require decreased function in several LV segments, which might not be present in patients with relatively limited myocardial scar. Both these indices have a weak ability to identify patients with minimal myocardial damage. More superior 2D speckle tracking derived echocardiographic parameters over WMSI and LVEF, 2D LVEF by Simpson's biplane method is dependent on imaging plane and observer experience. Its accuracy varies with image quality. 2D LVEF has limitations of reproducibility, and it is also not able to detect small changes in contractility. LVEF is a both pre-load and after-loading dependent parameter whereas strain has been shown to be less affected by loading conditions. In addition, 2D STE is relatively less operator-dependent and more reproducible than LVEF Recent studies reported that myocardial deformation imaging by STE after MI predicts cardiovascular outcomes such as new onset heart failure and cardiovascular death.

Limitations of the study

We have done the DESL at the time of admission only. We failed to follow up all patients in outpatient department because most of the patients are non-compliant.

CONCLUSION

Management of NSTE ACS patients is not well defined as that of STEMI. The requirement of early revascularization is dependent on various complex scoring systems. Echocardiographic evaluation by ejection fraction and wall motion abnormality may not be of help as most of the patients have normal or near normal ejection fraction. In our study, more than eighty percent of patients have normal or near-normal ejection fraction and WMSI. However, the DESL was significantly prolonged in NSTE ACS as compared with the control group. The present study also demonstrated its good correlation with other echocardiographic parameters such as LVEF, WMSI, and GLS. Very short or lack of DESL is associated with minimal myocardial damage while prolonged DESL is associated with a larger infarct or occluded artery. As DESL is afterload independent, it may be superior to GLS in assessing myocardial damage. Several studies including ourselves show that DESL of <50 milliseconds may be the cutoff value to reveal minimal myocardial damage.

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Authors' Contributions:
DP- Definition of intellectual content, literature survey, prepared the first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation and submission of an article; **LA**- Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; statistical analysis and interpretation; **SS-** Review manuscript; literature survey and preparation of figures; coordination and manuscript revision.

Work attributed to:
R G Kar Medical College Kolkata.

Orcid ID:
Dayanand Paswan - https://orcid.org/0009-0006-1431-8767
Lipika Adhikari - https://orcid.org/0000-0002-3927-5197
Sandip Sarkar - https://orcid.org/0000-0002-0621-024X

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