ORIGINAL ARTICLE

CORRELATION OF GLOBAL LONGITUDINAL SYSTOLIC STRAIN WITH SEVERITY OF CORONARY ARTERY DISEASE IN NON-ST-ELEVATION ACUTE CORONARY SYNDROME HAVING NORMAL EJECTION FRACTION

Muhammad Khaleel Iqbal[1], Muhammad Saleem Awan[2], Usman Mahmood Butt[1], Shahzad Tawwab[1], Muhammad Furrakh Maqbool[3]

[1]Cardiology Department, Allama Iqbal Medical College/ Jinnah Hospital, Lahore-Pakistan
[2]Cardiology Department, Ayub Medical College/ Teaching Hospital, Abbottabad-Pakistan
[3]Cardiology Department, D.G. Khan Medical College, D.G. Khan-Pakistan

Background: In patients of non-ST-elevation acute coronary syndrome (NSTEACS), the global longitudinal peak systolic strain (GLPS) has been used to detect the presence of coronary artery disease (CAD) before left ventricular ejection fraction (LVEF) is affected. We tried to find out the correlation between the GLPS and severity of CAD in such patients. **Methods:** A descriptive correlational study was conducted from March 2018 to January 2020 at Jinnah Hospital Lahore. Two hundred and sixteen patients of NSTEACS with EF of ≥60% were included. Patients were divided according to angiographic results into those having non-significant, one-vessel, two-vessel or three-vessel disease. These four groups were compared regarding left ventricular end-systolic dimension (LVESD), left ventricular end-diastolic dimension (LVEDD), LVEF, global longitudinal peak systolic strains in apical long axis view (GLPS-APLEX), in apical 4-chamber view (GLPS-A4C), in apical 2-chamber view (GLPS-A2C) and average of these (GLPS-AVG). All these parameters were also compared between patients having and those not having left main coronary artery (LMCA) disease. **Results:** Out of 216 patients, males and females were 124(57.4%) and 92 (42.6%) respectively. There were 28 (13.0%), 83 (38.4%), 62 (28.7%) and 43 (19.9%) patients who had non-significant, one-vessel, two-vessel and three-vessel CAD respectively. With increase in severity of CAD, GLPS-AVG progressively decreased from non-significant CAD being 20.6±0.7 to three-vessel CAD being 16.1±0.7. There was a significant negative correlation between severity of CAD and all of the GLPS-APLEX, GLPS-A4C, GLPS-A2C and GLPS-AVG (p<0.001 in all). GLPS-AVG was significantly low in patients having LMCA disease (16.5±0.7) than those not having LMCA disease (18.2±1.5) with p-value of <0.001. All other types of GLPSs showed the similar trend. **Conclusion:** Global longitudinal peak systolic strain has a significant negative correlation with severity of coronary artery disease in non-ST-elevation acute coronary syndrome having normal ejection fraction.

Keywords: Acute coronary syndrome; Longitudinal systolic strain; Coronary artery disease

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INTRODUCTION

The disease spectrum named as non-ST-elevation acute coronary syndrome (NSTEACS) consists of two types of coronary artery diseases (CAD). One is unstable angina and the other is non-ST-elevation myocardial infarction (NSTEMI).[1] Non-ST-elevation ACS is the major cause of mortality and morbidity across the globe. Six months mortality of patients with NSTEMI and unstable angina were 13% and 8% respectively and thirty day mortality was 9.1% despite best medical facilities.[2–4] Each year, NSTEACS leads to 2–2.5 million hospital admissions worldwide.[5] In Indian population, the coronary artery disease (CAD) was found to have a prevalence of 11% in the year 2001.[6] In Pakistan, ischemic heart disease (IHD) contributes to 11% of all deaths making it the second leading cause of death at all ages.[7] According to a Pakistani study, 28.2% of all the patients presenting with typical chest pain had unstable angina while 55% had NSTEMI making a total of83.2% who had NSTEACS.[8]

A large proportion of patients presenting with NSTEACS have normal left ventricular ejection fraction (LVEF) on echocardiography[1] but still they have significant coronary artery disease on angiography. The studies have shown that measurement of longitudinal systolic strain by speckle tracking method has led to detection of subclinical left ventricular (LV) dysfunction before the conventional parameters like ejection fraction (EF) have derranged.[9] Some such studies have also

been done on acute cardiovascular diseases.[10] Longitudinal Systolic strain has not only been used to diagnose and confirm the acute coronary syndrome (ACS) patients[11,12] especially those having normal ejection fraction but also to risk stratify the patients of ACS[13]. The speckle tracking derived systolic strain has also been used to rule out the presence of CAD in patients presenting with NSTEACS.[14–16] There is however much less DATA available on correlation of severity of CAD on angiography with systolic strain especially in our country where ACS is a major health problem. So, we conducted this study to find a correlation between global longitudinal systolic strain (GLPS) and severity of coronary artery disease (CAD) in patients with NSTEACS so that we are able to predict the CAD severity by just a non-invasive tool.

MATERIAL AND METHODS

The study was conducted at cardiology department, Jinnah Hospital, Lahore from March 2018 to January 2020. The study design was descriptive correlational. A sample size of 215 was calculated with 95% confidence interval (z-score=1.96) and 5% margin of error (ε=0.05) with expected percentage of ACS being 83.2% (*p*=0.832) from the previous study using the formula n= z^2xp (1-p) / ε^2.[8] The research was approved from ethical review board of the Jinnah hospital, Lahore. Sampling was done by purposive, non-probability technique. After taking informed consent, a total of 216 patients having >18 years of age, presenting to emergency with typical chest pain and diagnosed as NSTEACS on the basis of history, clinical examination and ECG, and having ejection fraction ≥60% were included. Exclusion criteria were age less than 18 years, ST elevation myocardial infarction (old or recent), history of percutaneous coronary intervention or open-heart surgery, left or right bundle branch block or non-sinus rhythm on ECG and severe valvular disease. All patients underwent both echocardiography and angiography.

Echocardiographies were done with VIVID-7 GE machine. In parasternal long axis view, M-mode was used to take left ventricular end-systolic dimension (LVESD) and left ventricular end-diastolic dimension (LVEDD). Simpson's biplane method was used to measure left ventricular ejection fraction (LVEF). Speckle tracking method was used to measure global longitudinal peak systolic strain (GLPS) in apical long axis, i.e., APLEX view (GLPS-APLEX), in apical 4-Chamber, i.e., A4C view (GLPS-A4C), in apical 2-Chamber, i.e., A2C view (GLPS-A2C), and average global longitudinal peak systolic strain (GLPS-AVG)

Severity of CAD was seen in angiography of each patient. The significant coronary artery disease (CAD) was defined as 70% or more of the diameter stenosis in any of the major epicardial vessels or 50% or more of the diameter stenosis in case of left main coronary artery (LMCA). The severity of coronary artery disease was graded as non-significant disease, one-vessel, two-vessel and three-vessel coronary artery disease. The presence or absence of left main coronary artery (LMCA) disease was also noted and recorded as a separate variable.

Data was analyzed with SPSS 22.0. Scale variables like age, LVESD, LVEDD, LVEF, GLPS-A4C, GLPS-A2C, GLPS-APLEX, and GLPS-AVG were presented by means and standard deviations. Categorical variables like gender, severity of coronary artery disease and presence or absence of LMCA disease were represented by frequencies and percentages. ANOVA test was used to compare scale variables between groups of different severities of CAD. The correlation of severity of CAD and different types of global longitudinal peak systolic strains (i.e., GLPS-APLEX, GLPS-A4C, GLPS-A2C and GLPS-AVG) was measured by using Spearman's rank correlation coefficient test. As a subgroup analysis, we compared the global longitudinal systolic strains taken in different views as well as average global systolic strain between the patients having and those not having LMCA disease using ANOVA test. Value of *p* was taken to be significant at ≤0.05.

RESULTS

Out of a total of 216 patients, males and females were 124 (57.4%) and 92(42.6%) respectively. Regarding diagnoses, 127 (58.8%) patients were of unstable angina while NSTEMI was the diagnosis in 89 (41.2%) patients. The study subjects had a mean age of 53.5±11.5 years while the means of the echocardiographic measures of LVEDD, LVESD, LVEF and GLPS-AVG were 45.7±3.8, 22.0±2.3, 64.3±3.5 and 18.0±1.5 respectively. (Table-1)

Comparing the subjects having different severities of coronary artery disease (CAD), patients having non-significant, one-vessel, two-vessel and three-vessel coronary artery disease were 28(13.0%), 83(38.4%), 62 (28.7%) and 43(19.9%) respectively. When we compared the subjects with different severities of CAD regarding age, LVEDD, LVESD and LVEF using ANOVA test, *p*-values were insignificant in all of them (Table-2).

When the patients having different severities of CAD were compared regarding global longitudinal systolic strains (GLPSs), all types of global systolic strains decreased progressively between the groups with increasing severity of CAD. So, the non-significant CAD patients had a mean GLPS-AVG of 20.6±0.7 which decreased progressively to 16.1±0.7

in patients with three vessel CAD (Table-3, Figure-1). Similarly, the GLPS-APLEX, GLPS-A4C and GLPS-A2C had values of 20.5±1.3, 20.7±1.1 and 20.8±1.2 respectively in non-significant CAD which decreased by increasing the severity of CAD till they reached the values of 16.2±1.2, 16.0±1.0 and 16.3±1.4 respectively in patients with three-vessel CAD. (Table-3) The ANOVA test revealed the significant difference between the mean values of all types of global longitudinal systolic strains (GLPSs) when the different groups of severity of CAD were compared. *p*-values in all of the GLPS-APLEX, GLPS-A4C, GLPS-A2C and GLPS-AVG were <0.001. (Table-3)When Spearman's rank correlation test was applied between severity of CAD and global longitudinal systolic strain (Table-3), it was found that significant negative correlation existed between severity of CAD and all types of GLPS (in GLPS-APLEX, GLPS-A4C, GLPS-A2C and GLPS-AVG, *p*-value <0.001). As a subgroup analysis, the patients with LMCA disease were compared with those not having LMCA disease. ANOVA test revealed that there was a significant difference between patients having and those not having LMCA disease regarding all types of global longitudinal systolic strains (*p* values in all of the GLPS-APLEX, GLPS-A4C, GLPS-A2C and GLPS-AVG were <0.001). All types of GLPS were significantly low in patients with LMCA disease than those not having LMCA disease. (Table-IV)

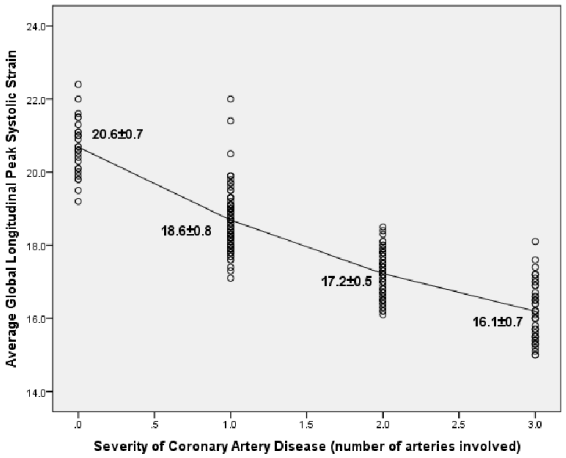

Figure-1: Graph between severity of coronary artery disease and average global longitudinal systolic strain

Table-1: General characteristics of study subjects

	Sex			Age (yrs)	LVEDD	LVESD	LVEF	GLPS-AVG
	Male N(%)	Female n (%)	Total n (%)					
Unstable Angina	75 (34.7%)	52 (24.1%)	27 (58.8%)	53.4±11.3	45.3±3.8	21.8±2.3	64.4±3.6	18.0±1.5
NSTEMI	49 (22.7%)	40 (18.5%)	89 (41.2%)	53.7±11.9	46.2±3.7	22.2±2.2	64.2±3.4	17.9±1.5
Total	124 (57.4%)	92 (42.6%)	216 (100%)	53.5±11.5	45.7±3.8	22.0±2.3	64.3±3.5	18.0±1.5

Table-2: Characteristics of study subjects having different severities of CAD

		Non-significant CAD	Single-vessel CAD	Two-vessel CAD	Three-vessel CAD	*p*-value (ANOVA)
SEX	**Male N(%)**	15(6.9%)	55(25.5%)	30 (13.9%)	24 (11.1%)	
	Female N(%)	13 (6.0%)	28 (13.0%)	32 (14.8%)	19 (8.8%)	
	Total N (%)	28 (13.0%)	83 (38.4%)	62 (28.7%)	43 (19.9%)	
Age		52.7±12.3	54.0±11.7	54.3±10.5	52.0±12.1	0.73
LVEDD		45.7±3.7	45.2±4.1	45.4±3.3	46.9±3.6	0.12
LVEDS		21.9±2.5	21.6±2.3	21.9±2.0	22.9±2.1	0.03
LVEF		65.1±4.1	64.7±3.6	64.3±3.4	63.2±3.1	0.09

Table-3: Comparison and correlation between global longitudinal systolic strain and severity of coronary artery disease

	Non-significant CAD	Single-vessel CAD	Two-vessel CAD	Three-vessel CAD	ANOVA *p*-value	Spearman Rank	
						Correlation Coefficient	*p*-value
GLPS-APLEX	20.5±1.3	18.6±1.1	17.1±1.0	16.2±1.2	**<0.001**	-0.750	**<0.001**
GLPS-A4C	20.7±1.1	18.9±1.2	17.2±0.8	16.0±1.0	**<0.001**	-0.825	**<0.001**
GLPS-A2C	20.8±1.2	18.5±1.3	17.2±1.0	16.3±1.4	**<0.001**	-0.696	**<0.001**
GLPS-AVG	20.6±0.7	18.6±0.8	17.2±0.5	16.1±0.7	**<0.001**	-0.888	**<0.001**

Table-4: Comparison between subjects having and those not having LMCA disease

	LVEDD	LVESD	LVEF	GLPS-APLEX	GLPS-A4C	GLPS-A2C	GLPS-AVG
LMCA disease Absent	45.6±3.7	21.9±2.3	64.5±3.6	18.2±1.7	18.3±1.8	18.2±1.9	18.2±1.5
LMCA disease Present	45.9±4.2	22.47±2.2	63.0±2.8	16.4±1.1	16.4±1.1	16.7±1.1	16.5±0.7
***p*-value (ANOVA b/w two groups)**	0.779	0.287	0.029	<0.001	<0.001	<0.001	<0.001

DISCUSSION

The conventional parameters of left ventricular function, like ejection fraction (LVEF) remain normal during a large number of episodes of non-ST-elevation acute coronary syndrome (NSTEACS).[1] The global longitudinal systolic strain (GLPS) can detect the subtle LV dysfunction in many cardiovascular diseases even before LVEF has dropped below the normal levels.[9,10]

In the previous studies, the longitudinal systolic strain has been used to diagnose the presence of coronary artery disease in NSTEACS with normal systolic function (i.e., normal LVEF).[11,17] Similarly, the longitudinal strain has also been used to predict adverse outcomes after the ACS episodes.[13] The systolic strain has also been seen to be correlated with SYNTAX score of CAD severity.[18,19] However, there is much less DATA available on the correlation of systolic strain with CAD severity regarding single, two or three vessel disease.

The prognosis of the patients having NSTEACS is strongly related to the severity of coronary artery disease (CAD) on angiography.[20] Hence, if we find out the relationship of global longitudinal systolic strain (GLPS) with the severity of CAD, we can predict not only the severity of CAD but also the prognosis of the patients of NSTEACS just on echocardiography derived GLPS. The main aim of the present study was to find out this correlation.

In the present study we included 216 patients of NSTEACS, performed their echocardiography and followed them to coronary angiography. We divided them into four groups regarding severity of CAD (i.e., patients having non-significant, one-vessel, two-vessel and three-vessel CAD). We then compared the echocardiographic features of these groups of different severities of CAD. No significant difference between these groups was found regarding conventional parameters of left ventricle function, i.e., LVEDD, LVESD and LVEF. It was already expected as we included only the patients of NSTEACS with normal LVEF. The same findings were also seen by Caspar T *et al*[11] who found no significant difference in LVEF and diastolic volume of LV between patients having and those not having significant CAD on angiography. Zhang L *et al*[21] found no significant difference between groups of CAD severity regarding LVEF and end diastolic (EDV) as well as end systolic (ESV) volumes.

There are two methods of measuring longitudinal systolic strain on echocardiography, i.e., tissue doppler method[22] and speckled tracking method[23]. In our study, we used 2D grey scale speckle tracking method because it is not an angle dependent modality like tissue doppler. Also, that it gives the global strain after averaging the systolic strain of all segments in three different apical views. The speckle tracking is done by automated function imaging (AFI) software in VIVI-7 machine of GE company. This method gives global longitudinal peak systolic strain (GLPS) in apical long axis view (GLPS-APLEX), in A4C view (GLPS-A4C), in A2C view (GLPS-A2C) and average of these (GLPS-AVG).

Our study showed progressively decreasing trend in all of GLPS-APLEX, GLPS-A4C, GLPS-A2C and GLPS-AVG with increasing severity of CAD from nonsignificant to single, two and three vessel CAD. Applying ANOVA test to compare the means of all types of GLPS between different groups of CAD severity showed significant difference in all types of GLPS ($p<0.001$). The same finding was seen in the study by Moustafa S. *et al*[24] who found significant difference between GLPS of the patients with different severities of CAD ($p=0.001$) although the difference was insignificant regarding conventional parameters, i.e., LVEF, LVEDD and LVESD.

Applying Spearman's rank correlation test, a significant negative correlation was seen in all types of GLPS and the severity of CAD ($p<0.001$ in all GLPSs). Hence, all of the GLPS-APLEX, GLPS-A4C, GLPS-A2C and GLPS-AVG decrease significantly and progressively with increase in severity of CAD in NSTEACS patients. Making a scatter plot between severity of CAD on X-axis and GLPS-AVG on Y-axis revealed linear inverse relationship between the two. Also, there were only a small number of outliers seen in the graph between these two (Figure-1).

Zhang L *et al*.[21] compared the groups of nonsignificant CAD, single or two vessel CAD and complex CAD. They found significant difference in global longitudinal (GLS) as well global circumferential (GCS) strains between these groups. These were the findings similar to our study. Zhang L *et al*.[21] found significant differences in endocardial, mid-myocardial and epicardial strains. So, the strains of all layers of cardiac wall are equally affected and are equally correlated with severity of CAD.

Radwan H *et al*.[25] found significant incremental decrease in global longitudinal strain (GLS) with increasing the number of coronary arteries involved. Their *p*-value was same as in our study, i.e, <0.001. In their study, a significant positive correlation was also seen between GLS and LVEF ($p=0.03$).

In our DATA, patients having left main coronary artery (LMCA) disease were compared with those not having LMCA disease as a subgroup

analysis. It was seen that global longitudinal peak systolic strain in these two groups were significantly different. This finding was seen in all types of GLPSs (p<0.001). The value of all types of GLPSs were significantly low in the group of patients having LMCA disease than those not having LMCA disease. The similar findings were seen by Sharma AK *et al*.[26], Bakhoum SWG *et al*.[27] and Hoshi H *et al*.[28] All of these three studies compared longitudinal systolic strain between high risk group (having LMCA disease/ three-vessel CAD) and low risk group (not having LMCA disease/ three-vessel CAD) and found significantly decreased longitudinal systolic strain in high risk group as compared to low risk group (p-values in Sharma *et al*, Bakhoum *et al* and Hoshi *et al* were <0.001, 0.03 and 0.007 respectively). Sharma AK *et al* used tissue doppler method for measuring longitudinal systolic strain while other two studies used speckle tracking method like our study. The difference between these three studies and our study was that none of them took LMCA disease as a separate entity to group the patients and compare the GLPS between them.

CONCLUSION

In patients of non-ST-elevation acute coronary syndrome (NSTEACS) having normal ejection fraction, global longitudinal peak systolic strain (GLPS) has a significant negative correlation with severity of coronary artery disease (CAD). So GLPS decreases significantly with increase in severity CAD in patients with NSTEACS having normal EF.

AUTHORS' CONTRIBUTION

MKI: Conceptualization, study design, data collection, data analysis, drafting. MSA: Rationale of the study, synopsis writing, sample size calculation, data entry/analysis, proof reading. UMB: Speckle tracking, concept, performing on echo machine, data collection, SPSS. ST: Getting ethical board's permission, data collection, and entry. MFB: Study design, drafting, figures, tables, SPSS.

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Address for Correspondence:

Muhammad Khaleel Iqbal, House No. 48-B, Block-B, Model Town, Lahore-Pakistan
Cell: +92 334 997 7598
Email: khleeldr@hotmail.com