Original Article

COMPARISON OF SPECKLE TRACKING DERIVED LEFT VENTRICULAR STRAIN AMONG PATIENTS WITH VARYING DEGREE OF LV SYSTOLIC DYSFUNCTION IN ASYMPTOMATIC PATIENTS WITH CHRONIC SEVERE RHEUMATIC MITRAL REGURGITATION

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ABSTRACT

OBJECTIVES: Comparing the global longitudinal peak systolic strain of left ventricle measured by speckle tracking method among the patients of chronic severe rheumatic MR having different severity of LV dilation and dysfunction and finding any correlation between LV dysfunction and strain.

METHODS & RESULTS: Subjects were studied under 4 groups Group-I: normal subjects (n =36) Group-II: Severe MR with EF ≥60% and LVESD ≤40mm (n=52), Group-III: Severe MR with EF ≥60% and LVESD 41-50 (n=16), Group-IV: Severe MR with EF <60 with any LVESD (n=8).Mean values of average global longitudinal peak systolic strain (GLPS-AVG) in group-I, II, III and IV were 20.6±2.03, 19.77±2.79, 21.02±3.66, 7.25±1.55 respectively. GLPS-AVG decreased insignificantly with mild LV dilation between groups I and II (p=0.46), and increased insignificantly with further LV dilation between groups II and III (p=0.35) but there was significant decrease in global longitudinal peak systolic strain when ejection fraction decreased below 60% (between group III and group IV, p= <0.001). Same trends were observed in global longitudinal strains measured in all three apical echocardiographic views.

CONCLUSION: Speckle tracking derived global longitudinal peak systolic strain changes insignificantly during LV dilation and shows significant decrease when ejection fraction drops in patients with asymptomatic chronic severe rheumatic mitral regurgitation.

KEYWORDS: Speckle Tracking, Left Ventricular Strain, LV Systolic Dysfunction, Chronic Severe Rheumatic Mitral Regurgitation

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INTRODUCTION:

The most common cause of Valvular Heart Disease in our country is Rheumatic heart disease (RHD).[1-3] According to a study conducted in Pakistan, the most common valvular lesion was mitral regurgitation (MR) which was 56%, even more common than mitral stenosis (MS) (20.3%)[4]. According to another Pakistani study, the severe MR was found in 22.5% of all MR patients[5]. So severe MR is a big health problem of our community.

According to AHA guidelines, Mitral valve surgery is indicated in severe MR if patient develops symptoms or left ventricular ejection fraction (LVEF) drops to ≤ 60% or left ventricle dilates (LVESD ≥ 40mm)[6]. Although EF (≤60%) was the first predictor developed to sort out asymptomatic patients of severe MR for surgery[7], it remains high during a long compensated phase of chronic severe MR and mortality even after surgery is high when EF drops[8,9]. So more sensitive parameters like left ventricular end systolic dimention (LVESD) and volume (LVESV) were devised for early detection of LV dysfunction in severe MR for referring patients to early MV surgery to get better outcomes[7,10,11]. Even the above mentioned parameters e.g LVESD are not reliable and early detectors of LV dysfunction as the studies have shown that waiting for the LVESD to reach ≥40 mm is independently associated with poor postoperative survival in severe MR[12]. So still better parameters are required for better post MV surgery results.

As we already know that compared to conventional echocardiographic parameters, measurement of myocardial strain and strain rate leads to an early detection of LV systolic dysfunction at subclinical stages[13,14]. In chronic severe MR, the research has been conducted to use tissue doppler derived strain imaging to find out subclinical LV dysfunction[15,16]. In these studies, the

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tissue doppler derived myocardial deformation i.e strain was measured and was associated with LV dysfunction.[15, 16]

In our study, we used 2D speckle tracking method for measuring the global longitudinal peak systolic strain (GLPS) of left ventricle (LV) and compared this global strain between patients with and without LV dysfunction to find out if there was any correlation of 2D speckle tracking derived strain with that of LV dysfunction as much less data is available on the 2D speckle tracking derived strain in patients with chronic severe rheumatic MR.

MATERIALS AND METHODS:

This cross sectional analytical study was conducted at Echo Department of Punjab Institute of Cardiology from December 2013 to December 2015 (Two Years) with non-probability purposive sampling. 76 patients of severe rheumatic asymptomatic MR and 36 healthy controls were included in study. Informed consent was taken. Healthy normal subjects were taken under group-I. Patients of severe MR were divided into three groups according to LVESD and EF i.e Group-II (severe MR with EF ≥60% and LVESD ≤40mm), Group-III (severe MR with EF ≥60% and LVESD 41-50), Group-IV (severe MR with EF <60 with any LVESD). Asymptomatic patients with chronic severe rheumatic MR were included. Patients with non rheumatic MR, Patients with Ischemic heart disease (IHD) (on the basis of history, clinical examination or segmental wall motion abnormalities (SWMAs) on echocardiography), patients with more than moderate degree of MS (mitral stenosis), AS (aortic stenosis), AR (aortic regurgitation) and patients with atrial fibrillation (AF) were excluded.

All echocardiographies were performed on VIVID-7 Dimensions machine. Standard parasternal long and short axis views were used to assess LVESD. Apical 4-chamber (A4C), 2-chamber (A2C) and long axis (APLEX) cine views were also saved and Speckle Tracking was performed on these images by Automated Function Imaging (AFI). Global longitudinal peak systolic strain (GLPS) was thus determined in Apical 4-Chamber i.e A4C view (GLPS-A4C), in Apical 2-Chamber i.e A2C view (GLPS-A2C), in Apical long axis i.e APLAX view (GLPS-APLAX) and average global longitudinal peak systolic strain (GLPS-AVG) was also determined. EF was calculated by Simpson's biplane method.

Mitral regurgitation severity: MR severity was assessed using vena contracta and jet area. Jet area > 50% of left atrial and vena contracta > 0.7 cm was taken as criteria for severe MR.

DATA was analyzed using SPSS 17.0. Variables under study were Age, gender, LVESD, LVEDD, EF, GLPX-A4C, GLPX-A2C, GLPX-APLAX, GLPS-AVG. All four groups were compared using ANOVA test regarding all four types of GLPX especially GLPS-AVG. Correlation between changes of GLPS-AVG by changing group were also assessed using Pearson's Correlation coefficient. p-value of <0.05 was considered as significant.

RESULTS:

Study Population: The study included 76 patients of chronic severe rheumatic MR and 36 normal healthy controls. Of the total subjects, 48(42.9%) were male and 64(57.1%) were females (Table-1). A total of 112 study subjects were divided into four groups. Group-I (controls) had 36(32.1%), Group-II had 52(46.4%), Group-III had 16(14.3%) and Group-IV had 8(7.1%) subjects. Overall mean age of study subjects was 31.02±9.9yrs with maximum

Table-1: General characteristics of the study subjects

		N	%	Mean Age (yrs)	LVESD	LVEDD	EF
SEX	Male	48	42.9%	35.13±6.7	31.4±9.1	51.2±7.1	62.1±12.7
	Female	64	57.1%	27.94±10.7	35.4±7.3	53.7±6.2	60.9±7.6
	Total	112	100%	31.02±9.9	33.7±8.3	52.6±6.7	61.4±10.1

Table-2: Groupwise characteristics of the study subjects

		Group-I (Controls)	Group-II (EF ≥60% and LVIDS ≤40mm)	Group-III (EF≥ 60% and LVIDS 41-50mm)	Group-IV (EF<60%)	P value
SEX	Male	28 (78%)	12 (23%)	04 (25%)	04 (50%)	
	Female	08 (22%)	40 (77%)	12 (75%)	04 (50%)	
	Total	36 (32.1%)	52 (46.4%)	16 (14.3%)	08 (7.1%)	
Age		32.2±5.9	32.27±11.8	27.75±9.0	24.0±8.5	0.065
LVIDS		24.5±5.4	34.9±2.7	43.3±2.1	48±3.2	<0.001
LVIDD		45.78±4.0	54.27±5.0	59.75±2.23	59.0±3.2	<0.001
EF		68.22±3.4	61.79±3.1	61.25±2.2	29.0±6.4	<0.001
GLPS-APLEX		20.8±2.97	19.36±2.94	20.95±3.71	7.8±1.06	**<0.001**
GLPS-A4C		19.6±2.08	19.97±3.17	21.1±3.22	6.65±2.51	**<0.001**
GLPS-A2C		21.5±2.87	19.66±3.16	20.7±4.95	7.25±1.01	**<0.001**
GLPS-AVG		20.6±2.03	19.77±2.79	21.02±3.66	7.25±1.55	**<0.001**

Table-3: ANOVA between four groups regarding all types of GLPS and applying Pearson's correlation coefficient

	Sum of Squares	Degrees of freedom	Mean Square	F value	P value	Pearsons Correlation	
						Coefficient	P value
GLPS-Average	1283.88	3	427.96	60.748	**<0.001**	-0.514	**<0.001**
GLPS-APLEX view	1183.49	3	394.5	43.98	**<0.001**	-0.500	**<0.001**
GLPS-A4C view	1355.08	3	451.7	56.33	**<0.001**	-0.434	**<0.001**
GLPS-A2C view	1366.67	3	455.55	41.86	**<0.001**	-0.536	**<0.001**

Table-4: Multiple comparisons between groups regarding GLPS-Average

GROUPS to Compare	Mean Differece (I-J)	Std. Error	P value	95% Confidence Interval	
				Lower Bound	Upper bound
Group-I wih Group-II	0.845	0.575	0.460	-0.656	2.347
Group-I with Group-III	-0.402	0.797	0.958	-2.484	1.678
Group-I with Group IV	13.372	1.037	**<0.001**	10.665	16.08
Group-II with Group-III	-1.248	0.758	0.358	-3.228	0.732
Group-II with Group-IV	12.526	1.008	**<0.001**	9.897	15.15
Group-III with Group-IV	13.775	1.149	**<0.001**	10.77	16.77

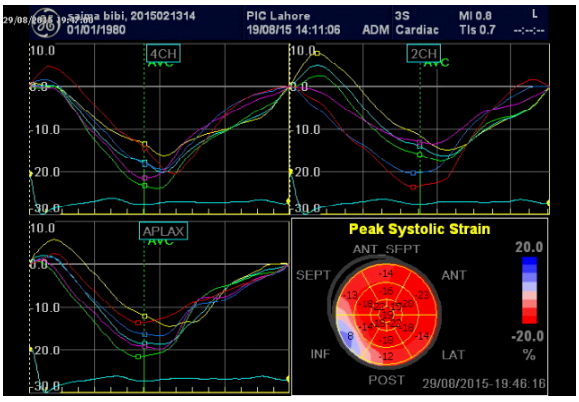

Figure-1: Quad picture obtained as a result of Speckle tracking of a patient showing curves of systolic longitudinal strain of different segments in three apical views i.e A4C, A2C and APLAX. Lower right corner shows bull's eye diagram showing segment-wise peak systolic strain

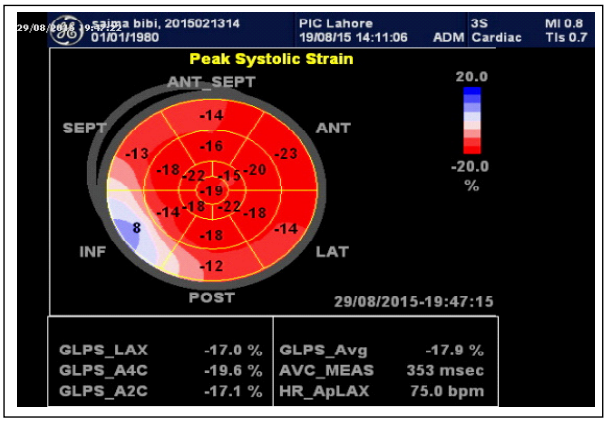

Figure-2: Bull's eye diagram after speckle tracking showing Peak systolic strain of each myocardial segment. Also showing GLPS-LAX, GLPS-A4C, GLPS-AC and GLPS-AVG

age of 54yrs and minimum of 13yrs. End-systolic dimention (LVESD) ranged from 18 to 51 with

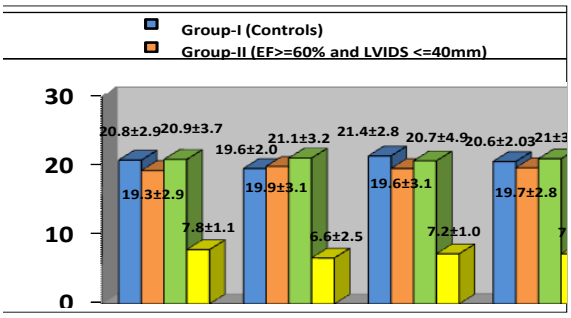

Figure-3: Comparison of all the four groups regarding mean values of GLPS-APLAX, GLPS-A4C, GLPS-A2C, GLPS-AVG

mean of 33.72±8.3mm, End-diastolic dimention (LVEDD) varied from 39 to 65 with mean of 52.6±6.7 and Ejection fraction (EF) varied from 23% to 74% with mean of 61.4±10.1. The group wise characteristics of the subjects are shown in the Table-2. Mean ages of groups I, II, III, IV were 32.2±5.9, 32.27±11.8, 27.75±9.0 and 24.0±8.5 respectively.

Global Longitudinal Peak Systolic Strain: Comparing the Average Global longitudinal peak systolic strain (GLPS-AVG) of the four groups, the mean values in group-I, II, III and IV were 20.6±2.03, 19.77±2.79, 21.02±3.66, 7.25±1.55 respectively (table-2). This showed progressive decreasing trend in GLPS-AVG from group-I to group IV except that GLPS-AVG showed increase between group-II and III. Almost similar type of trends were shown by other peak systolic strain parameters in three different apical views i.e GLPS-APLEX, GLPS-A4C and GLPS-A2C (Figure-1,2,3). Comparing the means of GLPS-AVG between the four groups using ANOVA test, p value turned out to be <0.001. Similarly applying ANOVA, means of all other types of peak strains (GLPS-A4C, GLPS-A2C and GLPS-APLAX) differed significantly between four groups (p <0.001)(table-3).

Applying pearson's correlation coefficient to find out correlation between GLPS-AVG of four groups showed p-value of <0.001 but as mentioned above the GLPS decreased with LV dysfunction except moving from Group II to III. So correlation did not hold practical in all groups.

Comparing the groups one by one regarding peak systolic strain:

As a post-hoc analysis, when we compared the groups, p-value (<0.001) was significant when we compared any of the groups with group-IV. This means that there is significant drop of GLPS-AVG when we move from any of group to group-IV.

Other groups compared with each other produce insignificant p-value (table-4).

DISCUSSION:

In asymptomatic chronic severe rheumatic MR, we usually plan for surgery on the basis of conventional parameters of LV function i.e. EF and LVEDS[17] but the EF and LVESD remains normal for a long period of time (compensated phase of MR) till EF decreases or LVESD increases, the LV has reached a point of irreversible damage.[15] Current guidelines suggest decision of surgery on basis of conventional parameters of LV dysfunction,[17] the mortality after surgery is high if we wait for these parameters to drop.[8,9] A newer echocardiographic paramater i.e Global Longitudinal Peak Systolic Strain (GLPS) detects very subtle amount of LV dysfunction even before there is any change in conventional parameters.[18] Therefore, in this study Average Global Peak Systolic strain (GLPS-AVG) of control group (Group-I) and other three groups of asymptomatic severe MR (Group-II with mild LV dilation, Group-III with Severe LV dilation and Group-IV with LV dysfunction i.e decreased EF) was compared to find out any relationship between progressive LV dysfunction and GLPS-AVG so we can refer the patients for surgery on the basis of GLPS-AVG even before LV dilation has started.

It was found that there was significant decrease in GLPS-AVG ($p = 0.001$) while moving from Group-I to Group IV. Similar results were seen by Gunjan et al[15] who compared the systolic longitudinal strain in patients with severe rheumatic MR with and without LV dilation and with and without decreased EF. It was found by them and also in the present study that with development of progressive LV dysfunction, peak systolic longitudinal strain significantly deceases. The better difference of the present study over their study is that they used Tissue doppler method of echocardiography which is more difficult to perform and because of being a doppler method, is angle dependent and has much noise pollution. These are not the problems of speckle tracking method which has been used in this study to calculate longitudinal strain. Moreover speckle tracking method gives Averaged Global strain which gives more global value of LV dysfunction of all myocardial segments as compared to doppler method which gives the strain of only the region of myocardium where the sample volume is placed and not the global strain. Till now almost no study have used this advanced speckle tracking method for calculating and comparing LV dysfunction in patients with rheumatic MR although studies have been performed for LV dysfunction in degenerative MR[19], ischemic MR[20], secondary MR (due to nonischemic dilated cardiomyopathy)[21] and functional MR (ischemic or non ischemic dilated cardiomyopathy)[22].

The results of our study differed from that of Gunjan et al in that although with decrease in LV function, longitudinal peak systolic strain decreased significantly ($p=<0.001$) while moving from group I-IV, there was no significant decrease in GLPS-AVG between group-I and group-II, even moving from group-II to group-III, the GLPS-AVG has actually increased, although not statistically significant. It means that with increase in LV dimensions i.e with progressive LV dilation, peak systolic strain first decreases with mild dilation of LV (LVESD $\leq$ 40mm) and then with further dilation (LVESD 41-50mm but EF $\geq$60%), it increases but with decrease in EF below 60%, this longitudinal peak systolic strain significantly decreases ($p<0.001$). This finding is contradictory to study by Gunjan et al but is well explained by the frank starling's law that with incearse in LV dimentions (LV dilation), as there is increase in length of myocardial fibers' length at the start of systole, the fibers contraction is more stronger and their shortening during systole increases and so longitudinal systolic strain also increases with severe LV dilation although with mild LV dilation, it has actually decreased. Same results are seen in study by Marciniak et al.[16] that with LV dilation, there is not much significant change in systolic strain which is significantly decreased with decrease in LVEF as in our study, although strain by Marciniak et al was measured by Tissue Doppler method and not speckle tracking as in our study.

Applying Pearson's correlation coefficient to average global peak systolic strain (GLPS-AVG) between the groups, the p-value of <0.001 gives the impression that GLPS-AVG is significantly correlated with progressive LV dilation and dysfunction (table-3) but looking at the scatter plot (fig-3) show that the GLPS-AVG although progressively decreases with more and more LV dysfunction, it actually increases between group II and III. Also decrease in GLPS-AVG is not smooth between groups and significant decrease is only between group III and IV. Moreover scatter plot shows significant influential outliers, so all these things make the above mentioned correlation invalid.

In the present study, in place of average longitudinal systolic strain, when different groups are compared regarding the longitudinal systolic strain in different views i.e in APLEX view (GLPS-APLEX),

in A4C view (GLPS-A4C), and in A2C view (GLPS-A2C), the same trends were seen in these separate strain types as those seen in average strain (GLPS-AVG) Table-2,3.

Study Limitations: The present study is a cross sectional and the data is not paired and has no longitudinal followup and also needs postoperative DATA to see postoperative condition of longitudinal systolic strain. Also software of speckle tracking does not give average peak strain (GLPS-AVG) in the presence of atrial fibrillation (AF) as varying cycle length does not have peak systole at the same time in cardiac cycle in all three views and most patients with severe MR develop AF so speckle tracking, although a very good method, will not be that useful in MR. That's why AF has been an exclusion criteria in this study and many patients were excluded due to AF. Moreover the patients having EF less than 60% are either operated before reaching this stage of LV dysfunction or get so sick (and develop SOB and hypotension) that they can not be taken to echo lab to be included in the study so the number of such patients (group IV patients) are very less in our study (only 8 patients).

CONCLUSION:

In chronic severe rheumatic MR patients, global longitudinal peak systolic strain measured by speckle tracking method shows an insignificant change with progressive LV dilation (increase in LVESD) and shows a significant decrease with development of LV dysfunction (i.e drop in LVEF).

Author's Contribution

MKI: Conducted the study and wrote the article. MFM: Helped in conducting the study and gave frequent advice.IS: Helped in collecting and re-analyzing the data.

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