ORIGINAL ARTICLE

# SYSTOLIC STRAIN RATE IN LEFT VENTRICULAR DYSFUNCTION CAUSED BY RHEUMATIC CHRONIC SEVERE MITRAL REGURGITATION

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**Background:** In rheumatic severe mitral regurgitation, earlier detection of left ventricular dysfunction is very necessary in order to refer the patients for surgery at appropriate time. This study tried to find a correlation between conventional parameters of left ventricular dysfunction with systolic strain rate. **Methods:** A descriptive correlational study conducted from September 2016 to March 2018. One hundred and ninety-two patients of severe rheumatic MR and fifty-eight healthy controls were included. Left ventricular ejection fraction (LVEF), end diastolic dimension (LVEDD) and end systolic dimension (LVESD) were measured. Healthy controls were taken as group-I and patients were divided into group-II (ejection fraction ≥60% and LVESD ≤40 mm), group-III (ejection fraction ≥60% and LVESD ≤41–50 mm), and group-IV (ejection fraction <60%). Systolic strain rate at medial wall (SSR-med), at lateral wall (SSR-lat) and average of both (SSR-avg) were also measured by tissue doppler method for each study subject. **Results:** Out of 250 study subjects, males were 113 (45.2%) and females were 137 (54.8%). Means of the age, LVEF, LVEDD and LVESD were 30.8±9.1, 60.0±8.3, 58.5±7.8 and 37.4±9.9 respectively. Group I, II, III and IV contained 58, 69, 67 and 56 subjects respectively. Comparing these groups, mean LVEF progressively decreased from 63.9%±2.2 in group-I to 46.2±6.5 in group-IV while means of LVEDD and LVESD progressively increased from 45.9±3.5 and 23.2±2.3 in group-I to 64.3±3.6 and 49.0±2.9 in group-IV respectively. Average systolic strain rate (SSR-avg) decreased progressively from 1.57±0.06 in group-I to 0.83±0.08 in group-IV. All the strain rates, i.e., SSR-med, SSR-lat and SSR-avg showed significant negative correlation with left ventricular dysfunction, i.e., the group number ($p$<0.001). **Conclusion:** Systolic strain rate measured by tissue doppler method have significant negative correlation with left ventricular dysfunction in patients having rheumatic chronic severe mitral regurgitation.

**Keywords:** Left ventricular dysfunction; Strain rate; Mitral regurgitation

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## INTRODUCTION

Rheumatic heart disease is one of the major health problems of our country. The prevalence of this commonest valvular disease in Pakistan between ages of 6–15 years is 14.6 per 900 patients.[1] According to one local study published in Pakistan, the most common valvular lesion found in rheumatic heart disease was mitral regurgitation (MR) being 56% followed by mitral stenosis being 20.3% of rheumatic patients.[2] In patients with severe mitral regurgitation (MR), the indications for surgery are the occurrence of symptoms or development of left ventricular dysfunction either in the form of drop in left ventricular ejection fraction (LVEF) below 60% or as dilatation of left ventricle which occurs when the left ventricular end systolic dimension (LVESD) is ≥40 mm.[3]

It has been seen that during a long phase in the history of chronic severe MR the LV ejection fraction is compensated and does not fall below 60%. So, if we wait for ejection fraction to drop, the surgery is delayed upto a high mortality stage. So after LVEF, another more sensitive predictor of LV dysfunction was added in the guidelines which was left ventricular end systolic dimension (LVESD).[3] Even if we wait for LVESD to increase utpo ≥40 mm the postoperative survival after surgery of severe MR is very poor.[3] So there are still more sensitive predictors of LV dysfunction are needed which detect the exact and earliest time when surgery is inevitable in the course of MR.

The systolic strain rate (SSR) is a parameter that has been proven to detect LV systolic dysfunction earlier as compared to the conventional parameters like ejection fraction in different diseases.[4–6] There are two methods of measuring strain rate in echocardiography lab which are speckle tracking in 2-D grey scale imaging[7] and tissue doppler imaging.[8] In the recent past, the studies on

severe MR have shown the peak systolic strain (PSS) to detect left ventricular dysfunction earlier than the traditional parameters like ejection fraction.[9,10] There are however very few studies in which systolic strain rate (SSR) has been compared with conventional parameters of LV function in severe MR although systolic strain rate is a less afterload dependent measure than peak systolic strain.[11] Moreover, rheumatic MR has been studied much less than other causes of MR. We conducted this study to compare the systolic strain rate between MR patients of different severities of LV dysfunction and find a correlation between LV dysfunction and SSR to develop a new parameter for detection of left ventricular dysfunction.

## MATERIAL AND METHODS

A descriptive correlational study was conducted in Punjab institute of cardiology from September 2016 to March 2018. Sample size of 185 was calculated from formula

$$n = \frac{z^2 \times \hat{p}(1-\hat{p})}{\varepsilon^2}$$

where Z= 2.05 (for 96% confidence interval), $p$=0.125 (as expected proportion of MR was 12.5% from previous study[12]) and ε=0.05 (for 5% margin of error).

After taking informed consent, one hundred and ninety-two patients of chronic asymptomatic severe rheumatic mitral regurgitation and fifty-eight healthy controls (all having ages between 15 and 55 years) were included. Patients having non rheumatic MR and MR due to ischemic heart disease (diagnosed on the basis of history, clinical examination, as well as ECG or echocardiography having segmental wall motion abnormalities) were excluded. Other exclusion criteria were mitral stenosis, aortic stenosis or aortic regurgitation of more than moderate degrees. Sampling was done with a purposive, non-probability and consecutive technique.

Echocardiography of all study subjects (controls and patients) was done using Vivid-7 GE machine. Severe mitral regurgitation was diagnosed if area of regurgitant jet was more than 50% of left atrial area and vena contracta of the jet was more than 0.7 cm. M-mode of left ventricle after making parasternal long axis view was taken and left ventricular end diastolic dimension (LVEDD) as well as left ventricular end systolic dimension (LVESD) were measured. Simpson's biplane method was also used to measure ejection fraction of left ventricle (LVEF).

Apical 4-chamber view was made and peak value of systolic strain rate (SSR) was measured by putting tissue doppler on left ventricle and placing the sample volume on basal medial (SSR-med) and basal lateral (SSR-Lat) walls. The average of these two SSRs was also measured and was called average systolic strain rate (SSR-Avg). Tissue doppler imaging was done at minimal optimal gain to reduce aliasing. Also, the angle of tissue doppler beam with left ventricular wall was always kept less than 20 degree. To reduce quantification noise (variance), the Nyquist limit, i.e., scale of the strain rate was kept as low as possible without creating aliasing. Sample length of strain rate was 12mm and sample was anchored with myocardium throughout the cardiac cycle by frame to frame manual tracking. In case of atrial fibrillation, the strain rate of a myocardial segment during ten consecutive cycles was averaged.

Study subjects were divided into group-I (healthy controls), group-II (patients having ejection fraction ≥60% and LVESD ≤40 mm), group-III (patients having ejection fraction ≥60% and LVESD 41–50 mm) and group-IV (patients having ejection fraction <60%).

Variables under study were age, sex, LVEDD, LVEF, LVESD and systolic strain rates at medial wall (SSR-med), systolic strain rate at lateral wall (SSR-lat) and average systolic strain rate (SSR-Avg). All types of SSRs of different groups having different severities of LV dysfunction were compared using ANOVA test. Also, the correlation between average systolic strain rate (SSR-Avg) and the group number (i.e., LV dysfunction) was seen by applying spearman rank correlation test. Same spearman rank test was used to see the correlation of SSR-med and SSR-lat with LV dysfunction (group number). "$p$" was considered significant if it had a value of <0.05.

## RESULTS

Out of a total 250 study subjects, males were 113 (45.2%) and females were 137(54.8%). Means of the age, LVEF, LVEDD and LVESD were 30.8±9.1, 60.0±8.3, 58.5±7.8 and 37.4±9.9 respectively.

Dividing the study subjects into groups, the group I, II, III and IV contained 58, 69, 67 and 56 subjects respectively. When we compared these groups, LVEF showed progressively decreasing trend with mean LVEF being 63.9%±2.2 in group-I which decreased to 46.2±6.5 in group-IV with a significant $p$-value of <0.001 (ANOVA between groups). Similarly comparing LVEDD and LVESD between these groups showed progressive increasing trends with LVEDD reaching 64.3±3.6 in group-IV starting with 45.9±3.5 in group-I (ANOVA, $p$<0.001) while LVESD progressively increased from 23.2±2.3 in group-I to 49.0±2.9 in group-IV ($p$<0.001). When the groups were compared regarding systolic strain rate at medial (SSR-Med) and lateral walls (SSR-lat) as well as average

systolic strain rate (SSR-Avg), the values of these strains were 1.55±0.06, 1.59±0.05 and 1.57±0.06 in group-I respectively which decreased to 0.81±0.08, 0.85±0.08 and 0.83±0.08 in group-IV respectively.

When the groups having different severities of left ventricular dysfunction were compared regarding SSR-med, SSR-lat and SSR-Avg using ANOVA test, a significant difference was found between the groups regarding all types of SSR ($p$<0.001 in each SSR). A significant negative correlation was found between LV dysfunction (group number) and average strain rate (SSR-Avg) using spearman rank correlation test (correlation coefficient -0.965, $p$ value <0.001).

Similar negative correlation was also found between the group number and SSR at both medial (SSR-medial) and lateral (SSR-lateral) walls applying spearman rank test ($p$<0.001 in both SSRs).

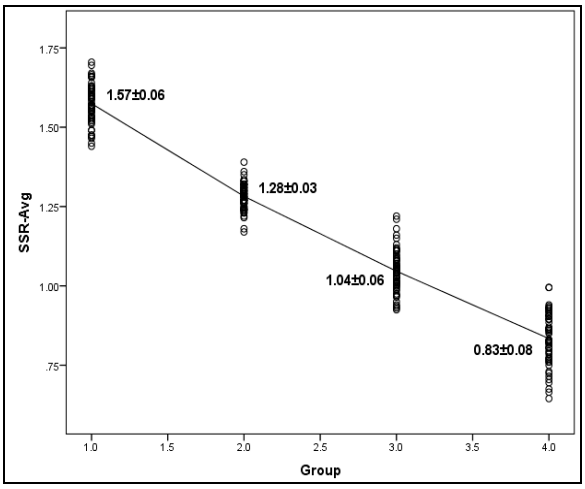


**Figure-1: Correlation between average systolic strain rate (SSR-Avg) and group number**

**Table-1: General characteristics of the study subjects**

| | n (%) | Age (yrs) | LVEF | LVEDD | LVESD | Average Systolic Strain Rate ($sec^{-1}$) |
|---|---|---|---|---|---|---|
| **Male** | 113(45.2%) | 32.1±9.0 | 59.7±8.5 | 58.5±8.6 | 37.3±10.4 | 1.18±0.29 |
| **Female** | 137(54.8%) | 29.7±9.1 | 60.1±8.2 | 58.5±7.1 | 37.5±9.4 | 1.18±0.26 |
| **Total** | 250(100%) | 30.8± 9.1 | 60.0±8.3 | 58.5±7.8 | 37.4±9.9 | 1.18±0.27 |

**Table-2: Group-wise characteristics of the study subjects**

| | | Group-I | Group-II | Group-III | Group-IV | $p$-value (ANOVA) |
|---|---|---|---|---|---|---|
| **SEX** | **Male** | 29 (50%) | 29 (42%) | 28 (41.8%) | 27 (48.2%) | |
| | **Female** | 29 (50%) | 40 (58%) | 39 (58.2%) | 29 (51.8%) | |
| | **Total** | 58 (100%) | 69 (100%) | 67 (100%) | 56 (100%) | |
| **Age** | | 31.3±8.7 | 30.2±9.3 | 29.7±9.0 | 32.3±9.4 | 0.373 |
| **LVEF** | | 63.9%±2.2 | 65±2.9 | 63.0±1.8 | 46.2±6.5 | <0.001 |
| **LVEDD** | | 45.9±3.5 | 61.5±3.6 | 61.6±3.0 | 64.3±3.6 | <0.001 |
| **LVESD** | | 23.2±2.3 | 34.0±3.3 | 43.5±1.8 | 49.0±2.9 | <0.001 |

**Table-3: Comparison of systolic strain rate (SSR) between different groups**

| Systolic Strain Rate | Group-I | Group-II | Group-III | Group-IV | ANOVA $p$-value | Spearman Rank | |
|---|---|---|---|---|---|---|---|
| | | | | | | Correlation Coefficient | $p$-value |
| **SSR-Med** | 1.55±0.06 | 1.26±0.04 | 1.02±0.06 | 0.81±0.08 | <0.001 | -0.966 | <0.001 |
| **SSR-Lat** | 1.59±0.05 | 1.29±0.04 | 1.06±0.06 | 0.85±0.08 | <0.001 | -0.965 | <0.001 |
| **SSR-Avg** | 1.57±0.06 | 1.28±0.03 | 1.04±0.06 | 0.83±0.08 | <0.001 | -0.965 | <0.001 |

## DISCUSSION

Mitral regurgitation is one of the commonest lesion to occur in rheumatic heart disease.[2] As many as 56% of the patients of rheumatic heart disease in Pakistan have mitral regurgitation out of which 8.8% patients are having severe mitral regurgitation.[2] In asymptomatic patients of severe MR, the conventional indicators used for detecting left ventricular dysfunction are ejection fraction (LVEF) and end systolic dimension (LVESD). However, still these parameters remain normal for a long phase in chronic severe MR and if we wait for these parameters of LV function to drop, the postoperative mortality is still high.[13,14]

Systolic strain rate (SSR), whether measured by tissue Doppler method[8] or by speckle tracking method[13,15], is a new parameter which can detect LV dysfunction even when conventional measures like LVEF and LVESD are intact and dysfunction is subtle[15]. So, in this study, we took asymptomatic patients of rheumatic chronic severe mitral regurgitation and divided them into three groups according to left ventricular function and took a group of healthy controls. We compared SSR between these groups and also assessed a correlation between SSR and LV function.

Group-I consisted of healthy controls. Group-II, III and IV were patients of severe MR with mildly dilated LV, severely dilated LV and decreased

ejection fraction respectively. So, moving from group-I to group-IV, subjects had progressive impairment in LV function. Regarding LV dimensions, it was seen that both end-systolic (LVESD) and end-diastolic (LVEDD) dimensions showed significant increasing trends (i.e., dilatation of left ventricle seen) while moving from group-I to group-IV (ANOVA, $p<0.001$) and LVEF also decreased significantly between group I to IV ($p<0.001$). Hence, according to conventional parameters, significant increase in LV dysfunction was seen as we moved from group-I to IV. This was already expected as we made the groups accordingly. So, these groups served the purpose very well.

We used tissue doppler imaging to measure systolic strain rate (SSR) on basal medial (SSR-Med) and basal lateral (SSR-Lat) walls and average of these two SSRs (SSR-Avg) was also taken. When these three types of SSRs were compared between the four groups of the study subjects, all types of systolic strain rates showed decreasing trends with increase in LV dysfunction, i.e., moving from group-I to group-IV. The trend was found significant using ANOVA test ($p$-value <0.001 in all SSR-med, SSR-lat and SSR-Avg). The same finding was seen in the previous study by Gunjan *et al*[16], the only study we found which compared the systolic strain rate in patients of left ventricular dysfunction caused by rheumatic severe MR. Gunjan *et al*[16] also found the significant ($p<0.05$) correlation between strain rate and conventional indices like EF and LVESD.

Another study by Yurdakul *et al*[4] found that peak systolic strain rate was significantly decreased in asymptomatic severe MR as compared to healthy controls ($p<0.001$) which also further and even more significantly decreased on 12 months follow-up. The difference between their study and ours was that they used velocity vector imaging (VVI) to measure the strain rate rather than tissue doppler imaging used in our study. Tissue doppler imaging is more common than VVI and is incorporated in almost all echocardiography machines now-a-days. Moreover, they included the patients of all types of non-ischemic MR while in our study we took only the patients with rheumatic MR which has been very less studied in the west as it is now more a disease of developing countries like Pakistan.

The previous studies on mitral regurgitation (like study by Casas-Rojo *et al*) have compared and correlated the conventional parameters of LV function with the systolic strain but in our study we used the systolic strain rate (SSR) to quantify the LV dysfunction because strain rate is more load independent measure as compared to strain.[11]

When we tried to find out correlation between the LV dysfunction labelled by the conventional parameters (i.e., group number) and systolic strain rate (SSR) with the help of Spearman rank correlation coefficient, we found a significant negative correlation between systolic strain rate and LV dysfunction ($p<0.001$). It was also found that systolic strain rate taken at basal medial wall, at basal lateral wall as well as average of these had the same significant negative correlation with the LV dysfunction. Hence, by increase in LV dysfunction there was a drop-in systolic strain rate in patients with rheumatic severe mitral regurgitation as seen in the figure-1.

The studies[10,13] in the past used the speckle tracking method to measure and compare systolic strain rate with conventional parameters of LV function but we used tissue doppler in our study because the speckle tracking method needs regular rhythm in order to incorporate three different two-dimensional views of the heart while many patients of severe MR have atrial fibrillation. In tissue doppler method, instead, we can take strain rate in any particular echocardiographic view in even a single cycle. Moreover, we had taken tissue doppler derived strain rate in ten different cycles in the case of atrial fibrillation and have averaged those ten readings. The limitation of tissue doppler is that it is an angle dependent modality like all other doppler modalities of echocardiography. So, we had kept the angle of interrogation of tissue doppler beam less than 20 degree while measuring the strain rate.

## CONCLUSION

Left ventricular dysfunction and tissue doppler derived systolic strain rate have significant negative correlation in severe mitral regurgitation of rheumatic origin. There is a significant decrease in the systolic strain rate with increase in LV dysfunction.

**Conflicts of interest:** There are no conflicts of interest to be declared by authors.

## AUTHORS' CONTRIBUTION

MKI: Study design, synopsis writing, data collection, data analysis, drafting and proof reading. MFM: Concept and rationale of study, study design, data acquisition, data interpretation and analysis, writing and language correction. ST: Study design, data analysis and output, making out-put sheets on SPSS, drafting, proof reading. MSA: Main concept of study, sample size calculation, data entry on SPSS and its analysis, out-put sheets figures and tables. TN: Extensive work in data collection, entry and analysis through SPSS, corrected the tables and out-put, writing and proof reading. UMB: Contributed in study design, main concept, tissue doppler imaging, concept of echo machines, interpretation of data and its analysis, drafting and language correction.

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