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# CORRELATION OF SYSTOLIC TISSUE VELOCITY WITH LEFT VENTRICULAR DYSFUNCTION IN PATIENTS PRESENTING WITH RHEUMATIC SEVERE MITRAL REGURGITATION

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**Contribution**
MKI conceived the idea and designed the study. Data collection and manuscript writing was done by MFM, AM, ST, UMB, and IS. All the authors contributed equally to the submitted manuscript.

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## ABSTRACT

**Objective:** To detect correlation between systolic tissue velocity and left ventricular systolic dysfunction in patients presenting with severe rheumatic mitral regurgitation (MR).

**Methodology:** A comparative study was performed at Punjab Institute of Cardiology, Lahore between October 2016 and February 2018. Fifty eight controls and 192 patients with rheumatic severe MR were included. End systolic dimension (LVESD), end diastolic dimension (LVEDD) and ejection fraction (LVEF) of left ventricle (LV) were taken. Group-1 contained healthy controls. Groups II, III and IV contained the patients of severe MR with non-dilated LV (LVESD $\leq$40mm and LVEF $\geq$60%), dilated LV (LVESD $\leq$40mm and LVEF $\geq$60%) and decreased LVEF (LVEF$<$60%) respectively. Tissue doppler was used to measure peak systolic tissue velocity at medial annulus (SV-Med), lateral annulus (SV-Lat) and average velocity (SV-Avg) of each subject.

**Results:** A total of 250 study subjects contained 45.2% (n=113) males and 54.8% (n=137) females. Mean age of the study subjects was 30.8$\pm$ 9.1. Group-I consisted of 58 controls. There were 69, 67 and 56 subjects in groups II, III and IV respectively. Moving from group-I to group-IV, LVEF decreased from 63.9%$\pm$2.2 to 46.2$\pm$6.5, LVESD increased from 23.2$\pm$2.3 to 49.0$\pm$2.9 and LVEDD increased from 45.9$\pm$3.5 to 64.3$\pm$3.6 respectively. Average systolic tissue velocity (SV-Avg) progressively decreased from group-I being 9.64$\pm$0.22 to group-IV being 6.32$\pm$0.47. There was a significant negative correlation between LV dysfunction and SV-Avg (spearman's rank coefficient -0.921, p$<$0.001). A positive correlation was also found between LVEF and SV-Avg in patients with severe MR only (pearson's coefficient 0.859, p$<$0.001).

**Conclusion:** A significant negative correlation exists between the peak tissue systolic velocity and left ventricular dysfunction in patients presenting with severe rheumatic mitral regurgitation.

**Key words:** Mitral Regurgitation, Tissue Velocity, Left ventricular dysfunction

## INTRODUCTION

Rheumatic heart disease (RHD) has high prevalence of 14.5 for every 900 patients of ages between 6 to 15 years[1] and 5.7 per 1000 in rural areas of Pakistan.[2] Mitral valve is the most commonly involved valve in the rheumatic heart disease. According to one Pakistani study, as many as 56% of patients of RHD had mitral regurgitation (MR) which was the most common valvular lesion in RHD. Out of these patients, severe MR was present in 8.8%.[2]

For severe mitral regurgitation, surgery is indicated when the patient becomes symptomatic or when left ventricular (LV) function gets impaired in an asymptomatic patient of severe MR.[3] So the biggest task is to detect LV function impairment before the damage to left ventricle is irreversible. The conventional parameters of LV function to refer the asymptomatic patients of severe MR for surgery were left ventricular ejection fraction (LVEF) and end-systolic dimension (LVESD). But it has been seen that during a long phase in the history of severe MR, the LVEF and LVESD remain normal and compensated. So even waiting for LVEF to drop or dilation of LV to occur leads to poor medium and long term survival postoperatively.[3] Therefore, some new, more sensitive and load independent parameters of LV function are still needed to refer the patients for surgery at early and appropriate time.

The previous data suggests that the normal systolic as well as diastolic tissue velocities measured by tissue Doppler imaging (TDI) at mitral valve annulus depict the normal cardiac function with high sensitivity and specificity.[4] The previous studies have also shown that the tissue Doppler derived systolic velocity at medial or lateral annulus of mitral valve can detect left ventricular dysfunction earlier than the conventional echocardiographic parameters like LVEF in different diseases.[5-8] Also that tissue systolic velocity has been found to be load independent measure[9,10] so it will more accurately depict the LV function and is less likely to be changed by changes in after or preload. This modality has however much less studied in the mitral valve disease especially severe mitral regurgitation although such sensitive parameters are needed to early detect the left ventricular dysfunction and refer the patients for surgery in severe MR at appropriate time. So we studied the systolic tissue velocity in severe mitral regurgitation and tried to find a correlation between tissue velocity and LV dysfunction.

## METHODOLOGY

It was a comparative study which was performed at Punjab institute of cardiology, Lahore between October 2016 and February 2018. The formula $n = z^2 \times p\ (1-p) / e^2$ was used to calculate study sample size of 185 where 'z' score for 96% confidence interval was 2.05, 'e' with margin of error of 5% was 0.05 and population 'p' with expected proportion of MR as 12.5% from previous study11 was 0.12. After taking informed consent, 192 consecutive asymptomatic patients of severe mitral regurgitation of rheumatic type with ages between 15 to 55 years were included. Another group of 58 healthy people were taken included control group. Exclusion criteria were ischemic MR (based on history, clinical examination, ECG and echocardiography) and MR due to causes other than rheumatic heart disease. The patients having more than moderate severity of other lesions like aortic regurgitation, aortic stenosis and mitral stenosis were also excluded.

Vivid-7 Dimensions GE machine was used to do echocardiography of controls as well as patients of MR. Diagnostic criteria of MR were vena contracta of the MR jet being $\geq$0.7cm and area occupied by jet being >40% of LA area (if jet is not wall hugging otherwise only vena contracta of $\geq$0.7cm). M-mode at tip of mitral valve was used to take left ventricle dimensions at end diastole (left ventricular end diastolic dimension, LVEDD) and at end systole (LVESD). Left ventricular ejection fraction (LVEF) was measured Simpson's biplane method.

Tissue Doppler imaging region of interest (ROI) was put on LV in apical four-chamber view and Q analysis was used to measure the peak of systolic wave of tissue velocity signal tracing (S'). This gave peak systolic tissue velocity (SV). Such peak systolic velocities were taken at both medial annulus (SV-Med) and lateral annulus (SV-Lat) of mitral wall. Average of both velocities (SV-Avg) was also measured. Angle between Tissue Doppler beam and LV wall was kept less than 20 degree. And tissue Doppler gain was kept minimal (to avoid the aliasing phenomenon) and scale of tissue velocity was kept low (in order to avoid the variance i.e. quantification noise) but it was just above the aliasing point. In patients with atrial fibrillation, all variables including LV dimensions and all tissue velocities (SV-Med, SV-Lat, SV-Avg) were averaged during 10 consecutive cycles and mean of ten cycles was taken.

We divided the study subjects into four groups. Group-I consisted of healthy controls. Group-II, Group-III and Group-IV contained patients with severe MR having non-dilated LV with normal EF (LVESD $\leq$40mm with LVEF $\geq$60%), dilated LV with normal EF (LVESD 41-50 with LVEF $\geq$60%) and decreased EF (LVEF <60%) respectively.

The studied variables were gender, age, left ventricular end systolic dimension (LVESD), Left ventricular end diastolic dimension (LVEDD) and left ventricular ejection fraction (LVEF) along with systolic tissue velocity at lateral (SV-Lat) and medial (SV-Med) annulus of mitral valve as well as average systolic tissue velocity (SV-Avg). The groups were compared regarding all types of systolic tissue velocities (SV-Med, SV-Lat, SV-Avg) using ANOVA test. The

Spearman rank correlation coefficient test was used to find the correlation between LV dysfunction (i.e. group number) and each type of tissue systolic velocity separately (i.e SV-Med, SV-lat and SV-Avg). As a subgroup analysis, we applied the pearson's correlation test between average systolic tissue velocity and LVEF in patients having severe MR (only groups II, III and IV). p value of $<0.05$ was considered significant.

## RESULTS

A total of two hundred and fifty study subjects consisted of 113(45.2%) males and 137(54.8%) females. Mean age of the study subjects was 30.8±9.1 while means of LVESD, LVEDD, LVEF and average systolic velocity (SV-Avg) were 37.4±9.9, 58.5±7.8, 60.0±8.3 and 7.75±1.18 respectively.

**Table-I: General features of the study subjects**

| | N (%) | Age (yrs) | LVEDD | LVESD | LVEF | SV-Med | SV-Lat | SV-Avg |
|---|---|---|---|---|---|---|---|---|
| **Male** | 113 (45.2%) | 32.1±9.0 | 58.5±8.6 | 37.3±10.4 | 59.8±8.5 | 7.73±1.25 | 7.83±1.25 | 7.78±1.24 |
| **Female** | 137 (54.8%) | 29.7±9.1 | 58.5±7.1 | 37.5±9.4 | 60.1±8.2 | 7.68±1.14 | 7.78±1.12 | 7.73±1.13 |
| **Total** | 250 (100%) | 30.8±9.1 | 58.5±7.8 | 37.4±9.9 | 60.0±8.3 | 7.70±1.19 | 7.80±1.18 | 7.75±1.18 |

**Table-II: Group-wise features of the study subjects**

| | N (%) | Age | LVEDS | LVEDD | LVEF | SVavg |
|---|---|---|---|---|---|---|
| **Group-I** | 58 (23.2%) | 31.3±8.7 | 23.2±2.3 | 45.9±3.5 | 63.9±2.2 | 9.64±0.22 |
| **Group-II** | 69 (27.6%) | 30.2±9.3 | 34.0±3.3 | 61.5±3.6 | 65.0±2.9 | 7.66±0.19 |
| **Group-III** | 67 (26.8%) | 29.7±9.0 | 43.5±1.8 | 61.6±3.0 | 63.0±1.8 | 7.40±0.16 |
| **Group-IV** | 56 (22.4%) | 32.3±9.4 | 49.0±2.9 | 64.3±3.6 | 46.2±6.5 | 6.32±0.47 |
| **ANOVA between groups (p value)** | | 0.373 | **<0.001** | **<0.001** | **<0.001** | **<0.001** |

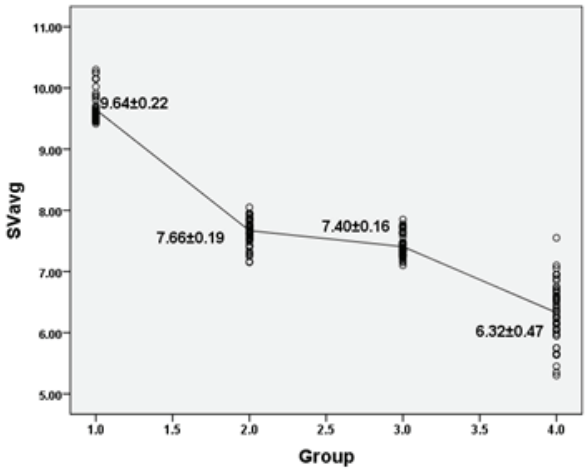
There were 58 (23.2%) subjects in group-I, 69 (27.6%) in group-II, 67 (26.8%) in group-III and 56 (22.4%) in group-VI. A progressive increase in both the systolic (LVESD) and diastolic (LVEDD) dimensions of left ventricle was seen as we moved from group-I to group-IV (by increasing LV dysfunction). In group-I, LVESD and LVEDD were 23.2±2.3 and 45.9±3.5 respectively which increased progressively with increasing the group number till they reached 49.0±2.9 and 64.3±3.6 respectively. Similarly, ejection fraction (LVEF) showed progressive decrease from group-I being 63.9±2.2 to group-VI being 46.2±6.5. Comparing the means of LVESD, LVEDD and LVEF between groups by ANOVA test revealed that each of these variables have significant difference between groups ($P<0.001$ in all the three).

The systolic tissue velocities i.e. SV-Med, SV-Lat and SV-Avg showed progressive decrease with increasing LV dysfunction (i.e. increasing group number). The systolic tissue velocities at medial annulus (SV-Med), at lateral annulus (SV-Lat) and average systolic velocity (SV-Avg) in group-I were 9.59±0.19, 9.69±0.26, 9.64±0.22 respectively which decreased progressively between groups to reach 6.25±0.48, 6.39±0.47 and 6.32±0.47 in group-IV respectively. ANOVA test showed significant between group difference regarding all three types of tissue velocities ($p<0.001$ in each systolic velocity). Also spearman rank correlation coefficient test revealed significant negative correlation between group number (i.e LV dysfunction) and average tissue systolic velocity (SV-Avg) with correlation coefficient of -0.921 and p value of $<0.001$. Similar results were seen by applying spearman rank test on SV-Med and SV-Lat (table-III).

**Table-III: Comparison between different groups regarding systolic tissue velocities.**

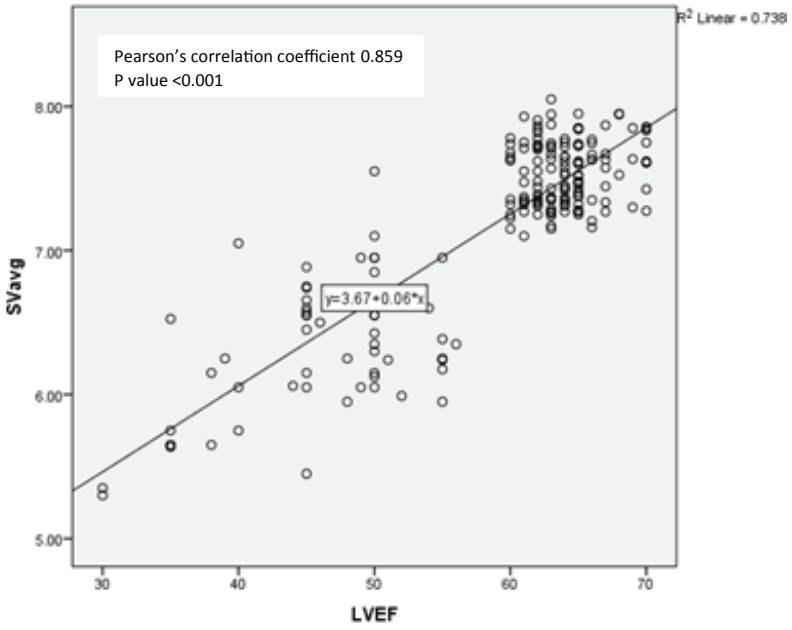
| Systolic Tissue Velocity (SV) | Group-I | Group-II | Group-III | Group-IV | ANOVA P value | Spearman Rank | |
|---|---|---|---|---|---|---|---|
| | | | | | | Correlation Coefficient | P value |
| SV-Med | 9.59±0.19 | 7.63±0.19 | 7.36±0.16 | 6.25±0.48 | <0.001 | -0.926 | <0.001 |
| SV-Lat | 9.69±0.26 | 7.70±0.19 | 7.45±0.17 | 6.39±0.47 | <0.001 | -0.918 | <0.001 |
| SV-Avg | 9.64±0.22 | 7.66±0.19 | 7.40±0.16 | 6.32±0.47 | <0.001 | **-0.921** | **<0.001** |

**Fig-I: Correlation between group number (LV dysfunction) and average systolic tissue velocity**




As a subgroup analysis, we took only patients with severe MR i.e. only groups II, III and IV and found a significant positive correlation between LVEF and SV-Avg using Pearson's correlation coefficient test (coefficient 0.859, p <0.001).

**Figure-II: Scatter graph between LVEF and SV-Avg in patients with severe MR (i.e. groups II, III and IV). Also shown is the Pearson's correlation coefficient and p value.**



## DISCUSSION

Rheumatic heart disease (RHD) is the cause behind 22% of cases of valvular heart disease in the developed nations like Europe[12] and in Pakistan the health problem is still bigger.[1,2] The most frequent valvular lesion found in RHD is mitral regurgitation (MR) being 56%. The most common valvular involvement leading to heart failure is MR. According to one study, the most frequent lesion found in patients of heart failure was MR having a proportion of 12.5%.[11] Another study showed most prominent cause of mitral regurgitation was rheumatic heart disease being the disease behind in 41.1% of isolated MR.[13]

In the treatment of mitral regurgitation, the surgery is indicated on development of either the symptoms or the impairment of LV function.[3] So for those patients who are asymptomatic, the detection of LV dysfunction and referral for surgery at an earlier stages in disease process is very necessary to get good postoperative results.[3] The conventional parameters of LV function like LVEF and LVESD remain normal during a long compensated phase of severe MR and mortality is still high if these are waited to get worse.[14] So we tried to correlate the LV function with a more sensitive and load independent parameter i.e. tissue doppler derived peak systolic velocity (SV) to early detect the LV dysfunction in severe MR.

In the present study, when the groups as defined earlier were compared regarding conventional parameters, we found significant progressive LV dilatation i.e. both LVESD and LVEDD increased between the groups ($p < 0.001$). However ejection fraction (LVEF) dropped progressively and significantly while moving from group I to IV ($p < 0.001$). This was exactly what was expected and needed from the groups so these groups served their purpose.

When we compared the tissue velocities taken at medial (SV-Med) and lateral (SV-Lat) annulus as well as average tissue velocity (SV-Avg) between the groups, we found significant between group difference in each of these velocities (ANOVA p value $< 0.001$). Also there was a significant correlation between average tissue velocity (SV-Avg) and the group number i.e LV dysfunction (spearman rank coefficient -0.921, $p < 0.001$). This correlation was negative. It means that with increase in LV dysfunction there was a significant decrease in SV-Avg. Almost similar type and significance of correlations were found in SV-Med and SV-Lat. We saw same trend in scatter graph between group number and SV-Avg and also we saw not much outliers in the graph. Also it is worth noting that tissue velocity correlated with LV dysfunction even when it still had not reached the critical level of fulfilling the criteria for surgery (i.e. in groups I and II).

The above mentioned observations were in harmony with the previous study by Gunjan et al.[15] who also found significant positive correlation between the conventional measures of LV function and tissue doppler derived parameters like systolic tissue velocity ($p < 0.05$) in rheumatic severe MR.

Florescu M et al.[16] conducted study on asymptomatic severe primary MR and fond that severe MR patients had significantly decreased systolic tissue velocities than age matched healthy controls ($p=0.0001$). These decreased velocities further showed a significant decrease with drop in LVEF postoperatively ($p=0.0001$). They however did not compare the systolic tissue velocities between different severities of LV dysfunction in MR patients as we did in our study.

Another study by Polat TB et al.[17] on rheumatic carditis showed that in tissue systolic velocity is not reduced as compared to controls in acute attack of MR which is significantly reduced in chronic MR on follow-up visit especially in MR of grade II or more ($p<0.001$). Still they did not study the correlation of tissue velocity with LV function in severe MR.

Agricola E et al.[18] also studied tissue doppler derived systolic velocity in postoperative patients of severe MR and found the systolic tissue velocity to be significantly decreased with decrease in EF and both was correlated significantly ($p=0.0001$).

As a subgroup analysis of our study, we took only the patients of severe MR (only groups I, II and III) and looked for presence of any correlation between ejection fraction (LVEF) and SV-Avg in these patients. We found a significant positive correlation between SV-Avg and LVEF using pearson's correlation coefficient test (correlation coefficient 0.859, $p < 0.001$). It meant that average peak systolic velocity (SV-Avg) also decreases significantly when LVEF drops down. As the tissue velocity is a load independent measure, it can give us a better picture of patients' LV function as compared to conventional parameters like LVEF. We can extend our research to find the relationship of other tissue doppler derived measures like the systolic strain and strain rate with LV function as compared to tissue velocity alone.

## CONCLUSION

A significant negative correlation exists between left ventricular dysfunction and systolic tissue velocity in patients presenting with asymptomatic severe rheumatic mitral regurgitation. There is also a significant positive correlation between left ventricular ejection fraction and tissue velocity in such patients.

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