“Changes of left and right ventricles function in rheumatic mitral stenosis patients”

Master thesis

A thesis submitted in part fulfilment for the degree of Master of Medicine

Supervisor
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SUMMARY

Author's name and surname: Jessica Theodorie

Research title: “Changes of left and right ventricles function in rheumatic mitral stenosis patients.”

Aim: This study aims to establish changes of left ventricle (LV) and right ventricle (RV) function and mechanics in patients with rheumatic mitral stenosis (MS) using 2D echocardiography and two-dimensional speckle tracking imaging.

Objectives: 1. To assess changes of RV geometry, function and pulmonary artery pressures in rheumatic MS using 2D echocardiography. 2. To assess changes of LV geometry, function and myocardial deformation parameters in rheumatic MS.

Methodology: 22 patients with mitral stenosis were enrolled, clinical data such as NYHA functional class, coexisting diseases, medicament treatment were collected. The control group consisted of 23 age and gender matched persons with normal valvular function. 2D echocardiography was performed for all patients. Parameters such as mitral valve area, left ventricle end-diastolic diameter, indices of LV end-diastolic and systolic volume, LV ejection fraction, diameters of right and left atriums, as well as left atrium volume, RV diameter, indices of longitudinal RV function (TAPSE, s’) as well as global RV function (FAC) were calculated, tricuspid valve regurgitation degree and systolic pulmonary artery systolic pressure were evaluated. LV global longitudinal strain was assessed using two-dimensional speckle tracking imaging. Parameters were analyzed by SPSS software.

Results: Reduced LV ejection fraction and global LV longitudinal strain was found in MS patients (p<0.001), while LV diastolic diameter and volume index did not differ between groups (p=0.6 and p=0.84 respectively). The correlation between MV area and LV global longitudinal strain, LA volume and the velocity of TV regurgitation was revealed. The smaller MV area (<1,4 cm²) correlated with lower LV global longitudinal strain (r=-0.436, p=0.042), lower LV EF (r=0.533, p=0.01), more dilated LA (p=0.025) and higher TV regurgitation velocity (r=-0.579, p=0.005). There was no significant correlation found between MV area and LV end diastolic diameters and volumes (p=0.2 and p=0.3), as well as RV diameter and RV longitudinal function parameters.

Conclusions:
1. LV global longitudinal strain and LV ejection fraction was lower in rheumatic MS group patients when compared to control group and was related to the severity of valve stenosis.
2. There was no significant correlation found between MV area and LV end diastolic diameter and volume indices, as well as RV diameter and RV longitudinal function parameters, but the relation was found between MV area and LA volume and velocity of tricuspid regurgitation.
ACKNOWLEDGEMENTS

I owe my sincere gratitude to my supervisor Prof. Eglė Ereminienė, for her continuous encouragement and support. I am also thankful to Doctor Ali Aldujeli for his guidance and efforts. Finally, I would like to express my appreciation to Irena Nedzelskiene for the help provided in statistics analysis. This research would hardly have been completed without their contribution.
CONFLICT OF INTEREST

The author reports no conflict of interest.
ETHICS COMMITTEE CLEARANCE

The ethics committee in the bioethics center at Lithuanian University of Health Sciences allows the medical student Jessica Theodorie, from VI course, on 2017-12-15 by her request Nr. BEC-MF-140, to proceed with her scientific research “Changes of left and right ventricle function in rheumatic mitral stenosis patients”. It involves changes assessment of RV geometry, function and pulmonary hypertension in rheumatic MS using 2D echocardiography and of LV geometry, function and myocardial deformation parameters.
All the research is fully conducted under the supervision of Prof. Eglė Ereminienė from Cardiology department.
ABBREVIATION LIST

2D – two-dimensional
RHD – rheumatic heart disease
TTE – transthoracic echocardiography
MV – mitral valve
MVA – mitral valve area
NYHA – New York heart association
2D STE – two-dimensional speckle tracking echocardiography
EF – ejection fraction
LV – left ventricle
LA – left atrium
RA – right atrium
RV – right ventricle
LVEDV – left ventricular end-diastolic volume
LVEDVi – left ventricle end-diastolic volume index
LVESD – left ventricular end-systolic diameter
LVEDD – left ventricle end-diastolic diameter
LVEDDi – left ventricle end-diastolic diameter index
LVESV – left ventricular end-systolic volume
LVESVi – left ventricle end-systolic volume index
FAC – fractional area change
TAPSE – tricuspid annular plane systolic excursion
PA – pulmonary artery
sPAP – pulmonary artery systolic pressure
AT – acceleration time
LVOT – left ventricle outflow tract
STE – speckle tracking echocardiography
STI – speckle tracking imaging
TDI – tissue Doppler imaging
PH – pulmonary hypertension
AF – atrial fibrillation
BSA – body surface area
PMV – percutaneous mitral valvuloplasty
Sr – strain rate
INTRODUCTION

Valvular heart disease is one of many heart pathologies, it can include rheumatic heart disease, known to be a chronic sequel of rheumatic fever. Rheumatic heart disease (RHD) is a preventable condition, in which the incidence and prevalence varies among different age groups and regions worldwide [1][2]. However, cases have been rarely reported in developed countries whereas in developing ones, higher rate of morbidity and mortality are being recorded [2]. Interestingly, despite the decline of identified new cases, it still remains a major disease involving all heart valves, especially the mitral valve (consisting of leaflets, chordae and papillary muscles), being mostly affected. Morphological changes consist of commissural fusion and shortening of the chordae, causing mobility restrictions of the leaflets and eventually contributing to narrowing of the orifice; and hence mitral stenosis being the hallmark of the disease [3].

This abnormal alteration in the mitral valve affects the hemodynamic flow primarily by blocking the forward flow into the left ventricle (LV) from the left atrium (LA), causing volume and pressure overload of LA [4], passively resulting in pulmonary hypertension (PH) from the backflow of blood to the lungs, and deterioration of right ventricular (RV) function mainly when it fails to cope with PH [5,6]. Although LV systolic dysfunction has been reported in MS, the impact of the stenotic mitral valve on intrinsic LV myocardial contractility remains an issue of debate for over 3 decades. There is still controversy whether LV dysfunction in this context is a result of functional or myocardial factors. Evidence from early studies suggested that impaired LV systolic function may be due to rheumatic myocardial fibrosis or as a consequence of scarring of subvalvular apparatus, reduction of LV compliance, abnormal right-left septal interaction, increased afterload, and reduced LV filling. Nevertheless, other evidences reveal that in patients with isolated MS, ventricular contractility is normal [6][7].

Within the progress of this study, we tried to assess changes of biventricular geometry and function parameters as well as pulmonary artery pressure in rheumatic MS using 2D echocardiography in addition to evaluating the changes of LV myocardial deformation parameters in this group of patients.
AIM AND OBJECTIVES OF THE THESIS

Aim:
This study aims to establish changes of left ventricle and right ventricle function in patients with rheumatic mitral stenosis using 2D echocardiography and two-dimensional speckle tracking echocardiography.

Objectives:
1. To assess changes of right ventricle geometry, function and pulmonary artery pressure in rheumatic mitral stenosis using 2D echocardiography.

2. To assess changes of left ventricle geometry, function and myocardial deformation parameters in rheumatic mitral stenosis using 2D echocardiography and two-dimensional speckle tracking analysis.
Rheumatic heart disease (RHD) is a long-lasting outcome of acute rheumatic fever which is recognized as an autoimmune inflammatory response against the offending agent group A streptococcal infection (streptococcal pharyngitis). Moreover, the worldwide use of penicillin G benzathine that prevents the recurrence of this illness has impacted the overall incidents of rheumatic heart disease, as many cases are still documented due to other contributing factors such as poverty, malnourishment and overcrowding. An estimate of 30 million individuals are affected globally by rheumatic heart disease; with approximately 300000 deaths reported in 2015. Females being affecting twice as much when compared with males [8].

RHD was traditionally diagnosed by the presence of new cardiac murmur on auscultation until echocardiography has become the newly comprehensive noninvasive diagnostic tool to establish the presence pathological valve. Rheumatic carditis can affect all four heart valves with mitral valve being predominantly altered, mitral stenosis remains the main pathophysiological change that occurred during rheumatic disease [9]. 2D echocardiography shows commissural fusion and shortening of the chordae, causing mobility restrictions of the leaflets and eventually contributing to narrowing of the orifice.

In normal physiology, the mitral valve opens during diastole phase of the cardiac cycle. The blood flow is sustained to be unidirectional from the left atrium to left ventricle under pressure gradient as long as the pressure in the left ventricle is lower. Mitral stenosis is mechanical obstruction, the obstruction affects the hemodynamics primarily by blocking the forward flow into the left ventricle (LV) from the left atrium (LA), causing LA volume and pressure overload [4], passively resulting in pulmonary hypertension (PH) from the backflow of blood to the lungs, and deterioration of right ventricular function mainly when it fails to cope with PH [5]. Summation of these changes or independent long term hemodynamic effects are directly proportionate with the severity of stenosis.

Left ventricular systolic performance is usually preserved in pure mitral stenosis patients [9] yet, some publications presented with existence of varying degrees of ventricular dysfunction in approximately a quarter of mitral stenosis patients. However, the factors contributing to the dysfunction is still controversial, hemodynamic and structural conditions are related to LV dysfunction. Proposed etiologies include widespread inflammation through myocardium, with the long term effect of inflammation causing the scarring of subvalvular apparatus, decreased LV filling hence, decreasing the preload and subsequent increase in afterload, impaired right-left septal collaborations and pulmonary hypertension [10].
Assessment of left ventricle performance in mitral stenosis

Echocardiographic examination, principally by determining ejection fraction (EF) has been the method used to evaluate the global left ventricular contractile function. Moreover, ejection fraction is load dependent measurement, high prevalence of atrial fibrillation and the inability to establish subclinical dysfunction of LV in mitral stenosis patients has led to limitations in predicting LV dysfunction. Nowadays, tissue doppler imaging (TDI) and 2D Speckle tracking echocardiography (2D-STE) derived strain/strain rate imaging are the techniques used to evaluate LV systolic function without the limitation seen in EF. TDI is more sensitive modality when compared to EF, nevertheless it has the disadvantage of being angle dependent, whereas, 2D STE is angle independent and therefore provides better comprehensive assessment of LV deformation – early changes of LV dysfunction. From 2D images, LV strain parameters express myocardial deformation, and strain rate (Sr) express the rate of deformation. Both of these methods provide quantitative assessment of global in addition to local myocardial function [11].

Theories explaining left ventricular dysfunction

Mechanical obstruction produced from the structural changes on the mitral valve has influenced the LV filling. A chronic inflow reduction to the LV has been believed to be the main reason behind the decline in cardiac performance. Hence, many studies have investigated the relationship between the left ventricle end diastolic volume (LVEDV) and LV dysfunction after percutaneous mitral valvuloplasty (PMV). As PMV theoretically should alleviate the obstruction. However, the results have been conflicting, with some studies showing that PMV provides an immediate improvement in LVED volume whereas, others reported the contrary with no change or slight increase after the procedure.[12]

Another theory proposed that back pressure from LA and subsequent pulmonary hypertension from long standing MS can have an impact on LV dysfunction, and that is due to unequal filling of both ventricles. An earlier filling is noted in the right ventricle during early diastole when compared to the left ventricle, that results in leftward displacement of the interventricular septum. This could be explained by absence of obstruction in the right side. Researchers proposed that the effects on the septum can predispose left ventricular systolic dysfunction. [6]

Alternative theory was long term pancardiac inflammation with resultant fibrosis that causes abnormal wall motion, and subsequent LV dysfunction. A study by A. M. Soesanto and colleagues [13] evaluated the extend of myocardial fibrosis concluding, greater fibrosis can be associated to subclinical LV dysfunction regardless of the mitral valve area. Similar findings were obtained by E. Bilen et al [7]. These results demonstrate that subclinical dysfunction seen in MS is dependent on
rheumatic changes including myocardial factor rather than hemodynamic factors.

A rise in afterload has also been investigated to be a probable cause of LV dysfunction in MS, as the fall in ejection performance can be explained partially by high LV afterload that is not compensated by increase in preload due to apparent restriction of orifice opening during diastole. They assumed the higher LV afterload is an outcome of inadequate end systolic wall thickness, in this manner increases wall stress at normal LV systolic pressure. Nonetheless, no certain mechanism has been established.

Sufficient knowledge of the disease process is essential in selecting optimal management strategy. Mitral stenosis is mechanical obstruction disorder, medical therapy can improve symptoms but does not have any impact on flow obstruction. Surgical intervention whether by valve replacement or repair are recommended in mitral stenosis until current years when noninvasive treatment modalities came into practice and have been preferred like percutaneous mitral valvuloplasty. PMV provides an effective therapy in dilating the orifice and hence relieving the obstruction. The purpose of the intervention is to improve long term risk of mortality. However, more incidence of adverse events are noted and that is due to several factors impacting the success and mortality rates, for instance, atrial fibrillation (AF) in old patients, a study by Y. Soga et al.[14] has showed that higher event rates are seen in AF patients when compared with sinus rhythm patients after undergoing successful PMV. There are various additional factors that may affect mortality such as age, pulmonary hypertension, concomitant disease (coronary artery disease), LVEF. However, little is known how the impaired LV function clinically affects the prognosis.

Difficulties

It is important to keep in mind that although there are several hypothesis proposed to explain the overall status of systolic LV dysfunction in patients with MS; findings remain controversial, likewise, the fundamental pathophysiologic mechanisms are not clearly recognized.
RESEARCH METHODOLOGY AND METHODS

A sample of 22 patients who underwent 2D echocardiographic evaluation in the tertiary teaching hospital, Department of cardiology, at the Lithuanian University of Health Sciences, between the period of May 2016 and December 2018 were enrolled prospectively in this study. The research was approved by LSMU bioethical centre, the ethics committee of the hospital. The control group consisted of 23 age and gender matched persons with normal valvular function.

Clinical data including NYHA functional classification, medical history (atrial fibrillation, arterial hypertension, diabetes mellitus), were reviewed attentively for all the selected subjects.

Echocardiographic examination and measurements

Echocardiographic evaluation was performed by a single experienced cardiologist using commercially available system (Vivid Seven, General Electric-Vingmed Ultrasound AS, Horten, Norway), with a 3.5 MHz transducer, according recommendations of the American Society of Echocardiography [15][16]. All the patients were examined in the left lateral decubitus position using TTE with two dimensional, continuous wave doppler and speckle tracking echocardiographic modalities.

Many variables were calculated including diameters of LV, LA, RA, RV, indices of LV end diastolic and systolic volumes.

Parameters to determine global LV systolic function: LV end systolic volume (LVESV), LV end diastolic volumes (LVEDV) were determined from the four and two chamber views using the modified Simpson’s rule and LVEF was calculated using the following formula: EF = (EDV-ESV)/EDV. To compare between individuals with different body size, chamber measurements were indexed to basal surface area (BSA).

Analysis of RV systolic function included: fractional area change (FAC), DTI-derived tricuspid lateral annular systolic velocity wave (S’), tricuspid annular plane systolic excursion (TAPSE) from apical 4 chamber view.

Pulmonary artery systolic pressure (sPAP) was derived from tricuspid regurgitant jet velocity using Bernoulli equation. Mean pulmonary artery (PA) pressure approximated by the PA acceleration time (AT).

Peak longitudinal global LV strain using speckle tracking echocardiography measured in three standard apical views (2C, long axis view, 4C) and calculated as an average of three apical views.
Quantification of mitral stenosis

Mitral valve area was assessed directly through 2D planimetry in parasternal short-axis view at the tip of leaflet as well as by Doppler evaluation. Pressure half time (P1/2t) was assessed - the time interval between the maximum mitral gradient in early diastole and the time point where the gradient becomes half of the peak initial value, expressed in milliseconds. Valve area is inversely related to the decline of the velocity of diastolic transmitral blood flow. MVA was derived using an empirical formula: MVA = 220/P1/2t cm². P1/2t was derived by tracing the slope of deceleration of E wave on Doppler spectral display of transmitral flow, and the valve area was calculated automatically by the software. [17][18].

Statistical analysis

All data was evaluated in Microsoft Excel® and IBM SPSS Statistics © (SPSS Inc, Chicago, IL, USA). The level of significance was accepted when the p value was less than 0.05 (p < 0.05). Continuous variables were expressed as mean ± SD. To compare control group with study subjects, Mann-Whitney test was used. Correlation between continuous variables were tested by nonparametric Pearson correlation analysis.
RESULTS

The study examined 22 patients with mitral stenosis. MV area was calculated as 1.22±0.2 cm², with medium gradient in diastole 10.3±0.7mmHg. High proportion were females (95.5%) with mean age 63.5[57.0-75.8]. The frequency of coexisting diseases (diabetes mellitus, arterial hypertension, dislipidaemia) did not differ between groups. Analyzing NYHA functional class in MS patients - II NYHA functional class was diagnosed in 13 (61.9%), while III-IV functional class was found in 8 (38.1%) of the group patients. 68% of the MS group patients had paroxysmal atrial fibrillation, though during the echocardiographic investigation all the patients were in sinus rhythm. The patients reported taking cardiovascular agents, the used agents were Beta blockers (82%), diuretics (77%), anticoagulant (64%) and ACEi (55%). Clinical characteristics parameters of patients group and control group are detailed in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total n=45</th>
<th>MS group n=22</th>
<th>Control group n=23</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, n(%) Men/Women</td>
<td>4(8.9)/41(91.1)</td>
<td>1(4.5)/21(95.5)</td>
<td>3(13.0)/20(87)</td>
<td>0.608</td>
</tr>
<tr>
<td>Age, Median[25-75%], years</td>
<td>59.0[55.0-65.5]</td>
<td>63.5[57.0-75.8]</td>
<td>58.0[54.0-59.0]</td>
<td>0.003</td>
</tr>
<tr>
<td>Body surface area [25-75%], m²</td>
<td>1.82[1.76-1.92]</td>
<td>1.8[1.74-1.89]</td>
<td>0.72</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, n(%)</td>
<td>4(8.9)</td>
<td>1(4.5)</td>
<td>3(13.0)</td>
<td>0.608</td>
</tr>
<tr>
<td>Arterial hypertension n(%)</td>
<td>11(24.4)</td>
<td>7(31.8)</td>
<td>4(17.4)</td>
<td>0.26</td>
</tr>
<tr>
<td>Dislipidaemia n(%)</td>
<td>15(33.3)</td>
<td>6(27)</td>
<td>9(39.1)</td>
<td>0.399</td>
</tr>
</tbody>
</table>

Analyzing the echocardiographic parameters of LV geometry and function we found that LV diastolic diameters and volumes did not differ between groups, but end systolic volume was higher and LVEF was lower in MS group patients (Table 2) as well as LV global longitudinal strain (-14.9±3.34 in MS group vs -24.7±1.69 in control group, p<0.001) (Figure 1).

LA diameter as well as LA volume index was increased when compared with control group data (p<0.001) (Table 3). While analyzing right heart geometry and function we concluded that though indices of RV longitudinal function (TAPSE and s’) as well as parameter of global RV function (FAC) were within normal values, they were statistically significantly lower when compared with control group data (Table 4). Systolic pulmonary artery pressure was higher in MS group (Table 4).
Table 2. *LV geometry and function parameters between the groups*

<table>
<thead>
<tr>
<th>Variables</th>
<th>MS group (n=22)</th>
<th>Control group (n=23)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median [25-75%]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV EDD</td>
<td>46.0[43.0-50.3]</td>
<td>48.6[42.8-50.3]</td>
<td>0.666</td>
</tr>
<tr>
<td>LV EDDi</td>
<td>26.8[24.5-29.2]</td>
<td>25.9[24.6-27.5]</td>
<td>0.525</td>
</tr>
<tr>
<td>LV EDV(ml)</td>
<td>88.5[72.5-115.5]</td>
<td>84.0[74.0-100.0]</td>
<td>0.593</td>
</tr>
<tr>
<td>LV EDVi (ml/m2)</td>
<td>47.8[39.9-59.6]</td>
<td>48.8[41.6-56.2]</td>
<td>0.842</td>
</tr>
<tr>
<td>LV ESV (ml)</td>
<td>42.0[38.0-57.0]</td>
<td>29.5[24.8-36.0]</td>
<td>0.001</td>
</tr>
<tr>
<td>LV ESVi (ml/m2)</td>
<td>23.7[21.0-30.7]</td>
<td>17.4[14.0-20.4]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV EF (%)</td>
<td>51.5[50.0-55.0]</td>
<td>64.0[61.0-74.0]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LV – left ventricle, EDD – end diastolic diameter, EDDi – end diastolic diameter index, EDV – end diastolic volume, EDVi end diastolic volume index, ESV – end systolic volume, ESVi – end systolic volume index, EF – ejection fraction, p value – analyzed with non-parametric Mann – Whitney test for two independent sample volumes
Figure 1 *Comparing LV global longitudinal strain between groups*

![Box plot comparing LV global longitudinal strain between groups](image)

Table 3. *Diameters and volumes of left and right atriums between the groups*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MS group (n=22)</td>
<td>Control group (n=23)</td>
</tr>
<tr>
<td></td>
<td>Median[25-75%]</td>
<td>Median[25-75%]</td>
</tr>
<tr>
<td>RA diameter (mm)</td>
<td>40.0[38.0-44.5]</td>
<td>34.0[30.0-38.0]</td>
</tr>
<tr>
<td>LA diameter (mm)</td>
<td>48.5[15.8-56.0]</td>
<td>32.6[30.0-36.4]</td>
</tr>
<tr>
<td>LA volume (ml)</td>
<td>100.0[91.0-142.5]</td>
<td>47.0[40.0-58.0]</td>
</tr>
<tr>
<td>LA volume index (ml/m2)</td>
<td>56.0[48.3-81.1]</td>
<td>26.2[21.9-31.4]</td>
</tr>
</tbody>
</table>

RA – right atrium, LA – left atrium
Table 4. *RV size, hemodynamics and function parameters between study groups*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MS group (n=22)</td>
<td>Control group (n=23)</td>
</tr>
<tr>
<td></td>
<td>Median[25-75%]</td>
<td></td>
</tr>
<tr>
<td>TAPSE (mm)</td>
<td>21.0[17.0-26.0]</td>
<td>26.9[23.0-28.6]</td>
</tr>
<tr>
<td>FAC (%)</td>
<td>36.5[30.2-39.9]</td>
<td>55.9[51.9-63.0]</td>
</tr>
<tr>
<td>S’(cm/s)</td>
<td>11.5[9.5-14.7]</td>
<td>15.0[14.0-17.0]</td>
</tr>
<tr>
<td>RV diameter (mm)</td>
<td>34.0[30.0-37.0]</td>
<td>31.3[26.7-35.8]</td>
</tr>
<tr>
<td>TVR degree</td>
<td>2.0[1.4-2.5]</td>
<td>1.0[0-1.0]</td>
</tr>
<tr>
<td>PAS sist (mmHg)</td>
<td>50.0[45.0-55.0]</td>
<td>28.0[26.5-31.5]</td>
</tr>
</tbody>
</table>

TAPSE – tricuspid annular plane systolic excursion, FAC – fractional area change, RV – right ventricle, S’ – tricuspid lateral annular systolic velocity wave, TVR – tricuspid valve regurgitation, PAS sist – systolic pulmonary artery pressure

We analyzed MS group patients for the impact of MV area on biventricular geometry and function. 8 patients had MV area >1,4 cm², 14 patients - ≤1,4 cm². The significant correlation between MV area and LV function parameters, LA volumes and the velocity of TV regurgitation (Figures 2,3,4,5) was revealed. The smaller MV area correlated with lower LV global longitudinal strain, lower LV EF, more dilated LA and higher TV regurgitation velocity. There was no significant correlation found between MV area and LV end diastolic diameters and volumes (p=0.2 and p=0.3), as well as RV diameter and RV longitudinal function parameters.
Figure 2 Correlation between MVA and LVEF in MS patients ($r=0.533$, $p=0.01$)

$MV$ – mitral valve, $EF$ – LV ejection fraction
Figure 3 Correlation between MVA and LV global longitudinal strain in MS patients
\((r=-0.436, p=0.042)\)

MV – mitral valve, strain – LV global longitudinal strain
Figure 4 Correlation between MVA and LA volume in MS patients (p=0.025)

MV – mitral valve, LA - left atrium
Figure 5 Correlation between MVA and TV regurgitation velocity in MS patients
\( (r=-0.579, p=0.005) \)

\( MV \) – mitral valve, \( TV \) – tricuspid valve, \( v \) – velocity.
DISCUSSION OF THE RESULTS

This study analyzed changes of biventricular geometry and function in rheumatic MS patients and the relation of MV area on LV systolic function, the size of LA and pulmonary artery pressures. The results have shown that MV stenosis cause significant variations on the cardiac parameters that were measured by 2D echocardiography.

One of the new echocardiographic modalities used in this study was 2D speckle tracking. This method is angle independent in the assessment of global ventricular function. The LV global longitudinal strain measurements were obtained and compared between MS patients and healthy control group. The results indicated that patients with MS had significantly decreased measurement of LV global longitudinal strain when compared with control groups. (-14.9±3.34 vs -24.7±1.69, p<0.001). Similar results were identified by E. Bilen et al. who obtained depressed LV strain and strain rate values in 72 mitral stenosis patients who were enrolled in the study. However, the values did not vary among patients within different group when considering the severity of stenosis [19]. Current results support the theory that subclinical LV dysfunction observed in MS patients, would probably depends on myocardial factors as well as hemodynamic factors – we found significant relation between MV area and global LV longitudinal strain (r=-0.436, p=0.042)

Parameters collected from conventional echocardiography (LVEDV, LVEDD, LVESV, LVEF) showed some differences between compared groups. LV end diastolic diameter and volume did not differ between groups (p=0.2 and p=0.3), while LV ESV was higher (p<0.001) and LVEF was lower in MS patients (p<0.001) though the absolute numbers were in normal value range. M. A. Sowdagar and Y. V. Subba Reddy performed an observational study on 30 patients with severe mitral stenosis (MVA < 1.0 cm2), he observed the changes after successful PMV which was described as (MVA > 1.5 cm2). His results showed an increase in LVEDD and LVEF with a decrease in LVESD after successful repair [20]. This seemingly discloses increased left ventricular filling after alleviation of the obstruction which again validates the results of the study conducted. However, their study included only severe stenosis patients while ours has limited sample size so the results are generalized upon all MS patients.

As anticipated, MS patients in comparison to control group, have revealed an increase in both LA diameter and volume; that can be clarified from chronic inflow reduction through the valve, which over time, causes gradual increase in loading pressure in the LA. Furthermore, atrial function can be altered in two ways, either from chronic loading pressure as it may cause fibrosis or from the potential chronic rheumatic inflammatory changes on the myocardium or can be from both. [21]. Our data confirmed the significant correlation between LA volume and MVA, the more narrow the area, the
higher the LA volume. RA remodeling in MS patients is observed as well with increased diameter of RA.

The relationship between RV performance and MS were also analyzed in our study. Parameters that assess global RV systolic function and longitudinal contractile pattern such RV FAC, TAPSE and doppler tissue imaging derived tricuspid lateral annular systolic velocity wave (S’) were shown to be lower in MS though not severely reduced whereas, systolic pulmonary artery pressure is significantly increased. The observed results can be simplified from the pathophysiological point of view. The pathological obstruction related to MS leads to LA pressure and volume overload, passively resulting to backward transmission that adversely influence the pulmonary circulation as the disease progress. As a result a buildup of pulmonary artery systolic pressure develops which was proved in our results [22]. Deterioration of right ventricular function mainly when it fails to cope with PH initially by dimensional dilation. Our study did not show significant correlation between MVA and RV diameter. This can be due to limited population size involved.

In our study, some evidence of relation of tricuspid regurgitation velocity and MV area in mitral stenosis patients has been shown (r=-0.579, p=0.005). R. Ahmed and colleagues have conducted a study to evaluate the correlation between tricuspid regurgitation and mitral stenosis severity in rheumatic heart disease. Thirty five MS patients were enrolled and were divided into subclasses depending on MVA into mild (mitral valve area >1.8 cm²), moderate (mitral valve area >1.0–1.8 cm²) or severe (mitral valve area <1.0 cm²). The number of patients in each group were 9, 9, 17 respectively. The study results revealed 22 out of 35 patients who presented with tricuspid regurgitation with mean MVA 0.84±0.3cm², the other 13 patients did not demonstrated TR with mean MVA 1.83±0.7cm². These findings conclude that tricuspid regurgitation is often exhibited in mitral valve disease; this was clearly recognized as more than one third of the patients with severe mitral stenosis have shown at least moderate tricuspid regurgitation when it was nonexistent in mild stenosis patients [23].
CONCLUSIONS

1. LV global longitudinal strain and LV ejection fraction was lower in rheumatic MS group patients when compared to control group and was related to the severity of valve stenosis.

2. There was no significant correlation found between MV area and LV end diastolic diameter and volume indices, as well as RV diameter and RV longitudinal function parameters, but the relation was found between MV area and LA volume and velocity of tricuspid regurgitation.
PRACTICAL RECOMMENDATIONS

The study results show the importance of detail evaluation of LV geometry, function and deformation parameters in MS patients using conventional and new echocardiographic modalities. Further studies are of great importance to find out the impact of LV dysfunction on treatment outcomes.
LITERATURE LIST


