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Association of Posterior to Anterior Mitral Valve Leaflets Length Ratio with Severity of Rheumatic Mitral Stenosis

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Background: Rheumatic mitral stenosis (RMS) is the cause of mitral valve disease commonly found in developing countries. Determining severity of RMS is very important, related with prognosis and management of the disease. Current echocardiography methods have advantages and disadvantages in determining the severity of RMS. Posterior to anterior mitral valve leaflets length ratio (PMVL/AMVL ratio) was proposed to be one of the semi-quantitative measurement which offered a simple, easy and accurate method in determining the severity of RMS. The aim of this study was to see the association of posterior to anterior mitral valve leaflets length ratio with severity of rheumatic mitral stenosis.
Methods: This was a cross-sectional descriptive analytic study. The subjects were all patients with rheumatic mitral stenosis who underwent echocardiography examination to measure the PMVL/AMVL ratio as well as determining the severity based on mitral valve area (MVA) planimetry. One-way ANOVA analytic test was used to assess the association of ratio PMVL/AMVL and severity of the RMS.
Results: Of 71 patients included in this study, there were 19 mild RMS, 19 moderate RMS and 33 severe RMS patients. Majority of the subjects were female with age range from 38 to 43 years and have atrial fibrillation. From echocardiography examination, the mean EF +/- 55% with increased LAVI and SPAP according to the severity of the RMS (LAVI; 44±1.3 vs. 55±1.5 vs. 74±1.7 ml/m^2 SPAP; 29±1.2 vs. 46±9.0 vs. 68±1.4 mmHg). There was a significant difference in the length of PMVL in mild, moderate and severe RMS (28±5.6 vs. 22±4.0 vs. 17±5.2 mm; $p<0.001$), but no significant difference in the length of AMVL (33±5.5 vs 33±5.4 vs 32±5.1mm; $p=0.93$) respectively. The PMVL/AMVL ratio had statistically significant association with severity of RMS ($p<0.001$).
Conclusion: The PMVL/AMVL ratio is significantly associated with severity of RMS.

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Penelitian Klinis

Hubungan antara Rasio Panjang Katup Mitral Posterior-Anterior dan Derajat Keparahan Stenosis Mitral Rematik

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Latar Belakang: Stenosis mitral rematik (SMR) merupakan penyebab penyakit pada katup mitral yang banyak ditemukan di negara berkembang. Penentuan derajat keparahan SMR sangat penting terkait dengan prognosis dan tatalaksana terhadap penyakit tersebut. Metode ekokardiografi saat ini memiliki kelebihan dan kekurangan dalam penentuan derajat keparahan SMR. *Posterior to Anterior Mitral Valve Leaflets Length Ratio* (Rasio PMVL/AMVL) dapat menjadi salah satu metode semikuantitatif yang sederhana, mudah, serta akurat dalam menentukan derajat keparahan SMR. Penelitian ini bertujuan untuk mengetahui hubungan antara rasio panjang katup mitral posterior-anterior dan derajat keparahan stenosis mitral rematik.
Metode: Penelitian ini adalah penelitian deskriptif analitis dengan desain potong lintang. Subjek penelitian adalah semua pasien stenosis mitral rematik yang mendapatkan pemeriksaan ekokardiografi untuk mengukur rasio PMVL/AMVL serta menentukan derajat keparahan berdasarkan *mitral valve area* (MVA) planimetri. Uji analisis pada penelitian ini menggunakan *one-way ANOVA*.
Hasil: Dari 71 pasien SMR terdapat 19 pasien SMR ringan, 19 pasien SMR sedang dan 33 pasien SMR berat. Mayoritas subjek adalah perempuan dengan rentang usia 38 sampai 43 tahun dan irama atrial fibrilasi. Pada pemeriksaan ekokardiografi didapatkan rerata EF +/- 55% dengan peningkatan LAVI dan SPAP yang bertambah sesuai beratnya keparahan SMR (LAVI; 44±1,3 vs. 55±1,5 vs. 74±1,7 ml/m^2 SPAP; 29±1,2 vs. 46±9,0 vs. 68±1,4 mmHg). Terdapat perbedaan panjang PMVL pada berbagai derajat keparahan SMR (28±5,6 vs. 22±4,0 vs. 17±5,2 mm; p<0,001), namun tidak terdapat perbedaan yang bermakna pada panjang AMVL 33±5,5 vs. 33±5,4 vs 32±5,1 mm; p=0,93). Pada uji *post-hoc* didapatkan bahwa rasio PMVL/AMVL bermakna secara statistik terhadap derajat keparahan SMR (p<0,001).
Kesimpulan: Rasio PMVL/AMVL berhubungan secara bermakna dengan derajat keparahan SMR.

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Kata kunci: Rasio PMVL/AMVL, derajat keparahan SMR

Introduction

Mitral stenosis (MS) is a condition where there is disruption of flow from left atrium to the ventricle due to disorder of mitral valve opening. The most common etiology of MS is rheumatic heart disease

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(rheumatic mitral stenosis/RMS). RMS prevalence has decreased in developed countries but remains a health problem in developing countries. Based on data from the World Heart Federation in 2011, rheumatic heart disease which continues to be RMS are found in children and young adolescents in low-income countries and caused the deaths of 233,000 people per year.[1,2] Therefore, the determination of severity of RMS becomes very important related to the management and prognosis of the rheumatic heart disease.[3,4]

Two-dimensional Doppler echocardiography (2D) is a noninvasive modality that became the gold standard to determine the diagnosis and severity of mitral stenosis. According to the American Society of Echocardiography (ASE) on Assessment of Valve Stenosis in 2009, measurements of mitral valve area (MVA) can be performed using several methods such as planimetry, pressure half time (PHT), transmitral gradient/mean pressure gradient (mPG) and continuity equation where a variety of ways such measurements have advantages as well as limitation.[5]

Measurement of posterior to anterior mitral valve leaflets length (PMVL/AMVL) ratio can be used in diagnosis of MS. It was based on the change in the length of both mitral leaflets due to adhesions process of commissure and shortening of the chordae tendinea. This method was introduced by Mahfouz to predict the outcome of the Percutaneous Mitral Balloon Valvulopalsty (BMV).[6] From these studies, it was found that the ratio of PMVL/AMVL was related to MVA ($p<0.001$). The ratio of PMVL/AMVL measured only by using 2D echocardiography modalities. Measurements are not influence by hemodynamic changes or lesions on the valves.[7] This study aims to determine the relationship between the ratio of PMVL/AMVL to the severity of rheumatic mitral stenosis.

Methods

This was a cross-sectional descriptive analytic study. The subjects were consecutive patients with rheumatic mitral stenosis that being treated or from outpatient clinic in Non–Invasive diagnostic division of Cardiac Integrated Services Installation of Dr. M. Djamil Padang Hospital from April to September 2016 who meet the inclusion and exclusion criteria. Patients with poor echogenicity and mitral regurgitation due to prolapse or flail were excluded. We used transthoracic echocardiography machine of Toshiba (HD11XE).

Measurement of PMVL/AML ratio was use of two-dimensional echocardiography in the parasternal long-axis view (PLAX) at the end-diastolic phase characterized by ECG shortly before Q waves. The distance of anterior valve was measured from the base of the valve adjacent to the posterior portion of the aortic root until the tip of anterior valve, posterior valve length measured from the base of the posterior valve adjacent to the left atrium until the end of the posterior valve leaflets (**Figure 1**). The average value of both valves was taken three to five times in patients with atrial fibrillation. Two investigators acquired images and supervised by an expert cardiologist in echocardiography. Inter-observer variability test was performed using Bland-Altman test.

Severity of rheumatic mitral stenosis determined by

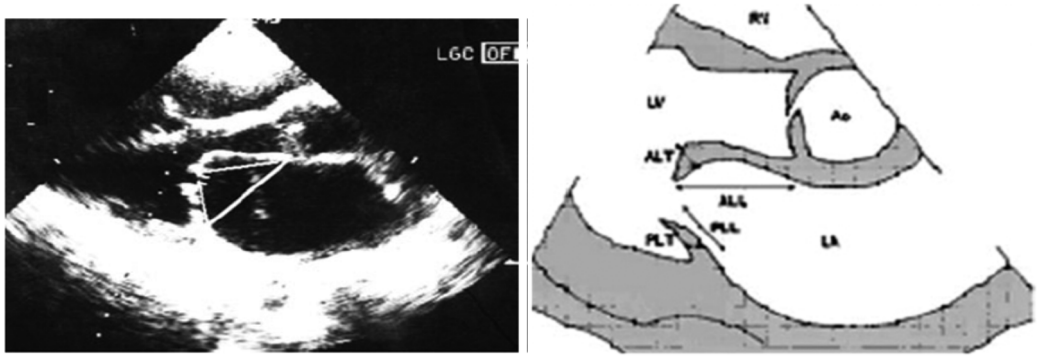

Figure 1. Measurement of PMMVL ratio (Mahfouz RA. Utility of the posterior-anterior mitral valve leaflets length ratio in prediction of outcome of percutaneous balloon mitral valvuloplasty. Echocardiography Wiley Periodicaly. 2011:168-178).

planimetry parameter based on the recommendation of American Society of Echocardiography (ASE). Planimetry measured using two-dimensional echocardiography in parasternal short axis view (SAX) in the mid-phase diastolic on mitral valve. Tracing of orifice mitral valve measured by using caliper mode on enlarged picture. The average values of planimetry taken three times in patients with atrial fibrillation. The severity of mitral stenosis was determined by the results of planimetry as follows; severe when MVA<1.0 cm^2; moderate when MVA planimetry 1.0-1.5 cm^2; mild when MVA planimetry>1.5 cm^2.

Statistics

Numerical variables that contain descriptive data are presented in the form of average standard deviation, whereas categorical variables are presented in the form of frequency and percentage. Data were analyzed by one-way ANOVA when the distribution data was normal and data variants were same. If the data distribution was not normal or variant data were not similar, the Kruskal-Wallis test was conducted. If one-way ANOVA test was significant, it was continued by Bonferroni post-hoc test, and post-hoc Games-Howell test was done when the Kruskal-Wallis test was found meaningful. Data were analyzed using the Statistical Package for Social Sciences (SPSS) for Windows.

Result

Characteristics of patients with rheumatic mitral stenosis are shown in **Table 1**. 71 patients with RMS were divided into three groups based on the severity of their RMS. Founding showed that patients with RMS were dominated by women with the mean age of patients with severe RMS were younger than the mean age of patients with mild RMS (38±1.0 vs. 43±1.3

Table 1. Characteristics of patient with rheumatic mitral stenosis.

Variables	Mild Rheumatic MS n=19	Moderate Rheumatic MS n=19	Severe Rheumatic MS n=33
Age, year (mean±SD)	43±1.3	40±1.1	38±1.0
Female, n (%)	14 (74%)	16 (84%)	24 (72%)
Atrial fibrillation, n (%)	10 (53%)	9 (47%)	27 (81%)
Echocardiography Parameters			
LA Dimension, mm (mean±SD)	48±1.0	49±1.0	49±8.0
EF, % (mean±SD)	55±1.3	54±9.0	53±9.9
LVEDD, mm (mean±SD)	54±9.6	48±1.0	44±7.4
LVESD, mm (mean±SD)	36±8.6	32±9.3	32±7.2
TAPSE, cm (mean±SD)	2.2±0.4	2.1±0.4	1.8±0.3
LAVI, ml/m^2 (mean±SD)	44±1.3	55±1.5	74±1.7
RVS' Velocity, cm/s (mean±SD)	11±2.5	10±3.5	11±2.7
Wilkin Score (mean±SD)	6±1	8±1	9±1
SPAP, mmHg (mean±SD)	29±1.2	46±9.0	68±1.4
Mitral PG, mmHg (mean±SD)	5±1.5	10±2.6	16±3.8
MVA Planimetri, cm^2 (mean ± SD)	1.8±0.2	1.2±0.1	0.7±0.2
MVA PHT, cm^2 (mean ± SD)	1.7±0.2	1.2±0.1	0.8±0.2
Medicaments, n (%)			
Diuretic	15 (78%)	10 (53%)	25 (76%)
Beta bloker	18 (94%)	17 (89%)	23 (69%)
Digoxin	6 (32%)	4 (21%)	15 (45%)
Oral Anticoagulan	8 (42%)	8 (42%)	27 (81%)
Aldosteron antagonis	11 (58%)	15 (78%)	31 (94%)

LA= left atrium; EF=ejection fraction; LVED= left ventricular end-diastolic diameter; LVESD= left ventricular end-systolic diameter; TAPSE= tricuspid annular plane systolic excursion; LAVI= left atrium volume index; RVS' Velocity= right ventricle systolic velocity; SPAP= systolic pulmonary artery pressure; PG= pressure gradient; MVA= mitral valve area; PHT= pressure half time

years). Echocardiographic parameters showed that patients with severe RMS had lower left ventricular pump function than those of other RMS with lower degrees of severity. Echocardiographic parameters that indicate mechanical implications for mitral stenosis namely left atrial volume index (LAVI) and an increase in pulmonary artery systolic pressure (systolic pulmonary artery pressure/SPAP) show a much lower increase in severe RMS compared with moderate or mild RMS.

Table 2 shows that the average length of the anterior valve does not differ at each severity but the distance of posterior valve has an approximate mean difference between the respective degrees of severity RMS.

From the test results of one-way ANOVA followed by post-hoc analysis Bonferroni, there was a significant difference between the ratios of PMVL/AMVL with the severity of the RMS as shown in **Table 3**. The result of post-hoc shows that the values of PMVL/AMVL ratio between various degrees of RMS severity were statistically significant as shown in **Table 4**.

veins and right heart function due to mitral valve stenosis in accordance with the degree of severity. All patients with RMS in this study already have dilated left atrium. The more severe degrees of severity RMS, more increasing LAVI value and higher SPAP value indicates an increase in pressure due to backflow into left atrium. However, the widening of the left atrium, increasing the value of LAVI and SPAP has yet to prove objectively the severity of RMS.[8, 9]

In this study there was no significant difference in AMVL. This is due to changes in the relative lengths of the anterior valve depends on the degree of commissural fusion.[10] Commissural fusion can occur eccentric or central so the length of the valve is not the same even though they remain at the same level of severity. When commissure undergo fusion with different degrees, change in length of anterior valve becomes less meaningful.[11]

Inflammatory process that occurs in the chordae tendinea also influences the size of the valve. Inflammation of the chordae tendinea creates two effects in the form of shortening the cord, but on the

Table 2. Differences in the length of AMVL and PMVL

Variables	Mild rheumatic MS n=19	Moderate rheumaric MS n=19	Severe rheumatic MS n= 33	P
AMVL, mm (mean±SD)	33±5.5	33±5.4	32±5.1	0.93
PMVL, mm (mean±SD)	28±5.6	22±4.0	17±5.2	<0.001

Table 3. Association of PMVL/AMVL ratio with severity of RMS

	Severity of RMS	n	Mean±SD	P
PMVL/AMVL ratio	Mild	19	0.85±0.08	<0.001
	Moderate	19	0.68±0.04	
	Severe	33	0.53±0.08	

Table 4. Results of post-hoc analysis of the PMVL/AMVL ratio

	Mean difference	CI 95%		p
		Minimum	Maximum	
Mild vs. moderate	0.09	0.06	0.12	<0.001
Mild vs. severe	0.20	0.17	0.22	<0.001
Moderate vs. severe	0.10	0.07	0.12	<0.001

Discussions

This study describes the echocardiographic parameters overall of patients RMS depicting anatomic and hemodynamic changes in the left atrium, pulmonary

other hand, can elongated of chordae size indicates the progression of changes cause by rheumatic in the structure of the mitral apparatus.[10] Antemortem data found by Brock in 1952 showed that the elongation of the anterior valve due to the consolidation exudates

along the chordae tendinea until the end of anterior valve happens after valvulitis phase.[12] However, elongation because of exudates will eventually lead to secondary retraction and thickening chronically especially in the supporting cords in posterior valve while the anterior valve retraction effects do not leave significant contribution in influencing the length of the anterior valve.[13] These conditions explain the difference in length of the posterior valve significantly change with increasing the degree of severity of the RMS. Besides, because of narrowing area of posterior valve and also retraction effect, changes during the rheumatic process of the chordae tendineae have more effects in relative length of the posterior valve.[10]

The PMVL/AMVL ratio is an overall picture of rheumatic processes that occur on the valves and chordae tendinea. This ratio reflects the variety of types of rheumatic mitral apparatus although the analysis of changes in length of each valve is different. The PMVL/AMVL ratio is associated with the severity of mitral stenosis. From these three groups, there was statistically significant difference. Correlation of PMVL/AMVL ratio with the severity of RMS showed the highest significance value especially between the ratio of PMVL/AMVL, mild vs. severe after post-hoc test, which is 95% CI 0.20 (0.17 to 0.22), p<0.001. This study continues the findings of previous studies by Mahfouz et al.[6]

This study has limitations. The study only examined this ratio in patients with RMS. The relationship of this ratio in another cause of mitral stenosis is unknown.

Conclusion

There is a significant difference in the length of the posterior valve to the severity of the RMS, but there was no difference in the length of the anterior valve. There is also a significant correlation between the ratio of PMVL/AMVL with the severity of the RMS. Further research needs to be done to get the sensitivity and specificity value of PMVL/AMVL in varying degrees of RMS severity and research that measures the ratio of PMVL/AMVL in other causes of mitral stenosis.

Abbreviations

AHA: American Heart Association
AMVL: anterior mitral valve leaflet
ASE: American Society of Echocardiography
BMV: balloon mitral valvuloplasty
LAVI: left atrium volume index
mPG: mean pressure gradient
MVA: mitral valve area
PHT: pressure half time
PLAX: parasternal long axis
PMVL: posterior mitral valve leaflet
SAX: short axis
MS: mitral stenosis
RMS: rheumatic mitral stenosis
SPAP: systolic pulmonary artery pressure
2D: two dimension

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Ethical Clearance

No. 112/EP/FK/2016 from Research Ethics Committee, Faculty of Medicine, Universitas Andalas, Padang.

Publication Agreement

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