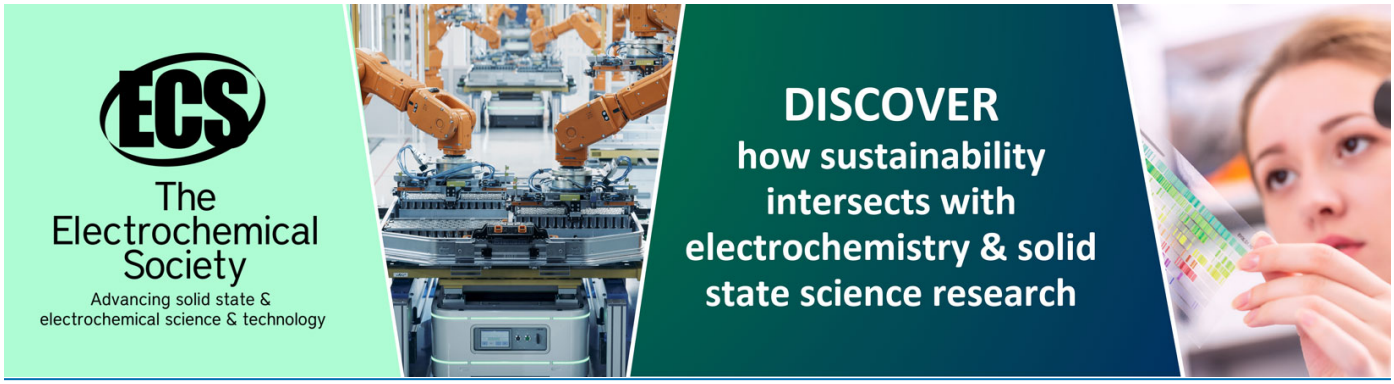
Left Atrial Volume Index (LAVI) as an Indicator of Severity and Pulmonary Hypertension in Mitral Stenosis



Left Atrial Volume Index (LAVI) as an Indicator of Severity and Pulmonary Hypertension in Mitral Stenosis

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Abstract. Left Atrial (LA) pressure and the trans-mitral pressure gradient chronically increases in Mitral Stenosis (MS), which results in LA enlargement and Pulmonary Hypertension (PH). We investigate the Left Atrial Volume Index (LAVI) as an indicator of severity and PH in MS. Fifty-nine subjects with MS (27 men and 32 women) mean ages 41.3±9.51 y.o were included in this study. We examined the correlation of LAVI and parameters of MS severity, and PH (Planimetry, MVA-PHT, MVA-VTI, MV-PHT, MV meanPG, TRmaxPG, and EstPASP). Most of the subjects had severe MS (77%), mild PH (40%) and AF (80%). LAVI value markedly increased in this study (Mean: 83.79 ± 38.32 ml/m^2). In subjects with severe MS, LAVI was significantly higher than that in moderate MS (91.88±38.41 vs 54.83±19.28, p<0..05). LAVI was significantly correlated with Planimetry, MVA-PHT, MVA-VTI, MV-PHT, MV MeanPG, and EstPASP (-0.40; -0.42; -0.29; 0.42; 0.27 and 0.29, p<0.05, respectively). LAVI cut-off value as an indicator for severe MS was 59.72 ml/m^2, with the sensitivity and specificity was 75.3% and 66%, respectively. LAVI was correlated well with severity and PH parameters in MS. LAVI also can be used as an indicator for severe MS.

1. Introduction

Rheumatic Heart Disease (RHD) which often manifests as Mitral Stenosis (MS), is still a significant healthcare problem in developing countries [1]. Data show that the prevalence of MS was 5 per 1000 children in India and Pakistan, and about 2.5 per 1000 children and adolescent in Africa [2].

The normal mitral orifice is 4-6cm^2. In physiological condition, there is a transient increase of pressure gradient between Left Atrial (LA) and Left Ventricle (LV) in early diastolic. This causes the trans-mitral pressure gradient to be relatively at the same level during the diastolic phase. In MS, the obstruction of mitral orifice increases the pressure gradient during the diastolic period [3].

Chronic increase of LA pressure in MS induces tissue to stretch and promotes subsequent structural changes that results in LA enlargement. This condition is the predisposing factor of Atrial Fibrillation (AF) and thromboembolic events [4]. Many studies showed that LA enlargement significantly increases the risk of AF, stroke, heart failure with preserved ejection fraction, and cardiovascular mortality. It also leads to pulmonary congestion due to increased pulmonary capillaries and vein pressures. Chronic pulmonary venous hypertension induces vasoconstriction of pulmonary arterioles and pulmonary vascular changes causing pulmonary hypertension (PH) [5,6]. PH increases the risk

of cardiovascular events not only during the valve replacement or repair but also in successful corrective surgery and conservative strategy [7].

Echocardiographic LA volume measurement is a simple and accurate method to estimate LA size [4,8]. Current guideline recommends the Left Atrial Volume Index (LAVI) to measure the LA size and its remodeling. LAVI measurement can be performed by biplane method using apical four chambers (A4C) and apical two chambers (A2C) view as shown in Figure 1 [9]. Maximal LAVI is measured at the end-systolic phase where LA reaches its maximal volume. Standard references limit of LAVI was 22 ± 6ml/m^2 [10]. LAVI was the critical parameter of diastolic function, but its role in MS was unknown. This study aimed to examine the correlation between LAVI and mitral stenosis and

pulmonary hypertension severity in subjects with mitral stenosis. We also determined the LAVI cut-off value as an indicator for severe MS.

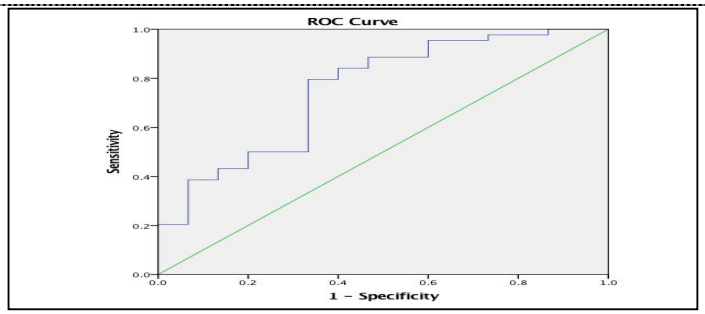

Figure 1. ROC Analysis Between LAVI and Severe MS.
Area Under Curve (AUC): 0..753

2. Methods

2.1. Population

We collected echocardiographic data of MS patients between January 1st to December 31st, 2017 from database. The exclusion criteria were: 1) Moderate to severe mitral regurgitation; 2) History of valve intervention (Percutaneous Transluminal Mitral Commissurotomy/PTMC) or surgery (Mitral Valve Repair or Replacement/MVR);3) Any congenital heart disease; 4) Intracardiac tumor; 5) Mitral valve vegetation; 6) Pericardial disease; and 7) Incomplete echocardiographic data.

2.2. Echocardiography

Demographic data, 2-D echocardiography, M-Mode, Doppler, and Tissue Doppler Imaging (TDI) were collected from the database. MS severity was measured by five parameters: 1) Mitral Valve Area (MVA) by Planimetry, 2) MVA by Mean Pressure Half Time (PHT), 3) MVA by Velocity Time Integral (VTI), 4) Mean Pressure Gradient (PG), and 5) Mean PHT, and qualitatively using Wilkins Score [11]. LAVI was measured by biplane method from A4C and A2C view, at the end of the systolic phase, then calculated based on the American Society of Echocardiography (ASE) guideline

[10]. LV Ejection Fraction (EF) was calculated by M-Mode (Teich) and 2-D (Simpson Biplane) method. Right and left atrial dimensions were measured by longest vertical (major) and horizontal (minor) diameter on A4C view. Right Ventricle (RV) diameter was measured using RV Diameter Basal (RVDB) on A4C view. RV systolic function was measured by Tricuspid Annular Plane Systolic Excursion (TAPSE). Tricuspid Regurgitation (TR) was measured by Tricuspid Maximum Pressure Gradient (TR maxPG). RA Pressure (RAP) was estimated from Inferior Vena Cava (IVC) diameter and collapsibility. The severity of PH was measured and classified by estimation of Pulmonary Artery Systolic Pressure (estPASP) from TR MaxPG and estimated RAP [12].

2.3. Statistical Analysis

Basic demographic and echocardiographic data were analyzed using descriptive statistics, consisting of mean, standard deviation, number, and percentage. Student t-test or Mann Whitney U test was performed to compare continuous variables between two groups. Pearson or Spearman correlation test was performed to measure the relationship between LAVI and MS severity as well as PH on all subjects. Risk factors or independent variables, i.e., MVA planimetry, MVA VTI, MVA PHT, MV mean PG, MV mean PG, TR Vmax, TR Max PG, and EstPASP, were selected based on clinical and statistical significance with the cut-off of p-value < 0.05. The ROC curve analysis is used to determine the LAVI cut-off value for severe MS. All statistical analysis was performed with SPSS version 22.

3. Result

A total of 59 subjects, who met the inclusion and exclusion criteria, were analyzed in this study. The baseline characteristics of the research subjects are summarized in Table 1. Most of the subjects were female (55%) with an average age of 41.9 ± 9.51 years and Body Surface Area (BSA) 1.54 ± 0.16m2. The most common basic electrocardiography found during echocardiography was Atrial Fibrillation (AF) (80%). Aortic valve involvement in various severity was found in 59% of subjects. All subjects were classified as severe MS (78%) and moderate MS (22%). There was no subject with mild MS in this study. Pulmonary hypertension at various severity levels occurs in most subjects, i.e., severe (22%), moderate (20%), and mild (40%).

Table.1 Baseline Characteristic

Variables	Value
Age (y.o)	41.3 ± 9.51
Sex (n=59)	
• Male (%)	27 (45)
• Female (%)	32 (55)
Rhythm (n=59)	
• Sinus (%)	12 (20)
• AF (%)	47 (80)
BSA (m^2)	1.54 ± 0.16
Aortic Disease (n=59)	
• Yes (%)	35 (59)
• No (%)	24 (41)
MS Severity (n=59)	
• Severe (%)	46 (77)
• Moderate (%)	13 (23)
• Mild (%)	0 (0)

PH (n=59)	
• Severe (%)	13 (22)
• Moderate (%)	12 (20)
• Mild (%)	23 (40)
• No PH (%)	11 (18)

Baseline echocardiographic data of the subjects are summarized in Table 2. The mean values LA and RA dimension (Major & Minor) were 7.5 ± 1.1cm; 5.6 ± 1.1cm; 6.2 ± 1.2 3.7 ± 0.9cm, respectively. It is concluded that the average value of LA and RA dimensions in this study were above the reference value. The mean of Left Ventricle Inner Diastolic Dimension (LVIDd) and LV diastolic mass index (LVDMI) in this study were within normal limits of 4.4 ± 0.8cm, and 85.6 ± 36g/m2. The average of RVDB measurements was above the normal limit, 3.03 ± 0.5cm, but RV systolic function based on TAPSE was within the normal range of 1.9 ± 0.3cm. The average of LVEF with Teich and Simpson (Biplane) methods was 61.4% ± 13.16 and 63.47 ± 6.44%, respectively. The means of the five parameters for assessing mitral valve severity; MVA planimetry, MVA VTI, MVA PHT, MV mean PG, and MV mean PHT were 0.80 ± 0.26cm2; 0.81 ± 0.26cm2; 0.79 ± 0.27cm2; 13.15 ± 5.07mmHg, and 299.47 ± 98.8ms, respectively. The mean of mitral valve morphology measured qualitatively by Wilkins score was 8.47 ± 1.45. The mean values of tricuspid valve regurgitation parameters, TR Vmax and TR MaxPG were 2.86 ± 1.81m/s and 42.7 ± 29.63mmHg, respectively. The severity of pulmonary hypertension based on the average PASP measurement was 52.07 ± 34.6mmHg.

Table. 2 Baseline Echocardiographic Data

Echocardiographic Parameters	**Mean ± SD**
LA Diameter	
• Major (cm)	7.5 ± 1.1
• Minor (cm)	5.6 ± 1.1
RA Diameter	
• Mayor (cm)	6.2 ± 1.2
• Minor (cm)	3.7 ± 0.9
LV Diameter	
• LVIDd (cm)	4.4 ± 0.8
LV Mass	
• LVDMI (g/m2)	85.6 ± 36
RV Diameter	
• Diameter Basal (RVDB) (cm)	3.03 ± 0.5
RV Systolic Function	
• TAPSE (cm)	1.9 ± 0.3
LV Systolic Function	
• EF by Teich (%)	61.4 ± 13.16
• EF by Biplane (%)	63.47 ± 6.44
MS Severity	
• MVA by Planimetry (cm^2)	0.80 ± 0.26
• MVA by Mean PHT (cm^2)	0.81 ± 0.26
• MVA by VTI (cm^2)	0.79 ± 0.27
• MV Mean PG (mmHg)	13.15 ± 5.07
• MV Mean PHT (ms)	299.47 ± 98.8
• Wilkins Score	8.47 ± 1.45

Tricuspid Valve	
• TR Vmax (m/s)	2.86 ± 1.81
• TR Max PG (mmHg)	42.7 ± 29.63
PH Severity	
• Est PASP (mmHg)	52.07 ± 34.6
Atrial Volume	
• LAVI (ml/m^2)	83.79 ±38.32

All of the subjects had an abnormal LAVI value, with an average of 83.79 ± 38.32ml / m2 (Table 3). The mean value of LAVI based on the various variables summarized in Table 4. Subjects with AF had a significantly higher LAVI score than with sinus rhythm (90.5 ± 37.57 vs. 57.32 ± 28.68ml/m2, p <0.05). Subjects with severe MS had a significantly higher LAVI compared to moderate MS (91.88 ± 38.47 vs. 38.41 ± 19.28ml/m2, p <0.05). When compared to subjects with mild and non-PH, subjects with moderate and severe PH had higher mean LAVI values, but not statistically significant (92.84 ± 40.91 vs. 75.17 ± 34.62ml/m2, p >0.05). Among the subjects with and without the involvement of aortic disease, the mean value of LAVI was not significantly different (88.19 ± 41.5 vs. 80.78 ± 36.29ml/ms, p> 0.05).

Table. 3 Comparison Analysis of LAVI According to Variables

Variables	LAVI (ml/m^2)	Sig.
Rhythm		**0.011***
• AF (n=47)	90.5 ± 37.57	
• Sinus (n=12)	57.32 ± 28.68	
Aortic Disease		0.415*
• Yes (n=35)	80.78 ± 36.29	
• No (n=24)	88.19 ± 41.5	
MS Severity		
• Severe MS (n=46)	91.88 ± 38.41	**0.000****
• Moderate MS (n=13)	54.83 ± 19.28	
PH Severity		0.054**
• Moderate-Severe (n=25)	92.84 ± 40.91	
• Mild or no PH (n=34)	75.17 ± 34.62	

* Analyzed by *Student t-test*
** Analyzed by *Mann Whitney-U test*

The correlations between LAVI and various variables are summarized in Table 4. There was a negative correlation between LAVI and Mitral Valve Area (MVA) measured by planimetry, Mean PHT, and VTI. LAVI positively correlated with variable MV mean PG, MV mean PHT, TR Vmax, TR maxPG, and EstPASP. There was a significant correlation between LAVI and MVA planimetry, MVA by mean PHT, MVA VTI, MV mean PG, MV mean PHT, and estPASP (p <0.05). The correlation between LAVI to TR Vmax, and TR MaxPG was not statistically significant (p> 0.05). The ROC analysis curve between LAVI and the incidence of severe MS is illustrated in Figure 1. With the LAVI cut-off of 59.72ml/m2 had a sensitivity of 75.3% and specificity of 66% as an indicator of severe MS.

Table. 4 Korelasi antara nilai LAVI dengan berbagai variabel

Variables	r	Sig.
MVA by Planimetry	- 0.40	**0..002***

MVA by Mean PHT	-0..42	**0.001***
MVA by VTI	-0.29	**0.026****
MV Mean PG	0.27	**0.03***
MV Mean PHT	0.42	**0.001***
TR Vmax	0.21	0.156**
TR MaxPG	0.21	0.147**
Est PASP	0.29	**0.041****

* Analyzed by *Pearson Correlation test*
** Analyzed by *Spearman Correlation test*

4. Discussion

A chronic elevation in LA pressure is caused by MS, leading to LA dilatation. This condition also induces strain and structural changes in LA, triggering the occurrence of AF [5]. This study involves most subjects with severe MS (77%) with no mild MS degree (0%) (Table 1). LA dilation, characterized by LAVI value> 40ml/m2, could be classified to severe dilation [13]. In the previous study, the average value of LAVI was 83.79 ± 38.32ml/m2 (Table 2), and most of the subjects had AF (80%) (Table 1).

Persistent increase of LA pressure and the presence of AF may result in pulmonary venous hypertension, pulmonary arteriolar constriction reflexes, obliterative changes in pulmonary vascular, pulmonary artery hypertension (PH), right ventricular hypertrophy or dilation, tricuspid valve dysfunction, systemic venous congestion, decreased LV filling, and subnormal cardiac output states. Furthermore, pulmonary arterioles may react by triggering vasoconstriction, intimal hyperplasia, and medial hypertrophy, which will aggravate the PH. In previous study, the mean RV dimension measured by RVDB was 3.03 ± 0.5cm (Table 2) or above the references values (2.2-2.8cm).[10] PH at various degrees was obtained in 82% of subjects, most of whom had a mild PH (40%) (Table 1).

In previous study, the mean value of LAVI in patients with AF rhythm was significantly higher compared to patient with sinus rhythm (90.5 ± 37.57 vs. 57.32 ± 28.68m/m2, p <0.05). Subjects with severe MS had a significantly higher mean value of LAVI compared to moderate MS (91.88 ± 38.47 vs. 38.41 ± 19.28ml/m2 (p <0.05). Among the subjects with and without aortic disease, the mean value of LAVI was not significantly different (88.19 ± 41.5 vs. 80.78 ± 36.29ml/ms, p> 0.05) (Table 3). The data proved that the magnitude of the LAVI was significantly proportional to the degree of mitral valve stenosis severity. This study showed that LAVI was negatively correlated with MVA and positively correlated with mean PG, mean PHT, TR Vmax, TR MaxPG, and Est RAP. According to the ROC analysis, LAVI above the cut-off of 59.72ml/m2 can be used as an indicator of severe MS with a sensitivity and specificity of 75.3% and 66%, respectively.

5. Conclusion

LAVI significantly correlates with the severity of mitral valve stenosis and PH in MS. LAVI can also be considered as an indicator of severe MS on echocardiography and can be a guide for determining management steps in patients with MS.

References

[1] Pourafkari L, Ghaffari S, Ahmadi M, Tajlil A, Aslanabadi N and Nader N D 2016 Pulmonary hypertension in rheumatic mitral stenosis revisited *Herz* 1–6
[2] Iung B 2008 Mitral stenosis still a concern in heart valve diseases *Arch Cardiovasc Dis* **101** 597–599
[3] Carabello B A 2005 Modern Management of Mitral Stenosis *Circulation* **112** 432–437
[4] Patel D A, Lavie C J, Milani R V, Shah S and Gilliland Y 2009 Clinical Implications of Left Atrial Enlargement: A Review *Ochsner J* **9** 191–196

[5] Neema P K 2015 Pathophysiology of Mitral Valve Stenosis *MAMC J Med Sci* **1** 25
[6] Neema P K and Rathod R C 2012 Pulmonary artery hypertension in mitral stenosis: Role of right ventricular stroke volume, atrio-ventricular compliance, and pulmonary venous compliance *J Anaesthesiol Clin Pharmacol* **28** 261–262
[7] Magne J, Pibarot P, Sengupta P P, Donal E, Rosenhek R and Lancellotti P 2015 Pulmonary Hypertension in Valvular Disease *JACC Cardiovasc Imaging* **8** 83–99
[8] Abhayaratna W P, Seward J B, Appleton C P, Douglas P S, Oh J K, Tajik A J and Tsang T S M Left Atrial Size *J Am Coll Cardiol* **47** 2357–2363
[9] Lang R M, et al. 2005 Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr Off Publ Am Soc Echocardiogr* **18** 1440–1463
[10] American Society of Echocardiography 2005 *American Society of Echocardiography: Guideline Reference Book*
[11] Osvelt R J and Salomon S J 2007 Mitral Stenosis *Essensial of Echocardiography* Humania Press
[12] Aguillar D and Bulwer B E 2007 Echocardiography in Pulmonary Embolism and Secondary Pulmonary Hypertension *Essential of Echocardiography* Humania Press
[13] Yıldız A, Karakurt A and Amikoğlu G 2014 Predictive Value Of Left Atrial Volume Index And Right Ventricular Dilatation In Mitral Stenosis For Atrial Fibrillation *Cukurova Med J* **39** 772–778