Original Article

Correlation between Left Atrial Volume Index and Pulmonary Hypertension in Patient with Moderate to Severe Aortic Stenosis

Apisit Leedumrongwattanakul, MD[1,2], Jarugit Sangmaneepimai, BSc[1], Kanjana Intasang, BSc[1], Pimporn Herwutthiwong, BSc[1]

[1] Cardiology Unit, Department of Medicine, Pranangklao Hospital, Nonthaburi, Thailand

[2] Faculty of Medicine, Siam University, Bangkok, Thailand

Background: Left atrial dilatation is a response to pressure overload in aortic stenosis (AS).

Objective: To study the correlation between left atrium volume index (LAVI) and the pulmonary hypertension in patients with moderate to severe AS.

Materials and Methods: The authors retrospectively studied patients with moderate to severe AS (either one or all echocardiographic criteria of aortic valve area [AVA]) smaller than 1.5 cm^2, AV Vmax of more than 3 m/s, AV mean PG of more than 30 mmHg who underwent transthoracic echocardiography at Pranangklao Hospital between January 2015 and December 2019.

Results: One hundred thirty-four patients (age 72.31±12.32 years, 46.3% male) were enrolled. In pulmonary hypertension group, proportion of atrial fibrillation (75%) were significantly higher Sinus Rhythm (26.3%). Right ventricular systolic pressure (RVSP) tended to increase when LAVI increased (r=0.695, p<0.001). The mean RVSP in four groups of LAVI (less than 35 ml/m^2, 35 to 41 ml/m^2, 42 to 48 ml/m^2, and more than 48 ml/m^2) were 35.11±8.97, 38.22±11.71, 39.0±8.57, and 60.05±31 mmHg, respectively. RVSP in patients with LAVI of more than 48 ml/m^2 was significantly higher than those of the other group (p<0.001). LAVI in patients with RVSP of less than 50 and more than 50 mmHg were 35.13±6.86 and 65.22±11.55 ml/m^2, respectively (p<0.001).

Conclusion: Moderate to severe AS, RVSP increase when LAVI increases.

Keywords: Echocardiography, Left atrium volume index, Aortic stenosis, Pulmonary hypertension

Received 23 Mar 2020 | Revised 29 May 2020 | Accepted 2 Jun 2020

J Med Assoc Thai 2020;103(8):824-8
Website: http://www.jmatonline.com

Calcific aortic stenosis (AS) is the most prevalent valvular heart disease in high-income countries, and the burden of the disease is expected to increase dramatically in the next 20 years with the aging of the population[1].

Correspondence to:

Leedumrongwattanakul A.

Cardiology Unit, Department of Medicine, Pranangklao Hospital, Muang Nonthaburi, Nonthaburi 10705, Thailand.

Phone: +66-2-5284567

Email: apisit_lee@hotmail.com

How to cite this article:

Leedumrongwattanakul A, Sangmaneepimai J, Intasang K, Herwutthiwong P. Correlation between Left Atrial Volume Index and Pulmonary Hypertension in Patient with Moderate to Severe Aortic Stenosis. J Med Assoc Thai 2020;103:824-8.

doi.org/10.35755/jmedassocthai.2020.08.11229

Left atrial (LA) enlargement is common in patients with AS[2] and is an established marker of increased left ventricular (LV) filling pressures[3]. LA enlargement reflects the effect of increased LA pressure over time and is a morphological indicator of chronically increased hemodynamic burden[4,5]. LA enlargement has been reported as a predictor of death[6-8], incident heart failure[9], atrial fibrillation (AF)[10], and stroke[7] in the general population.

Recently, Généreux et al[11] proposed a new staging classification characterizing the extent of extra-aortic valve cardiac damage and reported that this staging system has strong prognostic implications in patients with severe symptomatic AS undergoing aortic valve replacement (AVR).

The presence of pulmonary hypertension, a frequent consequence after AS, has prognostic implication pre- and post-operatively[12]. The authors do not know the association between the left atrium

volume index (LAVI) and the pulmonary artery pressure in patients with moderate to severe AS in Thai patients.

Materials and Methods

Between 2015 and 2019, patient 18 years or older diagnosed as having moderate to severe AS (aortic leaflet calcification or peak aortic jet velocity (Vmax) of 3 m/s or greater, mean PG AV of 30 mmHg or greater, or aortic valve area (AVA) of less than 1.5 cm^2) were included in this study. The following patients were excluded 1) those with more than mild aortic regurgitation, 2) those with prosthetic valves, congenital heart disease, supravalvular or subvalvular AS, or dynamic LV outflow tract obstruction, 3) those with more than mild mitral stenosis or mitral regurgitation.

Echocardiography

The echocardiographic data from the transthoracic echocardiography (TTE) including LV dimension, wall thickness, and ejection fraction (LVEF), LA diameter (M-mode, parasternal short axis view), LAV and LAVI by biplane area-length method, right ventricular systolic pressure (RVSP), and the severity of AS were collected. Pulmonary hypertension in patients with chronic moderate to severe AS was defined as RVSP of more than 50 mmHg. LAV was measured by the biplane area-length method as previously described[13,14]. LA area (A) and length (L) were measured from apical 4-chamber (A1 and L1) and apical 2-chamber view (A2 and L2). LAV was calculated by the formula $(0.85 \times A1 \times A2)/L$ when L was LA length as the average of L1 and L2. LAVI was equal to LAV divided by body surface area.

Statistical analysis

Descriptive statistics, including frequency and percentage, were used for categorical variables. Continuous variables were reported as mean ± standard deviation (SD). The normality of the distribution of variables was examined by the Kolmogorov-Smirnov test. The comparison of normally distributed continuous variables between two groups used the Independent t-test and chi-square test for categorical data. The comparison between more than two groups used the one-way ANOVA and post hoc multiple comparisons by Bonferroni test. Pearson's correlation between LAV index and RVSP. For all tests performed, a two-tailed p-value of less than 0.05 was considered statistically significant. IBM SPSS Statistics, version 22 (IBM Corp., Armonk, NY, USA) was used to perform all statistical analyses.

Results

According to Pranangklao Hospital echocardiographic database, 134 patients were diagnosed with moderate to severe AS between January 2015 and December 2019.

Baseline characteristics

Baseline clinical characteristics are shown in Table 1. The mean age was 72.31±12.32 years and 46.3% were male. Patients had hypertension (82.8%), diabetes mellitus (30.6%), and coronary artery disease (22.4%). There was a statistically significant difference in echocardiographic between patients with more pulmonary hypertension AF in the RVSP of more than 50 mmHg group.

Echocardiographic data

Echocardiographic data is shown in Table 2. Moderate to severe AS was quantitatively assessed by continuous equation method with at AVA 0.99±0.29 cm^2, AV Vmax at 4.28 m/s, and AV mean PG at 41.02 mmHg. Mean LVEF by modified Simpson's method was 68.8±10.92%. LAV and LAVI were 75.38±34.85 ml and 47.61±21.65 ml/m^2, respectively. There was no statistically significant difference in AVA, AV Vmax, AV mean PG, and LVEF LV mass, LV mass index, and E deceleration time between patients with pulmonary hypertension. Patients with pulmonary hypertension had higher E/A ratio, E/e', LAV, and LAVI than non-pulmonary hypertension patients.

Correlations between LAVI size and right ventricular systolic pressure

Correlations between LA size and RVSP are demonstrated in Figure 1. There was a positive correlation between LAVI and RVSP. RVSP tends to increase when LAVI increases (Pearson's correlation coefficient 0.695, $p<0.001$).

Correlation between the four groups[15] of LAVI and RVSP is demonstrated in Table 3 and Figure 2. Furthermore, LAVI was divided into four groups and mean RVSP:

LAVI of less than 35 ml/m^2 (n=40), mean RVSP 35.11±8.97 mmHg

LAVI of 35 to 41 ml/m^2 (n=25), mean RVSP 38.22±11.71 mmHg

LAVI of 42 to 48 ml/m^2 (n=21), mean RVSP 39±8.57 mmHg

LAVI of more than 48 ml/m^2 (n=48), mean RVSP 60.05±16.31 mmHg

Table 1. Baseline clinical characteristics of the entire patient population and groups

Variables	Total (n=134) n (%)	RVSP ≤50 (n=89) n (%)	RVSP >50 (n=45) n (%)	p-value
Age (year); mean±SD	72.31±12.32	72.78±12.67	71.4±11.68	0.544
≥75	63 (47.0)	42 (47.2)	21 (46.7)	
Sex				
Male	62 (46.3)	41 (46.1)	21 (46.7)	0.948
BSA (m^2); mean±SD	1.58±0.17	1.59±0.17	1.58±0.15	0.770
SBP (mmHg); mean±SD	130.97±19.77	131.84±19.68	129.29±20.05	0.484
EKG				
AF	20 (14.9)	5 (5.6)	15 (33.3)	<0.001*
Underling disease				
Hypertension	111 (82.8)	75 (84.3)	36 (80)	0.355
DM	41 (30.6)	27 (30.3)	14 (31.1)	0.993
CAD	30 (22.4)	18 (20.2)	12 (26.7)	0.437

RVSP=right ventricular systolic pressure; SD=standard deviation; BSA=body surface area; SBP=systolic blood pressure; EKG=echocardiographic; AF=atrial fibrillation; DM=diabetes mellitus; CAD=coronary artery disease

* p<0.05 is statistically significant

Table 2. Echocardiographic parameters of all patients with moderate to severe aortic stenosis and the comparisons between patients with and without pulmonary hypertension

Variables	Total (n=134) Mean±SD	RVSP ≤50 (n=89) Mean±SD	RVSP >50 (n=45) Mean±SD	p-value
AVA (cm^2)	0.99±0.29	1.00±0.30	0.97±0.28	0.483
Index AVA (cm^2/m^2)	0.41±0.15	0.41±0.16	0.40±0.14	0.657
Peak AV (m/s)	4.28±2.48	4.02±0.90	4.80±4.07	0.086
meanAV (mmHg)	41.02±19.20	40.09±20.38	42.88±16.66	0.428
LVOT VTI (cm)	24.39±5.85	24.45±5.85	24.28±5.89	0.872
SV (ml)	85.90±19.74	86.32±19.91	85.08±19.61	0.732
HR (bpm)	73.27±12.25	72.84±10.30	74.11±15.51	0.622
LV mass index (g/m^2)	128.70±45.48	124.30±45.56	137.41±44.56	0.115
E/A ratio	0.89±0.38	0.79±0.26	1.17±0.52	0.001*
E DT (ms)	271.29±84.95	274.10±81.55	263.45±94.88	0.558
E/e' ratio	22.83±11.73	19.72±7.88	31.54±15.89	<0.001*
LAV (ml)	75.38±34.85	58.95±16.13	107.89±39.05	<0.001*
LAV index (ml/m^2)	47.61±21.65	37.21±10.69	68.19±23.17	<0.001*
RVSP (mmHg)	45.23±16.70	35.13±6.86	65.22±11.55	<0.001*

RVSP=right ventricular systolic pressure; SD=standard deviation; AVA=aortic valve area; AV=aortic valve; LVOT VTI=left ventricular outflow tract velocity time integral; SV=stroke volume; HR=heart rate; LV=left ventricular; E DT=E deceleration time; LAV=left atrium volume

* p<0.05 is statistically significant

Multiple comparisons between each quartile of LAVI demonstrated that RVSP of LAVI size greater than 48 ml/m^2 was significantly higher than that of other groups (p<0.001).

Correlation between pulmonary hypertension and LAVI size is shown in Figure 3. LAVI in patients with and without pulmonary hypertension were 37.21±10.69 and 68.19±23.17 ml/m^2, respectively. LAVI was significantly different between the two groups of RVSP (p<0.001).

Table 3. The Compare between 4 groups of LAVI level for RVSP

	LAVI (ml/m^2); mean±SD				p-value
	<35 (n=40)	35 to 41 (n=25)	42 to 48 (n=21)	>48 (n=48)	
RVSP (mmHg)	35.11±8.97[a]	38.22±11.71[b]	39±8.57[c]	60.05±16.31[a,b,c]	<0.001*

LAVI=left atrium volume index; RVSP=right ventricular systolic pressure; SD=standard deviation

* p<0.05 is statistically significant

ANOVA test and post hoc multiple comparisons by Bonferroni test

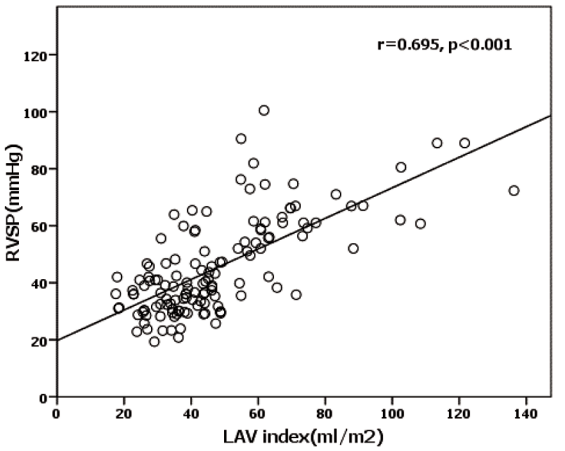

Figure 1. Correlations between LAVI and RVSP.

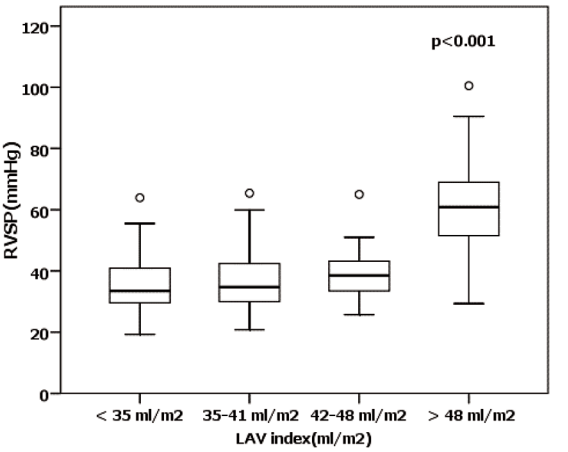

Figure 2. Correlation between 4 groups of LAVI size and RVSP.

Looking at the proportion of pulmonary hypertension and cardiac rhythm, in the pulmonary hypertension group, the proportion of AF (75%) was significantly higher sinus rhythm (26.3%).

Discussion

Most common patients with moderate to severe AS were elderly. The study showed that LAVI was correlated with RVSP. Patients with higher LAVI (especially, those with LAVI greater than 48 ml/m² group) had significantly higher RVSP than those with LAVI of less than 48 ml/m² group. Patients with pulmonary hypertension had higher LAVI than those without pulmonary hypertension.

In patients with AS, LA enlargement is the reflection of chronically elevated LV filling pressures necessary to maintain adequate LV filling and cardiac output. In patients with moderate AS, indexed LAV is significantly correlated with AVA, significant mitral regurgitation, hypertension, LV end-diastolic volume, LV hypertrophy, and restrictive LV filling pattern[2]. Christensen et al suggested that patients with asymptomatic severe AS with greater LAV have a high hemodynamic burden and pulmonary pressure, especially in the presence of an increased E/e' ratio[5].

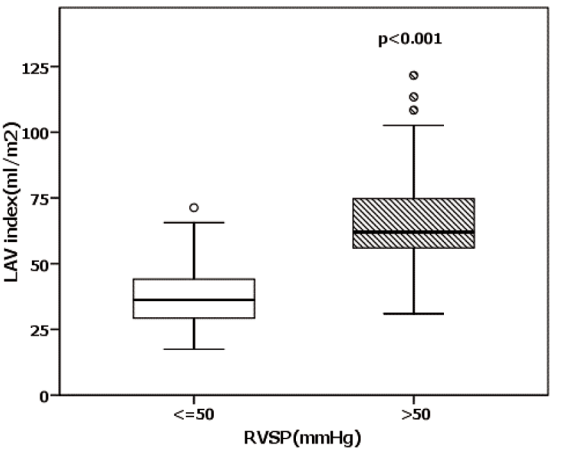

Figure 3. Correlation between pulmonary hypertension and LAVI size.

At present, the authors do not have a cut-off value for LAVI to indicate the optimal timing for AV surgery in patients with moderate to severe AS. The additional prognostic roles of LAVI in patients with moderate to severe AS will be further determined by larger prospective studies.

Limitations of the present study are the retrospective design and a small number of the study population and the questionable accuracy and validity of the echocardiographic measurement.

Conclusion

In moderate to severe AS, RVSP increase when LAVI increases.

What is already known on this topic?

There is a positive correlation between LAVI and RVSP. RVSP tends to increase when LAVI increases (Pearson's correlation coefficient 0.695, $p<0.001$).

What this study adds?

In Thai patients, LAVI in patients with and without pulmonary hypertension were 37.21±10.69 and 68.19±23.17 ml/m², respectively.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Lindman BR, Clavel MA, Mathieu P, Iung B, Lancellotti P, Otto CM, et al. Calcific aortic stenosis. Nat Rev Dis Primers 2016;2:16006.
2. Dalsgaard M, Egstrup K, Wachtell K, Gerdts E, Cramariuc D, Kjaergaard J, et al. Left atrial volume in patients with asymptomatic aortic valve stenosis (the Simvastatin and Ezetimibe in Aortic Stenosis study). Am J Cardiol 2008;101:1030-4.
3. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2016;29:277-314.
4. Dahl JS, Christensen NL, Videbæk L, Poulsen MK, Carter-Storch R, Hey TM, et al. Left ventricular diastolic function is associated with symptom status in severe aortic valve stenosis. Circ Cardiovasc Imaging 2014;7:142-8.
5. Christensen NL, Dahl JS, Carter-Storch R, Bakkestrøm R, Jensen K, Steffensen FH, et al. Association between left atrial dilatation and invasive hemodynamics at rest and during exercise in asymptomatic aortic stenosis. Circ Cardiovasc Imaging 2016;9.
6. Gardin JM, McClelland R, Kitzman D, Lima JA, Bommer W, Klopfenstein HS, et al. M-mode echocardiographic predictors of six- to seven-year incidence of coronary heart disease, stroke, congestive heart failure, and mortality in an elderly cohort (the Cardiovascular Health Study). Am J Cardiol 2001;87:1051-7.
7. Benjamin EJ, D'Agostino RB, Belanger AJ, Wolf PA, Levy D. Left atrial size and the risk of stroke and death. The Framingham Heart Study. Circulation 1995;92:835-41.
8. Laukkanen JA, Kurl S, Eränen J, Huttunen M, Salonen JT. Left atrium size and the risk of cardiovascular death in middle-aged men. Arch Intern Med 2005;165:1788-93.
9. Takemoto Y, Barnes ME, Seward JB, Lester SJ, Appleton CA, Gersh BJ, et al. Usefulness of left atrial volume in predicting first congestive heart failure in patients >or=65 years of age with well-preserved left ventricular systolic function. Am J Cardiol 2005;96:832-6.
10. Vaziri SM, Larson MG, Benjamin EJ, Levy D. Echocardiographic predictors of nonrheumatic atrial fibrillation. The Framingham Heart Study. Circulation 1994;89:724-30.
11. Généreux P, Pibarot P, Redfors B, Mack MJ, Makkar RR, Jaber WA, et al. Staging classification of aortic stenosis based on the extent of cardiac damage. Eur Heart J 2017;38:3351-8.
12. Cremer PC, Zhang Y, Alu M, Rodriguez LL, Lindman BR, Zajarias A, et al. The incidence and prognostic implications of worsening right ventricular function after surgical or transcatheter aortic valve replacement: insights from PARTNER IIA. Eur Heart J 2018;39:2659-67.
13. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. 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 2005;18:1440-63.
14. Messika-Zeitoun D, Bellamy M, Avierinos JF, Breen J, Eusemann C, Rossi A, et al. Left atrial remodelling in mitral regurgitation--methodologic approach, physiological determinants, and outcome implications: a prospective quantitative Doppler-echocardiographic and electron beam-computed tomographic study. Eur Heart J 2007;28:1773-81.
15. Edvardsen T, Gerber B, Donal E, Maurovich-Horvat P, Maurer G, Popescu BA. The year 2015-16 in the European Heart Journal-Cardiovascular Imaging. Part II. Eur Heart J Cardiovasc Imaging 2017;18:1322-30.