

Clinical and Echocardiographic Parameters and Score for the Left Atrial Thrombus Formation Prediction in the Patients with Mitral Stenosis

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Background: Rheumatic mitral stenosis is one of the important health problems, especially in Thailand. Thromboembolic complications from this disease remain the major problem in these patients. These complications are usually related to the left atrial thrombus formation.

Objective: To determine the parameters that can predict the presence of left atrial thrombus in these patients.

Material and Method: Two hundred and sixty Thai patients with mitral stenosis from Siriraj Hospital were prospectively recruited in the study. The baseline clinical characteristics of these patients which were related to thrombus formation were properly collected. All patients underwent the transthoracic and transesophageal echocardiography with the standard technique to detect the mitral valve area, mitral valve score, left atrial size, LV ejection fraction, right ventricular systolic pressure, spontaneous echo contrast (SEC) and associated valvular lesions. Transesophageal echocardiography was used as the gold standard for evaluation of left atrial thrombus. These parameters were analyzed to demonstrate association with the presence of left atrial thrombus by univariate and multiple logistic regression analysis. Equation with score for prediction of left atrial thrombus was also purposed.

Results: There were 77 men and 183 women in the present study. Left atrial thrombus was detected in 26% and previous thromboembolic complications occurred in 16.5%. Atrial fibrillation presented in 52.5%. From univariate analysis, atrial fibrillation (81.2% vs 42.9%, $p < 0.001$), male sex (37.7% vs 25.6%, $p < 0.050$), left atrial enlargement by electrocardiogram (45.5% vs 15.4%, $p < 0.001$), left atrial diameter (7.26 vs 6.97 cm, $p < 0.030$), left atrial volume (132.7 vs 113.5 cm³, $p < 0.001$), EF by Teich method (58.9 vs 62.5%, $p < 0.011$), EF by MOD-bp (60.7 vs 64.6%, $p < 0.005$), tricuspid regurgitation (46.4% vs 28.8%, $p < 0.008$), mitral regurgitation (10.1 vs 3.1%, $p < 0.022$), and RVSP (57.0 vs 49.7 mmHg, $p < 0.005$) can predict the presence of left atrial thrombus formation with statistical significance. Using multiple logistic regression model, only atrial fibrillation (OR 5.95, 95% CI 1.21-29.3, $p < 0.02$) and RVSP (OR 1.02, 95%CI 1.01-1.04, $p < 0.04$) were independent predictors. The authors proposed score for predicting probability of left atrial thrombus formation that equal to $-3.61 + 1.79 \text{ AF} + 0.03 \text{ RVSP}$ with AUC of 0.764. The best cut-off point for this score was -1.49, which gave a sensitivity of 91%, specificity of 56%, PPV of 48%, and NPV of 90%.

Conclusion: Prevalence of thromboembolic complications and thrombus formation is high in patients with mitral stenosis in Thailand. From the present study, the predictors for left atrial thrombus formation in the patients with mitral stenosis were atrial fibrillation and RVSP. The model for predicting left atrial thrombus formation was also proposed with high sensitivity and NPV.

Keywords : Echocardiographic Parameters, Left Atrial Thrombus Formation, Predication, Mitral Stenosis

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Rheumatic heart disease remains an important health problem in Thailand. Among rheumatic heart diseases, mitral stenosis is the most common valve pathology. Despite development in management including percutaneous mitral balloon valvulotomy (PBMV) and mitral surgery, there is still substantial mortality and morbidity among patients. Typical manifestations in patients with mitral stenosis are dyspnea and heart failure. However, the patients may also present with its complications such as systemic thromboembolism, infective endocarditis, hemoptysis, or compressive symptoms of dysphagia and hoarseness. Thromboembolic complications, especially cerebral embolism, is one of the major morbidities because these cause them to be disabled and necessitates that their relatives to take care of them⁽¹⁾. These events, which are much more common than in the normal population, occur in 10-20% in patients with mitral stenosis⁽²⁻⁵⁾. Obstruction of mitral valve caused by mitral stenosis causes stagnation of blood flow, leading to thrombus formation in the left atrium, especially the left atrial appendage. This clot can dislodge from the left atrium into the systemic circulation, when thromboembolic complication may occurs. The association between thromboembolic events and left atrial thrombus has been well recognized for a long time⁽⁵⁻⁸⁾.

However, the precise risk factors of left atrial thrombus formation are not well demonstrated. The previous studies have studied the factors which increased the incidence of left atrial thrombus in heterogeneous populations. The populations of these studies included the patients with rheumatic heart disease of various valve pathologies⁽⁹⁾, various kinds of mitral stenosis⁽¹⁰⁻¹³⁾, atrial fibrillation⁽¹⁴⁾, valvular atrial fibrillation⁽¹⁵⁾, non-valvular atrial fibrillation, or even normal sinus rhythm. Only a few predictors are consistent in all studies, whereas most predictors are controversial.

The best strategy to prevent this serious complication in high risk groups is anticoagulation⁽¹⁶⁻¹⁸⁾. The important problem is how to define high risk patients for thromboembolic complication. Despite the benefit of thromboembolic prevention, anticoagulation has some drawbacks, most importantly bleeding complication. The current guideline for valvular heart disease recommends anticoagulant only in patients with mitral stenosis with coexistent atrial fibrillation, prior history of thromboembolism, and presence of left atrial thrombus⁽¹⁹⁻²¹⁾.

Identification of these risk factors provides the benefit of assessing the high risk group for left atrial thrombus formation, which also predisposes members

of this group to the thromboembolic events. Furthermore, it may improve the strategies for preventing these complications such as prophylactic anticoagulant therapy in high risk patients other than those studied under the present guideline. However, most of the previous studies addressing risk predictors had been investigated in heterogeneous populations with rheumatic heart disease or patients with atrial fibrillation⁽²²⁾ and most studies were retrospective.

The purpose of the present study was to prospectively identify clinical and echocardiographic predictors and develop scores for prediction of left atrial thrombus formation in patients with rheumatic mitral stenosis in Thailand.

Objective

To investigate the clinical and echocardiographic variables and develop a score to predict the left atrial thrombus formation in patients with rheumatic mitral stenosis

Material and Method

Study population

From January 2002 to January 2004, two hundred and sixty Thai patients with rheumatic mitral stenosis from the inpatient and outpatient department of Siriraj Hospital were prospectively recruited in the present study. Diagnosis of mitral stenosis is met by echocardiographic criteria of mitral valve area < 2 cm².

Patients were excluded from the study if they met any of the following criterion : contraindication to

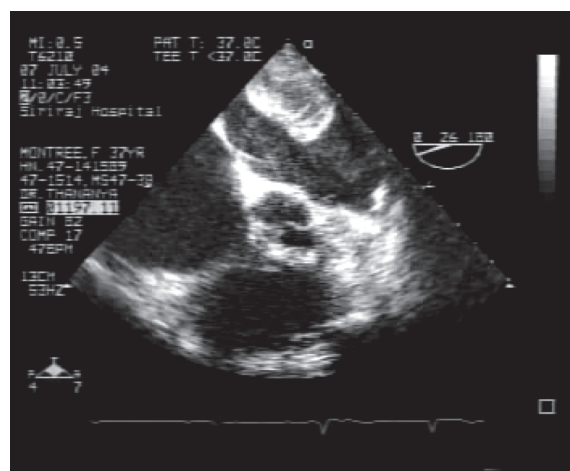


Fig. 1 Left atrial thrombus in left atrial body from transesophageal echocardiography

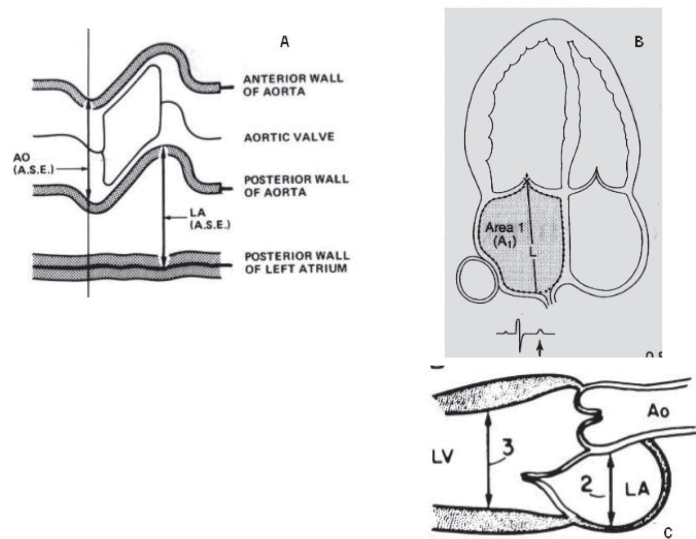


Fig. 2 Three methods for the measurement of left atrial size A) left atrial diameter from M-mode of parasternal short axis view, B) left atrial length and width from 4-chamber view and C) left atrial volume

transesophageal echocardiography such as some esophageal disorders, unconscious persons who can not cooperate or may take risk of aspiration, and uncorrectable coagulopathy. Patients were also excluded if they were unwilling to undergo transesophageal echocardiography. All patients gave informed consent.

Study procedures

All consecutive patients with mitral stenosis diagnosed by transthoracic echocardiography were enrolled in the present study. Then transesophageal echocardiography was performed to detect thrombus in left atrium and left atrial appendage. Clinical and echocardiographic variables which may predict the existence of left atrial thrombus were properly collected. Left atrial thrombus was diagnosed by the presence of a clearly defined echogenic intracavitary mass in at least two different planes⁽²³⁾ (Fig. 1) using transesophageal echocardiography which is currently the diagnostic method of choice for this purpose⁽²⁴⁾.

Clinical predictors : Clinical characteristics of the patients were obtained from their interview. The clinical data which were probably associated with left atrial thrombus formation were collected including

- Baseline characteristic data: age, gender
- Symptoms: Dyspnea, functional class, duration of symptom

- Atrial fibrillation: documented by physical examination and electrocardiogram
- Thromboembolic complications: transient ischemic attack, embolic stroke, and arterial embolism of other sites
- Anticoagulant and antiplatelet therapy

Echocardiographic predictors : Transthoracic echocardiography was performed with a Hewlett-Packard Sonos 5500 and 2 to 4-MHz transducer. These following echocardiographic parameters were recorded including

- Mitral valve area: measured by planimetry in the parasternal short-axis view and pressure half-time methods^(22,25)
- Mitral valve score
- Mitral regurgitation: graded by standard criteria as mild, moderate, and severe
- Other valvular pathology: Tricuspid regurgitation, Aortic regurgitation, Aortic stenosis
- Severity of pulmonary hypertension: assessed as right ventricular systolic pressure (RVSP)
- Left ventricular ejection fraction (LVEF): evaluated quantitatively by Teichholz and modified biplane methods
- Left atrial size: measured by three methods as diameter from M-mode echocardiogram in parasternal long axis, length (anteroposterior dimension) and width (lateral dimension) in apical 4-chamber view

Table 1. Clinical and echocardiographic variables in 260 patients with mitral stenosis

Variables	Mean $\pm$ SD or number (%)
Clinical variables	
Age (year)	42.3 $\pm$ 11.4
Men (%)	77 (28.8)
Previous emboli (%)	43 (16.5)
Atrial fibrillation (%)	136 (52.5)
Anticoagulant (%)	139 (53.5)
Previous PBMV (%)	14 (5.4)
Previous Valvulotomy (%)	8 (3.1)
Echocardiographic variables	
MVA (cm ²)	0.86 $\pm$ 0.24
MV score	8.59 $\pm$ 1.22
LA in short axis (mm)	55.82 $\pm$ 8.67
LA length (mm)	6.82 $\pm$ 1.56
LA width (mm)	5.69 $\pm$ 1.35
LA volume (mm ³)	118.69 $\pm$ 53.26
RVSP (mmHg)	51.71 $\pm$ 18.81
LVEF by Teich (%)	61.56 $\pm$ 9.94
Significant MR (%)	13%
Significant AR (%)	48%
Significant AS (%)	8%
Significant TR (%)	87%
LA thrombus by TEE (%)	26%
LA SEC by TTE (%)	14.2%

(Fig. 2), and left atrial volume calculated from the following formula

$$\text{Left atrial volume} = 0.523 \times D1 \times D2 \times D3$$

When D1 = diameter from M-mode echocardiogram in parasternal long axis

D2 = length in apical 4-chamber view

D3 = width in apical 4-chamber view

- Presence of left atrial spontaneous echo contrast (SEC): diagnosed by the presence of dynamic smoke-like echoes within the atrial cavity, with characteristic swirling motion distinct from white noise artifact

All patients underwent the transesophageal echocardiographic study using 5-MHz omniplane probes after informed consent. The patients fasted for at least 6 hours. The hypopharynx was sprayed with 10% topical lidocaine. The left atrial body and appendage were inspected carefully for the presence of thrombus and spontaneous echo contrast (SEC).

All echocardiograms were reviewed by two cardiologists with regard to the presence or absence of

thrombus and spontaneous echo contrast in the left atrium. Any discrepancy was resolved by the third cardiologist and consensus.

Statistical analysis

Quantitative variables were summarized as mean and SD. To test if there was a statistically significant difference in quantitative variables between patients with and without left atrium thrombus, unpaired t-test and Mann-Whitney U test were applied for normally and non-normally distributed data respectively. For categorical variables, chi-square test was employed to test the association between each variable and presence of left atrium thrombus. Regarding multivariable analysis, multiple logistic regression was used to determine the effect of each predictor on the presence of left atrium thrombus after controlling for the effect of other predictors in the model. Results were displayed as adjusted odds ratio (OR) and 95% confidence interval (CI).

All statistical analyses were performed using SAS Version 8.0. A p-value of less than or equal to 0.05 was considered statistically significant.

Results

From January 2002 to January 2004, two hundred and sixty Thai patients with rheumatic mitral stenosis from the inpatient and outpatient department of Siriraj Hospital were prospectively recruited in the present study. There were 77 men and 183 women, so male : female ratio was 2.38 : 1 with mean age of 42.3 $\pm$ 11.4 years (range 18 to 76 years). The left atrial thrombus was detected in 26% by transesophageal echocardiography which is currently the diagnostic method of choice for this purpose and previous thromboembolic complications occurred in 16.5%. 37 patients had cerebral thromboembolism whereas 3 had other sites of thromboembolism including 2 peripheral emboli in the leg and 1 ophthalmic arterial occlusion. Atrial fibrillation was found in 52.5% of the studied group. Anticoagulant was given in 139 patients. The INR levels in these patients were in the therapeutic range (1.5 to 2.5 times the control) with mean INR of 2.28. 22 patients had a previous history of mitral valve intervention including 14 patients with prior percutaneous balloon mitral valvuloplasty and 8 patients with surgical mitral valvulotomy.

In the present study, the authors included patients with mitral stenosis of all severities. There were severe mitral stenosis in 181, moderate mitral stenosis in 73, and mild stenosis in 6. Associated

Table 2. Univariable analysis of predictors of LA thrombi in patients with mitral stenosis

	With thrombus n = 67	Without thrombus n = 193	p-value
Clinical			
Age (year)	44.41 ± 10.40	41.50 ± 11.62	0.068
Male	37.7%	25.6%	0.050
Symptom	95.7%	93.2%	0.460
Duration of symptom (year)	3.68 ± 4.18	3.63 ± 4.32	0.941
Functional class			0.080
NYHA 1	10.2%	18.9%	
NYHA 2	69.5%	71.1%	
NYHA 3	18.9%	8.9%	
NYHA 4	1.4%	1.1%	
Previous emboli	15.8%	14.5%	0.800
Electrocardiography			
Atrial fibrillation	81.2%	42.9%	<0.0001
RAD	24.6%	37.7%	0.055
LAE	45.5%	15.4%	<0.001
RVH	36.2%	30.8%	0.420
Echocardiography			
MVA by trace (cm ²)	0.87 ± 0.27	0.93 ± 0.24	0.192
MVA by P1/2t (cm ²)	0.83 ± 0.28	0.93 ± 0.24	0.142
LA short axis (mm)	58.04 ± 10.41	55.02 ± 7.81	0.030
LA length (mm)	7.26 ± 0.92	6.97 ± 1.20	0.081
LA width (mm)	5.84 ± 0.79	5.52 ± 1.03	0.164
LA volume (mm ³)	132.78 ± 56.02	113.59 ± 51.43	0.001
EF by Teich (%)	58.96 ± 10.91	62.50 ± 9.42	0.011
EF by MOD-bp (%)	60.78 ± 11.24	64.63 ± 9.07	0.005
MR moderate-severe	10.1%	3.1%	0.022
AR moderate-severe	21.7%	17.3%	0.413
TR moderate-severe	46.4%	28.8%	0.008
RVSP (mmHg)	57.08 ± 18.68	49.77 ± 18.53	0.005
SEC by TTE (%)	18.8%	12.6%	0.200

moderate to severe mitral regurgitation was found in 13 patients, whereas moderate to severe tricuspid regurgitation presented in 87 patients. The other valvular pathologies were significant aortic regurgitation in 48 patients and significant aortic stenosis in 6 patients. Transesophageal echocardiography could be successfully performed in all patients without any complications. Image of left atrium and its appendage was successfully visualized in all of them. An excellent inter- and intra-observer agreement in all cases between 2 cardiologists was found on the presence of left atrial thrombus from transesophageal echocardiography (K 1.00).

Clinical, electrocardiographic, and echocardiographic data in patients with and without left atrial thrombus are shown in Table 1. From univariate analysis, it was demonstrated that atrial fibrillation (81.2%

vs 42.9%, $p < 0.001$), male sex (37.7% vs 25.6%, $p < 0.050$), left atrial enlargement by electrocardiogram (45.5% vs 15.4%, $p < 0.001$), left atrial diameter (Mean 7.26 vs 6.97 cm, $p < 0.030$), left atrial volume (Mean 132.7 vs 113.5 cm³, $p < 0.001$), EF by Teich method (Mean 58.9 vs 62.5%, $p < 0.011$), EF by MOD-bp (Mean 60.7 vs 64.6%, $p < 0.005$), tricuspid regurgitation (Mean 46.4% vs 28.8%, $p < 0.008$), mitral regurgitation (10.1 vs 3.1%, $p < 0.022$), and RVSP (Mean 57.0 vs 49.7 mmHg, $p < 0.005$) can predict the presence of left atrial thrombus formation with statistical significance. Patients with and without left atrial thrombi did not differ in age, presence or absence of symptoms, duration of symptoms, previous thromboembolism, right axis deviation, severity of mitral stenosis, and presence of spontaneous echo contrast in transthoracic echocardiography.

Table 3. Final Multiple logistic regression analysis of predictors of LA thrombus in patients with mitral stenosis

	Odds ratio	95% CI	p-value
Atrial fibrillation	5.95	1.21–29.3	0.02
RVSP (mmHg)	1.02	1.01–1.04	0.04

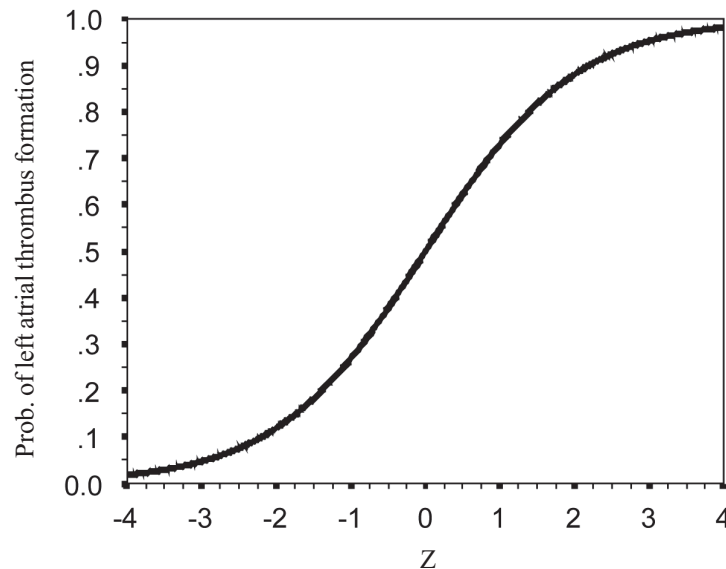


Fig. 3 Probability of left atrial thrombus formation using purposed equation

For evaluation of independent predictors of left atrial thrombus formation, 14 predictors with $p < 0.1$ from univariate analysis were entered multiple logistic regression analysis with forward stepwise method. Only two remaining parameters shown in Table 2, were independent parameters from multiple logistic regression models. These two predictors were atrial fibrillation (OR 5.95, 95% CI 1.21–29.3, $p < 0.02$) and RVSP (OR 1.02 95%CI 1.01–1.04, $p < 0.04$). To apply this simplified logistic model to practical use, and index score of these two predictors had to be first calculated according to equation (1) with AUC of 0.764. Probability of having left atrial thrombus formation can then be obtained using equation (2) or graph in Fig. 3.

$$Z = \text{Score} = -3.61 + 1.79 \text{ AF} + 0.03 \text{ RVSP} \dots \dots \dots (1)$$

where AF = 0 if absence of AF
1 if presence of AF

RVSP = Right ventricular systolic pressure in mmHg
P = Probability of left atrial thrombus formation

$$P = \frac{e^Z}{1 + e^Z} \dots \dots \dots (2)$$

To demonstrate the use of the authors' multiple logistic regression equation, if a patient has the following characters: A 45-year-old woman with severe mitral stenosis, atrial fibrillation, severe tricuspid regurgitation with RVSP of 70 mmHg. From equation (1), the calculated score was 2.67 and from Fig. 1, with a score of 2.67 the probability of the presence of left atrial thrombus becomes 0.95. From high probability achieved, this patient has a very high chance to have left atrial thrombus. In contrast, if another 45-year-old patient with severe mitral stenosis, has normal sinus rhythm and mild tricuspid regurgitation with RVSP of 30 mmHg, her score from equation (1) is -2.71 and

probability from Fig. 1 is only 0.01. From low probability achieved, this patient has a negligible chance of having left atrial thrombus.

The best cut-off point of this score was obtained from ROC curve of probability of left atrial thrombus. Score of -1.49 gave the highest accuracy with 91% sensitivity, 56% specificity, 48% PPV, and 90% NPV.

Discussion

From the present study, the factors that can predict the presence of left atrial thrombus in the patients with mitral stenosis are atrial fibrillation, male sex, left atrial enlargement by electrocardiogram, left atrial diameter, left atrial volume, EF by Teich method, EF by MOD-bp, tricuspid regurgitation, mitral regurgitation, and RVSP by univariate analysis. On the other hand, age, symptoms, duration of symptoms, previous thromboembolism, severity of mitral stenosis, left atrial volume, and presence of spontaneous echo contrast in transthoracic echocardiography can not demonstrate this association. By multivariable regression analysis, only atrial fibrillation and RVSP are identified as independent predictors. Using the authors' simple model purposed for predicting left atrial thrombus formation yields 91% sensitivity, 56% specificity, 48% positive predictive value, and 90% negative predictive value.

Prevalence of thromboembolic complications, mostly cerebrovascular accident, is still high in the authors' patients at 16.5%. Left atrial thrombus was found in 26% in the presented population. In this group, 53 patients had atrial fibrillation, whereas 13 patients were in sinus rhythm. According to the current guideline, some patients with thrombus may not receive anticoagulant due to not having atrial fibrillation. With the present model, the authors can identify patients who have a high probability of left atrial thrombus formation, and may thus choose to order anticoagulant or perform echocardiography to define the presence of thrombus.

As in most previous studies^(3-8,11), atrial fibrillation was the important risk factor for the occurrence of left atrial thrombus in the present study. There are also studies that demonstrated the close relationship between atrial fibrillation and thromboembolic complications. This leads to the revised guideline recommendation of anticoagulant prophylaxis in the patients with mitral stenosis and atrial fibrillation.

In contrast to atrial fibrillation, other predictors for left atrial thrombus remain controversial in many studies, including left atrial size, severity of mi-

tral stenosis as measured by mitral valve area, pulmonary hypertension, other associated valve pathology especially mitral regurgitation, and spontaneous echo contrast (SEC). The other independent predictor gleaned from the authors' study is right ventricular systolic pressure (RVSP). Pulmonary hypertension reflects both severity and chronicity of mitral stenosis. These two things can cause thrombus formation in patients with mitral stenosis.

Left atrial size is one of these controversial predictors for left atrial thrombus formation. Evaluation of this value is various and no standard technique nowadays prevails. Simple ECG criteria of left atrial enlargement can not applied in patients with atrial fibrillation, whereas echocardiographic value can be acquired from different methods including diameter measuring from M-mode in short axis view, length and width in apical four-chamber view, and left atrial volume calculated from various formula. In the present study the authors used one method from ECG and three methods from echocardiography for the assessment of left atrial size, including diameter measuring from M-mode in parasternal short axis view, length and width in apical four-chamber view, and left atrial volume calculated from diameter in short axis and length and width in apical four-chamber view as shown previously in the section of method. Left atrial size by ECG, diameter from short axis view, and volume demonstrated the association by univariate analysis in the present result. However, it could not declare significance in multiple logistic regression analysis. The explanation may be that there is no accurate method for left atrial size measurement and left atrial size may correlate with the presence of atrial fibrillation.

The present study could not demonstrate the association between severity of mitral stenosis, assessed by mitral valve area and the presence of left atrial thrombus. This predictor has contradictory results in previous studies. Some previous retrospective studies used spontaneous echo contrast as an indicator of increased risk for embolization⁽¹³⁻¹⁵⁾ However, subgroup analysis of one study did not confirm this finding but it had few patients in this subgroup. The present study found that spontaneous echo contrast cannot predict the presence of left atrial thrombus formation.

The coexistence of mitral regurgitation has been associated in clinical studies with reduced incidence of embolization. The reason behind this finding is that the regurgitant blood disrupts left atrial stasis. However, direct evidence of lower incidence of left

atrial thrombus in patients with mitral regurgitation is limited and controversial. In one study in patients with mitral stenosis, mitral regurgitation was not mentioned as a factor affecting left atrial thrombus. In nonrheumatic atrial fibrillation, mitral regurgitation was only related to a lower embolic rate. In a recent study of rheumatic mitral valve disease, significant mitral regurgitation was associated with a decrease in thrombus formation⁽⁹⁾. According to the present study, the authors found the association of mitral regurgitation and presence of left atrial thrombus from univariate analysis, but not from multivariate analysis.

The authors' purposed model for predicting the presence of thrombus in left atrium is simple and yields high sensitivity and negative predictive value. Because left atrial thrombus may lead to thromboembolic complication, that is a serious problem and if this group of the patients is missed, it may be harmful. In contrast, if a false-positive result occurs that leads the patient to have transesophageal echocardiography, it is not harmful because transesophageal echocardiography can be done with a high safety profile. So, in this serious condition, model with high sensitivity and negative predictive value is appropriate.

Conclusion

The present study demonstrates atrial fibrillation and RVSP as the independent predictors for left atrial thrombus formation in patients with mitral stenosis. Together with a purposed model for predicting presence of left atrial thrombus, this can predict left atrial thrombus formation with high sensitivity and negative predictive value. The present study also emphasizes the higher incidence of left atrial thrombus and thromboembolism in patients with rheumatic mitral stenosis. Better identification of high risk patients for thrombus formation may lead to further investigation and effective prevention in order to reduce this serious thromboembolic complications in the future.

References

1. Sithi-Amorn C, Tatsanavivat P, Sawadsitang W, Keoyoo J, Mahawerawat U. Death and stroke rate in chronic rheumatic heart disease. *J Med Assoc Thai* 1988; 71: 302-9.
2. Rowe JC, Bland EF, Sprague HB, White PD. The course of mitral stenosis without surgery: ten- and twenty-year perspectives. *Ann Intern Med* 1960; 52: 741-9.
3. Daley R, Mattingly TW, Holt CL, Bland EF, White PD. Systemic arterial embolism in rheumatic heart disease. *Am Heart J* 1951; 42: 566-81.
4. Yipintsoi T, Jirathamopas W, Suntiparpluacha C, Jintapakorn W, Akaravinake A, Kunjara-Na-Ayudhya R. Embolism and atrial fibrillation. A longitudinal follow-up. *J Med Assoc Thai* 1992; 75: 73-8.
5. Karnchanapanddh P, Choon-Ngarm T, Puavilai W. Systemic embolism in rheumatic heart disease. *Thai Heart J* 2000; 13: 1217-31.
6. Chiang CW, Lo SK, Ko YS, Cheng NJ, Lin PJ, Chang CH. Predictors of systemic embolism in patients with mitral stenosis. A prospective study. *Ann Intern Med* 1998; 128: 885-9.
7. Hwang JJ, Kuan P, Lin SC, Chen WJ, Lei MH, Ko YL, et al. Reappraisal by transesophageal echocardiography of the significance of left atrial thrombi in the prediction of systemic arterial embolization in rheumatic mitral valve disease. *Am J Cardiol* 1992; 70: 769-73.
8. Chiang CW, Lo SK, Kuo CT, Cheng NJ, Hsu TS. Noninvasive predictors of systemic embolism in mitral stenosis. An echocardiographic and clinical study of 500 patients. *Chest* 1994; 106: 396-9.
9. Karatasakis GT, Gotsis AC, Cokkinos DV. Influence of mitral regurgitation on left atrial thrombus and spontaneous echocardiographic contrast in patients with rheumatic mitral valve disease. *Am J Cardiol* 1995; 76: 279-81.
10. Goswami KC, Yadav R, Rao MB, Bahl VK, Talwar KK, Manchanda SC. Clinical and echocardiographic predictors of left atrial clot and spontaneous echo contrast in patients with severe rheumatic mitral stenosis: a prospective study in 200 patients by transesophageal echocardiography. *Int J Cardiol* 2000; 73: 273-9.
11. Sahasakul Y, Chaithiraphan S, Panchavinnin P, Srivanasont N, Jootar P, Trisukosol D, et al. Multivariate analysis in the prediction of left atrial thrombi in patients with mitral stenosis. *J Am Soc Echocardiogr* 1995; 8: 742-6.
12. Raungratanaamporn O, Tresukosol D, Chotinai-watarakul C, Sahasakul Y, Raungratanaamporn S, Bhuripanyo K, et al. Transesophageal echocardiography to detect left atrial thrombi in patients with mitral stenosis before percutaneous balloon mitral valvuloplasty. *Asean Heart J* 1995; 3: 63-6.
13. Vigna C, de Rito V, Cricconia GM, Russo A, Testa M, Fanelli R, et al. Left atrial thrombus and spontaneous echo-contrast in nonanticoagulated mitral stenosis. A transesophageal echocardiographic study. *Chest* 1993; 103: 348-52.

14. Trakulratanawong K, Piamsomboon C, Saguanwong S, Laothavorn P. The prevalence of left atrial spontaneous echo contrast and thrombus in nonrheumatic and rheumatic atrial fibrillation assessed by transesophageal echocardiography. *Thai Heart J* 1994; 7: 69-75.
15. Gonzalez-Torrecilla E, Garcia-Fernandez MA, Perez-David E, Bermejo J, Moreno M, Delcan JL. Predictors of left atrial spontaneous echo contrast and thrombi in patients with mitral stenosis and atrial fibrillation. *Am J Cardiol* 2000; 86: 529-34.
16. Roy D, Marchand E, Gagne P, Chabot M, Cartier R. Usefulness of anticoagulant therapy in the prevention of embolic complications of atrial fibrillation. *Am Heart J* 1986; 112: 1039-43.
17. Ezekowitz MD, Bridgers SL, James KE, Carliner NH, Colling CL, Gornick CC, et al. Warfarin in the prevention of stroke associated with non-rheumatic atrial fibrillation. Veterans Affairs Stroke Prevention in Nonrheumatic Atrial Fibrillation Investigators. *N Engl J Med* 1992; 327: 1406-12.
18. Stroke Prevention in Atrial Fibrillation Study. Final results *Circulation* 1991; 84: 527-39.
19. ACC/AHA guidelines for the management of patients with valvular heart disease. A report of the American College of Cardiology/American Heart Association. Task Force on Practice Guidelines (Committee on Management of Patients with Valvular Heart Disease) *J Am Coll Cardiol* 1998; 32: 1486-588.
20. Fuster V, Ryden LE, Asinger RW, Cannom DS, Crijs HJ, Frye RL, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: executive summary. A Report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients With Atrial Fibrillation): developed in Collaboration With the North American Society of Pacing and Electrophysiology. *J Am Coll Cardiol* 2001; 38: 1231-66.
21. Hirsh J. Guidelines for antithrombotic therapy. 4th ed. Summary of the American College of Chest Physicians (ACCP) recommendations 2000. Hamilton: BC Decker; 2001: 34-7.
22. Bruce CJ, Nishimura RA. Newer advances in the diagnosis and treatment of mitral stenosis. *Curr Probl Cardiol* 1998; 23: 125-92.
23. Feigenbaum H. Echocardiography. 4th ed. Philadelphia: Lea & Febiger; 1986: 592.
24. Koca V, Bozat T, Akkaya V, Sarikamis C, Turk T, Vural H, et al. Left atrial thrombus detection with multiplane transesophageal echocardiography: an echocardiographic study with surgical verification. *J Heart Valve Dis* 1999; 8: 63-6.
25. Hatle L, Angelsen B, Tromsdal A. Noninvasive assessment of atrioventricular pressure half-time by Doppler ultrasound. *Circulation* 1979; 60: 1096-104.
26. Pollick C, Taylor D. Assessment of left atrial appendage function by transesophageal echocardiography. Implications for the development of thrombus. *Circulation* 1991; 84: 223-31.

ปัจจัยทางคลินิกและคลื่นเสียงสะท้อนความถี่สูงหัวใจ และสมการสำหรับการพยากรณ์การเกิดลิ่มเลือดในห้องหัวใจเอเทรียมซ้าย ในผู้ป่วยลิ้นหัวใจไม่ตรัสติบ

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ภูมิหลัง: โรคลิ้นหัวใจไม่ตรัสติบชนิดรูมาติก เป็นปัญหาสำคัญทางสาธารณสุขของประเทศไทย ภาวะลิ่มเลือดหัวใจอุดตันซึ่งเกิดจากโรคนี้เป็นผลแทรกซ้อนที่สำคัญและมีอันตรายแก่ผู้ป่วยภาวะนี้มีความสัมพันธ์กับการเกิดลิ่มเลือดในห้องหัวใจเอเทรียมซ้าย ปัจจัยที่สามารถพยากรณ์การเกิดลิ่มเลือดได้ยังไม่มีการศึกษาในผู้ป่วยโรคลิ้นหัวใจ ไม่ตรัสติบชนิดรูมาติกแบบ prospective และผลการศึกษาล้วนใหญ่ยังมีความขัดแย้งกัน การพยากรณ์การเกิดลิ่มเลือดในห้องหัวใจเอเทรียมซ้ายในผู้ป่วยเหล่านี้ได้อย่างแม่นยำจะทำให้แพทย์สามารถให้การป้องกันภาวะแทรกซ้อนที่สำคัญนี้ได้

วัตถุประสงค์ : เพื่อหาปัจจัยที่สามารถพยากรณ์การเกิดลิ่มเลือดในห้องหัวใจเอเทรียมซ้ายในผู้ป่วยโรคลิ้นหัวใจไม่ตรัสติบชนิดรูมาติก

วัสดุและวิธีการ: ผู้ป่วยโรคลิ้นหัวใจไม่ตรัสติบ จำนวน 260 คน ที่ได้รับการตรวจที่โรงพยาบาลศิริราช ถูกคัดเข้าในการศึกษานี้ ลักษณะพื้นฐานทางคลินิกที่อาจมีความสัมพันธ์กับการเกิดลิ่มเลือด ถูกเก็บข้อมูลอย่างถูกต้องและครบถ้วน ผู้ป่วยทุกรายได้รับการตรวจคลื่นเสียงสะท้อนความถี่สูงหัวใจ ชนิดตรวจผ่านทางหน้าอกและตรวจผ่านทางหลอดอาหาร เพื่อประเมินขนาดและลักษณะของลิ้นหัวใจไม่ตรัสติบ ขนาดของห้องหัวใจเอเทรียมซ้ายด้วย 3 วิธี สมรรถภาพการบีบตัวของหัวใจห้องล่างซ้าย ความดันในหลอดเลือดปอด และพยาธิสภาพของลิ้นหัวใจอื่นที่พบร่วมด้วย นอกจากนี้จากการตรวจคลื่นเสียงสะท้อนความถี่สูงหัวใจชนิดตรวจผ่านทางหลอดอาหารยังใช้ในการวินิจฉัยลิ่มเลือดในห้องหัวใจเอเทรียมซ้าย ปัจจัยต่างๆ ถูกนำมาวิเคราะห์หาความสัมพันธ์กับการเกิดลิ่มเลือดในห้องหัวใจเอเทรียมซ้าย และสร้างสมการสำหรับการพยากรณ์การเกิดลิ่มเลือดหัวใจในผู้ป่วยโรคลิ้นหัวใจไม่ตรัสติบต่อไป

ผลการศึกษา: มีผู้ป่วยเพศชาย 77 คน และเพศหญิง 183 คน พบการเกิดลิ่มเลือดในห้องหัวใจเอเทรียมซ้าย 26% และการเกิดภาวะลิ่มเลือดหัวใจอุดตัน 52.5% จากการวิเคราะห์พื้นฐานพบว่าภาวะหัวใจเต้นผิดจังหวะชนิด atrial fibrillation เพศชาย ขนาดห้องหัวใจเอเทรียมซ้ายใหญ่จากการตรวจคลื่นไฟฟ้าหัวใจ เส้นผ่าศูนย์กลางห้องหัวใจเอเทรียมซ้ายจากการตรวจคลื่นเสียงสะท้อนความถี่สูงหัวใจ ปริมาตรห้องหัวใจเอเทรียมซ้ายจากการตรวจ คลื่นเสียงสะท้อนความถี่สูงหัวใจ สมรรถภาพการบีบตัวของหัวใจห้องล่างซ้าย ภาวะลิ้นหัวใจไตรคัสปิดรั่ว ภาวะลิ้นหัวใจไม่ตรัสติบ และความดันในหลอดเลือดปอด มีความสัมพันธ์ต่อการเกิดลิ่มเลือดในห้องหัวใจเอเทรียมซ้าย แต่ปัจจัยที่มีนัยสำคัญทางสถิติหลังจากวิเคราะห์เพิ่มเติมแล้วคือ ภาวะหัวใจเต้นผิดจังหวะชนิด atrial fibrillation และความดันในหลอดเลือดปอดสูงเท่านั้น จากการศึกษานี้ได้เสนอสมการสำหรับการพยากรณ์การเกิดลิ่มเลือดหัวใจ โดยมีค่าความไว 91% และความจำเพาะ 56%

สรุป: อุบัติการณ์การเกิดภาวะลิ่มเลือดหัวใจอุดตัน และการเกิดลิ่มเลือดในห้องหัวใจสูงในผู้ป่วย โรคลิ้นหัวใจไม่ตรัสติบในประเทศไทย จากการศึกษาพบว่าปัจจัยที่สามารถพยากรณ์การเกิดลิ่มเลือดในห้องหัวใจ ได้แก่ ภาวะหัวใจเต้นผิดจังหวะชนิด atrial fibrillation และความดันในหลอดเลือดปอดสูง สมการสำหรับการพยากรณ์ลิ่มเลือดหัวใจที่ได้จากการศึกษานี้มีความไวสูง จึงมีความเหมาะสมในการใช้ประเมินความเสี่ยงต่อการเกิดลิ่มเลือดในห้องหัวใจ
