

Echocardiographic Predictors of Symptomatic Atrial Fibrillation In Patients with Rheumatic Mitral Stenosis and Normal Sinus Rhythm

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Abstract

Introduction: Rheumatic mitral stenosis (RMS) increases the risk of both atrial fibrillation (AF) and thromboembolism.

Methods: Patients with mitral stenosis and normal sinus rhythm were enrolled in the study prospectively. The present study was designed to study whether echocardiographic evaluation in patients with mitral stenosis and normal sinus rhythm could predict the occurrence of symptomatic AF. **Results:** Sixty-two patients (51 females) with mitral stenosis and normal sinus rhythm were included in the study. Seven patients (11.3%) developed symptomatic AF and the remaining 55 were free of AF during a followed-up of 22 ± 5 months. The following echocardiographic parameters were significantly increased and predicted the development of AF; left atrial (LA) mediolateral diameter (5.5 ± 0.5 cm vs 4.7 ± 0.7 cm), right atrial mediolateral diameter (4.7 ± 1.0 cm vs 3.6 ± 1.3 cm), LA area in the apical two chamber view (31 ± 3.2 cm² vs 25 ± 5.8 cm²), right atrial volume (52 ± 22 cm³ vs 34 ± 19 cm³), and interatrial conduction time (IACT) (142 ± 22 msec vs 115 ± 16 msec).

Conclusions: OThis study revealed that echocardiography can be used to predict symptomatic AF in patients with RMS and sinus rhythm.

Introduction

Background

In rheumatic mitral stenosis (RMS), mitral valve area is reduced, creating an obstruction to the blood flow between the left atrium (LA) and the left ventricle (LV), causing an elevation in LA pressure. Elevation in LA pressure has several important effects including enlargement of the LA, atrial arrhythmias, and an increase in pulmonary venous pressure. RMS increases the risk of both atrial fibrillation (AF) and thromboembolism, causing an important health care problem

in developing countries. The prevalence of AF in patients with MS is between 17 to 80% and related to both the severity of valve obstruction and patient age.¹ The incidence of systemic embolism is greater in rheumatic mitral valve disease than in any other common form of valvular heart disease.

Patients with AF and mitral stenosis have high incidence of thrombus formation in the LA.^{2,3} AF is the most commonly encountered cardiac arrhythmia in this subset of patients with an increased risk of thromboembolism.⁴ Although mitral stenosis is considered as a strong risk factor for AF, the parameters in mitral stenosis that predict the risk of

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future AF have not been determined. Echocardiography is the primary and relatively simple tool to follow up the patients with RMS. AF is generally associated with structural changes in the atria and echocardiography provides a detailed anatomical evaluation. In addition, flow characteristics and chamber pressure can also be detected by echocardiography.

The aim of the present study was to investigate cardiac parameters that may predict prospectively in preceding symptomatic AF in patients with mitral stenosis and normal sinus rhythm. Clinical and echocardiographic parameters were studied in prediction of AF.

Methods and materials

Patients

Patients with mitral stenosis and normal sinus rhythm have been selected prospectively among a total of 1512 patients seen in our out-patient clinic between July 2003 and July 2004. Any patient with a new or previous diagnosis of mitral stenosis was evaluated for the study. Patients with a history of AF or valve disease other than RMS (with an exception of mild tricuspid or pulmonary valve regurgitation), who had undergone valve replacement, or those with poor echocardiographic images were excluded. None of the patients included in this study were on anti-arrhythmic drugs. The initial evaluation of the patients included history, physical examination, electrocardiography (ECG) and trans-thoracic echocardiography. At the end of the follow-up, patients were grouped into those who developed AF (group 1) and those who were free from AF (group 2).

Echocardiography

The echocardiographic evaluation was performed by transthoracic approach (General Electrics-Vivid 3 USA) and included standard parameters and atrial volumes, mitral valve area, transmitral pressure gradient and interatrial conduction time (IACT).

Atrial volumes were calculated by the ellipse formula: Atrial volume: $4 \Pi / 3 \times D1/2 \times D2/2 \times D3/2$, where D1 (mm) is anteroposterior, D2 medio-

lateral and D3 superoinferior dimension.⁵ The anteroposterior dimension of the left atrium (LA) was measured in the parasternal view, and the mediolateral and superoinferior dimensions of LA were measured in the apical four-chamber view. For the right atrium (RA), the mediolateral diameter was used for both D2 and D3 in the formula. Mitral valve area was calculated by planimetry and the pressure half-time methods.

Interatrial conduction time was defined as the time interval between the onset of the P-wave and the LAA (left atrial appendage) ejection flow.⁶ After the apical two-chamber view was obtained, the transducer was angulated anteriorly until LAA came into the view. A pulse Doppler sample volume in 1/3 proximal portion of LAA was used to obtain flow recordings. The ECG was recorded simultaneously via a single lead. The IACT was measured as the time interval between the beginning of the P wave on the ECG and the onset of LAA flow. The mean IACT value over 5 cardiac cycles was used in the data analysis (Figure).

Follow-up

All patients in the study were followed up with clinical evaluation every three months. The patients were asked to visit their primary physician if they experienced any palpitations. Patients who reported palpitations at their follow-up visits were subjected to 24-hour Holter monitoring. Episodes of AF were defined to be relevant if they exceeded duration of 30 seconds per day and coincided with the symptoms. The patients who underwent cardiac surgery have not been excluded from the study but not been followed-up for further. Percutaneous valvuloplasty was not a criterion for exclusion from the study or from follow-up.

Statistical Analysis

The Mann-Whitney U test was used for comparison of data between those with AF and without AF. Multiple logistic regression analysis was used to assess whether clinical and echocardiographic parameters and IACT were related to AF occurrence. Spearman's test was used to detect whether any of the assessed parameters correlated with AF occurrence. P value less than .05 was regarded as signifi-

cant.

Results

A total of 64 patients (11 males and 53 females) with mitral stenosis and normal sinus rhythm were initially enrolled in the study. Two patients were excluded from the study due to poor visualization of LAA by trans-thoracic echocardiography. The remaining 62 patients were followed prospectively for a mean period of 22 ± 5 months. Seven (11.3%, 7/62) patients developed symptomatic AF during follow-up and were assigned to Group 1. Six of the group 1 patients were demonstrated to have an AF episode by ECG recordings obtained when they were admitted to an emergency room due to palpitations. 10 patients presented palpitation and received Holter monitoring. A mbulatory Holter ECG monitoring revealed an AF episode in one patient. Group 2 consisted of the remaining 55 (88.8%) patients who did not develop AF during follow-up. The demographics, drug usage, and other characteristics of the patients are listed and compared between groups (Table 1). Age, functional capacity and follow-up periods were similar between groups. During the follow-up period, eight patients underwent percutaneous mitral balloon valvuloplasty. One patient had anterior myocardial infarction. Six patients underwent mitral valve surgery and were not followed-up further. In these patients, the mean time of follow-up from the time of inclusion to the surgery was 13 ± 6 months in those patients. No other major cardiac events have been reported.

Echocardiographic Parameters

The basal echocardiographic parameters of the study population are summarized in Table 2.

Mitral valve area, trans-mitral pressure gradients, the degree of mitral regurgitation, LA volume, LA and RA superoinferior diameters and volumes obtained in apical 4-chamber and 2-chamber views did not differ between the groups. However, the following four echocardiographic parameters were found to be associated with AF occurrence: left atrial mediolateral diameter (LAML2), right atrial mediolateral diameter (RAML2), right atrial volume (RAV) in apical 4-chamber view, and left atrial area in apical 2-chamber view (LA area3). Those parameters were found to be independent predictors of symptomatic AF. IACT was statistically significantly prolonged in group 1 (Mean IACT value was 142 ± 22 msec in group 1, 115 ± 16 msec in group 2, $p = 0.04$). No significant correlation was detected between IACT and other AF-predictive echocardiographic parameters.

Discussion

To the best of our knowledge this is the first prospective study that determined the echocardiographic parameters that predict symptomatic AF in patient with rheumatic mitral valve disease and sinus rhythm. Previous studies have provided information about AF recurrence or have compared chronic AF patients to control subjects with a normal sinus rhythm.⁷ Some clinical, electrocardiographic and echocardiographic parameters have been proposed as predictors of AF recurrence such as advanced age, left atrial enlargement and structural heart disease, although the results are conflicting.^{8,9} The role of left atrial diameter in predicting AF remains controversial. Kinay et al found no significant difference in left atrial diameter in patients with and without recurrent AF.⁶ In contrast, Diker et al has suggested that age, left atrial diameter and mean trans-valvular gradient may predict AF occurrence in their retrospective study.¹⁰ In our

Table 1

The comparison of the demographics and patient characteristics between groups. (CVA: Cerebrovascular accident).

	All patients (n= 62)	Group 1 (n=7)	Group 2 (n=55)	p value
Age (years)	42 ± 9	42 ± 13	41 ± 9	0.913
Functional Class	1.85 ± 0.70	2.00 ± 0.58	1.84 ± 0.72	0.556
Follow-up period (months)	22 ± 5	24 ± 3	21 ± 5	0.244

study, left and right atrial mediolateral diameters at apical 4-chamber view were significantly large in group 1. But only the volume of right atrium was found to be significantly high in group 1. This can be explained by that the mediolateral diameter of the right atrium has been used for both D2 and D3 in the volume formula. Additionally, an eccentric enlargement of the atria can also contribute these results.

Age appears to be predictive of AF recurrence only in patients older than 70-year old.¹¹ However, age cannot be considered as a predictive parameter for AF recurrence in patients with mitral stenosis.

The presence of an interatrial conduction delay has been shown to be associated with occurrence and recurrence of AF and some authors claim that clinically reducing interatrial conduction time via bi-atrial pacing could reduce AF recurrences in patients with interatrial conduction delay.¹² Interatrial conduction delay may endorse AF by facilitating micro-reentry circuits.¹³ There is an ongoing debate concerning the mechanism of these issues. A standard non-invasive method of measuring interatrial conduction time is missing. Fuenmayor et al demonstrated that IACT measured invasively by electrode catheters, correlated with IACT measured by trans-thoracic echocardiography as the time interval from the beginning of the P wave to the beginning of the mitral A wave.¹⁴ Dilation of LA structures in patients with mitral stenosis makes it easy to view the LAA by trans-thoracic

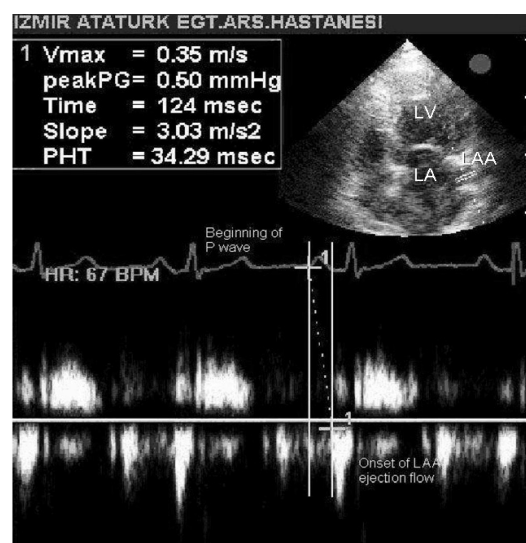
echocardiography, abolishing the need of more invasive trans-esophageal echocardiography.¹⁵ Although an electrophysiological test has not been performed in our patients, a significant correlation between IACT and electrophysiological IACT was previously reported by our group.¹⁶ In this study, IACT determined by trans-thoracic echocardiography correlated with symptomatic AF occurrence in patients with mitral stenosis, independent of any other clinical and echocardiographic parameters. Kinay et al. found that IACT was prolonged in patients with recurrent AF.⁶ But our study reveals that IACT has been prolonged before the episodes of symptomatic AF have been established.

There are conflicting results regarding whether enlarged atrial diameter predicts AF or occurs as a result of atrial remodeling due to AF. The present results support that atrial enlargement may be a structural substrate enabling symptomatic AF to occur. However large scale studies are needed to confirm this hypothesis.

Limitations

The design of our study does not include those patients without symptom due to AF, since we detected episodes of AF based on the symptoms. None of the patients who developed AF was detected coincidentally. This may cause underestimation of the patients with AF, and the patients with asymptomatic AF will be listed in group 2,

Figure 1: Interatrial conduction time is calculated as the time interval between the beginning of the surface p wave and the onset of LAA ejection flow. (LV: Left Ventricle, LA: Left Atrium, LAA: Left Atrial Appendage).



instead of group 1. This will reduce the power of the statistics. For these reasons, conclusions of our study can not be applied to asymptomatic AF patients with MS. Asymptomatic AF is a clinical challenge and causes underestimation of the incidence of AF in clinical studies. The incidence of asymptomatic patients has been reported to be 17%¹⁷ In the literature, absence of symptoms are especially evident in old patients. In contrary, the average age of the patients in our study is around 40 and represents a relatively young population. Fortunately, the patients with mitral stenosis are tent to be symptomatic when they develop AF, since rapid heart rate causes relatively more hemodynamic deterioration. On this assumption and according to the above data, we expect less asymptomatic patients with AF in this particular group on comparison to general AF population. Termination of the follow-up of the patients who underwent the surgery may interfere the results. Following surgery the incidence of AF due to pericardial irritation reaches 50% in some series with normal LA. Finally, due to the limited number of the subjects studied and short time of follow-up, effects of gender, age,

and surgery could not be assessed.

In conclusion, the present study showed that echocardiographic IACT measurement and the other four echocardiographic atrial parameters may predict the development of symptomatic AF in patients with mitral stenosis and sinus rhythm. These parameters may point out the group of patients prone to symptomatic AF and those who need close clinical follow-up. These parameters may be new targets for studies to address novel approaches to identify patients who require additional attention and modified treatment, such as early anti-coagulation and anti-arrhythmic medications. Large scale studies are necessary before making a certain comment on these issues.

Clinical implications

The patients with rheumatic mitral valve disease and sinus rhythm still has a substantial risk of systemic embolism and is, therefore, they are possible candidates for long-term warfarin therapy. There are no reliable clinical markers in such cases. Based on our study, prolonged IACT and enlarged atri-

Table 2 Comparison of echocardiographic parameters between groups.

	All patients (n=62)	Group 1 (n=7)	Group 2 (n=55)	P value
MVA PIn (cm ²)	1.50 ± 0.41	1.60 ± 0.32	1.49 ± 0.32	P=0.445
MVA PHT (cm ²)	1.52 ± 0.42	1.58 ± 0.35	1.52 ± 0.43	P=0.632
PGr (mmHg)	16.84 ± 8.89	16.59 ± 5.43	16.88 ± 8.19	P=0.601
MGr (mmHg)	8.62 ± 5.32	7.44 ± 3.28	8.78 ± 5.53	P=0.647
MR (degree)	1.24 ± 0.83	1.50 ± 0.76	1.21 ± 0.84	P=0.406
TTGr (mmHg)	33.55 ± 16.52	33.86 ± 18.19	33.51 ± 16.48	P=0.845
LA AP1(cm)	5.33 ± 0.49	5.36 ± 0.50	5.10 ± 0.41	P=0.039
LA area (cm ²)	27.54 ± 6.10	31.48 ± 5.91	27.04 ± 5.99	P=0.071
LASL (cm)	7.11 ± 0.96	7.26 ± 1.08	7.09 ± 0.95	P=0.556
LAML2 (cm)	4.81 ± 0.68	5.51 ± 0.50	4.72 ± 0.65	P=0.002
LA area2 (cm ²)	28.23 ± 5.83	31.51 ± 5.23	27.81 ± 5.82	P=0.116
RAML2 (cm)	3.74 ± 1.32	4.74 ± 1.04	3.61 ± 1.31	P=0.013
RASL (cm)	4.94 ± 1.24	4.95 ± 1.77	4.93 ± 1.18	P=0.711
RA area 2 (cm ²)	15.08 ± 4.48	17.75 ± 6.65	14.74 ± 4.09	P=0.218
LAAP3 (cm)	5.63 ± 1.46	6.01 ± 1.27	5.58 ± 1.48	P=0.273
LASl3 (cm)	5.87 ± 1.29	6.00 ± 1.84	5.85 ± 1.23	P=0.485
LA area3 (cm ²)	25.91±5.79	30.70±3.17	25.30±5.78	P=0.006
LAV (cm ³)	107.84 ± 45.73	131.36 ± 42.63	104.85 ± 45.61	P=0.101
RAV (cm ³)	36.12 ± 20.12	51.94 ± 22.33	34.10 ± 19.12	P=0.018

al diameter can be used to select a subgroup of patients who may actually benefit from anticoagulant therapy in patients with RMS and sinus rhythm.

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