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Clinical Investigations

Evaluation of Left Atrial Filling Using Systolic Pulmonary Venous Flow Velocity Measurements in Patients with Atrial Fibrillation

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Summary

Background: The pattern of pulmonary venous flow velocity is useful for understanding the hemodynamic relationship between the left atrium and left ventricle in patients with a variety of diseases, and the systolic flow wave, in particular, is considered a clinically important parameter that reflects left atrial filling.

Hypothesis: The study was undertaken to determine whether systolic pulmonary venous flow velocity patterns can be used to evaluate left atrial filling in patients with atrial fibrillation.

Methods: We performed transesophageal pulsed Doppler echocardiography and cardiac catheterization in 34 patients with chronic atrial fibrillation (10 with hypertrophic cardiomyopathy, 5 with dilated cardiomyopathy, 7 with previous myocardial infarction, and 12 with isolated atrial fibrillation) and 15 normal controls in sinus rhythm.

Results: Mean pulmonary capillary wedge pressure, V-wave height in the pulmonary capillary wedge pressure curve, and left ventricular end-diastolic pressure were significantly higher in the hypertrophic cardiomyopathy and dilated failing heart (previous myocardial infarction and dilated cardiomyopathy) groups than in the isolated atrial fibrillation and normal groups. The peak velocity and time-velocity integral of the systolic pulmonary venous flow velocity, and percent left atrial emptying fraction were significantly lower in the dilated failing heart group than in the isolated atrial fibrillation, hypertrophic cardiomyopathy, and normal groups. The peak velocity and time-velocity integral of the systolic pulmonary venous flow velocity, percent left atrial emptying fraction, and V-wave height were comparatively constant when the preceding R-R intervals were relatively stable in the isolated atrial fibrillation group and in 4 of the 10 patients with hypertrophic cardiomyopathy. However, changes in these variables correlated with the preceding R-R interval in all patients with dilated failing hearts and in 6 of the 10 patients with hypertrophic cardiomyopathy.

Conclusion: Transesophageal pulsed Doppler echocardiographic measurements of systolic pulmonary venous flow velocity are valid indicators of left atrial filling in patients with atrial fibrillation.

Key words: atrial fibrillation, preceding R-R interval, left atrial filling, pulmonary venous flow velocity

Introduction

The R-R interval is always irregular in patients with atrial fibrillation, thus atrial fibrillation is called an absolute arrhythmia. In patients with this arrhythmia, the left ventricular (LV) function curve can be determined according to the Frank-Starling mechanism since the blood volume flowing into the left ventricle (preload) varies with every cardiac cycle.[1,2] The recent advances in transesophageal pulsed Doppler echocardiography have allowed accurate recording of pulmonary venous flow velocity. This flow velocity pattern is useful for understanding the hemodynamic relationship between the left atrium and ventricle in patients with a variety of heart diseases. The systolic flow wave, in particular, is considered a clinically important parameter that reflects left atrial filling.[3–7] The purpose of this study was to evaluate the physiologic significance of left atrial reservoir function based on the relationship between systolic pulmonary venous flow velocity and R-R interval in patients with chronic atrial fibrillation.

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Methods

Patient Population

We evaluated 34 consecutive patients with chronic atrial fibrillation who visited our hospital between April 1994 and August 1996. All drugs for treating heart failure and arrhythmias, including digitalis, beta-adrenergic blocking agents, angiotensin-converting enzyme inhibitors, diuretics, and calcium antagonists were stopped at least five drug half-lives before the study. The group consisted of 10 patients with hypertrophic cardiomyopathy, 5 patients with dilated cardiomyopathy, and 7 patients with previous myocardial infarction. The remaining 12 patients had isolated atrial fibrillation without significant organic cardiovascular disease. None of the patients had structural mitral valve disease or moderate to severe functional mitral regurgitation.

A diagnosis of hypertrophic cardiomyopathy was made based on echocardiographic demonstration of hypertrophied LV in the absence of any other cardiac or systemic disease capable of producing LV hypertrophy. All patients had asymmetric septal hypertrophy, with a ratio of the interventricular septal to LV posterior wall thickness of $\geqq 1.5$. A diagnosis of previous myocardial infarction was confirmed by the following criteria: (1) A history of previous myocardial infarction, (2) normal values of creatine kinase, (3) abnormal Q waves on the electrocardiogram, and (4) recent coronary angiography. Based on these criteria, all patients had organic stenoses (>75% luminal diameter) of three major coronary arteries by coronary angiography, defined as ischemic cardiomyopathy. All five patients with dilated cardiomyopathy were found to have congestive heart failure in the absence of coronary artery, hypertensive or valvular heart disease, or other underlying causes. In all these patients, normal coronary anatomy was demonstrated angiographically. All patients with dilated cardiomyopathy and previous myocardial infarction were diagnosed with dilated LV and diffuse wall asynergy by two-dimensional echocardiography and left ventriculography. Furthermore, the following criteria were demonstrated by transthoracic M-mode echocardiography: (1) LV end-diastolic dimension $\geqq 6.0$ cm, and (2) percent fractional shortening of the LV $\leqq 25\%$.

The normal controls consisted of 15 patients in sinus rhythm who were being evaluated for complaints of palpitation, chest pain, or dyspnea, but showed no organic abnormalities as assessed by phonocardiography, echocardiography, and cardiac catheterization. Left ventriculography demonstrated mitral regurgitation of grade 2 or less in two patients with hypertrophic cardiomyopathy, three with dilated cardiomyopathy, and three with previous myocardial infarction. Informed consent for participation in the study was obtained from all subjects.

Study Design

Right and left heart catheterization was performed on the same day as echocardiographic examinations in all patients. Pulmonary capillary wedge and LV pressure curves were recorded simultaneously with the patient in the supine position, using 7F and 6F high-fidelity manometer-tipped catheters, respectively (Millar Instruments Inc., Houston, Texas). Mean pulmonary capillary wedge and LV end-diastolic pressures were measured at the phase of the R-R interval corresponding to the baseline heart rate after the pressure curves were recorded between 30 and 60 s in each subject, and the mean of measurements made during 10 consecutive R-R intervals was calculated. The relationship between the V-wave height of the pulmonary capillary wedge pressure curve and the preceding R-R interval was also examined. Left ventriculography was performed in the 30° right anterior oblique projection, and the grade of mitral regurgitation was determined by Sellers' classification.[8] Selective coronary angiograms were then obtained in multiple views.

Transthoracic and transesophageal echocardiography was performed in all subjects 3 h before cardiac catheterization, and no medical treatment was given during the study. LV end-diastolic dimension, percent fractional shortening of the LV, and end-diastolic thicknesses of the interventricular septum and the LV posterior wall were measured by transthoracic M-mode echocardiography. A horizontal section including the left atrium, interatrial septum, and right atrium, was set, and the maximum left atrial dimension (max LAD) at end-systole was measured by transesophageal M-mode echocardiography (Fig. 1A). The minimum left atrial dimension (min LAD) at end-diastole was also measured, and the percent left atrial emptying fraction [=(max LAD−min LAD)/max LAD]× 100 was calculated.

Pulmonary venous inflow to the left atrium was evaluated at the level of the horizontal section of the left atrium, including the left superior pulmonary vein, using color Doppler flow imaging, and a sample volume was set at the venous opening into the left atrium. The peak systolic velocity (PVS) and time-velocity integral (PVSI) were measured from the systolic wave of the pulmonary venous flow velocity (Fig. 1B). For the patients with atrial fibrillation in this study, the first systolic wave of the pulmonary venous flow velocity could not be recorded;[9] thus the second systolic wave was evaluated. Parameters were measured during a period of relatively stable R-R intervals, which corresponded to the baseline heart rate, after the flow velocity patterns were recorded between 30 and 60 s in each subject, and the mean of measurements made during 10 consecutive R-R intervals was calculated.

Transthoracic echocardiography was performed using a Toshiba SSH-160A (Toshiba Corp., Tokyo) with a 2.5 MHz probe, and transesophageal echocardiography was performed using an Aloka SSD 870 (Aloka Co., Ltd., Tokyo) with a 5 MHz probe.

Statistical Analysis

Differences in mean group values were analyzed by analysis of variance (ANOVA) and Scheffe's test. Linear regression coefficients were determined to analyze the correlations among variables. Values are expressed as the mean ± standard deviation (SD). A p value of < 0.05 was considered significant.

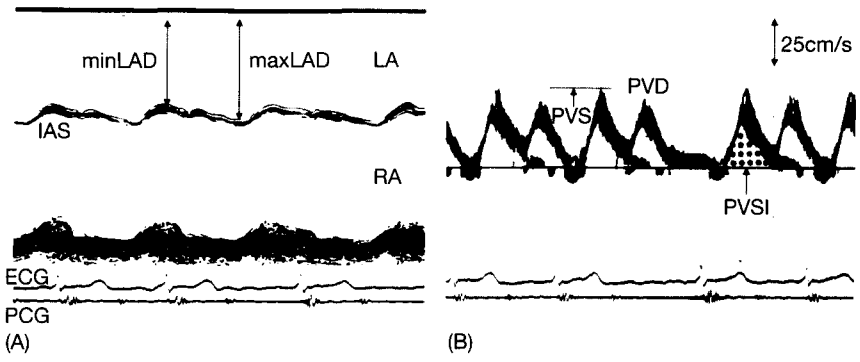

FIG. 1 M-mode and pulsed Doppler echocardiographic measurements of interatrial septal motion (A) and pulmonary venous flow velocity (B). min LAD = minimum left atrial dimension at end-diastole, max LAD = maximum left atrial dimension at end-systole, LA = left atrium, IAS = interatrial septum, RA = right atrium, PVS = peak systolic pulmonary venous flow velocity, PVSI = time-velocity integral of the systolic pulmonary venous flow velocity, PVD = early diastolic wave of the pulmonary venous flow velocity, PCG = phonocardiogram.

Results

There was no significant difference in age and heart rate between the normal controls and the four patient groups, although the mean age of the patients in the isolated atrial fibrillation group was significantly lower than that of the previous myocardial infarction group (Table I).

Hemodynamic Variables

The mean pulmonary capillary wedge pressure and V-wave height of the pulmonary capillary wedge pressure curve were significantly higher in the hypertrophic cardiomyopathy and dilated failing heart groups than in the isolated atrial fibrillation and normal groups, and were highest in patients with dilated cardiomyopathy (Table I). The LV end-diastolic pressure was also significantly higher in the hypertrophic cardiomyopathy and dilated failing heart groups than in the isolated atrial fibrillation and normal groups, but there was no significant difference in this value between the patients with previous myocardial infarction and dilated cardiomyopathy. There were no significant differences in mean pulmonary capillary wedge and LV end-diastolic pressures between the isolated atrial fibrillation and normal groups.

Transthoracic M-Mode Echocardiographic Variables

The LV end-diastolic dimension was significantly larger, and the percent fractional shortening of the left ventricle was significantly lower in the dilated failing heart group than in the hypertrophic cardiomyopathy, isolated atrial fibrillation, and normal groups (Table II). However, there was no significant difference in either of these parameters between the two patient groups with dilated failing hearts, and among the hypertrophic cardiomyopathy, isolated atrial fibrillation, and normal groups.

Transesophageal M-Mode and Pulsed Doppler Echocardiographic Variables

The maximum left atrial dimension was significantly larger in the hypertrophic cardiomyopathy and dilated failing heart

TABLE I Clinical and hemodynamic parameters

Group	No. of patients	Age (years)	Heart rate (beats/min)	mPCWP (mmHg)	V (mmHg)	LVEDP (mmHg)
Controls	15	46 ± 10	76 ± 13	8 ± 2.4	10 ± 1.2	9.7 ± 4.5
Atrial fibrillation						
Isolated	12	40 ± 12	78 ± 18	10 ± 2.8	13 ± 2.3[b]	11 ± 6.2
HCM	10	48 ± 11	69 ± 15	15 ± 5.3[b,d]	16 ± 6.7[a,d]	19 ± 7.3[b,d]
MI	7	56 ± 14[d]	74 ± 10	16 ± 3.6[c,e]	18 ± 3.5[c,e]	18 ± 2.4[b,d]
DCM	5	50 ± 17	75 ± 11	20 ± 5.1[c,f]	22 ± 7.4[c,e]	22 ± 4.6[c,d]

[a]$p<0.01$, [b]$p<0.001$, [c]$p<0.0001$ vs. controls.
[d]$p<0.01$, [e]$p<0.001$, [f]$p<0.0001$ vs. isolated atrial fibrillation.
Abbreviations: mPCWP = mean pulmonary capillary wedge pressure, V = V-wave height in the pulmonary capillary wedge preseeure curve, LVEDP = left ventricular end-diastolic pressure, HCM = hypertrophic cardiomyopahty, MI = previous myocardial infarction, DCM = dilated cardiomyopathy.

TABLE II M-mode and pulsed Doppler echocardiographic parameters

Group	LVDd (cm)	%FS (%)	max LAD (cm)	%LAEF (%)	PVS (cm/s)	PVSI (cm)
Controls	4.6±0.5	36±4	3.2±0.3	26.6±3.4	63±15	8.5±0.8
Atrial fibrillation						
Isolated	4.7±0.9	35±6	3.7±0.8[g]	12.3±4.2[c,i]	55±10	8.2±1.3
HCM	4.4±0.7	33±5	4.4±0.5[c,d]	5.6±1.7[c,f]	50±12	7.6±2.0
MI	6.5±0.9[c,f,i]	21±4[c,f,i]	4.2±0.6[c]	3.8±1.2[c,f,g]	33±11[a,e,g]	4.6±1.5[c,f,g]
DCM	6.8±0.8[c,f,i]	20±7[c,e,h]	4.3±1.0[b]	3.0±1.6[c,f,g]	28±17[b,g]	3.4±1.1[c,f,g]

[a]p<0.01, [b]p<0.001, [c]p<0.0001 vs. controls.
[d]p<0.01, [e]p<0.001, [f]p<0.0001 vs. isolated atrial fibrillation.
[g]p<0.01, [h]p<0.001, [i]p<0.0001 vs. HCM.
Abbreviations: LVDd = left ventricular end-diastolic dimension, %FS = percent fractional shortening of the left ventricle, max LAD = maximum left atrial dimension at end-systole, %LAEF = percent left atrial emptying fraction, PVS = peak systolic pulmonary venous flow velocity, PVSI = time-velocity integral of the systolic pulmonary venous flow velocity, HCM = hypertrophic cardiomyopathy, MI = previous myocardial infarction, DCM = dilated cardiomyopathy.

groups than in the normal group (Table II). The percent left atrial emptying fraction was significantly lower in the dilated failing heart group than in the normal, isolated atrial fibrillation, and hypertrophic cardiomyopathy groups, and it was slightly lower in patients with dilated cardiomyopathy than in patients with previous myocardial infarction. The peak velocity and time-velocity integral of the systolic pulmonary venous flow velocity were significantly lower in the dilated failing heart group than in the normal, isolated atrial fibrillation, and hypertrophic cardiomyopathy groups, but there were no significant differences between the two patient groups with dilated failing hearts, and among the hypertrophic cardiomyopathy, isolated atrial fibrillation, and normal groups.

Relationships between the Preceding R-R Interval and the Hemodynamic and Echocardiographic Variables

The peak velocity and time-velocity integral of the systolic pulmonary venous flow velocity, percent left atrial emptying fraction, and V-wave height in the isolated atrial fibrillation group remained fairly constant when the preceding R-R intervals were relatively stable. In 4 of the 10 patients in the hypertrophic cardiomyopathy group, as well as all the patients in the isolated atrial fibrillation group, the above variables were not significantly affected by the preceding R-R interval. However, in the remaining six patients with hypertrophic cardiomyopathy, the peak velocity and time-velocity integral of the systolic pulmonary venous flow velocity, and the percent left atrial emptying fraction correlated positively with the preceding R-R interval, and the V-wave height correlated negatively with the preceding R-R interval. In all 12 patients with dilated failing hearts, the peak velocity and time-velocity integral of the systolic pulmonary venous flow velocity, and percent left atrial emptying fraction correlated positively with the preceding R-R interval, and the V-wave height correlated negatively with the preceding R-R interval. In three of the patients with dilated cardiomyopathy, the slopes of the regression lines between these variables and the preceding R-R interval were less steep than in the remaining nine patients with dilated hearts.

Figures 2, 3, and 4 indicate the relationships between the preceding R-R interval and the peak systolic pulmonary venous flow velocity, percent left atrial emptying fraction, and V-wave height, respectively, in the five representative patients with atrial fibrillation.

Discussion

Preload, afterload, and myocardial contractility vary with every cardiac cycle in patients with atrial fibrillation since the R-R interval is not constant.[10] Therefore, the beat-to-beat LV

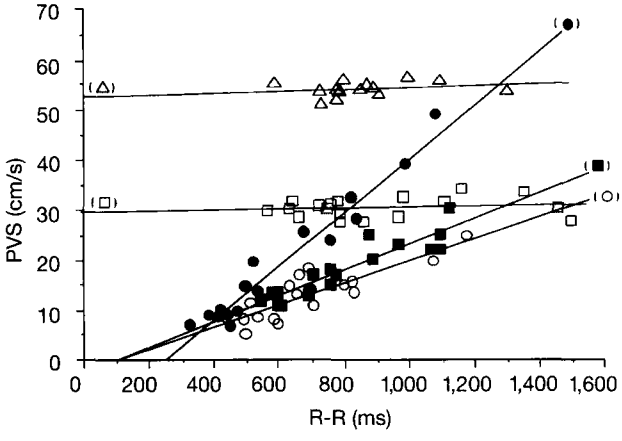

FIG. 2 Correlation between the peak systolic pulmonary venous flow velocity (PVS) and the preceding R-R interval in five patients with atrial fibrillation. ■ (r = 0.92, p < 0.0001), □ = hypertrophic cardiomyopathy; ○ (r = 0.85, p < 0.0001) = dilated cardiomyopathy; ● (r = 0.96, p < 0.0001) = previous myocardial infarction; △ = isolated atrial fibrillation.

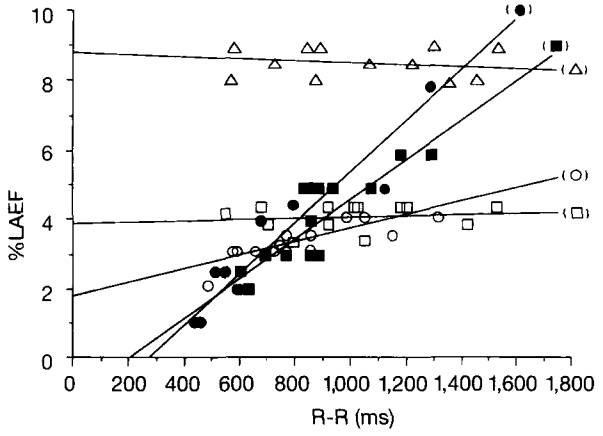

FIG. 3 Correlation between the percent left atrial emptying fraction (% LAEF) and the preceding R-R interval in five patients with atrial fibrillation. ■ ($r = 0.85$, $p < 0.0001$), □ = hypertrophic cardiomyopathy; ○ ($r = 0.75$, $p < 0.001$) = dilated cardiomyopathy; ● ($r = 0.96$, $p < 0.0001$) = previous myocardial infarction; △ = isolated atrial fibrillation.

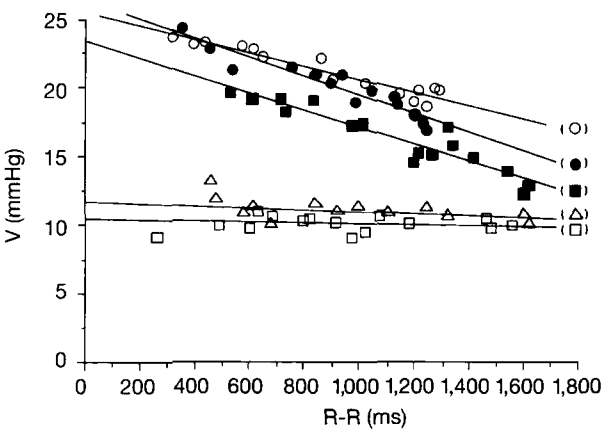

FIG. 4 Correlation between the V-wave height (V) in the pulmonary capillary wedge pressure curve and the preceding R-R interval in five patients with atrial fibrillation. ■ ($r = -0.94$, $p < 0.0001$), □ = hypertrophic cardiomyopathy; ○ ($r = -0.96$, $p < 0.0001$) = dilated cardiomyopathy; ● ($r = -0.95$, $p < 0.0001$) = previous myocardial infarction; △ = isolated atrial fibrillation.

function curve is determined by the Frank-Starling mechanism in these patients. It is clinically useful to be able to evaluate the severity of underlying heart disease using changes in the slopes of the LV filling and function curves following medical or surgical treatment.[1, 2] Generally, the mortality of patients with underlying heart disease and atrial fibrillation is higher than in those with isolated atrial fibrillation.[11, 12]

The recent advances in transesophageal echocardiography have allowed accurate recording of pulmonary venous flow velocity. Using parameters obtained from these flow velocity patterns as well as from LV function, information on reservoir, conduit, and systolic functions of the left atrium can be obtained. The second systolic pulmonary venous flow velocity reflects left atrial filling, and a number of studies have demonstrated its relationship with left atrial pressure,[4, 5] mitral regurgitation,[6, 7] and LV systolic function.[3, 5]

Left atrial systolic function in patients with stiff and failing hearts is very important for LV filling during ventricular diastole.[13] If atrial fibrillation occurs in these patients, the loss of an effective atrial contribution may result in a decrease in LV filling, which can markedly affect LV function.[14] Generally, cardiac output is not significantly affected even when atrial pump function is lost in patients with isolated atrial fibrillation because the reservoir and conduit functions of the left atrium are maintained.[15] Our results suggest that LV filling is essentially complete during early diastole even when left atrial contraction is lost in patients with isolated atrial fibrillation at rest, and that a sufficient volume of blood is present in the left atrium to be used for optimal LV filling. Thus, cardiac output may be maintained within a normal range in such patients.

With regard to left atrial filling in patients with hypertrophic cardiomyopathy, Sanada *et al.*[16] have shown that left atrial stiffness, as measured by the left atrial volume–pressure curve, is increased in patients with LV hypertrophy, and the degree of left atrial stiffness correlates negatively with the left atrial reservoir volume and cardiac output. It has also been shown that a stiff left atrium decreases pulmonary venous return, resulting in a decrease in cardiac output.[17] Therefore, loss of atrial contraction due to atrial fibrillation will significantly affect LV function under conditions where the left atrial reservoir function is decreased,[18] as in six patients with hypertrophic cardiomyopathy in this study. Thus, the cardiac output was probably maintained by the Frank-Starling mechanism in the left atrium, in which the relatively high pulmonary capillary wedge pressure acted to increase atrial preload.[19]

In 9 of the 12 patients with dilated failing hearts, in whom these parameters varied with changes in the preceding R-R interval, it may be possible that this atrial Frank-Starling mechanism was also recruited, as in the above six patients with hypertrophic cardiomyopathy. A recent study has demonstrated histopathologically that areas of left atrial fibrosis are significantly larger in patients with dilated cardiomyopathy than in those with previous myocardial infarction.[20] In some patients with dilated cardiomyopathy, therefore, left atrial systolic dysfunction may not be fully explained by left atrial mechanical overload alone, and may also be due to the presence of left atrial myopathy.[21, 22] In such patients, the Frank-Starling mechanism can no longer be utilized effectively, and this may contribute to a poorer prognosis in these patients.

Study Limitations

We did not obtain simultaneous measurements of intracardiac pressure and M-mode and pulsed Doppler echocardiography; therefore, we could not evaluate directly the relationship between the pressure and echocardiographic variables. However, transthoracic and transesophageal echocardiography was performed within 3 h before cardiac catheterization, and no medical treatment was given during the study. Furthermore, we used a high-fidelity manometer-tipped pulmonary

capillary wedge catheter to approximate left atrial pressure. Although some researchers involved in hemodynamic studies do not accept pulmonary capillary wedge pressure tracings because of their multiple assumptions, many studies have demonstrated that pulmonary capillary wedge pressure is a clinically acceptable and useful estimate of left atrial pressure.[23–25]

Conclusions

Transesophageal pulsed Doppler echocardiographic measurements of systolic pulmonary venous flow velocity are valid indicators of left atrial filling in patients with atrial fibrillation.

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