CLINICAL STUDIES METHODS

Estimating Mean Pulmonary Wedge Pressure in Patients With Chronic Atrial Fibrillation From Transthoracic Doppler Indexes of Mitral and Pulmonary Venous Flow Velocity

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Objectives. **We sought to obtain a noninvasive estimation of mean pulmonary wedge pressure (MPWP) in patients with chronic atrial fibrillation (AF).**

Background. **It has previously been demonstrated that MPWP can be reliably estimated from Doppler indexes of mitral and pulmonary venous flow (PVF) in patients with sinus rhythm. Doppler estimation of MPWP has not been validated in patients with AF.**

Methods. **MPWP was correlated with variables of mitral and pulmonary venous flow velocity as assessed by Doppler transthoracic echocardiography in 35 consecutive patients. The derived algorithm was prospectively tested in 23 additional patients.**

Results. **In all patients the mitral flow pattern showed only a diastolic forward component. A significant but relatively weak correlation (r = −0.50) was observed between MPWP and mitral deceleration time. In 12 (34%) of 35 patients, the pulmonary vein flow tracing demonstrated only a diastolic forward component; a diastolic and late systolic forward flow was noted in the remaining 23 patients (66%). A strong negative correlation was observed between MPWP and the normalized duration of the diastolic flow (r = −0.80) and its initial deceleration slope time (r = −0.91). Deceleration time >220 ms predicted MPWP ≤12 mm Hg with 100% sensitivity and 100% specificity. When estimating MPWP by using the equation MPWP = −94.261 PVF deceleration time − 9.831 Interval QRS to onset of diastolic PVF − 16.337 Duration of PVF + 44.261, the measured and predicted MPWP closely agreed with a mean difference of −0.85 mm Hg. The 95% confidence limits were 4.8 and −6.1 mm Hg.**

Conclusions. **In patients with chronic AF, MPWP can be estimated from transthoracic Doppler study of PVF velocity signals.**

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Analysis of mitral and pulmonary venous flow (PVF) by both transesophageal and transthoracic pulsed Doppler echocardiography has provided new insights into the evaluation of left ventricular diastolic properties (1–6). It has been demonstrated (7–14) that mean pulmonary wedge pressure (MPWP) can be reliably estimated from variables of mitral flow and PVF in a spectrum of heart disease. Atrial fibrillation (AF), with its loss of mechanical atrial activity and irregular heart rhythm, is the most common sustained cardiac arrhythmia (15–17). Doppler estimation of MPWP has received little study in the presence of AF, in part because several variables are not available for analysis and also because venous and mitral flow velocities vary continually (7–14). Given the high incidence of AF among patients with left ventricular systolic or diastolic dysfunction, or both, it would be desirable to know whether filling pressures can be estimated by using standard transthoracic Doppler mitral and pulmonary venous variables. We therefore designed this study to determine whether MPWP can be estimated from transthoracic pulsed Doppler analysis of mitral flow and PVF in patients with chronic AF.

Methods

Patients. The initial study group comprised 38 consecutive patients (aged 49 to 80 years) admitted to our institutions between September 1995 and January 1996. All patients >45 years old with chronic (i.e., >3 months, known by previous electrocardiograms [ECG]) AF without echocardiographic evidence of mitral stenosis who underwent right or combined right and left heart catheterization were included. No patients were receiving mechanical ventilation at the time of cardiac catheterization or echocardiography. Echocardiographic and invasive pressure evaluations were recorded simultaneously in the 25 patients studied in the intensive care unit for whom

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Abbreviations and Acronyms

AF	= atrial fibrillation
ECG	= electrocardiogram, electrocardiographic
MPWP	= mean pulmonary wedge pressure
PVF	= pulmonary venous flow

invasive right heart and arterial pressure monitoring was considered necessary. In the 13 patients undergoing elective cardiac catheterization, the echocardiographic evaluation was performed just before the invasive procedure (mean interval ± SD between procedures 28 ± 12 min [range 10 to 33]). We excluded three patients: two whose Doppler recordings were inadequate and one from whom pulmonary wedge pressure tracings could not be obtained. Therefore, 35 patients were included in the study group. The equation derived to estimate MPWP was assessed prospectively in a test group of 23 consecutive patients (age range 50 to 76 years) with heart failure due mostly to either ischemic or nonischemic dilated cardiomyopathy. The criteria for enrollment were the same as those for the study patients; in the test group, Doppler and pressure data were obtained simultaneously. The study protocol was approved by the Ethical Committee of Treviso Regional Hospital and Legnago Civic Hospital. All patients gave written informed consent to both procedures.

Cardiac catheterization. Right-sided pressures were obtained with a 7F balloon-tipped pulmonary artery catheter (Swan-Ganz, Baxter Healthcare) introduced through a jugular or femoral percutaneous approach. The catheter was connected to a strain gauge pressure transducer and referenced to the midaxillary line to obtain MPWP and right atrial and pulmonary artery pressures. Pulmonary wedge position was verified by chest fluoroscopy, by noting a ≥5-mm Hg decrease in mean pulmonary artery pressure and changes in pressure phasic waveform. Uncertain positions were verified by measuring oxygen saturation. MPWP was obtained at end-tidal apnea. In patients undergoing simultaneous invasive and echocardiographic evaluation, the echocardiographer had no access to pressure values. In patients undergoing elective cardiac catheterization, the mean heart rate and systolic and diastolic blood pressures measured during invasive and echocardiographic evaluation were compared. Thermodilution cardiac output was performed in triplicate, and the results were averaged. Arterial pressure was measured by using a radial cannula or a 7F pigtail catheter placed in the descending thoracic aorta.

Echocardiography. All patients were examined in the left lateral position by precordial M-mode, two-dimensional and Doppler echocardiography. Hewlett-Packard Sonos 1500 and 2500 ultrasound units with a 2.5-MHz transducer were used. Images were stored on a Panasonic videotape recorder (model AG-7330E) for later playback and analysis. Mitral flow velocities were recorded by using an apical four-chamber view, placing a 0.5- to 1.0-cm pulsed wave Doppler sample volume between the tips of the mitral leaflets, where maximal flow velocity was recorded. PVF velocities were obtained from an apical four-chamber view by placing a 0.5- to 1.5-cm sample volume 0.5 to 1 cm into the upper right pulmonary vein. Color Doppler imaging was used to obtain a beam direction as parallel as possible to PVF. No angle correction was used. Filters were set to the minimum and gain settings were adjusted carefully at each depth to obtain optimal spectral display. From each patient five cardiac cycles obtained during end-tidal volume apnea with the most satisfactory signal/noise ratio were selected for analysis and averaged. Cardiac cycles with fusion of two consecutive diastolic waves, as a consequence of a short RR interval, were excluded from analysis. The PVF curves were selected from cardiac cycles considered representative of the average heart rate of each patient with the shortest and longest cycles discarded. Mean RR interval was calculated by obtaining a continuous 2-min ECG record. Left atrial diameter (18), left ventricular ejection fraction (19) and mitral regurgitation (20) were assessed by using previously described methods.

Mitral flow and PVF signals were digitized off-line with the aid of a computer and custom-made software. The mitral flow and PVF variables evaluated are shown in Figure 1. These included 1) duration of the diastolic anterograde flow; 2) time from the onset of the QRS wave of the ECG to the onset of anterograde diastolic flow; 3) time from the onset of the QRS wave of the ECG to peak diastolic flow; and 4) velocity-time integral of diastolic flow. All these variables were normalized by the squared RR interval. We also evaluated the peak velocity and the deceleration time of diastolic flow, calculated as the time between peak diastolic velocity and the upper deceleration slope extrapolated to the zero baseline. Therefore, in the presence of a bimodal deceleration slope, only the initial and steeper deceleration slope was considered to obtain the deceleration time (Fig. 1). Finally, the presence of a late systolic forward flow on the PVF tracing was evaluated.

Statistical analysis. Results are expressed as mean value ± SD. Statistical analysis between groups was performed by analysis of variance for independent samples with the Scheffé F test. Doppler variables were correlated with MPWP by using a multiple stepwise regression analysis that allowed detection of the effect of age, gender, mean RR interval, systolic and diastolic blood pressure, cardiac output, central venous pressure, left ventricular ejection fraction, left atrial diameter and presence and severity of mitral regurgitation. Mean heart rate was correlated with MPWP to evaluate whether PVF time intervals and PVF duration of flow were independent predictors of MPWP. Values for heart rate and systolic and diastolic blood pressure during nonsimultaneous echocardiographic and invasive evaluations were compared with the Student *t* test for paired data. The degree of correlation between MPWP and mitral flow and PVF Doppler variables was evaluated by linear regression analysis. Stepwise multilinear regression was performed for MPWP to determine the relative importance of each PVF variable for MPWP and to generate multivariate equations to predict the individual MPWP (21). To evaluate

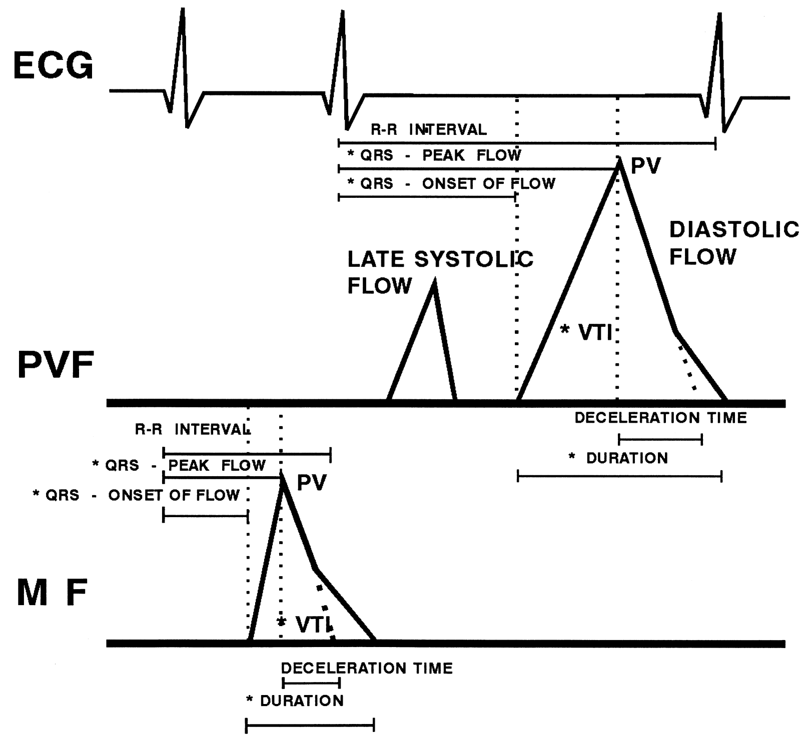

Figure 1. Measurements of mitral flow (MF) and PVF velocities in the presence of AF. Deceleration time of the diastolic component was calculated as the time between peak diastolic velocity and the upper deceleration slope extrapolated to the zero baseline. **Asterisk** indicates variables that have been normalized by the squared RR interval. PV = peak velocity; VTI = velocity-time integral.

the agreement between PVF variables and MPWP, data were processed by the Bland-Altman method (22). The 95% limits of agreement were expressed in absolute value. To test intraobserver and interobserver variability, two independent observers measured mitral flow and PVF variables on videotape recordings containing selected beats (identified by using the frame counter) from 20 randomly selected patients. The same beats were analyzed by one of the two observers 1 month later. Interobserver and intraobserver variability were calculated as the coefficient of variation. A probability level <0.05 was considered significant. Sensitivity and specificity were calculated with standard formulas.

Results

There were no significant differences between the study and the test patients with regard to clinical characteristics and hemodynamic data (Table 1). In patients undergoing elective cardiac catheterization, mean heart rate and systolic and diastolic arterial blood pressure values did not differ significantly when measured during echocardiography or cardiac catheterization.

Mitral flow and PVF patterns. The mitral flow pattern was characterized by the presence of only a diastolic forward component in all patients. No late diastolic waves were noted on Doppler mitral velocity tracings in any patient. Systolic high velocity flow was noted in all 35 patients because of the presence of various degrees of mitral regurgitation.

The PVF was biphasic in 23 (66%) of the 35 patients, with a predominant diastolic forward wave and smaller late systolic forward wave (Fig. 1). In 12 patients (34%), only a diastolic component was present. No reverse flow velocity in the pulmonary vein was seen in any patient. The presence of a biphasic PVF pattern did not correlate with patient age, presence and degree of mitral regurgitation, left ventricular ejection fraction, pulmonary wedge pressure or left atrial diameter.

Table 1. Clinical, Hemodynamic and Echocardiographic Characteristics of the Study and Test Groups

	Study Group (n = 35)	Test Group (n = 23)
Age (yr)*	66 ± 7	69 ± 5
Gender (M/F)*	21/14	14/9
Mean RR interval(s)*	0.720 ± 0.110	0.680 ± 0.150
Cardiac output (liters/min)*	4.1 ± 1.6	3.8 ± 1.5
Pressures (mm Hg)*		
Mean right atrial	5.6 ± 1.9	8.0 ± 5.0
Pulmonary artery systolic	38 ± 5	42 ± 6
Pulmonary artery diastolic	20 ± 8	22 ± 6
Mean pulmonary wedge	19 ± 3	21 ± 5
Left ventricular ejection fraction*	0.41 ± 0.13	0.38 ± 0.12
Left atrial diameter (mm)*	54 ± 6	52 ± 13
Dilated cardiomyopathy	12	10
Coronary artery disease	9	9
Hypertensive heart disease	10	4
Severe aortic stenosis	3	—
Severe aortic regurgitation	1	—
Moderate mitral regurgitation	21	14
Mild mitral regurgitation	13	9

*p = NS comparing the study and test groups. Data are presented as mean value ± SD or number of patients. F = female; M = male.

Table 2. Correlation of Doppler Variables of Pulmonary Venous and Mitral Flow With Mean Pulmonary Wedge Pressure

Doppler Variables	r	SEE	F Ratio
Pulmonary venous flow			
Normalized diastolic velocity-time integral	−0.26	4.30	2.50
Normalized duration of diastolic flow	−0.80	0.06	59.6
Normalized interval QRS to onset of flow	−0.22	0.08	1.78
Normalized interval QRS to peak velocity	−0.23	0.08	1.75
Deceleration time	−0.91	0.02	167.2
Deceleration time × normalized duration of diastolic flow	−0.86	0.0023	86.3
Peak velocity of diastolic flow	0.26	19.35	2.50
Mitral flow			
Normalized diastolic velocity-time integral	0.31	2.98	3.58
Normalized duration of diastolic flow	0.01	0.03	0.004
Normalized interval QRS to onset of flow	−0.29	0.63	3.16
Normalized interval QRS to peak velocity	−0.31	0.04	3.62
Deceleration time	−0.50	26.47	11.10
Peak velocity of diastolic flow	0.10	11.81	0.33

Correlation of mitral flow and PVF variables with MPWP. Regression analysis performed on mitral flow and PVF data derived from all patients did not show any significant correlation between peak velocity, normalized velocity-time integral of diastolic flow, variables related to the timing of the forward diastolic flow with reference to the QRS complex, and MPWP (Table 2). Among mitral variables only deceleration time showed a significant, but relatively weak (r = −0.50), negative correlation with MPWP. A much stronger negative correlation (r = −0.80) was observed between MPWP and the normalized duration of the forward diastolic PVF. No correlation was observed between mean heart rate and MPWP in the study group. Among the Doppler-derived indexes the deceleration time of the diastolic PVF showed the strongest (r = −0.91) correlation with MPWP (Fig. 2 and 3). PVF deceleration time >220 ms predicted MPWP ≤12 mm Hg with 100% sensitivity and 100% specificity. The relation between deceleration time and MPWP did not depend on the level of left ventricular systolic function. In patients with depressed ejection fraction (<45%), the relation between PVF deceleration time and MPWP was slightly higher (r = −0.94) than in patients with preserved left ventricular systolic function (r = −0.87), but this difference did not reach statistical significance.

Estimation of MPWP in the test group. The equation derived from multiple linear regression analysis in the training group (Table 3) (i.e., MPWP = −94.261 Deceleration time − 9.831 Interval QRS to onset of diastolic PVF − 16.337 Duration of PVF + 44.261) was prospectively applied to estimate MPWP in the test group. The mean difference between predicted and measured pressures was −0.85 mm Hg, and the 95% confidence limits were 4.8 and −6.1 mm Hg (Fig. 4). The sensitivity and specificity for MPWP ≤12 mm Hg were 99% and 83%, respectively; accuracy was 93%.

Intraobserver and interobserver variability. Coefficients of intraobserver and interobserver variability were not statistically significant for any of the mitral flow and PVF variables measured.

Discussion

Previous studies based on analysis of mitral flow and PVF patterns as assessed from pulsed Doppler echocardiography (7,10–14) have suggested several noninvasive methods for estimating left ventricular filling pressures. In these studies AF has generally been considered an exclusion. The significant prevalence of chronic AF among patients with left ventricular dysfunction currently excludes a significant group of patients with heart disease.

Pattern of PVF velocities in the presence of sinus rhythm and AF. PVF velocities are believed to reflect phasic changes in left atrial pressure and the events of left atrial filling (23–27).

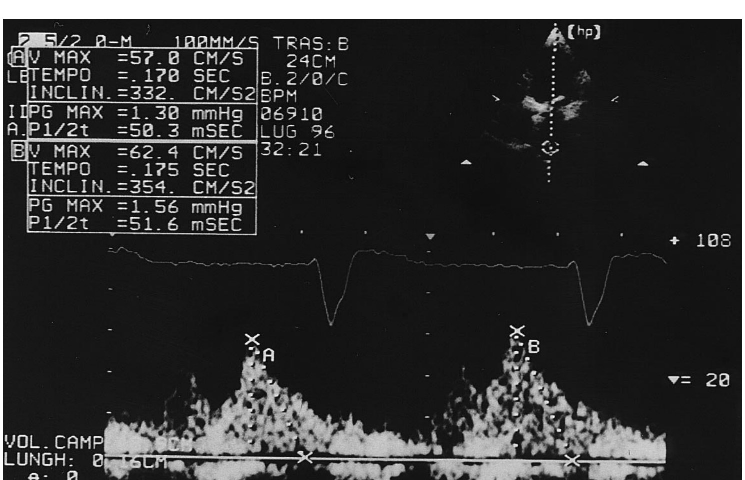

Figure 2. Transthoracic pulsed wave Doppler recording in a patient with chronic AF and dilated cardiomyopathy (MPWP was 24 mm Hg). The deceleration time of the diastolic flow (see the value indicated as "tempo") (calculated as the time interval between peak diastolic velocity and the upper deceleration slope extrapolated to the zero baseline) showed little variation (170 to 175 ms) over two consecutive beats (A and B).

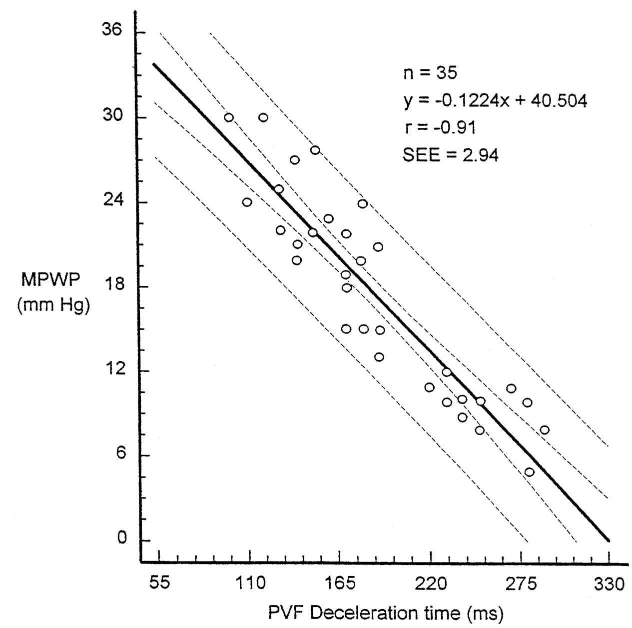

Figure 3. Scatterplot and correlation between deceleration time of the diastolic PVF and MPWP. There are 33 points because of overlapping of values in two pairs of patients who had identical Doppler and pressure values. Confidence limits appear on the plot as the **pair of dotted lines closest to the regression line**. Prediction limits appear as the **pair of dotted lines farthest from the regression line**.

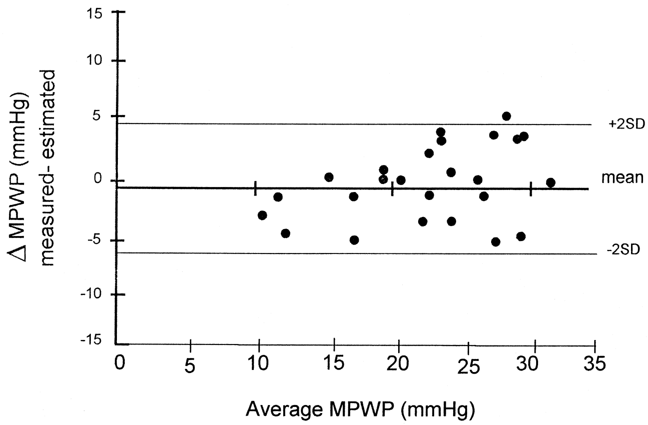

Figure 4. Bland-Altman plot of differences (delta) between measured and estimated MPWP versus their mean values in the test group.

In normal subjects PVF is triphasic or quadriphasic, with one or two forward components during systole, a forward component during diastole and a reverse flow velocity component that occurs as a result of atrial contraction (23,24,27). There is a loss of the early systolic forward component and the reverse flow at atrial contraction due to AF. In agreement with the study of Ren et al. (28), we also found this loss. However, Ren et al. (28) found a late systolic anterograde component in all patients with AF, whereas we found it in 23 of 35 patients. This systolic flow velocity is generally a low velocity signal. Technical difficulties in recording this signal by transthoracic pulsed wave Doppler study in patients in the intensive care unit and catheterization laboratory may be the most likely explanation for the discrepancy between our results and those of Ren et al. (28), who used transesophageal echocardiography.

Correlation of PVF velocity variables with MPWP. By analyzing the correlation between MPWP and Doppler variables in patients with chronic AF we found a strong significant negative correlation between MPWP and the duration of PVF. This variable is strictly dependent on the length of the cardiac cycle; therefore, it should be used as a predictor of MPWP only

Table 3. Multiple Linear Regression Analysis Relating Pulmonary Venous Flow Velocity Variables to Mean Pulmonary Wedge Pressure

	Cumulative r Value
Deceleration time	0.91
Deceleration time + PV	0.91
Deceleration time + PV + Interval QRS to onset of flow	0.92
Deceleration time + PV + Interval QRS to onset of flow + Duration of flow	0.93
Deceleration time + PV + Interval QRS to onset of flow + Duration of flow + VTI	0.93
Deceleration time + PV + Interval QRS to onset of flow + Duration of flow + VTI + N. VTI	0.93
Deceleration time + PV + Interval QRS to onset of flow + Duration of flow + VTI + N. VTI + N. duration of flow	0.94
Deceleration time + PV + Interval QRS to onset of flow + Duration of flow + VTI + N. VTI + N. duration of flow + N. interval QRS to onset of flow	0.94
MPWP = −85.437 Deceleration time + 0.007 PV − 51.016 Interval QRS to onset of flow + 78.000 Duration of flow − 0.796 VTI + 0.694 N. VTI − 84.239 N. duration of flow + 31.583 N. interval QRS to onset of flow + 44.871	
Deceleration time + Duration of flow	0.93
Deceleration time + Duration of flow + Interval QRS to onset of flow	0.93
MPWP = −94.261 Deceleration time − 9.831 Interval QRS to onset of flow − 16.337 Duration of flow + 44.261.	

MPWP = mean pulmonary wedge pressure; N. = normalized by the squared RR interval; PV = peak velocity; VTI = velocity-time integral.

after normalization by the RR interval. The lack of correlation between MPWP and heart rate shows that the normalized duration of diastolic PVF can be considered an independent predictor of MPWP. This correlation may reflect the more rapid equalization of left atrial and left ventricular pressures, which occurs earlier in diastole in the presence of increased left ventricular filling pressure.

Deceleration time of diastolic PVF was the best predictor of MPWP, irrespective of heart rate. It is very important to outline that the deceleration slope of PVF is often bimodal, with two different slopes (Fig. 1 and 2). The first starts at peak velocity and is generally steeper than the second, which reaches the zero line. The first component may be mainly dependent on the initial driving pressure of the PVF and the specific compliance of the receiving chamber (29). The second component is probably affected by the duration of left ventricular relaxation, left ventricular compliance and heart rate. In our patients, the first component extrapolated to the zero line was rather constant, whereas the second slopes varied largely with variation in RR interval. Thus, only the initial deceleration slope correlates with MPWP. The influence of left ventricular systolic function on the correlation between Doppler-derived deceleration time and left ventricular filling pressure is controversial. Some investigators (1,2,11) excluded this influence, whereas Nagueh et al. (30) found that in patients with AF mitral deceleration time correlated with MPWP only in the presence of depressed (<45%) ejection fraction. In an experimental model (29), the mitral deceleration time was found to be strictly dependent on left ventricular chamber stiffness. The correlation found by Nagueh et al. (30) between mitral deceleration time and left ventricular ejection fraction may depend on the fact that their patients with normal ejection fraction had a wide variety of heart diseases or had no cardiac abnormalities at all. Although these investigators did not report data on left ventricular volumes, it is conceivable that the range was very wide; such a range might have resulted in scattered values for left ventricular chamber stiffness and mitral deceleration time in patients with preserved left ventricular systolic function and different levels of MPWP.

Correlation of mitral flow velocity variables with MPWP. Among the variables of mitral flow, only deceleration time showed a correlation ($r = -0.50$) with MPWP, although at a lower level than the corresponding PVF. In a recent study (31) performed in patients with sinus rhythm, a much stronger negative correlation ($r = -0.90$) was found between deceleration time of early diastolic mitral flow and MPWP. Considering the poor correlation values reported by Nagueh et al. (30) ($r = -0.42$) and by Pozzoli et al. (32) ($r = -0.50$) in patients with AF, it appears that the correlation between MPWP and the deceleration time of mitral flow is significantly lower in the presence of AF.

The discrepancy between the strong correlation of PVF deceleration time and the poor correlation of mitral deceleration time with MPWP could be the result of several factors. 1) When considering the relation between mitral flow velocity pattern and left ventricular filling pressures, it is generally assumed (29) that in early diastole the left atrium and the left ventricle act as a common conduit. This theoretic analysis depends on the simplifying assumption that left atrial stiffness is very low (33,34). Low atrial stiffness can occur in patients with a normal left atrium, but it is very unlikely in the presence of chronic AF. In an experimental model, White et al. (35) found that AF alters atrial hemodynamics and metabolism, determining a significant increase in left atrial pressure and stiffness. As MPWP reflects the mean left atrial pressure it is not surprising that MPWP correlates better with PVF deceleration time than with mitral deceleration time. 2) The presence and continual variation in the degree of mitral regurgitation after changes in the RR interval may determine continual changes in early diastolic deceleration of mitral flow. Pozzoli et al. (36) recently found that in patients with sinus rhythm the correlation between mitral deceleration time and MPWP was significantly stronger in patients without mitral regurgitation. 3) Because deceleration time appears to be such a useful variable, the position of the sample volume is crucial. It has been emphasized (27,37) that different sites of mitral flow sampling (too medial, too far into the left ventricle or at the annulus) influence the flow velocity curve and may result in different values for deceleration time, peak velocity and duration. However, because the proximal portion of the pulmonary veins resembles a straight conduit, the sample volume can be moved only proximally and distally to the mouth of the vein, and this factor may result in variation in peak velocity, but not in deceleration time (38).

Limitations of the study. We did not evaluate patients with new onset AF. Such patients may have a heart rate faster, more RR variation and more atrial activity than patients with chronic AF. In such patients it would be more difficult to reproducibly separate the first from the second component of the deceleration slope of the diastolic PVF, and the correlation between this variable and MPWP might be weaker. Therefore, our findings may not be applicable to patients with recent AF. Other key limitations of our study are the small size of the patient group and the fact that pressure measurements and Doppler analysis were not simultaneous in all patients. The success rate in sampling PVF velocities in the present study is higher than that reported by some other groups (14,26,38). This difference may reflect the experience of our laboratories where PVF velocities have been routinely assessed for many years in all patients undergoing transthoracic Doppler study. We did not evaluate the changes in mitral flow and PVF patterns after changes in MPWP. However, volume expansion and reduction were not possible in the present study because they would have prolonged the examination time and would have increased risks, which could not be tolerated for ethical reasons in patients with severe congestive heart failure or patients undergoing elective cardiac catheterization.

Effects of age. As previously demonstrated by different investigators (39,40), mitral flow and PVF variables change with age in normal subjects. This variation is mainly dependent on the physiologic impairment of left ventricular relaxation observed in elderly subjects (41). In our study the mean age was not significantly different between patients with normal and increased MPWP and did not influence the correlation between Doppler variables and MPWP. Although younger patients (<45 years old) were excluded from the study to avoid a large age bias, and 65.7% of patients were ≥65 years old, the age range was quite large. It is conceivable that age distribution may modify the cutoff value for normal and elevated MPWP without reducing the strength of correlation between MPWP and PVF variables. However, it should be considered that the incidence of AF in patients <45 years old is low (17). Further studies are needed to establish the cutoff value for normal MPWP in groups of different ages.

Conclusions. In conclusion, PVF velocity variables obtained by routine transthoracic Doppler echocardiography technique appear to be a promising method for estimating MPWP in patients with chronic AF. Given the significant incidence of this arrhythmia among patients with signs and symptoms of left ventricular dysfunction and the inability of current noninvasive techniques to estimate left ventricular filling pressures in this situation, our study results may significantly expand the use of the Doppler technique to assess left ventricular diastolic performance. Further studies in larger patient groups appear warranted to validate our results and to investigate the same variables in other patient groups with AF.

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