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Reassessment of Valve Area Determinations in Mitral Stenosis by the Pressure Half-Time Method: Impact of Left Ventricular Stiffness and Peak Diastolic Pressure Difference

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Estimation of the orifice area is of major importance in the timing of valve dilation or surgery in patients with mitral stenosis. Determination of the area has traditionally been accomplished at cardiac catheterization by the Gorlin equation. The valve area can also be estimated noninvasively with Doppler echocardiographic measurements of the pressure half-time, which is inversely proportional to the area. This method has gained widespread acceptance, but its accuracy has recently been questioned and factors other than reduction of orifice area appear to modify the pressure half-time. In the present study, the influence of left ventricular stiffness (defined as diastolic pressure rise per milliliter of mitral flow) and peak atrioventricular pressure difference on the pressure half-time was examined both in a hydraulic model and by review of data from 35 patients with mitral stenosis. Left ventricular stiffness <0.13 mm Hg/ml was considered normal.

In the model study, the orifice area correlated only moderately with inverted pressure half-time (1/PHT) ($r = 0.67$). By multiple linear regression, inverted pressure half-time was shown to be dependent on valve area, chamber stiffness and peak pressure difference ($R = 0.89$), area and stiffness being most important ($R = 0.85$). In the clinical study, an increased ventricular stiffness was found in 22 of the 35 patients. The pressure half-time method overestimated the Gorlin-derived area by an average of 72% in these patients compared with only 10% in 13 patients with normal stiffness ($p < 0.001$). The overestimation was >100% in seven patients with coronary heart disease or aortic valve disease (or both), of whom all had a stiffness >0.2 mm Hg/ml.

In conclusion, the pressure half-time is shortened and the valve area thus overestimated if left ventricular stiffness is increased, which is often the case in patients with mitral stenosis associated with coronary heart disease or aortic valve disease.

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The clinical manifestations of mitral stenosis do not invariably reflect the severity of left ventricular inflow obstruction, and optimal timing of valvular surgery is dependent on accurate quantification of the mitral orifice area (1). The valve area can be calculated from data obtained at cardiac catheterization (2,3), which is generally accepted as a reference method. Quantification of the valve area can also be accomplished by noninvasive methods (4,5) suitable for initial evaluation and serial follow-up. Hatle and coworkers (6,7) described a noninvasive approach to estimate the mitral valve area that has gained widespread acceptance. Doppler echocardiographic measurements of the transmitral flow velocity are used to calculate the time required for the pressure difference across the valve to decrease to one half of its initial value (the pressure half-time), which varies inversely with the valve area (6–9). The Doppler-derived and invasive area determinations may, however, differ substantially (10–13). Using computer simulation, Thomas et al. (12) suggested that the pressure half-time is dependent not only on the valve area but also on the square root of the early peak diastolic pressure difference across the valve as well as the combined left ventricular and left atrial compliance.

The present study was undertaken to examine the influence of left ventricular stiffness and the initial peak transvalvular pressure difference on valve area determination by

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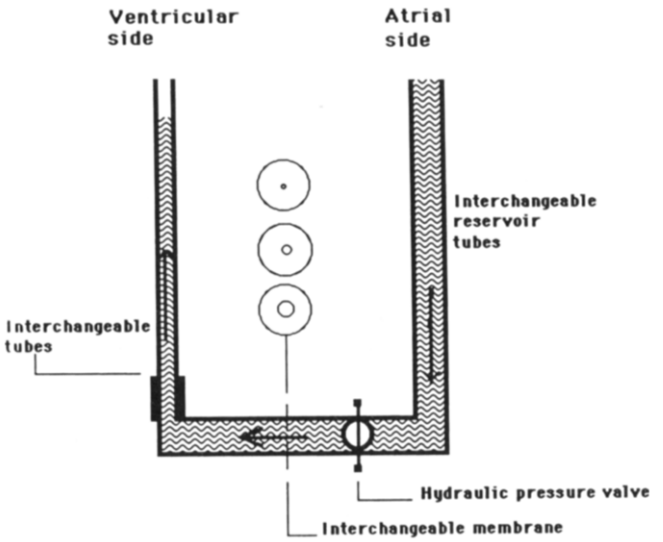


Figure 1. Schematic diagram of the hydraulic model.

the pressure half-time method, both in a hydraulic model and in patients with mitral stenosis.

Methods

Model Study

A hydraulic model consisting of two standpipes connected through a tube was constructed (Fig. 1). Interchangeable membranes with circular holes with areas ranging from 0.2 to 3.0 cm^2 could be inserted in the tube to simulate different severity of valvular stenosis. Different peak pressure differences were obtained by variation of the initial height of the pressure-generating fluid column in the proximal "atrial" standpipe. Variation of chamber stiffness was achieved by the use of outlet standpipes of different cross-sectional areas. Simultaneous pressure registrations on both sides of the interchangeable membrane were recorded on paper at 100 mm/s for documentation and analyses. The peak pressure difference was varied from 12 to 30 mm Hg and the chamber stiffness (pressure increase/volume inflow) from 0 to 0.77 mm Hg/ml, values chosen to correspond to those likely to be encountered in clinical cases.

Clinical Study

Study patients. Invasive and noninvasive data from 59 patients referred for evaluation of suspected mitral stenosis between 1981 and 1987 were reexamined. Twenty-four patients with significant combined mitral and aortic regurgitation were excluded because invasive determinations of the transmitral flow were considered insecure. Of the remaining 35 patients, 11 were men and 24 women, and their ages ranged from 42 to 78 (mean 62) years.

Cardiac catheterization and angiography. All measurements were made in the rest state. Pressures were recorded with use of fluid-filled catheters connected to mechano-electrical transducers interfaced with a multichannel UV recorder, and a hydrostatic standard was used for calibration. The left ventricular and pulmonary capillary wedge pressures were recorded simultaneously, and the area between the curves during the diastolic filling period was measured by planimetry. The mean diastolic pressure difference was obtained as the mean of at least five beats. Left ventriculography was performed in biplane 45° right and 45° left anterior oblique projections, and left ventricular end-diastolic and end-systolic volumes were calculated with a biplane method (14). Left ventricular stroke volume was obtained both by the Fick method and as the difference between the ventriculographic end-diastolic and end-systolic volumes. The severity of coexistent mitral regurgitation was graded according to Dexter and Grossman (15): mild (1+), moderate (2+), moderately severe (3+) and severe (4+). Aortography was performed in the 45° left and 45° right anterior oblique projections, and the severity of aortic regurgitation was also graded as described by Dexter and Grossman (15). The mitral valve area (MVA) was calculated with use of a modified Gorlin equation (3):

$$MVA = SV/(37.9 \times DFT \times \sqrt{\Delta P_{mean}}),$$

where SV = the stroke volume, DFT = diastolic filling time and ΔP_{mean} = mean diastolic transvalvular pressure difference. The Fick stroke volume was used to determine the flow across the mitral valve in patients without or with only mild (1+) mitral regurgitation, whereas the angiographic stroke volume was used in patients with ≥2+ mitral regurgitation (16). The diastolic increase in left ventricular pressure per unit of mitral volume inflow was used as an estimate of left ventricular stiffness (17). A value of 0.13 mm Hg/ml, the mean value + 3 SD in the series of Diamond and Forrester (17), was considered as the upper normal limit. Coronary angiography was performed with the Judkins method, and multiple projections of the coronary vessels were obtained. Obstruction of a major coronary artery resulting in a diameter reduction >50% was considered as a significant stenosis.

Noninvasive examinations. Echocardiographic examinations were performed with an ATL Mark 300 C (Advanced Technology Laboratories), CV 100 (Diasonics) or CFM 700 (Vingmed A/S) ultrasound system for verification of the diagnosis. Views of the heart were obtained from the apical, parasternal and subcostal transducer positions (18). Two-dimensional echocardiographic measurements of the mitral valve area were not routinely performed. Continuous wave Doppler examinations were performed with a nonimaging Pedof Doppler system with use of a 2.0 MHz transducer (Vingmed A/S) or with the CFM 700 ultrasound system using

a nonimaging 2.0 MHz transducer or a multimode 3.0 MHz transducer. The patients were examined in the left lateral supine position, and the transmitral flow was recorded from the apical view. Recognition of maximal blood flow velocities was aided by the direct audio output, and the highest audible frequency and a regular smooth velocity profile indicated an optimal transducer position. No angle correction was used. The pressure half-time (PHT) was obtained by dividing the peak velocity by $\sqrt{2}$ and measuring the time, in milliseconds, from the peak velocity to the point where this decrease was found (6,7). If there was a short early diastolic high velocity peak, this was omitted (6,7). A minimum of five representative beats were analyzed and the results averaged. The mitral valve area (MVA) was calculated (7): MVA = 220/PHT, where 220 = an empirically derived constant.

Statistical analysis. Correlation and simple and multiple linear regression were used to analyze data. Student's *t* test for unpaired variables was used to examine differences between subgroups.

Results

Model Study

By multiple linear regression, the inverted pressure half-time (1/PHT) was directly correlated with the membrane hole area and the chamber stiffness and inversely correlated with the peak pressure difference (R = 0.89). If only the area and chamber stiffness was used in the regression model, R = 0.85 was obtained, whereas using the area and peak pressure difference resulted in R = 0.72. The area alone correlated only moderately with 1/PHT (r = 0.67). The interrelation between 1/PHT on one hand and hole area, chamber stiffness and peak pressure difference on the other, are shown in Figures 2 and 3.

Clinical Study

Patient characteristics. Individual data of the 35 patients with mitral stenosis are presented in Table 1. The mitral valve area ranged between 0.28 and 1.71 cm^2 by the Gorlin formula, and between 0.57 and 2.14 cm^2 by the pressure half-time method. Mitral regurgitation was present in 22 patients and aortic regurgitation in 14. Aortic stenosis was found in nine patients, of whom three had an aortic valve area of <1 cm^2. Significant coronary artery lesions were present in nine patients. The diastolic flow across the mitral valve ranged between 40 and 225 ml/s, left ventricular stiffness ranged between 0.068 and 0.483 mm Hg/ml and peak diastolic transmitral pressure difference varied from 6 to 34 mm Hg.

Pressure half-time area versus Gorlin-derived area. For all 35 patients, there was only a moderate degree of correlation between Gorlin and pressure half-time valve area determinations (r = 0.51, SEE = ±0.34 cm^2, $p < 0.005$) (Fig. 4). The Gorlin area was systematically overestimated by the pressure half-time method, the mean difference (±SD) being 47 ± 46%. The largest difference observed was 172%. In patients with pure mitral stenosis (n = 13) the correlation between the two methods was somewhat closer (r = 0.67, SEE = ±0.38 cm^2, $p < 0.05$) (Fig. 4).

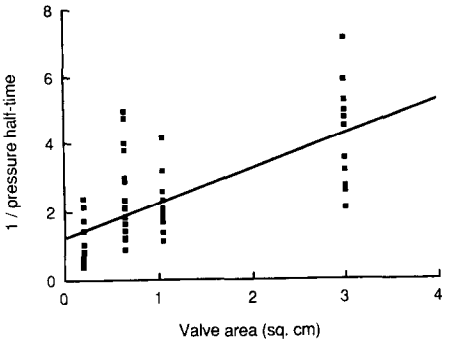


Figure 2. The inverted pressure half-time plotted against the membrane hole area in the hydraulic model. The variation of 1/pressure half-time for each area is caused by changes in peak pressure difference or changes in simulated chamber stiffness. Thus, a decrease in peak pressure difference or an increase in chamber stiffness (or both) increases 1/pressure half-time at any given hole area (regression line is shown, r = 0.67).

Ventricular stiffness and peak diastolic pressure difference. By multiple linear regression, the mitral valve area determined by the pressure half-time method was directly related to the Gorlin area and left ventricular stiffness (R = 0.74). Inclusion of the peak diastolic pressure difference in the multiple regression model influenced the correlation only modestly (R = 0.79). The patients were classified into two groups, one with normal ventricular stiffness (<0.13 mm Hg/ml) and one with increased stiffness. The mean percent

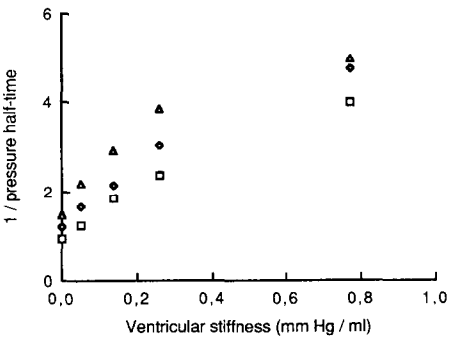


Figure 3. The inverted pressure half-time plotted against simulated chamber stiffness in the hydraulic model. A membrane hole area of 0.64 cm^2 is used for all readings. Inverted pressure half-time increases as chamber stiffness increases; the variation at each stiffness value is caused by variation of the peak pressure difference. **Triangles** correspond to a low, **diamonds** to an intermediate and **rectangles** to a high pressure difference.

Table 1. Clinical and Hemodynamic Data in 35 Patients With Mitral Stenosis

Patient No.	Concomitant			CHD	ΔP/ΔV (mm Hg/ml)	MVA (Cath) (cm^2)	MVA (PHT) (cm^2)
	MR	AR	AS				
1	1+	1+	0	+	0.164	0.52	0.80
2	1+	0	+	0	0.333	0.69	1.49
3	0	0	0	0	0.118	0.61	0.69
4	0	0	0	+	0.350	0.61	1.10
5	1+	0	0	0	0.186	0.96	1.29
6	1+	0	0	0	0.077	1.32	1.65
7	1+	1+	+	0	0.254	0.82	1.56
8	1+	0	0	0	0.119	1.71	1.48
9	1+	0	+	0	0.149	1.11	1.33
10	1+	1+	0	0	0.127	0.97	0.99
11	1+	0	0	0	0.127	1.30	1.31
12	0	0	0	0	0.222	1.00	1.47
13	0	0	0	0	0.216	0.74	1.00
14	1+	1+	0	0	0.068	1.24	1.22
15	2+	0	0	+	0.108	1.01	1.03
16	1+	0	0	0	0.127	0.64	1.03
17	0	1+	0	0	0.088	1.67	1.85
18	0	2+	+	0	0.111	0.96	1.16
19	2+	0	0	0	0.114	0.96	1.07
20	1+	0	0	0	0.160	1.10	1.21
21	0	3+	0	+	0.261	1.26	2.53
22	1+	1+	+	+	0.483	0.58	1.58
23	1+	0	0	+	0.194	0.67	1.20
24	1+	1+	+	0	0.323	0.28	0.57
25	0	0	0	0	0.078	0.94	0.80
26	0	0	0	0	0.222	0.87	1.05
27	1+	2+	0	0	0.150	0.82	1.20
28	0	0	0	+	0.205	0.58	1.25
29	3+	0	+	0	0.129	0.95	1.38
30	1+	1+	0	+	0.226	1.01	2.14
31	1+	1+	+	0	0.300	0.57	1.01
32	2+	0	0	+	0.235	0.77	1.75
33	0	2+	+	0	0.143	1.35	1.35
34	0	0	0	0	0.278	0.60	1.13
35	0	1+	0	0	0.236	1.09	1.57

AR = aortic regurgitation; AS = aortic stenosis; CHD = coronary heart disease; MR = mitral regurgitation; MVA (Cath) = mitral valve area at cardiac catheterization; MVA (PHT) = mitral valve area by the pressure half-time method; ΔP/ΔV = left ventricular stiffness (that is, left ventricular diastolic pressure rise/ml mitral inflow). See text for details.

overestimation of the valve area was 10% in 13 patients with normal and 72% in 22 patients with increased stiffness, the difference between the groups being highly significant ($p < 0.001$). The deviation of valve area estimated by the pressure half-time method and the Gorlin area correlated strongly with left ventricular stiffness ($r = 0.83$, SEE = ±26%, $p < 0.001$ [$n = 35$]) (Fig. 5).

Discussion

Model study. The pressure half-time was found to be dependent not only on the membrane hole area but also on chamber stiffness and peak pressure difference in the experimental study. After area, chamber stiffness was the most important factor. Because of variations in chamber stiffness or peak pressure difference, the pressure half-time could be longer with an area of 3.0 cm^2, which is nearly normal, than with an area of 0.2 cm^2, corresponding to a very tight stenosis, (Fig. 2).

Limitations of reference methods in the clinical study. Although the validity of catheter data has largely been accepted, errors in the magnitude of 20 to 40% may be obtained by the Gorlin formula (19,20). To obtain accurate area determinations with the Gorlin formula, the actual transmitral flow must be determined. The Fick method undervalues the flow across the valve when mitral stenosis is associated with regurgitation. There was angiographic evidence of substantial (≥2+) mitral regurgitation in four pa-

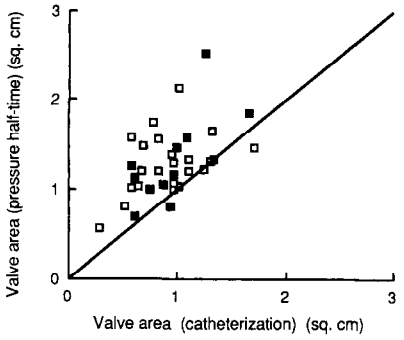
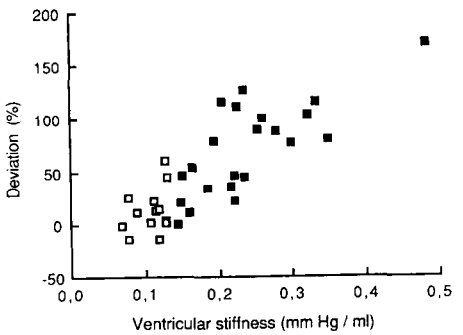


Figure 4. Mitral valve area estimated noninvasively by the pressure half-time method plotted against the valve area determined by the Gorlin formula at cardiac catheterization in 35 patients ($r = 0.51$, SEE = ± 0.34 cm^2, $p < 0.005$; $Y = 0.75 \times 0.54$, $n = 35$). **Solid squares** indicate patients with pure mitral stenosis (line of identity is shown).

tients, in whom angiographic stroke volume was used (16). However, there may be beat to beat variations in angiographic stroke volume in patients with atrial fibrillation. No routine invasive method provides accurate determination of the transmitral flow when mitral regurgitation is associated with aortic regurgitation. The differences observed between area determinations obtained by the pressure half-time method and the Gorlin formula were considerable, and it seems unlikely that they can be explained by errors in the invasive method.

The method used to determine left ventricular stiffness in this study is an approximation, and it is appropriate only if the total diastolic inflow to the left ventricle and the increase in diastolic pressure can be accurately measured. However, our data show that estimated stiffness, measured as ventricular diastolic pressure increase per milliliter of *mitral* inflow, affects the pressure half-time irrespective of whether it is caused by an actual increase in ventricular stiffness or by additional diastolic inflow due to aortic regurgitation. A regurgitant flow would accelerate the increase in ventricular pressure and thus equalization of the atrioventricular pressure difference.

Figure 5. The relative overestimation of the Gorlin area by the pressure half-time method (deviation) plotted against estimated left ventricular stiffness. **Solid squares** indicate patients with a stiffness >0.13 mm Hg/ml mitral inflow.



Significance of ventricular stiffness in coronary heart disease and aortic stenosis. An increased left ventricular stiffness in patients with coronary heart disease has been reported (17), and eight of our nine patients with coronary artery lesions had an estimated stiffness >0.13 mm Hg/ml. Increased left ventricular stiffness has also been reported in patients with aortic stenosis (21) and was also found in seven of our nine patients with aortic stenosis. The Doppler pressure half-time method overestimated the Gorlin area by >100% in 7 (20%) of the 35 patients. They had either coronary heart disease or aortic stenosis (or both) and all had a ventricular stiffness >0.20 mm Hg/ml.

Our results are at variance with some reports demonstrating an excellent correlation between invasive and noninvasive mitral valve area determinations (6,7,9). This variance may to some extent be explained by differences in patient groups examined. The mean age of our patients was high and the prevalence of associated valve disease or coronary heart disease was high, whereas only occasional patients with coronary heart disease have been reported previously (22). Considerable differences between determinations by the pressure half-time method and the Gorlin method have also been observed in patients with moderate or severe aortic regurgitation (22).

Atrial compliance. The present model and patient study both show that left ventricular stiffness has a major impact on the pressure half-time. The temporal differences of left atrial filling during the cardiac cycle reported by Keren et al. (23) in different patient groups may render determination of left atrial compliance unreliable, and the contribution of left atrial compliance to differences in the valve area determinations by the pressure half-time method and the Gorlin method was not assessed in the present study.

Clinical implications. Our results indicate that the pressure half-time method should not be uncritically used to estimate mitral valve area and that it should be abandoned in patients in whom increased left ventricular stiffness is suspected, as might be the case in patients with concomitant coronary heart disease or aortic valve disease.

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