MEASUREMENT

Limitations of Doppler ultrasound in the assessment of the function of prosthetic mitral valves

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Abstract
Pressure half time has been assumed to be a relatively flow-independent measure of orifice area, but it may also be influenced by atrial and ventricular factors. Pressure half time and peak left ventricular inflow velocity were measured by continuous wave Doppler ultrasound in 164 patients with normally functioning Carpentier-Edwards, Björk-Shiley, and Starr-Edwards mitral prostheses. Pressure half time was shorter in the Björk-Shiley than in the other valve types and peak transmitral velocity was highest in the Starr-Edwards prostheses. These differences, however, were partly explained by coexistent differences in transmitral flow. Filling time accounted for 19% and stroke volume for 15% of the variance in pressure half time compared with only 5.6% for prosthetic design and 0.4% for annulus diameter when each of these variables was considered alone. The design of the prosthesis explained 18% of the variance in peak transmitral velocity, while cardiac output and annulus diameter did not contribute significantly. With Doppler ultrasound it is impossible to define reliable normal ranges for prosthetic function independently of atrial

and ventricular function. Formulas for orifice area based on peak transmitral velocity and flow seem more likely to reflect the behaviour of normally functioning prostheses than those based on pressure half time.

There are numerous published reports of mean values for pressure half time and peak transmitral velocity (or derived gradient and orifice area) in normally functioning mitral prostheses¹⁻¹¹ (table 1). The implicit assumption has been that dysfunction can be detected as a departure from these values, but this has not been established and important, unexplained inconsistencies remain.

Pressure half time is assumed to be a reliable indicator of orifice area but it rarely correlates inversely with annulus diameter and may be surprisingly similar in prostheses of widely different design.^{5 6 10} Furthermore, the mean pressure half time for one valve type can be highly variable^{1 3 7} and is far longer for a tricuspid prosthesis than for a mitral prosthesis of the same diameter.¹ Evidence is growing that factors other than the behaviour of the prosthesis may affect pressure half time; these include the shape and time course of left ventricular filling, stroke volume, and the transmitral pressure difference at the start of diastole.¹²⁻¹⁵ Except for

Table 1 Published values for pressure half time and effective orifice area (mean (SD))

Study	Porcine bioprosthesis	Björk-Shiley	Starr-Edwards
Effective orifice area (Hatle formula):			
Williams and Labowitz ¹⁰	2.1 (0.7) ^{H,C} (n = 16)	2.5 (0.8) (n = 36)	2.0 (0.3) (n = 10)
Panidis <i>et al</i> ⁵	2.2 (0.7) ^{H,C} (n = 6)	2.2 (0.7) (n = 8)	2.1 (0.5) (n = 3)
Sagar <i>et al</i> ⁹	1.3-1.9 ^H (n = 23)	2.1-2.2 (n = 17)	
Fawzy <i>et al</i> ⁴	1.5 (0.3) ^C (n = 14)		
Alam <i>et al</i> ⁸	2.0 (0.5) ^C (n = 105)		
Cooper <i>et al</i> ¹¹	2.6 (0.7) ^C (n = 25)		
Pressure half time:			
Ryan <i>et al</i> ³	136 (18) ^C (n = 29)		
Hatle and Angelsen ⁷	135 (25) ^C (n = 13)		
Gibbs <i>et al</i> ¹²	90 (23) ^C (n = 38)	77 (18) (n = 31)	127 (24) (n = 5)
Present study	105 (35) ^C (n = 78)	90 (30) (n = 56)	115 (45) (n = 30)

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early work by Holen *et al*,¹⁶ no study of prosthetic function by Doppler ultrasound has reported flow information.

The aim of this study was to compare the contribution of valve type or annulus diameter and blood flow to pressure half time and peak transmitral velocity in three different types of mitral prosthesis—a porcine bioprosthesis (Carpentier-Edwards) and tilting disc (Björk-Shiley) and caged ball (Starr-Edwards) mechanical prostheses.

Patients and methods

PATIENTS

A total of 182 consecutive patients with Carpentier-Edwards, Björk-Shiley, or Starr-Edwards prostheses were referred either for routine assessment or because dysfunction was suspected. Fourteen prostheses were excluded: 10 because of appreciable aortic or mitral regurgitation on continuous wave Doppler and colour flow mapping (area of jet (by planimetry) more than 20% of receiving chamber area)¹⁷ and four because cusp thickness exceeded 3 mm.¹⁸ No patient had reduced occluder motion. Four further patients were excluded because recordings were of poor quality. Abnormal left ventricular function was not a criterion for exclusion. Thirty five patients were in sinus rhythm, three were in paced rhythm, and the rest were in atrial fibrillation.

DOPPLER STUDIES

A phased array system was used (Hewlett Packard 77020A) with 1.9 MHz continuous wave and 2.5 MHz duplex probes. A full examination was performed in all views with sector imaging and colour flow Doppler to look for abnormalities of cusp or occluder motion and for significant aortic or mitral regurgitation. M mode recordings were taken at standard levels. A continuous wave probe was then placed at the apex, aimed towards the mitral valve, and its position adjusted until optimal signal quality was obtained. Left ventricular inflow recordings were made on to thermal paper run at 100 mm/s.

STATISTICAL ANALYSIS

All diastolic measurements were made on the

same three cycles in each patient. Most waveforms had a non-linear deceleration phase. Pressure half time¹⁹ was therefore calculated first by constructing a vertical line passing through the point of maximum velocity. A second line was then drawn parallel to the baseline at $0.7 \times$ peak velocity. Pressure half time was taken as the distance along the second line from the first vertical line to the outline of the waveform (figure). The diastolic time interval was measured from the start of the mitral opening artefact to the midpoint of the closing artefact. On long cardiac cycles where ventricular filling ended before the end of diastole, the filling period was taken to end where transmitral velocity had fallen to less than 0.2 m/s for more than 200 ms. The filling period was shorter than the diastolic time interval in 34 (7%) of 492 cardiac cycles in a total of 19 patients. In all other instances the two periods were of identical length. The RR interval was measured from the end of the preceding diastolic period (figure). Mean values for pressure half time, peak transmitral velocity, diastolic time interval, filling period, and RR interval were calculated.

Stroke volume was calculated from M mode left ventricular recordings by the corrected cube formula described by Teicholz *et al*,²⁰ which is not applicable in the presence of left ventricular dyskinesia. The formula could not, therefore, be applied in four cases. Cardiac output was calculated by the equation:

$$CO = (SV \times \text{rate})/10^3 \quad (1)$$

when CO is cardiac output (l/min), SV is mean stroke volume (ml), and rate is heart rate derived from the mean cycle length over three cycles. Transmitral flow was calculated on each cardiac cycle from the formula:

$$Q = 10^3 \times SVm/DFP \quad (2)$$

when Q is flow (ml/s), SVm is mean stroke volume (ml), and DFP is diastolic filling period (ms).

We used the SPSS^x program on the University of London computer for statistical analysis. It was first performed using the three individual values for pressure half time and peak transmitral velocity, but this gave results similar to those with the mean values for each patient. This may have been because there was little beat to beat variation in RR interval ($F = 0.97$; $p = 0.38$ by one way analysis of variance). Mean values were therefore used for further analysis. The factors controlling pressure half time and peak transmitral velocity were then assessed by multiple regressions by entering variables from among the following: diastolic time interval, diastolic filling period, transmitral flow, valve type, annulus diameter, cardiac output, presence of aortic regurgitation. The results for diastolic time interval were skewed and required log transformation before being analysed. Dummy variables were constructed for prosthetic type and annulus diameter. A p value of 0.01 was taken as significant for the multivariate analysis.

Left ventricular inflow recorded by continuous wave Doppler. DTI, diastolic time interval; $T_{1/2}$, pressure half time; $V_{\max}$, peak left ventricular inflow velocity.

Table 2 Results for all annulus diameters combined (mean (SD))

Variable	Carpentier-Edwards (n = 78)	Björk-Shiley (n = 56)	Starr-Edwards (n = 30)	F value	p value*
T½ (ms)	105 (35)	90 (30)	115 (45)	4.0	<0.05
V max (m/s)	1.5 (0.3)	1.5 (0.4)	1.8 (0.3)	19.1	<0.0001
RR (ms)	760 (150)	760 (175)	790 (145)	0.9	
DTI (ms)	365 (130)	395 (140)	440 (120)	2.4	
Fill (ms)	365 (130)	355 (80)	415 (115)	5.5	<0.01
Age of valve (mnth)	35 (38)	51 (43)	107 (90)	—	
Age at surgery (yr)	59 (13)	56 (8)	49 (10)	—	
	n = 77	n = 53	n = 30		
SV (ml)	60 (25)	55 (20)	68 (20)	2.2	
CO (l/min)	4.8 (1.8)	4.6 (1.7)	4.9 (1.9)	2.6	
Flow (ml/s)	170 (60)	165 (55)	165 (80)	2.1	

T½, pressure half time; RR, RR interval; V max, peak left ventricular inflow velocity; DTI, diastolic time interval; Fill, diastolic filling period; SV, stroke volume; CO, cardiac output.
*By one way analysis of variance.

Table 3 Results for Carpentier-Edwards prostheses by diameter (mean (SD))

Variable	27 mm (n = 2)	29 mm (n = 30)	31 mm (n = 27)	33 mm (n = 19)	F values	p value*
T½ (ms)	90 (10)	115 (35)	105 (40)	95 (30)	1.2	
V max (m/s)	1.7 (0.7)	1.5 (0.3)	1.5 (0.3)	1.4 (0.2)	0.8	
RR (ms)	645 (135)	830 (155)	755 (150)	680 (100)	4.9	<0.001
DTI (ms)	270 (85)	435 (130)	365 (115)	335 (70)	4.1	<0.001
Fill (ms)	270 (85)	405 (105)	355 (100)	330 (70)	4.2	<0.001
	n = 2	n = 30	n = 27	n = 18		
SV (ml)	45 (15)	60 (20)	60 (30)	60 (20)	0.2	
CO (l/min)	4.3 (2.3)	4.3 (1.6)	4.9 (2.1)	5.4 (1.5)	2.2	
Flow (ml/s)	180 (110)	145 (50)	180 (70)	185 (45)	2.9	<0.05

See footnote to table 2 for abbreviations.
*By one way analysis of variance.

Results

MEAN PRESSURE HALF TIME AND PEAK TRANSMITRAL VELOCITY

These are shown for each valve type (table 2) and by annulus diameter within each valve type (tables 3–5). Pressure half time was shorter in the Björk-Shiley prosthesis than in either of the other valve types ($p < 0.05$) and peak transmitral velocity was highest in the Starr-Edwards prostheses ($p < 0.0001$). The relative contribution of prosthesis related and other factors was, however, unclear from this preliminary analysis because there were coexistent differences in cardiac output and filling period between different valve types and annulus diameters. Further multivariate analysis was therefore performed to try to dissociate these factors.

MULTIVARIATE ANALYSIS OF PRESSURE HALF TIME Filling time and stroke volume were the variables that best explained the variance in mean pressure half time (table 6). Valve design also contributed, but annulus diameter, transmitral flow, or the presence of mild aortic regurgita-

tion did not. All the contributory variables together explained 32% of the variance in pressure half time.

Even when each valve type was considered separately, annulus diameter did not explain a significant proportion of the variance in pressure half time (Carpentier-Edwards 4.9%, $F_{3,72} = 1.2$; Björk-Shiley 4.5%, $F_{3,51} = 0.8$; Starr-Edwards 7.7%, $F_{2,25} = 1.1$). The effect of filling time was greater in the Björk-Shiley prostheses (24%, $F_{1,53} = 16.7$; $p = 0.0001$) than in the Starr-Edwards (20%, $F_{1,26} = 6.7$; $p = 0.016$), or Carpentier-Edwards prostheses (13%, $F_{1,74} = 10.6$; $p = 0.0017$).

To exclude the possibility that filling period was controlled by valve type or annulus diameter and that pressure half time could therefore be related indirectly to prosthetic factors, further analysis of filling period was performed. The filling period was strongly related to the RR interval (68%, $F_{1,162} = 343$; $p < 0.00001$) in all three prosthetic designs and multivariate analysis showed little contribution from valve design alone (5.0%, $F_{2,161} = 4.2$; $p = 0.016$) or annulus diameter alone (4.0%, $F_{3,160} = 2.2$; $p = 0.09$).

Table 4 Results for Björk-Shiley prostheses by diameter (mean (SD))

Variable	25 mm (n = 1)	27 mm (n = 18)	29 mm (n = 19)	31 mm (n = 13)	33 mm (n = 5)	F values
T½ (ms)	100	100 (35)	90 (25)	90 (25)	75 (25)	0.7
V max (m/s)	1.9	1.6 (0.3)	1.4 (0.4)	1.6 (0.3)	1.3 (0.6)	1.4
RR (ms)	1065	755 (180)	760 (185)	760 (170)	710 (165)	0.8
DTI (ms)	615	405 (130)	395 (155)	390 (130)	340 (105)	0.9
Fill (ms)	485	360 (70)	350 (85)	360 (80)	315 (70)	1.1
	n = 1	n = 18	n = 16	n = 13	n = 5	
SV (ml)	60	50 (20)	60 (25)	65 (20)	45 (10)	1.4
CO (l/min)	3.4	4.2 (1.9)	5.0 (1.6)	5.0 (1.5)	4.0 (1.5)	0.7
Flow (ml/s)	125	145 (60)	175 (45)	180 (50)	150 (55)	1.2

See footnote to table 2 for abbreviations.

Table 5 Results for Starr-Edwards prostheses by diameter (mean (SD))

Variable	28 mm (n = 7)	30 mm (n = 14)	32 mm (n = 9)	F values	p value*
T ₁ (ms)	130 (25)	100 (40)	125 (60)	1.1	
V max (m/s)	1.8 (0.2)	1.8 (0.2)	1.9 (0.4)	0.3	
RR (ms)	840 (85)	740 (170)	775 (190)	0.5	
DTI (ms)	460 (75)	445 (125)	415 (150)	0.3	
Fill (ms)	440 (50)	415 (135)	395 (130)	0.3	
	n = 7	n = 14	n = 9		
SV (ml)	70 (10)	50 (15)	70 (20)	6.9	<0.01
CO (l/min)	5.2 (0.9)	4.1 (1.7)	5.9 (2.4)	5.4	<0.02
Flow (ml/s)	165 (35)	135 (65)	210 (105)	2.4	

See footnote to table 2 for abbreviations.

*By one way analysis of variance.

Table 6 Results of multivariate regression analyses of the variance in pressure half time

Variable	Variance explained	F value	p value	Standard error
Diastolic filling time	19%	37	<0.00001	33
Stroke volume	15%	26	<0.00001	35
Diastolic time interval	11%	19	<0.00001	35
Prosthetic design	5.6%	4.6	<0.02	36
Mean transmitral flow	2.0%	2.0	0.12	38
Coexistent aortic prosthesis	0.7%	1.3	0.25	37
Annulus diameter	0.4%	0.2	0.95	37
Presence of aortic regurgitation	0.0	0.0	0.85	37

MULTIVARIATE ANALYSIS OF PEAK TRANSMITRAL VELOCITY

Prosthetic design, cardiac output, and annulus diameter together explained 22% of the variance in peak transmitral velocity, of which most was explained by design alone (18%, ($F_{2,161} = 17.2$; $p < 0.00001$)). Cardiac output explained only 2.7%, ($F_{1,158} = 4.3$) and annulus diameter alone was not a determinant of peak transmitral velocity even within each prosthetic design (Carpentier-Edwards 3.5%, $F_{3,74} = 0.8$; Björk-Shiley 6.0%, $F_{3,52} = 1.1$; Starr-Edwards 2.0%, $F_{2,27} = 0.3$). The prosthetic designs differed in their response to flow. Peak transmitral velocity was weakly but significantly correlated with cardiac output ($r = 0.443$; $SE\ 0.24$; $p < 0.02$).

Discussion

In the normally functioning mitral prostheses in this study, the variability in pressure half time was better explained by the diastolic filling period and stroke volume than by the design of the prosthesis. Annulus diameter did not contribute significantly.

DETERMINANTS OF PRESSURE HALF TIME

Theoretical work suggests that pressure half time is related not only to mitral orifice area, but also to the transmitral pressure difference at the start of diastole, to stroke volume, and to left atrial and ventricular compliance.^{14,15} In a flow simulator we showed that the pressure half time in mitral bioprostheses reflects the shape and time course of the left ventricular filling curve¹² and this can be regarded as a model for the effect of left atrial and ventricular compliance. Altered atrial compliance may also explain the deterioration soon after balloon dilatation in the correlation between pressure half time and the orifice area measured by planimetry in patients with native mitral stenosis.²¹

The present study gives clinical evidence for

a relation between pressure half time and both stroke volume and heart rate. All variables together, however, explained only 32% of the variance in pressure half time. Differences in ventricular compliance probably accounted for part of the residual variability, although inaccuracies in measurement or individual patient variability may also have contributed.

EFFECT OF HEART RATE ON PRESSURE HALF TIME

Morrow *et al* showed that in native mitral valves the proportion of left atrial pressure lost in the first 100 ms of diastole was high in pure mitral regurgitation, low in pure mitral stenosis, and intermediate in normal valves or in valves with combined stenosis and regurgitation.²² This observation led to the concept of pressure half time, which was the time taken for the peak transmitral pressure gradient at cardiac catheterisation to fall to one half.^{23,24} This was thought to be relatively independent of flow, but the original data show a large scatter in results with pressure half times of from 110 to 170 ms over a range of instantaneous heart rates from 63 to 86 beats/minute in atrial fibrillation.²⁴ Retrospective analysis of these data showed a statistically significant inverse relation between pressure half time and heart rate.¹⁴

An inverse relation between pressure half time and heart rate was also found during pacing in patients with permanent pacemaker systems and mitral prostheses.¹³ Heart rate probably affects pressure half time in several ways. Orifice area may sometimes increase at higher heart rates, although at the cardiac outputs seen in the present study most valves would be expected to have been fully open.²⁵ Furthermore, pressure half time also falls as rate increases in patients with St Jude bi-leaflet tilting disc prostheses, which are expected to be fully open at low flows.²⁶ Changes in heart rate may also affect left ventricular compliance, stroke volume, and left atrial pressure.²⁷⁻²⁹ The effect of these factors may differ in individuals

because in the present study the observed relation between heart rate and pressure half time varied widely. Therefore no simple correction of pressure half time for rate can be possible.

EFFECT OF ANNULUS DIAMETER AND TYPE OF PROSTHESIS

The inability of this study to show a major effect of prosthetic design and annulus diameter on pressure half time need not necessarily rule out an effect of orifice area. In the Carpentier-Edwards porcine bioprosthesis actual orifice area may vary by about 20% in valves of the same annulus diameter³⁰ and in the Starr-Edwards valve there is no simple central orifice. The Björk-Shiley tilting disc prosthesis, however, has an area available for flow that is expected to reflect the annulus diameter more closely, but even in this valve type pressure half time was not related statistically to annulus diameter. It is possible that the type of prosthesis might have contributed more to the variance in pressure half time had valves with larger orifice areas such as the St Jude prosthesis been studied.³¹ If, however, valve behaviour were a major determinant of pressure half time, this should have been found in the prostheses studied because these show wide differences during in vitro testing.^{32,33} Furthermore, we found that pressure half time is only moderately related to orifice area in vitro.¹² Thus there is good evidence that in normally functioning mitral prostheses pressure half time does not reliably reflect orifice area.

PEAK TRANSMITRAL VELOCITY

Peak transmitral velocity was most closely related to prosthetic design although in the Starr-Edwards prostheses it was also affected by cardiac output. This result is consistent with hydrodynamic work, showing that of the three valve types studied the Starr-Edwards offers the greatest resistance to flow and therefore produces the steepest slope when transmitral velocity is plotted against flow.^{32,33} A close relation between flow and peak velocity has also been shown in fixed diaphragm obstructions.³⁴

CLINICAL IMPORTANCE

The relatively minor effect of prosthetic design on pressure half time has important practical implications. Numerous studies have attempted to define normal ranges for prosthetic function based on pressure half time or effective orifice area derived from the Hatle formula (220/pressure half time) (table 1). Differences between studies are likely to be related more to atrial or ventricular factors than to prosthetic function. Thus the range in mean pressure half time reported as normal for Carpentier-Edwards prostheses, 90–136 ms, is wider than for the three prosthetic designs in this study.

It is therefore very unlikely that pressure half time can reliably detect minor changes in prosthetic function. Studies claiming that Doppler is highly sensitive for the detection of prosthetic obstruction have used patients already defined as normal or dysfunctional on clinical grounds.^{3,4,8,9} None the less, severe

prosthetic obstruction is associated with a lengthened pressure half time.³ Furthermore, aortic regurgitation has been reported to lengthen pressure half time when the mitral valve is normal, but to have no effect where there is severe mitral stenosis.^{35,36} These observations are consistent with the suggestion that orifice area is the most important constraint on pressure half time where there is significant mitral stenosis, whereas where the orifice is relatively large, other factors will be more important. The point at which this transition occurs is not yet known.

This study showed that pressure half time was statistically more closely related to diastolic filling time and stroke volume than to prosthetic design or annulus diameter. Peak transmitral velocity was related to prosthetic design and in the Starr-Edwards valve also to cardiac output. Pressure half time is unlikely to detect small changes in orifice area. Orifice area formulas based on transmitral velocity and flow such as the Gorlin formula²⁵ are likely to reflect prosthetic mitral behaviour more accurately than the Hatle formula, which should be applied with caution in normally functioning mitral valve prostheses.

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