

# Non-invasive assessment by Doppler ultrasound of 155 patients with bioprosthetic valves: a comparison of the Wessex porcine, low profile Ionescu-Shiley, and Hancock pericardial bioprostheses

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**SUMMARY** One hundred and fifty five patients with 167 bioprosthetic valves (68 Wessex porcine, 54 Hancock pericardial, and 45 low profile Ionescu-Shiley pericardial valves) were studied by Doppler ultrasound. Valve gradients were calculated from the mitral and aortic flow velocities by the modified Bernoulli equation. Mean mitral gradients were significantly smaller across the Ionescu-Shiley valves than across the Wessex porcine or Hancock pericardial valves. Mitral pressure half time was, however, significantly longer in the Hancock pericardial than in the Wessex porcine or Ionescu-Shiley valves. No significant differences were seen among the groups of aortic bioprostheses, though the comparable size of Wessex porcine valves showed significantly higher gradients. Bioprosthetic regurgitation was detected in 13 of 103 mitral and 11 of 59 aortic valves, though it was suspected clinically in only 12 mitral and six aortic bioprostheses.

Doppler ultrasound is a repeatable non-invasive method of acquiring haemodynamic information *in vivo* from a variety of bioprostheses and it can detect bioprosthetic regurgitation at an early stage.

There is considerable interest in the haemodynamic assessment of the newer bioprostheses. Although some *in vitro* haemodynamic information is available,<sup>1</sup> this is not easily extrapolated to the clinical situation. In addition the *in vivo* assessment of valve prostheses has usually been obtained intraoperatively<sup>2,3</sup> and rarely at cardiac catheterisation,<sup>4</sup> and there are no *in vivo* haemodynamic data on the bioprostheses that we studied. Non-invasive haemodynamic measurements are important in the continuing clinical assessment of new bioprostheses because the alternative is repeated invasive investigation, which has major ethical implications in otherwise healthy individuals. In addition, in patients in whom important prosthetic dysfunction is suspected, cardiac catheterisation is

nearly always required to evaluate its nature and severity. A non-invasive method of accurately assessing prosthetic function *in vivo* would be valuable. Echocardiography can show excellent structural detail but is an insensitive method for detecting prosthetic dysfunction and does not provide haemodynamic information.<sup>5,6</sup>

Doppler ultrasound predicts valve gradients in patients with mitral<sup>7-9</sup> and aortic<sup>10-12</sup> stenosis and can identify valve regurgitation in these patients.<sup>13-15</sup> More recently these techniques have been applied to the assessment of valve gradients in a small number of patients with either mechanical<sup>16-18</sup> or bioprosthetic<sup>18-20</sup> valve replacements. Doppler ultrasound was also of value in the assessment of prosthetic valve regurgitation in a larger series of mechanical and bioprosthetic valves.<sup>21</sup> We have shown the validity of Doppler ultrasound measurement of valve gradients across bioprosthetic valves *in vitro*<sup>22</sup> and have investigated the accuracy of assessing mitral prosthetic gradients

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and the presence and extent of mitral regurgitation by Doppler ultrasound *in vivo*.<sup>23</sup> The purpose of this study was to determine the value of Doppler ultrasound in the haemodynamic assessment of new types of bioprosthetic valve replacements.

### Patients and methods

We studied 155 patients (age range 33 to 76 years, mean 55.8 years) with 167 bioprostheses. This group comprised 68 with Wessex porcine bioprostheses (47 mitral, 21 aortic), 54 with Hancock pericardial bioprostheses (27 mitral, 27 aortic), and 45 with low profile Ionescu-Shiley pericardial valves (29 mitral, 16 aortic). Valve sizes ranged from 29 mm to 35 mm for the mitral bioprostheses and from 19 mm to 27 mm for aortic bioprostheses.

Before Doppler ultrasound examination all patients underwent cross sectional echocardiography with a Diasonics V3400R phased array echocardiographic imaging system. Measurements were made of left ventricular, right ventricular, and left atrial dimensions, and left ventricular wall thickness. Prosthetic valve function was assessed visually by leaflet separation and apposition and by the structure and motion of the valve ring. Doppler examination was performed by means of a Vingmed Alfred pulsed and continuous wave Doppler velocimeter with a 2 MHz transducer that was interfaced with a Doptek spectrum analyser. Doppler examination was performed with the patient at rest immediately after echocardiographic examination. The optimal Doppler signal was obtained by transducer manipulation and was based both on the audiosignal and on the visual display of a clearly demarcated spectral envelope on the spectrum analyser. Patients with a mitral bioprosthesis who were in atrial fibrillation had analysis performed on Doppler signals obtained during similar diastolic time periods.

Mitral flow was detected from the apical position and the peak mitral diastolic flow velocity was measured in the continuous wave mode. We calculated the transprosthetic valve gradient by means of the modified Bernoulli equation<sup>8</sup>:  $P=4V^2$ , where P is the valve gradient in mm Hg and V is the maximum velocity in m/s.

This equation was applied to the maximum mitral diastolic flow velocity at each 10 ms interval throughout the diastolic time period and these results were averaged to obtain the mean mitral valve gradient. In addition we measured the mitral pressure half time, that is the time taken for the mitral diastolic flow velocity to fall to the equivalent of half the initial calculated peak pressure drop. In mitral stenosis this provided an assessment of the degree of mitral obstruction that was independent of cardiac

output<sup>24</sup> and it has also been used to assess a small number of mitral valve prostheses.<sup>16</sup>

We used continuous wave Doppler from the apical position to assess mitral regurgitation, which was indicated by high velocity systolic flow away from the transducer into the left atrial cavity. The pulsed wave mode, which allowed depth resolution of the Doppler signal, was then used to estimate the degree of mitral regurgitation, as previously reported,<sup>23</sup> by measurement of the extent of flow into the left atrial cavity. Although it is not possible to provide precise quantification of the degree of mitral prosthetic regurgitation by this method it does allow identification of those patients with severe regurgitant lesions.

We measured aortic prosthetic flow velocity in the continuous wave mode from various precordial positions that have been used to assess aortic stenosis<sup>12</sup>—suprasternal notch, apex, subcostal, supraclavicular, and right parasternal in the right lateral decubitus position. The maximum systolic velocity with a clearly demarcated spectral signal was used to calculate the peak aortic valve gradient by the modified Bernoulli equation. The presence of aortic regurgitation was also determined from these precordial positions.

Tricuspid regurgitation was assessed from either the apical or left parasternal positions and when present it was used to estimate right ventricular systolic pressure derived from the gradient obtained across the tricuspid valve during systole. Assuming the absence of pulmonary valve disease the pulmonary artery systolic pressure could be determined.<sup>25</sup>

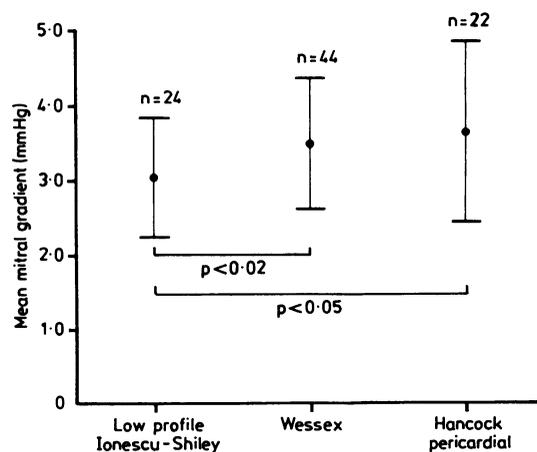


Fig. 1 Comparison of mean mitral gradients (mean (SD)) across all competent mitral bioprostheses.

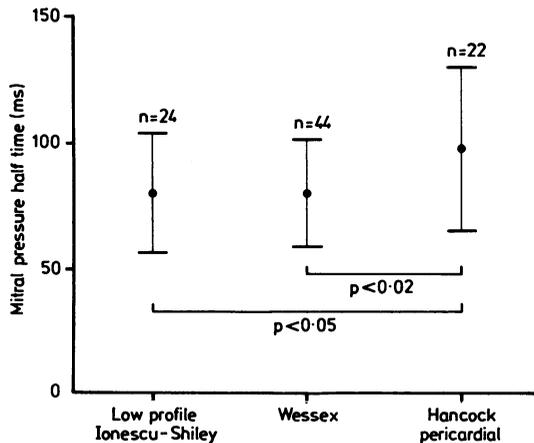


Fig. 2 Comparison of the mitral pressure half time (mean (SD)) for all competent mitral bioprostheses.

#### STATISTICAL METHODS

Mean and standard deviations were calculated, and statistical analysis was performed by the unpaired *t* test.

#### Results

We obtained satisfactory cross sectional echocardiograms in 133 (86%) patients but these did not show any structural abnormality suggestive of prosthetic valve dysfunction. Doppler examination gave satisfactory recordings in all 103 mitral prostheses and in 59 (92%) of the 64 aortic prostheses.

There was no significant difference in the resting heart rates between the three groups of patients (Wessex porcine 84 (7), Hancock pericardial 78 (5), low profile Ionescu-Shiley 82 (9) beats/min).

#### BIOPROSTHETIC GRADIENTS

Figure 1 shows the mean mitral valve gradients measured by Doppler ultrasound. The presence of important mitral regurgitation will increase the mitral diastolic flow velocity and hence the measured valve gradient. Although this would produce an increased gradient even at catheterisation, to obtain a direct comparison between the three types of valve prostheses we excluded those valves demonstrating mitral regurgitation on the Doppler examination. There was a narrow range of valve gradients for each type of bioprosthesis despite the variation in valve size, and significantly lower gradients were found with the Ionescu-Shiley low profile valve than with either the Wessex porcine bioprosthesis ( $p < 0.02$ ) or the Hancock pericardial valve ( $p < 0.05$ ). Mitral pressure half time (Fig. 2) was, however,

significantly longer with the Hancock pericardial bioprosthesis than with either the Wessex porcine bioprosthesis ( $p < 0.02$ ) or the low profile Ionescu-Shiley valve ( $p < 0.05$ ); there was no significant difference in pressure half time between the Wessex porcine and low profile Ionescu-Shiley valves.

There was no significant difference in the peak aortic gradients across the three types of bioprostheses (Fig. 3).

Table 1 shows a comparison of all the mitral prostheses of various sizes. Only two patients had a 35 mm mitral bioprosthesis (both Wessex porcine valves) and they were excluded. The 29 mm mitral bioprosthesis had a significantly longer pressure half time than either the 31 mm or 33 mm sizes. There was no difference, however, in either the peak mitral flow velocity or mean mitral valve gradient among the three valve sizes. Table 2 compares the results for the three different bioprostheses of the same size. A significantly higher peak mitral flow velocity was demonstrated with the 29 mm Wessex porcine valve than with the other two bioprostheses, though this difference was not found with the 31 mm valves. For aortic bioprostheses with a diameter of 23 mm a significantly ( $p < 0.005$ ) higher gradient was demonstrated across the Wessex porcine valve (21.4 (9.8) mmHg,  $n=8$ ) than across the pericardial bioprostheses (Hancock pericardial 15.1 (5.6) mmHg,  $n=13$  and low profile Ionescu-Shiley 15.6 (4.4) mmHg,  $n=7$ ).

#### BIOPROSTHETIC REGURGITATION

Mitral regurgitation was detected in 13 (12.6%) of 103 mitral bioprostheses: three of 47 Wessex porcine, five of 29 low profile Ionescu-Shiley, and five of 27 Hancock pericardial prostheses. It had been sus-

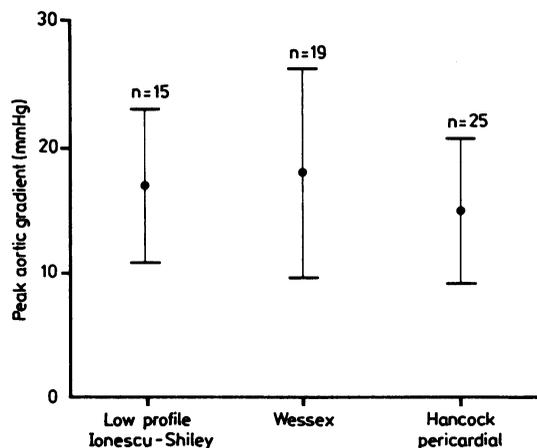


Fig. 3 Comparison of peak valve gradients (mean (SD)) across all competent aortic bioprostheses.

Table 1 Haemodynamic variables (mean (SD)) and valve sizes for all mitral bioprostheses

	Valve size (mm)		
	29 (n=36)	31 (n=40)	33 (n=13)
Peak mitral flow velocity (cm/s)	145.7 (22.7)	141.1 (23.4)	146.5 (26.2)
Mean mitral gradient (mm Hg)	3.52 (1.07)	3.22 (0.82)	3.51 (1.38)
Mitral pressure half time (ms)	90.6 (32)	80.0 (20.0)*	74.6 (19.0)**

\*p<0.05; \*\*p<0.02 compared with value for 29 mm valve. Two patients with 35 mm bioprostheses were not included in analysis.

Table 2 Haemodynamic variables (mean (SD)) for bioprostheses of same size (29 mm and 31 mm)

	29 mm			31 mm		
	Wessex (n=9)	Hancock pericardial (n=14)	Low profile Ionescu-Shiley (n=13)	Wessex (n=22)	Hancock pericardial (n=8)	Low profile Ionescu-Shiley (n=10)
Peak mitral flow velocity (cm/s)	166.4 (17.1)	141.7 (14.4)***	135.7 (25.3)***	141.1 (24.9)	151.0 (26.9)	133.2 (14.2)
Mean mitral gradient (mm Hg)	3.69 (0.61)	2.61 (1.39)	3.31 (0.96)	3.31 (0.83)	3.57 (1.02)	2.74 (0.37)**
Mitral pressure half time (ms)	83.3 (19.4)	105 (36.3)*	80 (30.3)	80 (21.4)	81.2 (23.0)	79 (15.2)

\*\*\*p<0.005 compared with 29 mm Wessex; \*\*p<0.01 compared with both 31 mm Wessex and Hancock pericardial; \*p<0.05 compared with both 29 mm Wessex and low profile Ionescu-Shiley.

pected clinically in 12 of the 13 patients. Table 3 shows the severity of mitral regurgitation graded by the extent of left atrial systolic flow. Three patients were graded as having severe mitral regurgitation, and all subsequently required operation. Additional evidence of severe bioprosthetic regurgitation was obtained in the two patients with a low profile Ionescu-Shiley bioprosthesis who, in the presence of a normal pressure half time, had peak mitral diastolic flow velocities of 240 and 232 cm/s, which is well outside the range for the competent prostheses (Table 4). The peak mitral velocity in the remaining patient with severe mitral regurgitation (in a Hancock pericardial bioprosthesis) and the peak mitral velocities associated with mild or moderate regurgitation all fell within the range for the competent valve prostheses.

Aortic regurgitation was detected in 11 (18.6%) of 59 bioprostheses (five of 19 Wessex porcine, three of 15 low profile Ionescu-Shiley, and three of 25 Hancock pericardial), though this was suspected clinically in only six of the 11 patients.

Tricuspid regurgitation was detected by Doppler ultrasound in 30 (29%) of the 103 mitral bioprostheses but was not found in any patient with single aortic valve replacement. Although the presence of tricuspid regurgitation was identified in 30 patients, a clearly demarcated spectral signal from which the peak velocity could be measured was obtained in only 24 of the 30 patients. The estimated pulmonary systolic pressure ranged from 15 to 33

mm Hg (mean 21.9 mm Hg) in the 21 patients with a competent bioprosthesis, and was 22 mm Hg, 33 mm Hg, and 57 mm Hg in the remaining three patients with mitral regurgitation.

## Discussion

Doppler ultrasound has great potential as a non-invasive method of assessing bioprosthetic valve function. Although in vitro studies can provide data on the haemodynamic profile of various bioprostheses it is difficult to extrapolate from these results to the clinical situation.

The newer pericardial bioprostheses presented

Table 3 Severity of mitral regurgitation graded by extent of left atrial systolic flow

	Mild	Moderate	Severe
Wessex (n=3)	3	—	—
Low profile Ionescu-Shiley (n=5)	3	—	2
Hancock pericardial (n=5)	1	3	1

Table 4 Peak mitral diastolic flow velocities (cm/s) for the competent bioprostheses

	Range	Mean
Wessex (n=44)	92–200	149
Low profile Ionescu-Shiley (n=24)	88–180	134
Hancock pericardial (n=22)	116–204	143

less obstruction to flow than the porcine bioprostheses when they were studied *in vitro*<sup>22</sup> and *intraoperatively*,<sup>3</sup> though it is not certain whether this is of clinical relevance.

The range of mean valve gradients for bioprostheses in the mitral position was quite narrow and gradients in all competent prostheses were acceptably low. We expected the valve gradients in the low profile Ionescu-Shiley pericardial valve to be lower than in the Wessex porcine bioprosthesis, but we did not expect them to be significantly lower than in the Hancock pericardial valve. Similarly the longer mitral pressure half time in the Hancock pericardial prosthesis suggests that the *in vivo* obstructive characteristics of this valve differ from those that were established *in vitro*.

The mean mitral valve gradient was significantly lower for the low profile Ionescu-Shiley valve only at the 31 mm size and not at the 29 mm size. The prolonged pressure half time noted with the Hancock pericardial valve, however, occurred only at 29 mm and not at 31 mm. Because the pressure half time relates more to the initial phase of diastole and the mean mitral gradient relates to the whole diastolic time period, the difference in pressure half time noted with the Hancock pericardial valve could be explained by an increased restriction to flow during the first part of diastole, possibly as a result of less rapid leaflet opening, which may only be of relevance at the smaller valve size.

Similarly the low profile Ionescu-Shiley pericardial valve may be less obstructive throughout diastole and hence produce a significantly lower mean valve gradient with the 31 mm valve than Wessex or Hancock valves of similar size. This effect was also seen with the 29 mm size valves, but it was not significant. *In vitro* studies had not led us to expect these differences in mean valve gradient and mitral pressure half time, and such discrepancies indicate the complexity of the pressure flow relation across the mitral valve *in vivo*.

The slight reduction in the mitral pressure half time with the larger bioprostheses indicates a tendency to increased obstruction with smaller bioprostheses. There was no difference in the mean mitral valve gradients, however, which suggests that this may only have an effect at rest in the early diastolic period when valve flow is greater.

Although there was no overall difference between the three groups of aortic bioprostheses, the Wessex porcine valve, as expected, produced significantly higher peak aortic gradients than different valve types of similar size.

The ability of Doppler ultrasound to identify bioprosthetic valvar regurgitation may be valuable in the assessment of prosthetic valve dysfunction. In

this study not only did we identify three patients with severe mitral regurgitation who required reoperation, but we detected mitral bioprosthetic regurgitation in 10 further patients who were symptom free. Although difficulties arise when pulsed Doppler is used to quantitate mitral regurgitation from the extent of left atrial systolic flow, the technique can allow identification of those with severe regurgitation, particularly where mitral diastolic flow velocity is also increased. Valvar regurgitation in patients with bioprostheses can be the result of leaflet tears, and by detection of regurgitation, Doppler ultrasound may identify at risk patients at an early stage. It is difficult to distinguish between a periprosthetic and a through-valve leak by Doppler ultrasound alone, and simultaneous cross sectional echocardiographic imaging, or more particularly real time colour coded Doppler,<sup>26</sup> may improve performance. The question whether patients suspected of having less important mitral regurgitation will subsequently develop major leaflet tears will only be resolved by careful patient follow up and examination at reoperation.

Aortic regurgitation was identified in 11 aortic bioprostheses, one of which had to be replaced because of leaflet tear. Although it is not possible to measure aortic regurgitation accurately by Doppler ultrasound, its identification in conjunction with clinical and other non-invasive assessment may predict the development of important prosthetic dysfunction at an early stage.

The estimation of right ventricular and therefore pulmonary artery systolic pressure in patients with tricuspid regurgitation is a useful adjunct to the assessment of bioprosthetic valve function. This was possible in several patients with mitral bioprostheses who had tricuspid regurgitation, presumably as a result of right ventricular dilatation associated with previous mitral valve disease. In all patients with a competent mitral bioprosthesis pulmonary pressures were satisfactory at rest, though they were significantly increased in a patient with mitral regurgitation.

This study has demonstrated the successful application of Doppler ultrasound techniques in a large series of patients with bioprosthetic valves. It allowed a comparison of the haemodynamic function of different bioprosthetic valves *in vivo*. Because it is both non-invasive and can be repeated it is likely to have a major impact on the continuing assessment of the newer types of bioprostheses. The ability to identify the presence of bioprosthetic regurgitation in these patients and to provide information on its severity in patients with mitral bioprostheses suggests that non-invasive assessment of developing bioprosthetic dysfunction may be possible.

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