Significance of pulmonary valve prolapse *A cross sectional echocardiographic study*

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SUMMARY Many patients with congenital heart disease now undergo cardiac surgery based solely on clinical and echocardiographic findings, but those with intracardiac shunts still frequently require cardiac catheterisation because there is no reliable non-invasive method of measuring the pulmonary artery pressure. Blinded to the haemodynamic results two independent observers retrospectively studied the cross sectional echocardiograms of 59 patients with uncomplicated ventricular septal defect to assess whether diastolic backward bowing of the pulmonary valve leaflets towards the right ventricular outflow tract (pulmonary valve prolapse) was associated with pulmonary hypertension. There was considerable interobserver variation in the diagnosis of pulmonary valve prolapse, but concordance was achieved in 27 cases. Mean pulmonary artery systolic and mean and diastolic pressures and the ratios of aortic to pulmonary artery mean pressures were all significantly higher for the group with pulmonary valve prolapse diagnosed by both observers than for the group without, thus showing an association between pulmonary valve prolapse and pulmonary hypertension. Further studies are warranted to determine the usefulness of this cross sectional echocardiographic sign in routine clinical practice.

In many patients with congenital heart disease the relevant intracardiac anatomy can be clearly demonstrated by modern high resolution cross sectional echocardiography, but cardiac catheterisation remains necessary in many cases to assess the degree of pulmonary hypertension. In an attempt to obviate the need for these often repeated invasive procedures many studies have been performed predominantly using M mode echocardiographic observations of pulmonary valve motion. A few non-invasive markers of increased pulmonary artery pressure have been identified.¹⁻⁵ None of these has, however, found a routine place in clinical practice.

It is well known that severe pulmonary hypertension can cause clinically evident pulmonary regurgitation. We had noted during routine cross sectional echocardiography that some patients with pulmonary hypertension showed diastolic backward bowing or prolapse of the pulmonary valve leaflets and presumed that this might ultimately result in pulmonary incompetence. This observation prompted us to test the hypothesis that the cross sectional echocardiographic

appearance of pulmonary valve prolapse would be associated with pulmonary hypertension in a group of patients with a single anatomical lesion (that is, ventricular septal defect) and, if this was confirmed, to assess the reliability of detecting pulmonary hypertension by this approach.

Patients and methods

To define pulmonary valve prolapse one of us retrospectively studied the cross sectional echocardiograms of 38 patients with atrioventricular septal defects and known haemodynamics as well as 30 clinically normal patients who had not undergone cardiac catheterisation. These constituted the learning set, and the results are not presented. Pulmonary valve prolapse was defined as diastolic backward bowing of the pulmonary valve towards the right ventricular outflow tract beyond a horizontal line joining the points of attachment of the pulmonary valve leaflets to their annulus (Figs. 1 and 2).

Our initial study population consisted of all patients with simple ventricular septal defects (excluding those with atrioventricular septal defects) who had undergone both cardiac catheterisation and cross sectional echocardiography at our hospital between September

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Fig. 1 Diagrammatic representation of the definition of pulmonary valve prolapse as seen in the parasternal short axis cross sectional echocardiographic cut. Dotted line joins the points of attachments of the pulmonary valve leaflets to the annulus. RVOT, right ventricular outflow tract; MPA, main pulmonary artery; PVP, diastolic position of pulmonary valve leaflets when there was pulmonary valve prolapse; N, diastolic position of pulmonary valve leaflets when there was no pulmonary valve prolapse.

1979 and June 1983. Patients with coexistent persistent ductus arteriosus were, however, excluded since diastolic blood flow from aorta to main pulmonary artery may affect pulmonary valve motion.⁶ We also excluded patients who were studied after repair of the ventricular septal defect or who had pulmonary stenosis.

Fifty nine patients met these criteria, and these yielded 61 echocardiograms for review. These echocardiograms were examined by the same observer who had formulated the definition of pulmonary valve prolapse and by a second echocardiographer who had not previously studied pulmonary valve motion in detail. Although both observers used the same definition of pulmonary valve prolapse, observer 1 was prepared to identify the points on the opposite sides of the pulmonary trunk from which the pulmonary valve leaflets originated on different cross sectional echocardiographic frames, whereas observer 2 required that both these points be identified on the same stop frame. A classification of unknown was used if a decision could not be made because the quality of the echocardiogram prevented adequate visualisation of the pulmonary valve. When the echocardiograms were reviewed neither observer was aware either of the other's opinion or of the patient's catheterisation data.

All cross sectional echocardiograms were recorded using an Advanced Technology Laboratory (ATL) 500 Mark V mechanical sector scanner with a 3.0 MHz transducer and recorded on Sony U-matic 1 inch tape. These were reviewed on a Sony U-matic video cassette recorder (model VO-5800 ps) which has the facility for isolated stop frame analysis and vari-

Fig. 2 Subcostal short axis cross sectional echocardiographic cuts of (a) normal pulmonary valve end diastolic position and (b) end diastolic position of pulmonary valve leaflets when there is pulmonary valve prolapse. RVOT, right ventricular outlet tract; MPA, main pulmonary artery; PV, pulmonary valve leaflets; RV, right ventricle; LV, left ventricle; VSD, ventricular septal defect; s, superior; a, anterior; r, right.

able play back speed regulation. The pulmonary valve was usually best visualised in the parasternal short axis cut. Occasionally, the subcostal right ventricular outflow short axis cut or suprasternal examination of the long axis of the pulmonary trunk gave the best view of pulmonary valve motion and was therefore used. Cardiac catheterisation and angiocardiology

Table 1 Comparison of mean haemodynamic values between categories of echocardiograms according to whether pulmonary valve prolapse was present, absent, or unknown for two different observers

Category	Pulmonary artery pressures (mm Hg)			Ratio of PA mean to Ao mean pressure	Ratio of PA systolic to Ao systolic pressure
	Systolic	Diastolic	Mean		
Observer 1					
Present (Y)	70	29	45	0.76	0.82
Absent (N)	35	16	22	0.29	0.34
p value	<0.001	<0.001	<0.001	<0.001	<0.001
Present (Y)	70	29	45	0.76	0.80
Unknown (U)	50	17	31	0.50	0.60
p value	<0.05	<0.01	<0.05	NS	NS
Absent (N)	35	16	22	0.29	0.34
Unknown (U)	50	17	31	0.50	0.60
p value	NS	NS	NS	NS	NS
Present (Y)	70	29	45	0.76	0.82
Absent (N) and unknown (U)	41	16	26	0.37	0.43
p value	<0.001	<0.001	<0.001	<0.001	<0.001
Observer 2					
Present (Y)	69	27	44	0.74	0.79
Absent (N)	57	24	36	0.60	0.69
Difference	NS	NS	NS	NS	NS
Present (Y)	69	27	44	0.74	0.79
Unknown (U)	55	23	36	0.56	0.62
Difference/p value	<0.05	NS	NS	<0.05	<0.05
Absent (N)	57	24	36	0.69	0.79
Unknown (U)	55	23	36	0.62	0.65
Difference	NS	NS	NS	NS	NS
Present (Y)	69	27	44	0.79	0.74
Absent (N) and unknown (U)	56	23	35	0.65	0.58
Difference/p value	<0.05	NS	<0.05	<0.05	<0.05

PA, pulmonary artery; Ao, aortic.

were performed using standard techniques. Oxygen consumption was not routinely measured.

In analysing the results, the haemodynamic variables were categorised according to whether pulmonary valve prolapse was present (Y), absent (N), or unknown (U) for observer 1, observer 2, and for the combination of both the observers. The haemodynamic variables examined were pulmonary artery systolic pressure, pulmonary artery mean pressure, pulmonary artery diastolic pressure, the ratio of pulmonary to aortic systolic pressures, and the ratio of

pulmonary to aortic mean pressures. Haemodynamic results were analysed on an Amdahl mainframe computer using a statistical package (SPSS version 7.0, Northwestern University) and the standard unpaired *t* test.

Results

The time between performance of the cross sectional echocardiograms and cardiac catheterisation was 0-912 (mean 23.5) days. This interval was ≤ 1 day in 39 (64%) patients, 2 days in nine (15%), and >2 days in 13 (21%). When those whose echocardiograms were recorded ≤ 1 day before the haemodynamic study were considered, the overall results were the same as for the total group. For this reason all 61 echocardiograms (59 patients) are included in the analysis.

Table 1 shows the haemodynamic values for the echocardiograms according to whether pulmonary valve prolapse was present (Y), absent (N), or unknown (U).

Table 2 Observers' opinions of whether pulmonary valve prolapse was present, absent, or unknown. Figures are numbers of echocardiograms

	Observer 1			Total
	Present (Y)	Absent (N)	Unknown (U)	
Observer 2:				
Present (Y)	17	1	1	19
Absent (N)	11	5	2	18
Unknown (U)	12	7	5	24
Total	40	13	8	

Table 3 Comparison of haemodynamic values where there was observer concordance on whether pulmonary valve prolapse was present or absent

Pulmonary valve prolapse	Pulmonary artery pressures (mm Hg)			Ratio of PA mean to Ao mean pressure	Ratio of PA systolic to Ao systolic pressure
	Systolic	Diastolic	Mean		
Present (Y):					
Mean	71	28	47	0.78	0.82
Range	35-100	15-50	25-70	0.5-1.0	0.44-1.0
No of patients	17	17	17	14	15
Absent (N):					
Mean	38	14	24	0.30	0.36
Range	25-50	10-20	15-30	0.19-0.39	0.21-0.53
No of patients	5	5	5	5	5
Significance*	<0.001	<0.02	<0.005	<0.001	<0.001

*Student's unpaired *t* test.

OBSERVER 1

Pulmonary valve prolapse was diagnosed as present (Y) on 40 echocardiograms, absent (N) on 13 and unknown (U) on eight. The arithmetic means of all the haemodynamic values were significantly different ($p<0.001$) when the category (Y) was compared with category (N). When category (Y) was compared with category (U) all the arithmetic means were also significantly different ($p<0.05$) except for the pulmonary to systemic systolic and mean pressure ratios.

Fig. 3 Comparison between pulmonary valve prolapse groups where there was observer concordance for the ratio of pulmonary artery mean pressure to aortic mean pressure (PA:Ao mean pressure ratio). YY, both observers agree pulmonary valve prolapse present; NN, both observers agree pulmonary valve prolapse absent; UU, both observers agree neither pulmonary valve prolapse nor its absence could be diagnosed. In three of the 17 patients in whom there was observer agreement that there was prolapse (YY) no aortic mean pressure was available so no points are plotted.

There was no significant difference between haemodynamic values within categories (N) and (U). When category (Y) was compared with the combined categories (N) and (U) the mean values were significantly different ($p<0.001$).

OBSERVER 2

Pulmonary valve prolapse was diagnosed as present (Y) on 19 echocardiograms, absent (N) on 18, and unknown (U) on 24. No statistically significant difference was present in the haemodynamic values for the categories (Y) and (N). When category (Y) was compared with category (U) only pulmonary artery systolic pressure, pulmonary to aortic systolic ratio, and pulmonary to aortic mean ratio showed significant differences ($p<0.05$). The mean values for categories (N) and (U) were not significantly different for any of the haemodynamic variables. When categories (N) and (U) were combined and compared with category (Y) significant differences ($p<0.05$) were found for pulmonary artery mean pressure, pulmonary artery systolic pressure, pulmonary artery to aortic systolic pressure ratio, and pulmonary artery to aortic mean pressure ratio.

COMBINED RESULTS

There was agreement between observers in 27 of the 61 (41%) reviewed echocardiograms (Table 2); in 17 pulmonary valve prolapse was identified as present (Y), in five as absent (N), and in five as unknown (U). Observer 2 was three times as likely to be undecided as observer 1. For these 27 cases, the haemodynamic values for category (Y) were compared with those for category (N) (Table 3). There were significantly different values for all haemodynamic variables but there was considerable overlap in all the ranges except that for pulmonary artery to aortic mean pressure ratio; no echocardiogram in category (N) had a ratio >0.40 and none in category (Y) had a ratio <0.5 (Fig. 3). This finding was highly significant ($p<0.001$).

Discussion

Despite major advances in the non-invasive diagnosis of congenital heart disease due to the introduction of cross sectional echocardiography, cardiac catheterisation is still necessary in many cases for the reliable diagnosis of pulmonary hypertension. In our unit many patients now undergo surgery based on clinical and cross sectional echocardiographic findings alone,⁷ but we, like others,¹ still find it necessary for many patients with left to right shunts to have invasive measurement of pulmonary artery pressure.

Previous attempts to predict pulmonary hypertension non-invasively have been unreliable or beyond the routine resource and time constraints of most cardiac centres. Most of this work has involved the use of systolic time intervals measured from surface electrocardiography combined with M mode echocardiography of the tricuspid and pulmonary valves. Unfortunately, many of the results have been conflicting, as Silverman *et al* have previously discussed.¹ They tested the predictive value of the ratio of right ventricular pre-ejection period to right ventricular ejection time and found no statistically significant correlation between this ratio and either pulmonary vascular resistance or pulmonary artery mean pressure.¹ They also discussed the conflict in published studies regarding the reliability of pulmonary valve "a" wave amplitude in the prediction of pulmonary hypertension.

Boyd *et al* have highlighted other limitations of systolic time intervals.² They noted that a raised right atrial pressure, overt right heart failure, or right bundle branch block changed the measurements so that there was no longer a correlation with pulmonary artery pressure.

Other M mode echocardiographic features of pulmonary valve motion have been related to pulmonary artery pressure but again with conflicting results. Lew and Karliner found that mid-systolic notching of the pulmonary valve was 100% specific for pulmonary hypertension,³ but Heger and Weyman noted that isolated dilatation of the main pulmonary artery may cause the same finding in the absence of pulmonary hypertension.⁸ Nanda *et al* found a correlation between the pulmonary valve e-f slope and pulmonary hypertension,⁴ but Weyman *et al*⁹ and Lew and Karliner³ found it an unreliable sign owing to overlap with normal values. The only M mode echocardiographic predictor of pulmonary hypertension yet to be challenged is the finding of Serwer *et al*⁵ that in patients with ventricular septal defect the absence of any right to left shunt on contrast echocardiography was strong evidence against pulmonary hypertension.

Other factors may also affect some of these variables, further reducing their reliability in predicting

pulmonary artery pressure. Kerber *et al* showed that cardiac output, heart rate, and concurrent drug treatment each had an effect on the ratio of right ventricular pre-ejection period to ejection time.¹⁰ Furthermore, Green and Popp studied pulmonary valve motion in relation to other anatomical factors with M mode and cross sectional echocardiography and found that there was a relation between the motion of the posterior aortic wall and that of the pulmonary valve in late diastole.¹¹ They also showed that the size of the pulmonary valve "a" wave was related to motion of the entire cardiac base as well as to left atrial volume changes.

Stevenson *et al* used Doppler ultrasound to predict pulmonary hypertension in patients with persistent ductus arteriosus.¹² They found that when ductal blood flow occurred throughout the whole of diastole there was a normal pulmonary pressure. Nevertheless, there was a non-linear correlation between degrees of raised pulmonary pressure and the degree of abbreviation of ductal flow. More recently, using a nomogram described by Burstin,¹³ Hatle *et al* showed a linear correlation between pulmonary artery systolic pressure and the interval between pulmonary valve closure and tricuspid valve opening identified by Doppler ultrasound.¹⁴ Limitations of this technique were similar to those in previous studies with systolic time intervals. It proves unreliable when there is an increased right atrial pressure, increased right ventricular end diastolic pressure, tricuspid regurgitation, very low cardiac output, or pulmonary regurgitation, all of which can occur with chronic pulmonary hypertension. Furthermore, recording the time of pulmonary valve closure was not always easy in their study. Great accuracy in this is vital since a 10 ms error in timing will create an error of 10 mm Hg in pressure estimation. This technique is therefore unlikely to become useful clinically because of the difficulty in making the measurements and the large scope for error.

Studies assessing a non-invasive measurement against a gold standard are best tested with the independent opinions of more than one observer, each blinded to the true results. Few of the studies reviewed above fulfilled these criteria so it is perhaps not surprising that so few of the results reported have been reproducible by other workers. In only two of the studies^{2 12} was it stated that the echocardiographic measurements or observations were made before invasive testing—that is, blinded to the true results. Some missed the opportunity to test interobserver error, instead using the consensus of all investigators to arrive at their opinions.^{11 12}

In our study two independent observers compared the occurrence of pulmonary valve prolapse with various haemodynamic pressures and ratios which might

be expected to affect diastolic pulmonary valve motion. Pulmonary arteriolar resistance was not included among these because oxygen uptake is not routinely measured during cardiac catheterisation in our laboratories and assumed values in small patients with varying degrees of sedation and cardiac output are unreliable.¹⁵

Our results clearly show that pulmonary valve prolapse is associated with pulmonary hypertension. Although it is not clear whether systolic, diastolic, or mean pressure is the most important determinant there was no overlap for the pulmonary artery to aortic mean pressure ratio between the groups with and without prolapse. In theory, diastolic (closing) pressure is the most relevant.

The results also show that without further improvement in the resolution of cross sectional echocardiography it is unlikely that the observation of the presence or absence of pulmonary valve prolapse will prove to be either a specific or sensitive marker for pulmonary hypertension. The thickness of the pulmonary valve in most of these patients was such as to lie between the limits of the axial and lateral resolution of the equipment. As a result, in suprasternal cuts the coapted edges of the leaflets often appeared in diastole as a free floating line in the centre of and parallel with the pulmonary trunk, the remainder of the leaflets being invisible. By contrast, in short axis cuts the most easily identified portion of the leaflets was neither the coapted segments nor the origin of the leaflets but the region in between, lying in the short axis of the pulmonary trunk. Such views as were obtained of the origin of the leaflets from the pulmonary trunk were often only fleeting. It is clear that the requirement for the leaflet origins on both sides of the pulmonary trunk to be seen simultaneously (which is essential if the recognition of prolapse is to be truly objective) resulted in the classification of many cases, both of true positive and true negative prolapse, as unknown. For a technique to be generally adopted it is essential that it should be as objective as possible.

There are, however, four reasons why we believe pulmonary valve prolapse may merit further study as a marker for pulmonary hypertension. Firstly, the resolution of cross sectional echocardiographic equipment will doubtless improve and may make visualisation of the entire pulmonary valve a feasible proposition in all patients. Secondly, this was a retrospective study. Had the primary intention of the echocardiographic examination been to demonstrate the pulmonary valve, the results might well have been better. Thirdly, the association between pulmonary valve prolapse and pulmonary hypertension might have been closer had echocardiograms been recorded at the time of cardiac catheterisation in every case. Finally, if pulmonary valve prolapse were taken as

one indicant of pulmonary hypertension along with several other preferably independent non-invasive measures a multivariate model might have a higher predictive value.

In conclusion, we have shown for the first time that the cross sectional echocardiographic demonstration of pulmonary valve prolapse is associated with pulmonary hypertension. Nevertheless, further prospective studies are required to evaluate its use as a reliable echocardiographic sign in patients with left to right shunts.

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