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Five-Year Follow-Up After Balloon Pulmonary Valvuloplasty

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Objectives. The aim of this study was to assess results 5 years after balloon pulmonary valvuloplasty.

Background. Since the technique of balloon pulmonary valvuloplasty was first reported in 1982, it has become the treatment of choice for pulmonary valve stenosis. In contrast to surgical valvotomy, the long-term outcome after balloon pulmonary valvuloplasty is unknown.

Methods. We reviewed the findings in 34 patients 5.2 ± 0.8 (mean ± SD) years after balloon pulmonary valvuloplasty: 27 with isolated pulmonary stenosis, 5 with Noonan syndrome and 2 with previous surgical valvotomy. In eight patients (three with Noonan syndrome), a second balloon valvuloplasty was the index procedure for analysis.

Results. The transpulmonary gradient (mm Hg) was 74 ± 34 before balloon pulmonary valvuloplasty, 36 ± 26 immediately after, 22 ± 9 at cardiac catheterization in 29 patients 6 ± 0.6 months later and 19 ± 10 by Doppler study at 5 years. At 5 years 26 patients (group A) had a residual gradient of ≤20 mm Hg; the remaining 8 (group B) had a gradient of >20 mm Hg. Four group B patients had Noonan syndrome ($p = 0.01$). Balloon/pulmonary valve diameter ratio was larger for group A patients than for group B patients with isolated pulmonary stenosis (1.20 ± 0.10 vs. 1.00 ± 0.07, $p = 0.005$); larger balloons were used in group B patients with Noonan syndrome (1.30 ± 0.10). Group A patients were more likely than group B patients to have significant pulmonary incompetence (6 of 24 vs. 0 of 8) and had a greater right ventricle/left ventricle long-axis diastolic dimension ratio (0.47 ± 0.10 vs. 0.35 ± 0.04, $p = 0.05$). In the subgroup of five patients with Noonan syndrome and two with prior surgical valvotomy, the transpulmonary gradient was reduced from 74 ± 24 mm Hg before balloon valvuloplasty to 23 ± 12 mm Hg at 5 years. In addition, two patients with isolated pulmonary valve stenosis had pulmonary valve dysplasia by angiographic criteria: transpulmonary gradients of 85 and 56 mm Hg were reduced to 20 and 11 mm Hg, respectively, at 5 years.

Conclusions. Relief of obstruction persists at 5 years especially if oversized balloons are used. Acceptable results can be obtained in patients with a dysplastic valve. More complete relief of right ventricular outflow gradient is associated with increased right ventricular dimension, probably because more pulmonary incompetence is induced. This is well tolerated at 5 years but may be important in the longer term.

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Since the technique of balloon pulmonary valvuloplasty was first reported in 1982 (1), it has become the treatment of choice for pulmonary valve stenosis (2). In contrast to surgical valvotomy (3,4), the long-term outcome after balloon pulmonary valvuloplasty is unknown although our initial experience with it was favorable (5). Our main finding at that time was that an apparently poor immediate result did not preclude good relief of obstruction, especially in patients with the most severe pulmonary stenosis, because of the resolution of myocardial hypertrophy at the infundibular level, a finding later confirmed by others (6,7). The purpose of this study was to assess whether the beneficial effect of balloon pulmonary valvuloplasty was maintained at medium-term (5-year) follow-up.

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Methods

Patients. Of our first 40 patients to undergo balloon pulmonary valvuloplasty, 34 were available for follow-up. Six patients were excluded because of death (n = 2), residence overseas (n = 2), diffuse pulmonary artery branch stenoses (n = 1) or Ebstein's anomaly (n = 1). Both patients who died underwent neonatal balloon pulmonary valvuloplasty with an apparently good initial result. One, a dysmorphic neonate with a chromosomal abnormality, died of aspiration pneumonia at age 1 month. The other, a neonate with unusually large central pulmonary arteries, underwent ligation of the arterial duct at age 2 months; progress was apparently satisfactory until fatal mycoplasma pneumonia occurred at age 2 years.

Eight of the 34 patients available for follow-up had undergone two balloon pulmonary valvuloplasty procedures; the most recent procedure was selected for analysis. Patients were assessed a mean (± SD) of 5.2 ± 0.8 years after their most recent balloon dilation. Twenty-seven patients had isolated pulmonary stenosis, five had Noonan syndrome diagnosed by a clinical geneticist on the basis of

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phenotypic features (8) and two had undergone previous surgical valvotomy (performed at age 1 day for pulmonary atresia with intact ventricular septum in one, and at age 6 months for severe pulmonary valve stenosis in the other). Repeat cardiac catheterization was performed in 29 patients a mean of 6.0 ± 0.6 months after the initial dilation procedure. Repeat balloon dilation was performed at this procedure in eight patients, three of whom had Noonan syndrome. The balloon size used at the initial procedure was probably inadequate in these patients (5).

Clinical and echocardiographic evaluation were performed at the 5-year follow-up, and the data were compared with hemodynamic and angiographic data obtained before and after balloon pulmonary valvuloplasty. Outcome was assessed separately for patients with Noonan syndrome and postoperative patients and for those with isolated pulmonary stenosis who had angiographic features of pulmonary valve dysplasia. Pulmonary valve dysplasia in patients without Noonan syndrome was diagnosed by agreement between two observers when the pulmonary valve diameter was less than the mean value for body surface area (9), and there was marked asymmetric thickening of the valve cusps and limited cusp movement (10,11). All patients were asymptomatic.

Echocardiography. Right ventricle/left ventricle long-axis M-mode diastolic dimension ratio was measured with patients in the supine or left lateral decubitus position under two-dimensional control (12). Patient data were compared with measurements obtained from 33 age- and gender-matched normal children. Doppler echocardiographic measurement of systolic pressure decrease across the pulmonary valve was assessed by the modified Bernoulli equation; this value correlates well with the peak to peak systolic pressure difference measured at cardiac catheterization in patients with pulmonary valve stenosis. The spatial distribution of pulmonary regurgitant flow was assessed by color flow and pulsed Doppler interrogation. Pulmonary regurgitation was assessed as grade 1 when regurgitant flow was detected below the pulmonary valve, grade 2 when it was detected at the level of the pulmonary valve, grade 3 when it was detected in the pulmonary trunk and grade 4 if the regurgitant signal was present at the pulmonary artery bifurcation. Tricuspid regurgitation was considered mild if the regurgitant Doppler spectral signal was confined to early systole, and moderate when the spectral signal was pansystolic.

Patients were classified into two groups according to the severity of residual right ventricular outflow tract obstruction; a residual gradient of >20 mm Hg was arbitrarily chosen as indicative of incomplete relief of obstruction. Discriminating features between the groups were assessed.

Statistics. Results were expressed as mean value ± SD. A *t* test and an exact probability test were used to test significance, and statistical significance was assumed at the 5% level.

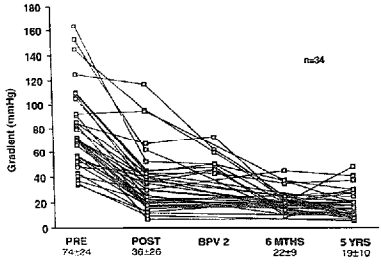


Figure 1. Transpulmonary systolic pressure difference (Gradient) before (PRE) and after (POST) balloon pulmonary valvuloplasty (BPV). BPV 2 indicates eight patients who underwent a second balloon pulmonary valvuloplasty procedure. MTHS = months. Mean values ± SD are shown on the abscissa.

Results

Systolic pressure gradients. Transpulmonary systolic pressure difference (mm Hg) was 74 ± 24 before balloon pulmonary valvuloplasty, 36 ± 26 immediately after dilation, 22 ± 9 at cardiac catheterization in 29 patients 6.0 ± 0.6 months later and 19 ± 10 by Doppler velocimetry at 5-year follow-up study (Fig. 1). The systolic pressure difference at 5 years was similar to or less than that previously documented 6 months after balloon dilation in all except one patient (Fig. 1). This was a girl who was 4 years old at the time of balloon dilation, which resulted in reduction of systolic pressure difference from 108 mm Hg to 30 mm Hg immediately after, and 20 mm Hg at 6 months, but an increase to 48 mm Hg at 5-year follow-up. The ratio of balloon diameter to pulmonary valve diameter was 1.0 in this patient.

The residual systolic pressure difference was ≤20 mm Hg in 26 patients (group A), whereas it was >20 mm Hg in 8 patients (group B). Group A included the 2 postoperative patients and 1 patient with Noonan syndrome, but the remaining 23 patients had isolated pulmonary stenosis. In comparison, group B included four patients with Noonan syndrome ($p = 0.01$) (Fig. 2). Groups A and B were similar with respect to age at the time of balloon valvuloplasty (mean 4.5 ± 4.0 vs. 4.5 ± 3.6 years [median 3.0 vs. 5.0] for group A and group B, respectively) and proportion of male patients (42% in group A vs. 50% in group B).

Right ventricular size and pulmonary incompetence. Right ventricle/left ventricle long-axis diastolic dimension ratio was 0.47 ± 0.1 in group A and 0.35 ± 0.04 in group B ($p = 0.05$). The right ventricle/left ventricle ratio for the matched control group was 0.29 ± 0.0(, which was lower than that in either patient group (group A, $p < 0.001$; group B, $p = 0.05$) (Fig. 3). The child who had undergone neonatal surgical pulmonary valvotomy had had a left modified Blalock-

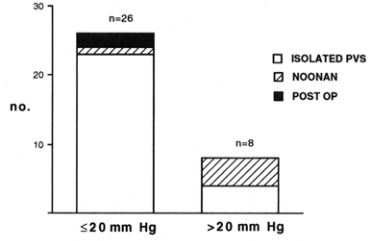


Figure 2. Proportion of patients with isolated pulmonary valve stenosis (PVS), Noonan syndrome or previous surgical pulmonary valvotomy (POST OP) according to the residual transpulmonary gradient at 5-year follow-up.

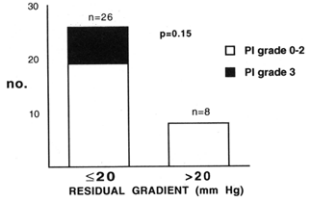


Figure 4. Grade of pulmonary incompetence (PI) according to residual transpulmonary gradient 5 years after balloon pulmonary valvuloplasty. See text for details.

Taussig shunt at the same procedure and was excluded from the analysis because of left to right shunting at the atrial level at 5-year follow-up.

Pulmonary incompetence was grade 3 in six patients from group A but was grade 1 or 2 in all other patients (Fig. 4). No patient had physical signs of severe pulmonary incompetence. Tricuspid regurgitation could not be detected by Doppler interrogation in 12 patients, was represented by a short early systolic spectral signal in 20 and was pansystolic in 2. These two patients were both from group A and had a right ventricle/left ventricle long-axis dimension ratio of 0.76 and 0.67, respectively.

The ratio of balloon diameter to pulmonary valve size of 1.20 ± 0.10 in group A patients was higher than the ratio of 1.00 ± 0.07 in the four group B patients with isolated pulmonary stenosis ($p = 0.005$, Fig. 5). However, for the patients with Noonan syndrome in group B, the balloon/pulmonary valve ratio of 1.30 ± 0.10 was higher than that in either of the other groups (Fig. 5).

Noonan syndrome and pulmonary valve dysplasia. Hemodynamic data for the five patients with Noonan syndrome and two patients with previous surgical pulmonary valvotomy are presented separately in Figure 6. For this group of seven patients, transpulmonary systolic pressure difference was reduced from 74 ± 24 mm Hg before balloon dilation to 23 ± 12 mm Hg at 5-year follow-up. Dilation resulted in little benefit in the two patients with Noonan syndrome with the least severe obstruction (Fig. 6). One of these was a 10-year old boy with a transpulmonary gradient of 41 mm Hg both before dilation and at 5-year follow-up. Balloon/pulmonary valve diameter ratio was 0.9 in this patient. In the other patient, who was 12 months old at balloon dilation, the transpulmonary systolic pressure gradient was 48 mm Hg before balloon dilation and 30 mm Hg at 5-year follow-up. Balloon/pulmonary valve diameter ratio was 1.5 in this patient. The remaining five patients with a predilation transpulmonary gradient of 70 to 109 mm Hg had generally satisfactory results, with gradients ranging from 9 to 37 mm Hg at 5 years.

Of the 27 patients with isolated pulmonary stenosis, only 2 had pulmonary valve dysplasia. One was a girl aged 1 year at balloon dilation with a transpulmonary systolic pressure difference of 85 mm Hg before dilation and 20 mm Hg at 5-year follow-up (Fig. 7). Balloon/pulmonary valve diameter

Figure 3. Right ventricle/left ventricle long-axis diastolic dimension ratio (RVd/LVd) according to residual transpulmonary gradient 5 years after balloon dilation of the pulmonary valve compared with the ratio in age- and gender-matched control subjects.

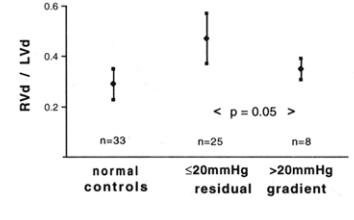
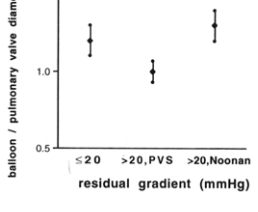


Figure 5. Balloon/pulmonary valve diameter ratio according to residual transpulmonary gradient for patients with isolated pulmonary valve stenosis (PVS) and Noonan syndrome.



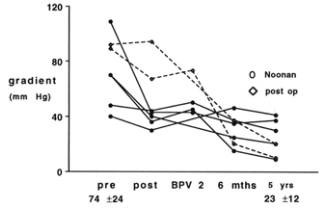


Figure 6. Transpulmonary systolic pressure difference (gradient) before and after balloon valvuloplasty for the seven patients with either Noonan syndrome **(solid lines, circles)** or previous surgical valvotomy **(dashed lines, diamonds)**. Format and abbreviations as in Figure 1.

ratio was 1.1. The other was a boy aged 3 years at balloon dilation (balloon/pulmonary valve ratio 1.2) whose transpulmonary gradient was reduced from 56 mm Hg to 11 mm Hg at 5 years.

Discussion

Gradient relief and right ventricular size. These data confirm that relief of right ventricular outflow tract obstruction persists up to 5 years after balloon dilation of the pulmonary valve for pulmonary stenosis, especially if balloons with an inflated diameter of 120% to 130% of the pulmonary valve diameter are used. In the only patient who had a pronounced increase in the transpulmonary gradient between the 6-month and 5-year follow-up, a balloon with inflated diameter no larger than the pulmonary valve had been used. It is tempting to speculate that incomplete relief of commissural fusion may have afforded reasonable relief of obstruction at first, but that restenosis occurred with body growth. It was the use of inadequately sized balloons that necessitated repeat dilation in eight patients who underwent their initial dilation procedure early in our experience (5).

The noninvasive assessment of right ventricular volume, and of the severity of pulmonary incompetence, is difficult. Although the right ventricle/left ventricle long-axis diastolic dimension ratio measures the dimension of only one part of the right ventricular cavity, this measurement could be obtained in all patients. Moreover, a previous two-dimensional echocardiographic study demonstrated that right ventricular diameter measured in this way was reproducible (13). Although the assessment of pulmonary incompetence by the distribution of the Doppler regurgitant signal must be regarded as semiquantitative at best, all patients with more than trivial pulmonary incompetence were in the group of those who had more complete relief of obstruction. Because right ventricular dimensions were also greater in this group, it seems reasonable to suppose that the increased right ventricular dimension was the consequence of pulmonary incompetence induced by the balloon dilation procedure. Even the two patients with pansystolic tricuspid regurgitation on Doppler assessment who had large right ventricular dimensions also had significant pulmonary incompetence assessed on Doppler study. Moderate pulmonary incompetence is very well tolerated in the medium term. All of our patients were asymptomatic at 5-year follow-up. However, moderate degrees of induced pulmonary regurgitation after surgery to correct right ventricular

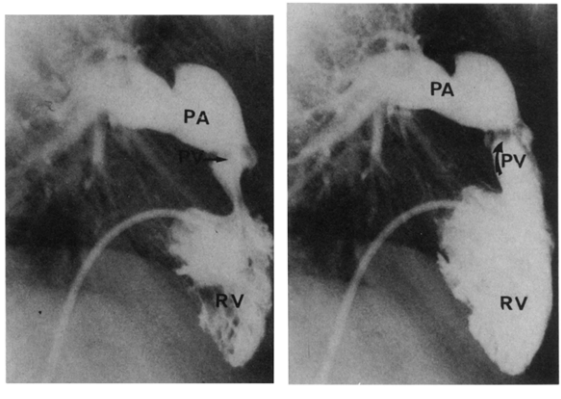


Figure 7. Lateral views of right ventricular angiogram in systole **(left)** and diastole **(right)** from a 1-year old girl with a dysplastic pulmonary valve **(arrows)** and a satisfactory result after balloon pulmonary valvuloplasty. See text for details. PA = pulmonary artery; PV = pulmonary valve; RV = right ventricle.

outflow obstruction decrease exercise capacity and hemodynamic responses to exercise (14); thus, the pulmonary regurgitation we have documented may become clinically manifest at late follow-up.

Noonan syndrome and pulmonary dysplasia. Satisfactory results from balloon dilation were obtained in the two patients with previous surgical pulmonary valvotomy, the three patients with Noonan syndrome with the most severe right ventricular outflow tract obstruction and the two other patients with isolated pulmonary stenosis who had a dysplastic valve. Although the results of balloon dilation for a dysplastic pulmonary valve are less satisfactory than in "typical" pulmonary valve stenosis (10,15,16), satisfactory palliation may be obtained in many patients. We were not able to predict the result of balloon dilation from the morphology of the pulmonary valve assessed angiographically. This finding suggests that balloon dilation should be the initial palliative procedure of choice even for children who have apparently dysplastic pulmonary valve morphology.

Comparative data. In a recently reported comparable study (17), patients were assessed 4.6 ± 1.9 years after balloon dilation of the pulmonary valve, with a 91% follow-up rate. The results were similar to our findings in that the residual transpulmonary gradient was 20 ± 13 mm Hg at late follow-up compared with 19 ± 10 mm Hg in our patients and, similarly, acceptable results were obtained in patients with Noonan's syndrome and those with a dysplastic valve. In contrast to our findings, however, there was no relation between balloon/pulmonary valve diameter ratio and either residual gradient or pulmonary regurgitation. Several factors may explain the apparent discrepancy. Data on individual patients were not provided in the Baltimore study (17). Significant residual obstruction was defined as a transpulmonary gradient of ≥36 mm Hg; this requirement would have been fulfilled by only three patients from our series (with a gradient of 37, 41, and 48 mm Hg, respectively, at 5-year follow-up). In the Baltimore study, smaller balloons were used with a balloon/pulmonary valve diameter of 0.67 to 1.22 (mean 1.01 ± 0.11). Pulmonary incompetence was assessed subjectively from the color flow signal but right ventricular dimension was not measured. The smaller balloons used might also account for the finding that patients aged <2 years at the time of the procedure were at risk of residual or recurrent obstruction, which was not the case in our patient group.

Conclusions. In summary, our data confirm that the encouraging early results of balloon dilation of the pulmonary valve are maintained at 5-year follow-up. Acceptable results can be obtained in many patients with an apparently dysplastic valve. Complete relief of obstruction was associated with increased right ventricular dimension, probably because more pulmonary incompetence was induced. The importance of this observation is uncertain, and these patients require longer follow-up. However, it suggests that the "ideal" result after balloon pulmonary valvuloplasty may be to limit the severity of pulmonary incompetence induced at the cost of a small residual transpulmonary gradient.

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References

1. Kan JS, White RI, Mitchell SE, Gardner TJ. Percutaneous balloon valvuloplasty: a new method for treating congenital pulmonary stenosis. N Engl J Med 1982;307:540–2.
2. Stanger P, Cassidy SC, Girod DA, Kan JS, Lababidi Z, Shapiro SR. Balloon pulmonary valvuloplasty: results of the valvuloplasty and angioplasty of congenital anomalies registry. Am J Cardiol 1990;65:775–83.
3. Mirowski M, Shah KD, Neill CA, Taussig HB. Long term (10 to 13 years) follow up study after transventricular valvectomy for pulmonary stenosis with intact ventricular septum. Circulation 1963;28:906–14.
4. Tandon R, Nadas AS, Gross RE. Results of open heart surgery in patients with pulmonic stenosis and intact ventricular septum. A report of 108 cases. Circulation 1965;31:190–201.
5. Sullivan ID, Robinson PJ, Macartney FJ, et al. Percutaneous balloon valvuloplasty for pulmonary valve stenosis in infants and children. Br Heart J 1985;54:435–41.
6. Radtke W, Keane JF, Fellows KE, Lang P, Lock JE. Percutaneous balloon valvotomy of congenital pulmonary stenosis using oversize balloons. J Am Coll Cardiol 1986;8:909–15.
7. Fontes VF, Esteves CA, Sousa JEMK, Silva MVD, Bemborn MCB. Regression of infundibular hypertrophy after pulmonary valvuloplasty for pulmonic stenosis. Am J Cardiol 1988;62:977–9.
8. Duncan WJ, Fowler RS, Farkas LG et al. A comprehensive scoring system for evaluating Noonan syndrome. Am J Med Genet 1981;10:37–50.
9. Ichida F, Aubert A, Denef B, Dumoulin M, van der Haumart L. Cross-sectional echocardiographic assessment of great artery diameters in infants and children. Br Heart J 1987;58:627–34.
10. Marantz PM, Huhta JC, Mullins CE, et al. Results of balloon valvuloplasty in typical and dysplastic pulmonary valve stenosis: Doppler echocardiographic follow up. J Am Coll Cardiol 1988;12:476–9.
11. Schneeweiss A, Blieden LC, Shem-Tov A, Goor D, Milo S, Neufeld HN. Diagnostic angiocardiographic criteria in dysplastic stenotic pulmonary valve. Am Heart J 1983;106:761–2.
12. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantification in M mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58:1072–83.
13. Foale R, Nihoyannopoulous P, McKenna W, et al. Echocardiographic measurement of the normal adult right ventricle. Br Heart J 1986;56:33–44.
14. Marx GR, Hicks RW, Allen HD, Goldberg SJ. Non-invasive assessment of haemodynamic responses to exercise in pulmonary regurgitation after operations to correct pulmonary outflow obstruction. Am J Cardiol 1988;61:595–601.
15. Musewe NN, Robertson MA, Benson LN, et al. The dysplastic pulmonary valve: echocardiographic features and results of balloon dilatation. Br Heart J 1987;57:364–70.
16. DiSessa TG, Albert BS, Chase NA, Birbaum SE, Watson SC. Balloon valvuloplasty in children with dysplastic pulmonary valves. Am J Cardiol 1987;60:405–7.
17. McCrindle BW, Kan JS. Long-term results after balloon pulmonary valvuloplasty. Circulation 1991;83:1915–22.