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Evolving management for critical pulmonary stenosis in neonates and young infants

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Abstract  Over the years, management of critical pulmonary stenosis in young infants has evolved from surgical reconstruction of the right ventricular outflow tract and closed pulmonary valvotomy to transcatheter balloon valvoplasty. Our study aimed at evaluating how the changing policy for management had affected the immediate and long term outcomes of babies with this cardiac lesion. Interventions were made in 34 infants at a median age of 8.5 days (2–90 days). Reconstruction of the right ventricular outflow tract reconstruction was performed in 10 patients, closed pulmonary valvotomy in 13, and balloon valvoplasty in 11. Initial procedure-related mortality was 50%, 15% and 0% respectively. Multivariate analysis revealed transannular patching of the right ventricular outflow tract, and male sex, to be significant factors for death. For the 27 survivors, the ratio of right ventricular to systemic systolic pressure decreased from 1.6 ± 0.3 to 0.3 ± 0.2 after reconstruction of the outflow tract, 1.8 ± 0.5 to 0.8 ± 0.4 after closed valvotomy, and 1.8 ± 0.6 to 0.9 ± 0.3 after balloon valvoplasty. The decrease was significantly greater after patch reconstruction (p=0.025) that required no further reinterventions. The overall rate of reintervention for the survivors was 37% (10/27). The freedom from reintervention after closed valvotomy was 82%, 64% and 51% at 1, 5 and 10 years respectively. The figure remained at 78% at both 1 and 5 years (p=0.66) after balloon valvoplasty. The higher reintervention rate for closed valvotomy corresponded to the significantly greater residual gradient across the pulmonary valve noted on follow-up (p=0.01). Reinterventions included balloon dilation (n=6), reconstruction of the outflow tract (n=4), and 1 each of ligation of an arterial duct and systemic-pulmonary arterial shunting. The risk factor for reintervention was a hypoplastic right ventricle. In conclusion, transcatheter balloon valvoplasty appears to be the optimum initial approach in view of its low mortality, efficacy at relieving the obstruction, and low rate of reintervention.

Keywords: Critical pulmonary stenosis; evolving management

I N T H E M A N A G E M E N T O F N E O N A T E W I T H C R I T I C A L pulmonary valvar stenosis, surgery has been the mainstay of treatment to alleviate obstruction of the right ventricular outflow tract obstruction.1,2 Since the first description of percutaneous balloon pulmonary valvuloplasty,3 the technique has increasingly been employed as the initial treatment for small infants and neonates with this condition. Comparative studies on the outcome of various treatment modalities for this group of sick babies, however, have been limited.4,5 Over the past 16 years, there has been a marked evolution in the polices for management of this critical condition. Surgical treatment had given way to transcatheter intervention as the initial treatment of choice. The objective of this study was to evaluate how the changing policy of management had affected the immediate and long term outcomes.

Methods

Patients
Between November 1980 and October 1996, 34
consecutive infants younger than 3 months of age were treated for critical pulmonary stenosis. They all had suprasystemic right ventricular pressure, with variable degrees of hypoxaemia. Patients with cardiac anomalies other than a persistent arterial duct were excluded. All their clinical records were reviewed up to the most recent follow-up or the time of death. There were 25 boys and 11 girls. The median age at clinical presentation and intervention were 1 day (1 to 60 days) and 8.5 days (2 to 90 days), respectively. The mean weight at intervention was 3.4 ± 0.7 kg.

Cineangiographic review

We reviewed the antero-posterior and lateral projections of the right ventriculograms taken immediately before interventions. The size of the catheter was used as the magnification factor. The diameters of the pulmonary outflow tract and tricuspid valve were measured at early systole and diastole, respectively. A mean value of the measurements was derived for the 2 projections. The mean dimensions of both the pulmonary outflow tract and tricuspid valve in relation to the body surface area were expressed as the Z value using the normograms published by Hanley et al. The value was regarded as hypoplastic if it was less than −2. The Z value was derived according to the equation:

\[ Z = \frac{\text{measured diameter} - \text{mean normal diameter}}{\text{SD of the mean normal diameter}} \]

The equation was used to predict the size of the descending aorta at the level of the diaphragm. All measurements were taken at end-diastole. The right ventricle was considered hypoplastic if the index was less than 11. The equation used for calculation was:

\[ \text{Index of hypoplasia} = \frac{\text{diameter of tricuspid valvar and right ventricular inlet and outlet dimensions, with normalization to the size of the descending aorta at the level of the diaphragm.}}{\text{at the level of diaphragm}} \]

Interventions

Over the past 16 years, there has been an evolution of management in our institution. Reconstruction of the right ventricular outflow tract was the only available treatment prior to 1984. From mid 1984 to early 1990, closed pulmonary valvotomy was the mainstay of treatment. With the introduction of the transcatheter technique, since 1990, this has become the initial treatment of choice.

Ten patients underwent cardiopulmonary bypass with reconstruction of the right ventricular outflow and transjunctional patching, 8 with a pericardial and 2 with a GoreTex patch. Closed surgical pulmonary valvotomy was undertaken in 13 patients, accomplished via the transventricular approach without cardiopulmonary bypass. Percutaneous transcatheter balloon valvoplasty was attempted in another 13 patients, according to the technique described previously. It was feasible in 85% (11/13) of the patients. Those in whom it failed were managed by closed pulmonary valvotomy. The ratio of the diameter of the balloon to the pulmonary outflow tract was 1.2 ± 0.4. Infusion of prostaglandin would be continued for babies who could not maintain satisfactory oxygenation (<90%) following the surgical or catheterization intervention. The initial procedure-related mortality was noted for the 3 groups of patients.

Assessment of the procedures

The efficacy of the procedures was assessed according to the reduction of the ratio of right ventricular to systemic systolic pressure, post-intervention complications, length of hospital stay, residual gradient across the pulmonary valve, and the need for further interventions. The residual pressure gradient was serially assessed by cardiac catheterization and Doppler studies. The initial Doppler assessment of the pressure gradient across the pulmonary valve during the neonatal period was not included, since this was frequently underestimated because of the high neonatal pulmonary arterial pressure. Systemic oxygen saturation was not included as an index of assessment because of the confounding influence of the use of prostaglandin and oxygen supplementation.

Statistical analysis

All the results were expressed as mean ± SD unless otherwise specified. The comparison of the demographic variables, haemodynamic data, right ventricular dimensions, and duration of hospital stay amongst the three groups of patients was performed using simple analysis of variance. Comparison by the Bonferroni test was performed if p < 0.05. The mortality of different interventions was compared by the Fisher's exact test. The reduction of the ratio of right ventricular to systemic systolic pressure was compared by the two-tailed paired Student t test. Kaplan-Meier analysis was used to evaluate the freedom from reintervention after the initial intervention. Comparison between different groups was
performed using the log rank test. Multivariate risk-factor analyses for death and the need for reintervention were performed. The independent variables entered into the multivariate analyses were listed in Table 1. A value of p<0.05 was taken as statistically significant.

Table 1. Variables entered into the multivariate analyses for early procedure-related mortality and the need for reinterventions

1. Demographic data
   - age at presentation; age and weight at intervention; gender

2. Morphologic variables
   - right ventricular size as quantitated by the index of hypoplasia(6); Z value of the pulmonary valve; Z value of the tricuspid valve

3. Haemodynamic variable
   - right ventricular to systemic systolic pressure ratio before the interventions; use of intravenous prostaglandin infusion

4. Procedural variables
   - right ventricular outflow tract reconstruction; use of transcatheter patch; closed pulmonary valvotomy; transcatheter balloon valvoplasty.

Results

Patients

There was no significant difference amongst the three groups of patients in terms of the age at presentation and intervention, weight at intervention, the right ventricular dimensions, and haemodynamic data prior to intervention (Table 2).

Right ventricular dimensions

The Z value of the diameter of the pulmonary outflow tract was $-2.8 \pm 1.5$, and that of the tricuspid valve was $1.1 \pm 1.2$ (p<0.005). Hence, none of our babies had a hypoplastic tricuspid valve (Z > -2). In contrast, the pulmonary outflow was hypoplastic in 70%, and the right ventricular cavity was hypoplastic (Index less than 11) in 60% of the babies.

Infusion of prostaglandin

Amongst the 20 babies started on intravenous infusion of prostaglandin E2 before surgery or balloon valvoplasty, the medication was stopped in 14 who could maintain satisfactory saturations of oxygen (>90%) after the interventions. Infusion was continued in 6 patients (1/5 after patch reconstruction, 3/9 after closed valvotomy and 2/8 after balloon valvoplasty) for a mean of 6 days (range 1 to 20 days).

Mortality

The hospital mortalities for reconstruction of the right ventricular outflow tract and closed pulmonary valvotomy were 50% and 15%, respectively. The difference, however, was not statistically significant (p=0.17). In contrast, transcatheter balloon valvoplasty as an initial interventional procedure had no procedure-related mortality (p=0.01).

There was one late death occurring after balloon pulmonary valvoplasty when performed as a re-interventional procedure for the relief of significant residual pulmonary stenosis after closed pulmonary valvotomy. The guidewire positioned in the left pulmonary artery could not be retrieved after successful balloon dilation of the valve. Three hours following surgical exploration and removal of the
wire, the patient developed bilateral pneumothoraces and could not be resuscitated. The overall mortality attributed to balloon valvoplasty was 5.9% (1/17).

Multivariate analysis identified reconstruction of the right ventricular outflow tract with transannular patching, and the male sex, to be significant risk factors for death. The latter was likely due to statistical bias related to multicollinearity between the two variables. Right ventricular dimensions, and the use of intravenous infusion of prostaglandin, were not significant determinants of mortality.

Efficacy
A significant reduction in the ratio of right ventricular to systemic systolic pressure could be achieved after all three interventional modalities (Fig. 1). The ratio after reconstruction (0.3 ± 0.2) was significantly less than that after closed valvotomy (0.8 ± 0.4) and balloon valvoplasty (0.9 ± 0.3) (p=0.025). These haemodynamic data were obtained 9.3 ± 9.0 months and 16±19.4 months after reconstruction and closed valvotomy, respectively (p=0.44), but taken immediately after balloon valvoplasty. The residual pressure gradient across the pulmonary valve, assessed at similar intervals after the respective interventions and prior to reinterventions, was significantly higher after closed valvotomy as compared to the other two groups (p=0.01) (Fig. 2).

Reinterventions:
The overall rate of reintervention for the survivors was 37% (10/27). Patients surviving the surgical reconstruction were free of reinterventions. The freedom from reintervention after closed pulmonary valvotomy was 82%, 64% and 51% at 1, 5 and 10 years respectively. That for balloon valvoplasty was 78% at both 1 and 5 years (p=0.66) (Fig. 3). Balloon dilation of the pulmonary valve was performed in 6 babies who had significant residual stenosis, 5 after closed valvotomy and 1 after previous balloon dilation. Surgical reconstruction of the outflow tract was performed in 4 infants after closed valvotomy before the introduction of the transcatheter technique into our institution. Ligation of the arterial...
duct was required in 1 neonate after closed valvotomy for congestive heart failure, while 1 baby required construction of a systemic-pulmonary arterial shunt because of persistent severe cyanosis after balloon valvoplasty. The only risk factor for reintervention identified by multivariate analysis was a hypoplastic right ventricle as reflected by an index of less than 11. A hypoplastic pulmonary outflow tract did not predict the need for reintervention.

Clinical course after the interventions
Transcatherter balloon valvoplasty was associated with the least post-procedural complications and the shorter duration of hospital stay (p<0.001) (Table 3). All survivors remained asymptomatic, with a biventricular circulation on follow-up. The median duration of follow-up was 5.8 years (0.1 to 16 years).

Discussion
Recent reports on the use of balloon valvoplasty supported its application as the initial intervention for the treatment of significant valvar pulmonary stenosis.6-11 Few studies, however, truly compared the efficacy of surgical valvotomy to percutaneous balloon valvoplasty in critically ill neonates with severe pulmonary stenosis.4-5 It is true that we are now in the era that, apparently, makes this
comparative study seem outdated. Nonetheless, we are also practicing in an era in which evidence-based medicine is flourishing. The findings of this study support the evolution of the strategies for management of neonates and young infants with critical pulmonary stenosis.

The available literature provided somewhat contradicting recommendations. A multi-institutional study suggested that survival after percutaneous balloon valvoplasty was comparable to the best surgical techniques. While the authors accepted balloon valvoplasty as the method of choice for initial management, they recommended that, when expertise with this method is not available at an institution that is otherwise experienced in neonatal surgery, surgical valvotomy is indicated under cardiopulmonary bypass. On the other hand, another study from a single institution experienced in neonatal surgery reported a high mortality for surgical valvotomy (25% versus 9% for balloon valvoplasty). The highest mortality was associated with open valvotomy under cardiopulmonary bypass (43% versus 19% for closed pulmonary valvotomy). Our results are in keeping with the latter study, suggesting that reconstruction of the right ventricular outflow tract with transannular patching under cardiopulmonary bypass does not appear to be an optimal initial strategy. While both centres noted an improved survival by closed pulmonary valvotomy, it was balloon valvoplasty and its associated lack of complications, zero immediate mortality and the short stay in hospital (5.8 ± 2.5 days), that put the procedure beyond any doubt as the choice of initial intervention for critical pulmonary stenosis. The sparse incidence of failure to pass a guidewire or the balloon catheter through the pin-hole opening of the stenotic valve should not discourage balloon valvoplasty as the initial interventional therapy. This would decrease with increasing experience, and with the availability of laser or radiofrequency perforation of the stenotic or imperforate pulmonary valve.

Relief of the severe obstruction in the pulmonary outflow tract in early infancy is vital to the development of the hypoplastic right ventricle. In our study, as many as 60% of our patients had a hypoplastic right ventricle as defined by an index of hypoplasia. The tricuspid valvar annulus, however, was within the normal range for all these patients. The so-called 'hypoplasia' probably represented hypertrophy of the trabecular portion in response to the severe obstruction of the outflow tract, leading to diminished size of the cavity. Relief of the pulmonary stenosis was associated with an increase in right ventricular size, regression of infundibular hypertrophy, improvement of right ventricular diastolic function, and morphologic maturation of the pulmonary valve. Multivariate analysis failed to identify any of the indexes concerning the right ventricular inflow, outflow or cavity as significant causal factors for procedure-related mortality. Thus, previous suggestions that the choice of treatment should be dependent on the degree of right ventricular hypoplasia are not valid, especially in view of a currently high success rate of balloon valvoplasty. Furthermore, the favourable outcome of balloon valvoplasty, including patients with a hypoplastic pulmonary outflow tract in this and other studies, further suggests that transannular patching may not be mandatory. Our results also suggested that a small index of hypoplasia was predictive of reintervention. A small index probably reflects severe myocardial hypertrophy as a result of significant obstruction to ventricular outflow that would be difficult to relieve by just a single interventional procedure. Immediately after balloon valvoplasty, the high right ventricular pressure usually did not drop significantly. Nonetheless, progressive regression of infundibular hypertrophy, and the associated dynamic narrowing, explain a small residual pressure gradient on follow-up. Irrespective of the choice of treatment modality, a biventricular circulation was feasible in our survivors.
A major limitation of the study is the different periods in which the treatments were offered. With the general improvement in early diagnosis and referral, advancement in nursing care of sick neonates, and possibly the concomitant use of a systemic-pulmonary shunt, surgical open valvotomy under cardiopulmonary by-pass in recent days should have a lower mortality. Nevertheless, this probably would not compare favourably to the presently available safe and effective balloon valvoplasty.14-16 While the use of the catheter as a magnification factor could be a potential source of error for the right ventricular dimension measurements, the method has been widely accepted for good quality angiograms. This could be further supported by the correct choice of balloon size, a measurement based on similar magnification factor, which led to the successful outcome of valvoplasty in our patients. The haemodynamic data measured at different times after the various treatment modalities apparently did not favour balloon valvoplasty, bearing in mind however that the recordings were taken immediately after the dilation. Nonetheless, regression of the infundibular hypertrophy after the therapeutic catheterization ultimately gave a good result on follow-up. Although survivors of surgical reconstruction had minimal residual pressure gradient and were free of reinterventions, the potential risks associated with pulmonary regurgitation in the long term must not be overlooked. Further studies to compare the degree of and morbidity related to pulmonary insufficiency after the different treatment modalities should be considered. On the whole, this study demonstrated that it is appropriate to switch from surgery to trans- is for neonates and young infants with critical pulmonary stenosis.

References