BALLOON DILATATION FOR TREATMENT OF OBSTRUCTIVE CARDIOVASCULAR LESIONS IN CHILDREN

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BALLONDILATATIE ALS BEHANDELING VOOR
OBSTRUCTIEVE CARDIOVASCULAIRE AFWIJKINGEN BIJ KINDEREN

PROEFSCHRIFT

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aan de Erasmus Universiteit Rotterdam
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Aan mijn ouders
Voor Machteld en de kinderen

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CHAPTER 1

INTRODUCTION

The use of balloon-tipped catheters for the treatment of cardiac malformations was initiated by Rashkind and Miller, with the introduction of the atrial septostomy catheter in 1966 (1). This was an important historical milestone because it was the first therapeutic interventional procedure performed in the cardiac catheterization laboratory. Since its introduction balloon atrial septostomy continues to be of major importance for the non-surgical creation of an atrial septal defect in neonates with inadequate mixing of pulmonary and systemic venous blood at atrial level. The use of catheters for dilatation of peripheral artery stenosis was reported previously by Dotter and Judkins in 1964 (2). Almost a decade passed before the next major step in therapeutic cardiac catheterization was made. In 1974 Grüntzig reported the use of small cylindrical high pressure balloons for the dilatation of atherosclerotic arteries (3). In 1982 Kan and coworkers reported the use of large balloon catheters for the treatment of congenital valvular pulmonary stenosis (4). In the following years many reports on the use of balloon dilatation catheters for the treatment of obstructive cardiovascular lesions in children were published (5 - 20). These lesions included valvular stenosis as well as stenosed veins and arteries. Since then, balloon valvuloplasty and angioplasty have been applied both for native stenoses, and for residual or recurrent stenotic lesions after surgery.

The substrate of balloon angioplasty has been studied in animals and humans. Lock studied the effect of balloon angioplasty in surgically created coarctation of the aorta in the lamb (21). Microscopic examination revealed tearing of the intima and media initially, with healing of the intima within months (23). In experimental balloon dilatation of surgically excised human coarctations and in resected specimens after unsuccessful balloon angioplasty this was confirmed and even transmedial tears were observed, which could eventually have led to fatal bleeding or pseudoaneurysm formation. Because of this, there is concern about balloon angioplasty for the treatment of native coarctation. In our department balloon angioplasty for native coarctation has not been performed because of these risks, and the reported occurrence rate of restenosis.

In balloon angioplasty for native pulmonary artery branch stenosis in lambs only intimal tearing was observed, with healing at longer follow up (24). However, in clinical studies vessel perforation and rupture has been observed, with fatal outcome in some cases (18).

The morphological substrate of congenital stenosis of semilunar valves is frequently partial fusion of commissures. The initial surgical approach for congenital valve stenosis in the growing individual is commissurotomy. In valvular pulmonary stenosis this is done quite liberally, whereas in valvular aortic stenosis only a small commissurotomy is performed to prevent possible valvular regurgitation in the presence of a high systemic afterload. Balloon valvuloplasty has been documented to induce commissural splitting, but partial rupture of the valve may occur (26, 27). In current valvuloplasty practice the difference in approach between valvular pulmonary and valvular aortic stenosis is reflected by the balloon/annulus ratio chosen. In valvular pulmonary stenosis the preferred balloon size is 1.2 to 1.4 times the angiographically determined annular ring (28). In aortic valve stenosis a balloon size slightly smaller than the annular ring is chosen.

The percutaneous transluminal balloon dilatation technique has been reported for both native stenosis and residual or recurrent stenosis after previous surgical intervention. For native stenosis the dilatation technique has been applied for various diagnoses, such as valvular pulmonary and aortic stenosis, right ventricular outflow tract obstruction in tetralogy of Fallot, pulmonary artery branch stenosis, subaortic stenosis and coarctation of the aorta (4 - 9, 11, 15, 16, 18, 19). The variety of stenotic lesions after earlier surgical intervention in which balloon dilatation has been performed, is even larger (7 - 14, 17 - 20). These include obstruction of the Mustard baffle after operation for transposition of the great arteries, residual right ventricular outflow tract obstruction, obstructed valved or non-valved conduits between the right ventricle and the pulmonary artery, pulmonary artery branch stenosis due to an earlier systemic-to-pulmonary artery shunt, residual aortic valve stenosis, recurrent coarctation

and stenosed systemic-to-pulmonary artery shunts. Except for valvular pulmonary and aortic stenosis, and coarctation many of the reported series are small. For most of the studies the follow up is limited.

The aim of the studies described in this thesis was to evaluate the initial haemodynamic changes and possible complications of balloon dilatation for obstructive cardiovascular lesions in infants and children and relate these findings with the longer term follow up results. The studies were performed in the department of Paediatric Cardiology of the Sophia Children's Hospital in Rotterdam, except for those reported in chapters 2 and 8, which also include results in children treated in the departments of Paediatric Cardiology of the University Hospitals of Groningen and Leiden, The Netherlands, and the Royal Hospital for Sick Children, Edinburgh, Scotland.

In chapter 2 the results and follow up are described of balloon valvuloplasty for valvular pulmonary stenosis in children over 6 months of age. Chapter 3 deals with the results and problems encountered in balloon valvuloplasty for pulmonary stenosis in neonates and infants up to 6 months of age. The immediate effect of balloon valvuloplasty for valvular pulmonary stenosis on left ventricular function, as assessed by changes in the end-systolic end end-diastolic pressure-volume relationship, is described in chapter 4. In chapter 5 the short- and long-term follow up results of balloon valvuloplasty for valvular aortic stenosis are reported. These include patients with native valvular stenosis as well as patients who previously underwent surgical valvulotomy.

Recurrent stenosis after earlier surgical repair of aortic coarctation has been used as an indication for balloon angioplasty in our clinic. The results and follow up are presented in chapter 6. Chapter 7 deals with the results of balloon dilatation for less common cardiovascular obstructions, such as stenosed Mustard baffles, post surgical right ventricular outflow tract obstructions and pulmonary artery branch stenoses. Monitoring of the interventional procedure is routinely performed with fluoroscopy. Transoesophageal echocardiography is another monitoring modality and may be used in addition to fluoroscopy. The results of the use of transoesophageal echocardiography during interventional cardiac catheterization in children are described in chapter 8. Due to the small size of the femoral vessels in infants and children a mismatch between these vessels, especially the femoral artery, and the balloon dilatation catheter frequently occurs. This may result in femoral artery thrombosis, which is difficult to manage surgically in young children. The use of thrombolytic therapy for femoral artery thrombosis after retrograde arterial catheterization is described in chapter 9. In chapter 10 the results of the studies and the future perspective of balloon dilatation in the paediatric cardiac catheterization laboratory are discussed.

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CHAPTER 2

BALLOON VALVULOPLASTY FOR VALVULAR PULMONARY STENOSIS IN CHILDREN OVER 6 MONTHS OF AGE: INITIAL RESULTS AND LONG-TERM FOLLOW UP

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(submitted for publication)

SUMMARY

The initial, short- and long-term follow up results of balloon valvuloplasty for valvular pulmonary stenosis in children over 6 months of age, treated between August 1984 and December 1990 are reported. Valvuloplasty was planned and performed in 92 children over 6 months of age (range 0.8 - 17.9 years). Valvuloplasty decreased the invasively determined mean peak systolic gradient from 61 ± 34 (mean ± SD) to 27 ± 20 mmHg ($p < 0.001$). At follow up cardiac catheterization performed in 22 patients after 13 ± 5 months the gradient was 22 ± 23 mmHg (NS). Initially the continuous wave Doppler gradient decreased from 61 ± 23 to 26 ± 12 mmHg ($p < 0.001$). The gradient remained unchanged at early follow up after 0.6 ± 0.3 years being 23 ± 12 mmHg. No change in residual mean continuous wave Doppler gradient at long-term follow up after 3 ± 1.7 years was observed (21 ± 10 mmHg, NS). In the 41 patients treated before end 1986 the mean residual continuous wave Doppler gradient at long-term follow up after 5.1 ± 0.8 years was 21 ± 10 mmHg.

Mild pulmonary regurgitation was present in 77% of the patients at early follow up and in 80% of the patients at latest follow up. Right ventricular hypertrophy on the electrocardiogram was present in 83% of the children before valvuloplasty. At early follow up it was present in 44% and at latest follow up in 24% of the patients.

Pulmonary balloon valvuloplasty can be safely and successfully performed in children over 6 months of age. Restenosis is rare and the relief of the gradient persists in the long-term. Pulmonary regurgitation remains mild. The electrocardiogram is of little value in the follow up of these patients.

INTRODUCTION

The introduction of balloon valvuloplasty as an alternative for surgical valvulotomy for the treatment of isolated valvular pulmonary stenosis was introduced by Kan in 1982 (1). Several reports confirmed the success of this approach, though most reports deal with initial or short-term results only (2 - 9). Pulmonary valvuloplasty usually results in an adequate reduction of the transvalvular gradient (2 - 7). Residual infundibular obstruction is noticed in some patients but tends to decrease within months (10, 11). Complications of the procedure are inversely related to age, and are especially observed in young infants in whom the valvuloplasty is not performed on an elective base (3). Here we report the combined experience with balloon valvuloplasty for valvular pulmonary stenosis in children over 6 months of age from three Dutch paediatric cardiology centers, since the introduction of this technique in 1984. Special em-

phasis is given to the long-term effect on the residual valve gradient and on pulmonary valve regurgitation.

PATIENTS AND METHODS

All children older than 6 months of age that underwent balloon valvuloplasty for valvular pulmonary stenosis between August 1984 and December 1990 were included in the study. Initially the indication for treatment was mainly based on clinical and electrocardiographic examination. Quantification of the transvalvular gradient with continuous wave Doppler was performed routinely since 1987. A continuous wave Doppler gradient > 50 mmHg was used as the indication for further invasive evaluation and eventual valvuloplasty.

Ninety two children entered the study. There were 45 girls and 47 boys. The mean age was 5.9 years (range 0.8 - 17.9), the mean weight was 23.3 kg (range 5.7 - 67.5). In 3 patients Noonan's syndrome was present. Additional cardiac malformations were observed in 15 patients. At cardiac catheterization in 9 a shunt at atrial level was found (Qp/Qs range 1.1 - 1.5). Aortic valve stenosis was present in 2 patients, supravalvular pulmonary stenosis in 2 patients, branch pulmonary artery stenosis in 1 patient. Another patient had previously undergone surgical treatment for valvular pulmonary atresia by means of a valvulotomy and a Blalock-Taussig shunt.

Non-invasive studies

Standard surface 12-lead electrocardiogram was recorded. According to criteria published by Park et al. right ventricular hypertrophy was judged to be either present or absent (12). Echo-Doppler studies were performed routinely since 1987. No sedation was used. The transvalvular gradient was determined with continuous wave Doppler. Absence or presence of pulmonary or tricuspid valve regurgitation was assessed by either pulsed or colour-coded Doppler. Moderate right ventricular dilatation was noted to be present or not. Follow up data relate to studies performed in the first year after the valvuloplasty and to studies performed at latest follow up.

Invasive studies

Right-sided cardiac catheterization was performed under general anaesthesia. Pressure measurements were obtained with fluid filled catheters. The peak systolic gradient between right ventricle and pulmonary artery was measured. The eventual presence of intracardiac shunts was determined oxymetrically. A right ventricular angiogram was performed to document the valvular obstruction and to measure the annular diameter from the lateral projection. The in-

flated diameter of the balloon chosen was preferably 1.2 - 1.3 times the valve annulus (13). Heparin was not routinely administered. After gentle dilatation of the entry site in the femoral vein the balloon catheter was advanced over a guide wire and positioned at valve level. The balloon was inflated 3 times. Single balloons were preferred, but because of a large annular width in 5 patients a trefoil balloon was used. Shortly before the actual dilatation procedure the fractional inspiratory oxygen concentration was temporarely raised from 30% to 100%. After the valvuloplasty both the pressure measurements and right ventriculography were repeated. Bleeding from the groin was controlled by attentive local manual compression. Most patients were discharged the next day.

Cardiac catheterization was repeated after 1 year in 22 patients either to evaluate the result in the early years, or to elucidate the reason for suspected residual stenosis.

DATA ANALYSIS

Group data are presented as mean ± standard deviation. Statistical analysis was performed using Student's paired or unpaired *t*-test. Differences were considered significant at a p level < 0.05.

RESULTS

Invasive studies

In all children planned for the pulmonary valvuloplasty the procedure could be performed. The mean peak systolic transvalvular gradient before the valvuloplasty was 61 ± 34 mmHg and decreased to 27 ± 20 mmHg ($p < 0.001$). The mean balloon/annulus ratio was 1.2 ± 0.2, range 0.8 - 1.4. Repeat cardiac catheterization for evaluation of the result was performed in the first consecutive 22 patients after a mean follow up of 13 ± 5 months. The mean peak systolic transvalvular gradient was 22 ± 23 mmHg (NS). In 5 of these 22 patients a residual gradient > 30 mmHg was present. In 3 patients, with gradients ranging fom 52 - 165 mmHg repeat balloon valvuloplasty was successful. In these 3 patients the balloon/annulus ratio at the first valvuloplasty was 0.8 - 1. One patient had a hypoplastic valve annulus and underwent valve replacement with a homograft. In one patient with a residual gradient of 40 mmHg, in part due to a shunt through an atrial septal defect ($Qp/Qs = 1.3$), the gradient was accepted.

Complications

Significant complications occurred in 4 patients. In 1 patient entrapment of the balloon in the tricuspid valve apparatus resulted in moderate tricuspid regurgitation, due to partial rupture of the chordae, which is clinically well tolerated. One patient experienced an atrial flutter during the positioning of the catheter and was treated with cardioversion. One patient presented with a focal insult at the outpatient clinic 3 days after the valvuloplasty, likely due to a paradoxic embolus through a patent foramen ovale. During the valvuloplasty heparin had been administered. He received anti-epileptic treatment and recovered completely within days. Neurological follow up was normal. In one patient at follow up collateral circulation was observed, probably as a consequence of femoral vein occlusion.

Although several patients showed evidence of moderate infundibular stenosis after the valvuloplasty, β-blocking drugs have not been used routinely. Only in one patient propranolol was administered for a longer time. However, at follow up this patient proved to have a significant residual valvular obstruction and underwent a successful repeat valvuloplasty.

Non-invasive studies

All patients remained in sinus rhythm during the follow up. Right ventricular hypertrophy could not be judged because of a right bundle branch pattern in 2 patients and pre-excitation in 1 patient. The electrocardiogram before the valvuloplasty showed right ventricular hypertrophy in 83% of the patients and was within normal limits in 17%. At early follow up at 0.6 ± 0.3 years right ventricular hypertrophy was still present in 44% of the patients ($p < 0.001$). At late follow up after 3 ± 1.7 years 23% of the patients showed signs of right ventricular hypertrophy ($p < 0.05$).

The transvalvular continuous wave Doppler gradient before valvuloplasty was 61 ± 23 mmHg and decreased to 26 ± 12 mmHg after the valvuloplasty ($p < 0.001$). At early follow up at 0.6 ± 0.3 years the gradient was measured in 75 patients and remained unchanged (23 ± 12 mmHg, NS). At late follow up after 3 ± 1.7 years, the gradient measured in 79 children was 21 ± 10 mmHg (NS). Seven patients were lost of follow up, 1 patient underwent valve replacement with a homograft, and in 5 patients no adequate Doppler signal could be obtained due to technical limitations. In these 5 patients clinical and electrocardiographic findings pointed at a low right ventricular pressure and no signs of a substantial residual outflow tract obstruction.

Mild pulmonary regurgitation was present in 50/65 patients in early follow up and in 66/83 patients at latest follow up. Slight right ventricular dilatation was sometimes noticed but no paradoxical motion of the interventricular septum was observed.

The effect of the valvuloplasty was judged to be inadequate in 9 patients, all 9 in the first 2 years of our experience. In 4 of these patients the initial balloon/annulus ratio was < 1. Three patients underwent successful redilatation. One patient underwent valve replacement because of inadequate growth of the annular ring. In 2 patients valve dysplasia precluded a adequate relief of the gradient. In 2 other patients there proved to be additional supravalvular stenosis which was the cause of the residual gradient.

In 5 of the 9 patients with an oxymetically proved left-to-right shunt at atrial level during cardiac catheterization, this shunt had been recognized echocardiographically before the valvuloplasty. At follow up it remained unchanged in 4 patients, in 1 spontaneous closure was documented. At follow up there were no clinical signs related to an eventual increase in left to right shunt.

Focussing on the first consecutive 41 patients, who underwent the pulmonary balloon valvuloplasty before the end of 1986, the mean residual continuous wave Doppler gradient was 19 ± 9 mmHg at early follow up, and 21 ± 10 mmHg at latest follow up after 5.1 ± 0.8 years (NS). Pulmonary regurgitation was present in 68% at early follow up and in 71% at latest follow up (NS).

DISCUSSION

The treatment of valvular pulmonary stenosis aims to relieve the pressure overload of the right ventricle to prevent or diminish the problems of right heart failure in adult life, as well as the impairment of left ventricular function (13 - 15). In children over the age of 6 months the clinical symptoms related to valvular pulmonary stenosis are mostly mild or absent, and treatment is performed electively. Because complaints are frequently absent, the effect of the treatment has to be judged by either invasive or non-invasive diagnostic techniques. Several authors have described a good initial result of pulmonary valvuloplasty with a low complication rate (2 - 6). In most studies the follow up period does not exceed 2 years (5, 6, 8, 11). Our study confirms the initial effectiveness and safety of balloon valvuloplasty for valvular pulmonary stenosis in children over 6 months of age, as documented initially by invasive studies and non-invasively in the patients treated later. Renewed cardiac catheterization was not scheduled anymore in the presence of a small or absent transvalvular gradient on continuous wave Doppler, since the correlation between a continuous wave Doppler gradient and a gradient obtained at cardiac catheterization has shown to be good. Passagere infundibular obstruction was present in several patients but did not lead to clinical problems. In these electively treated patients there was no need for β-blocking agents.

McCrindle and Kan recently described their long-term results after pulmonary valvuloplasty (9). The results of our study with respect to short and long-term residual gradient are comparable with their findings. However, we can not confirm their observation that age at valvuloplasty under 2 years is a risk factor for a substantial residual gradient. This may be true for patients under 6 months of age, who are rarely treated on an elective base.

Our early and late follow up results show persistence of the initial gradient reduction. Surgical valvulotomy without the use of an outflow or transannular patch results at early follow up in an invasively obtained mean residual gradient of 30 mmHg (16). Unpublished long-term follow up data of children, who underwent a surgical pulmonary valvulotomy in Rotterdam between 1968 and 1980 revealed a residual mean continuous wave Doppler gradient of 9 mmHg (Dr. F. J. Meyboom, personal communication). The results of balloon pulmonary valvuloplasty in our series are comparable with these findings.

Restenosis which is mentioned by several authors, occurred in only 1 patient who had an initial inadequate relief of the gradient (17, 18). Elevated right ventricular pressure at follow up was often related to the use of an improperly selected balloon size in the early years. Although questioned by some, we agree that the use of oversized balloons is essential for an optimal result (6, 19). Additional obstruction at supravalvular level, or valve dysplasia were the other reasons for inadequate relief of right ventricular hypertension. Valvuloplasty of a dysplastic valve has been reported to be less successful, however in this study the 3 patients with Noonan's syndrome and dysplastic valves had a result comparable to that in the other patients. Pulmonary valvuloplasty can safely be performed in patients with a limited shunt at atrial level.

Although pulmonary valve regurgitation is present in the majority of these patients after balloon valvuloplasty, it does not result in major right sided dilatation at longer term follow up. However, as demonstrated in patients after surgical repair for tetralogy of Fallot, the effect of a persisting volume overload of the right ventricle should lead to some concern in the longer term.

Unexpected complications of pulmonary valvuloplasty may arise from the use of relatively large and stiff guidewires, positioned through the tricuspid valve. This may be even more hazardous if a stiff back-up wire is used, which is sometimes useful for proper positioning of the balloon across the stenotic valve. Partial rupture of chordae of the tricuspid valve, as was demonstrated in 1 patient, may be prevented by the use of transoesophageal echocardiography as a monitoring technique (20).

The electrocardiographic part of the study confirms that even in moderate pulmonary valve stenosis the initial electrocardiogram is normal in 17% of the patients (21). At short- and long-term follow up a normalization of the electrocardiogram is observed in many, but at the latest follow up right ventricular

hypertrophy was still present in 23% of the patients. With respect to the residual stenosis the electrocardiogram is of limited value in the follow up of these patients.

The indication for treatment in children with mild-to-moderate valvular stenosis is still debatable. It has been shown that the severity of valvular pulmonary stenosis seldomly increases after the age of 2 years (14, 15). Mild and moderate pulmonary stenosis is generally well tolerated and has hardly any effect on cardiac performance. Since percutaneous pulmonary balloon valvuloplasty is easy to perform and complications are rare, there is a tendency to treat patients with only small gradients too. The benefits of such a policy are not yet clear. There is no evidence that on the long-term mild or eventually moderate pulmonary valve regurgitation is better tolerated than mild stenosis. Especially in infants with subsystemic peak systolic right ventricular pressures we postpone balloon valvuloplasty unless progression of the gradient occurs.

In summary, balloon valvulopasty for valvular pulmonary stenosis in children over the age of 6 months is a safe and effective technique, with relatively low costs and persistent results in the longer term.

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CHAPTER 3

DETERMINANTS FOR OUTCOME OF BALLOON VALVULOPLASTY FOR SEVERE PULMONARY STENOSIS IN NEONATES AND INFANTS UP TO 6 MONTHS OF AGE

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SUMMARY

In a retrospective study the results of percutaneous balloon valvuloplasty for severe pulmonary stenosis in neonates and young infants were analysed. Eighteen patients under 6 months of age underwent balloon valvuloplasty for the treatment of severe pulmonary stenosis. In 7 patients dilatation was not successful, mainly because the pulmonary valve could not be passed, or positioning of even a small balloon was impossible. In 11 patients the dilatation was initially successful, although 3 of them needed a second intervention after 8 to 12 months. The only complication was a haemopericardium which was drained by puncture. The patients in whom valvuloplasty failed had a significantly more severe tricuspid valve regurgitation score (2.0 ± 1.1 vs 0.7 ± 0.6 on a scale of 0 - 3, $p < 0.05$) and a smaller diameter of the pulmonary valvular annulus (6.4 ± 0.8 vs 8.8 ± 1.8 mm, $p < 0.05$).

It is concluded that balloon valvuloplasty for severe valvular pulmonary stenosis in neonates and young infants is the preferred procedure, because it is safe and reasonably successful. Severity of tricuspid valve regurgitation and size of the pulmonary valvular annulus are major determinants for the outcome and mark a subgroup of patients for whom surgery may be a better option.

INTRODUCTION

Many reports have shown that in older children balloon valvuloplasty for valvular pulmonary stenosis is a safe and effective alternative for surgical valvulotomy, and for that reason it is considered to be the preferred procedure (1 - 5). However, in young infants and neonates the results of balloon valvuloplasty are less satisfying, with reported failure rates varying from 17 to 45% (6 - 10). The lower success rate may be related to the smaller size of the patients, but also to differences in anatomy of the right ventricle and its valves, and in haemodynamics when compared to older children. Besides the lower success rate, complications of the procedure are more common in this age group (1, 7, 9). These include femoral vein thrombosis, paradoxic emboli, and perforation of the myocardium.

Here we report the experience of three Dutch paediatric cardiology centers with non-elective balloon valvuloplasty in children under 6 months of age, with special emphasis on determinants for the outcome.

PATIENTS AND METHODS

All neonates and infants up to 6 months of age, who presented with severe valvular pulmonary stenosis between 1985 and 1991 underwent cardiac catheterization with the intention to perform valvuloplasty. Indications for treatment were prostaglandin dependant pulmonary circulation, cyanosis and/or echocardiographic evidence of suprasystemic right ventricular pressure. None of the infants had coronary artery fistula. Eighteen infants entered the study (12 girls and 6 boys). The age was 64 ± 65 days (mean ± SD) and weight was 5.1 ± 1.4 kg.

Doppler-echocardiography was routinely performed in all children, without sedation. Morphology of the right ventricular and pulmonary valve were documented. Until 1987 studies were performed with single gated Doppler combined with high pulse repetition frequency. If necessary, right to left shunting was confirmed by contrast echocardiography. From 1987 onwards colour-coded and continuous wave Doppler were used. Since Doppler derived pulmonary valve gradients before dilatation were considered unreliable because of haemodynamic instability of the patients, and varying degree of elevated pulmonary arterial pressure if the ductus arteriosus was still open, these data were not taken into account. Measurements of residual Doppler gradients after treatment were performed 1 day after the valvuloplasty and then yearly. Before valvuloplasty the presence or absence of tricuspid valve regurgitation was determined and compared with the angiographic data. Cardiac catheterization was performed under general anaesthesia. Pressure measurements were obtained by fluid filled catheters. In all children the left side of the heart was catheterised via the foramen ovale. The presence of intracardiac shunts was determined oxymetrically. A right ventriculogram was made in frontal and lateral projection. The annulus of the pulmonary valve was measured from the lateral projection. The magnification factor was determined by measurement of the known diameter of the catheter used. When the angiogram showed a clear delineation of the descending aorta, the right ventricular index as described by Lewis, was used for the determination of right ventricular hypoplasia (9, 11). This index is calculated by averaging the sum of the biplane measurements of tricuspid valve annulus, length of right ventricular inlet and right ventricular outlet, divided by 2 times the diameter of the descending aorta at the level of the diafragm. If this index is < 11 the right ventricle is considered hypoplastic.

Tricuspid valve insufficiency was graded angiographically on a 4 point scale, and was correlated with echocardiography (0 = no insufficiency, 1 = mild or moderate insufficiency with a local jet, 2 = severe insufficiency with opacification of the whole right atrium and caval veins, 3 = massive insufficiency, without any difference in opacification between right ventricle and right atrium.

Variable	Units	Failure	Success	p
age	days	51.4 ± 78.4	77.6 ± 61.7	NS
weight	kg	3.7 ± 1.1	4.8 ± 1.4	NS
Lewis-index		12.2 ± 3.5	13.1 ± 2.8	NS
tricuspid/aorta ratio		2.43 ± 0.89	2.33 ± 0.50	NS
pulmonary valve annulus	mm	6.4 ± 0.8	8.8 ± 1.8	< 0.05
pulmonary valve dysplasia	pts	3 / 7	4 / 11	NS
RV/LV pressure ratio		1.29 ± 0.29	1.41 ± 0.34	NS
tric.valve regurgitation score		2.0 ± 1.1	0.7 ± 0.6	< 0.05
grade 2 or 3 tric. regurgitation	pts	6 / 7	4 / 11	< 0.01

NS = not significant, pts = number of patients, RV = right ventricle, LV = left ventricle, tric. = tricuspid

Table I: Patient data referring to non-successful or successful pulmonary valvuloplasty.

Preferably dilatation was performed with a balloon with an inflated diameter of 1.2 to 1.3 times the size of the pulmonary valvular annulus, although in 4 children a smaller balloon was used. Only single balloons were used. The balloon was inflated three times. Shortly before dilatation the inspired oxygen concentration was raised to 100%. After valvuloplasty pressure measurements and right ventriculography were repeated.

DATA ANALYSIS

Group data are presented as mean ± standard deviation. Statistical analysis was performed using Student's paired or unpaired *t*-test, χ^2-test or Mann-Whitney *U*-test when appropriate. Differences were considered significant at a p level < 0.05.

RESULTS

Overt cyanosis was present in 11 of the 18 patients, and 6 patients were prostaglandine dependent. One child with clinical suspicion of Noonan's syndrome, had concomitant aortic valve stenosis. In all 18 children, two-dimensional echocardiography revealed a tripartite right ventricle which appeared substantially smaller than normal in 2 of them. A dysplastic pulmonary valve was present in 7 children. Severe tricuspid valve insufficiency (grade 2 or 3) was present in 7.

In 7 children percutaneous balloon valvuloplasty was unsuccessful. In 3 of these 7 patients the pulmonary valve could not be passed with a guidewire. In another 3 patients it was impossible to position even a small coronary dilatation

balloon correctly. In one child positioning of the guide wire through the pulmonary valve led to an inacceptable low arterial oxygen saturation and the procedure was discontinued. These 7 children were referred for surgical repair.

Dilatation could be performed in 11 children. The mean balloon/annulus ratio was 1.2 (range 0.9 to 1.3). The mean peak systolic gradient decreased from 84 ± 32 to 46 ± 30 mmHg ($p < 0.001$). The relevant data regarding differences between patients in whom valvuloplasty could or could not be performed are shown in table I. The children in whom balloon valvuloplasty was unsuccessful had significantly more severe tricuspid valve regurgitation and smaller pulmonary valvular rings. There was no difference in age, weight, right to left ventricular pressure ratio, and in right ventricular size as expressed by the Lewis-index. In both groups 2 patients had right ventricles with a Lewis index < 11. Nor was the tricuspid valve ring to descending aorta diameter ratio different between both groups.

There was one severe complication. In a 3 week old infant a moderate haemopericardium had developed after valvuloplasty. This probably had been caused by a guide wire perforating the right ventricular wall silently before valvuloplasty. The pericardium was drained successfully by puncture and recovery was uneventful.

At follow up in 3 children a second interventional procedure was necessary. Two of these children, who had undergone a primary dilatation with a balloon of 0.9 and 1.0 times the pulmonary valvular annulus, underwent successful redilatation with larger balloons (1.2 times the diameter of the valvular annulus) at 8 and 12 months after the initial procedure. In one child, who showed restenosis because of inadequate growth of the pulmonary valvular annulus after 8 months, a transannular patch had to be inserted to relief the outflow obstruction.

The residual Doppler gradient in patients 1 day after valvuloplasty was 37 ± 18 mmHg. Of the 3 patients that needed reintervention the valve gradient at 1 day was 30 ± 10 and 66 ± 25 shortly before reintervention (NS). Of the other 8 patients the residual gradient the day after valvuloplasty was 41 ± 20 mmHg, at latest follow up after 26 ± 20 months the gradient was 24 ± 18 mmHg (NS). None of the valvuloplasty treated patients showed substantial pulmonary valve regurgitation leading to right ventricular dilatation. Tricuspid valve regurgitation in this group remained minimal.

DISCUSSION

Percutaneous balloon valvuloplasty is almost uniformly successful for the treatment of valvular pulmonary stenosis in older children, in whom treatment

is performed electively (1 - 5). However, in neonates and young infants the results of pulmonary valvuloplasty are less satisfying. Reported patient series are small and vary considerably in outcome. In this study valvuloplasty was successful in 67% of the patients. This compares well with the success rates reported, varying between 55 and 83% (6 - 10).

Severe valvular pulmonary stenosis in the neonate and young infant is a rare disease, which may limit the paediatric cardiologists' experience with valvuloplasty for this malformation. However, the failures were evenly spread over the years, while in the mean time considerable experience was obtained with valvuloplasty and angioplasty in older children. Major technical advances in balloon catheters resulting in smaller shafts and improved handling did not have an impact on the success rate over the years either. This may in part be due to the fact that from early on in our experience we used small (3 or 4 mm, 3 french) coronary balloons as an alternative approach in case the selected balloon catheter could not be passed trough the narrowed valve at once. This technique has been reported by other investigators as well (7, 10).

Morphology of the right ventricle and pulmonary valve are thought to have a major impact on the outcome of valvuloplasty in these infants. There is a wide variation with respect to right ventricular morphology in these patients. Caspi et al found a strong correlation between relative hypoplasia of the right ventricle and failure of valvuloplasty, using the Lewis index (9). In our series there was no relationship between right ventricular size, as expressed by the Lewis index, size of the tricuspid valve compared to the descending aorta, and outcome. However, patients in whom balloon valvuloplasty failed had angiographically a significantly smaller pulmonary valvular annulus and a considerably more severe tricuspid valve insufficiency. In fact the only child with valvuloplasty failure, which had less than severe tricuspid insufficiency had a right ventricular hypoplasia with a Lewis index of 9.4. Of the 7 patients treated surgically, 3 needed a transannular patch for adequate relief of the obstruction, supporting the importance of annular hypoplasia as a risk factor for failure of valvuloplasty.

The importance of tricuspid valve regurgitation as a risk factor has not been noticed before. Of the patients treated successfully there was only one with a severe (grade 2) tricuspid regurgitation. Moderate to severe tricuspid regurgitation interferes with (balloon)catheter and guidewire positioning. In the most successful series reported by Zeevi et al tricuspid valve regurgitation was only present in 1 of the 6 patients (6).

In contrast to our experience with older children, at follow up restenosis was observed in 25% of the patients that were initially treated successfully. Although repeated dilatation was effective in 2 patients, in one infant growth of the annulus was inadequate, despite a normal right-sided cardiac output. These

observations emphasize the different behaviour of severe pulmonary valve stenosis in the age group under 6 months, when compared to older children.

In neonates and young infants balloon valvuloplasty for valvular pulmonary stenosis is the procedure of choice. It is safe and reasonably successful in the majority of the patients. Next to small size of the pulmonary valvular annulus, severity of tricuspid valve regurgitation is a major determinant for outcome. In those patients where valvuloplasty fails, surgery is mandatory (12). However, transcatheter laser assisted balloon dilatation might be an alternative in the near future (13).

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CHAPTER 4

ACUTE EFFECTS OF PULMONARY BALLOON VALVULOPLASTY AND PACING ON LEFT VENTRICULAR PERFORMANCE IN CHILDREN, ANALYZED BY SYSTOLIC AND DIASTOLIC PRESSURE-VOLUME RELATIONSHIPS

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SUMMARY

Increased right ventricular overload of both volume and pressure, may affect left ventricular systolic and diastolic function. This has been shown in animal studies and has been suggested in non-invasive studies in man. Altered geometry of the left ventricle, myocardial hypertrophy and changes in contractile state may be responsible for the change in function. Balloon valvuloplasty is an effective treatment for isolated valvular pulmonary stenosis in children, and results in an immediate decrease of right ventricular systolic pressure. Whether this results in immediate changes in left ventricular performance is unknown. Eight anaesthetized children (age 5.2 to 13.9 years) with moderate valvular pulmonary stenosis underwent pulmonary balloon valvuloplasty. Left ventricular function measurements before and after valvuloplasty were performed using a combined micromanometer-conductance catheter to obtain end-systolic (ESPVR) and end-diastolic (EDPVR) pressure-volume relationships employing inferior vena cava occlusion both at normal and pacing-induced increased heart rates.

Pulmonary valvuloplasty resulted in a decrease of peak systolic right ventricular pressure from 62.8 ± 13.5 to 34.4 ± 7.3 mmHg ($p < 0.001$), without significant changes in left ventricular systolic and end-diastolic pressure, or in cardiac index. The ESPVR was fitted to a linear function to obtain the slope (E_{es}) and the volume intercept at 75 mmHg (V_{75}). The EDPVR was fitted to an exponential function. At baseline, E_{es} was 1.68 ± 0.99 mmHg.ml^{-1} and V_{75} was 33.6 ± 21.8 ml. Neither valvuloplasty nor pacing, which increased mean heart rate from 81 to 112 beats/min ($p < 0.001$), resulted in significant changes of the parameters E_{es} or V_{75}. The EDPVR was not affected by valvuloplasty either, but pacing resulted in a change of its stiffness constant from 0.042 ± 0.019 to 0.034 ± 0.018 ($p < 0.05$) and pressure intercept from 0.97 ± 0.51 to 1.37 ± 0.86 mmHg ($p < 0.05$). The effect of pacing on left ventricular function before and after valvuloplasty was comparable.

Neither balloon dilatation for moderate valvular pulmonary stenosis in children, nor pacing within the physiologic range results in immediate changes in left ventricular contractile performance.

INTRODUCTION

Both animal experiments and studies in isolated hearts have shown that an increased right ventricular overload of both volume and pressure affects systolic and diastolic left ventricular function (1 - 8). Clinical studies in children with right ventricular outflow tract obstruction and in adults with pulmonary artery

hypertension have revealed shifting of the interventricular septum to the left, thereby altering the geometry of the left ventricle (9 - 13). Longstanding right ventricular outflow tract obstruction results in myocardial hypertrophy which may extend to the left ventricle (6, 14). Both septal shifting and myocardial hypertrophy are factors that may result in impaired left ventricular function. Relief of chronic right ventricular pressure overload in man, caused by pulmonary hypertension and by supravalvular pulmonary stenosis, has been studied echocardiographically and suggests that left ventricular performance returns towards normal (11, 12).

In isolated valvular pulmonary stenosis impairment of left ventricular function may become clinically important, but whether this holds true for moderate stenosis is unknown. Since isolated valvular pulmonary stenosis can be treated instantaneously by means of balloon dilatation, such a treatment offers the possibility to assess the immediate effect of an acute decrease in right ventricular pressure on left ventricular pump function (15, 16). The possible effect of such a right ventricular pressure overload reduction on the left ventricular end-systolic (ESPVR) and end-diastolic pressure-volume relationship (EDPVR) is unknown but may now be studied with a combined micromanometer-conductance catheter (17 - 20). This instrument allows the continuous and simultaneous registration of left ventricular pressure and volume during a preload intervention which is required to obtain the above relationships (18 - 20). To prevent possible confounding of the results by heart rate changes, which are known to affect the left ventricular pressure-volume relationship in animals (21 - 23), studies were performed both at baseline heart rate and during atrial pacing before and after valvuloplasty. This procedure also enabled us to study the specific effect of an increased heart rate on the ESPVR and EDPVR.

Left ventricular end-systolic elastance (E_{es}), defined as the slope of the ESPVR, has been proposed as a sensitive index of ventricular contractility, which is largely independent of loading conditions (24). However, shifts in the volume intercept of the ESPVR also reflect changes in contractile state (25, 26). Both changes in slope and volume intercept of the ESPVR can be assessed accurately in man with a conductance catheter combined with a high-fidelity micromanometer transducer (19, 20, 27, 28).

METHODS

Patients

Eight children (5 girls and 3 boys) aged 5.2 to 13.9 years (mean 7.9 years) with moderate valvular pulmonary stenosis underwent percutaneous pulmonary balloon valvuloplasty. Body weight ranged from 19.7 to 50.5 kg (mean 31.1

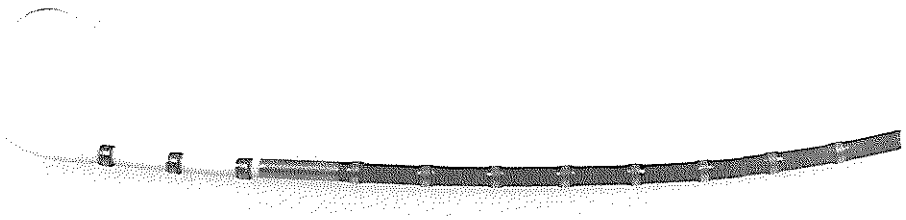

Figure 1: The conductance catheter in which a micromanometer transducer is incorporated.

kg). Informed consent was obtained and the study protocol was approved by the hospital ethical committee. The indication for treatment was isolated valvular pulmonary stenosis in the absence of other significant cardiac abnormalities, with a pressure gradient, assessed by continuous wave Doppler, of more than 50 mmHg, electrocardiographic evidence of right ventricular hypertrophy, and an invasively obtained indexed pulmonary valve area of less than 0.7 $cm^2.m^{-2}$.

Study protocol

Routine cardiac catheterization was performed with 0.02 mg/kg atropine and 0.1 mg/kg morphine as premedication. General anaesthesia was induced with midazolam 0.5 mg/kg and fentanyl 5 μg/kg, combined with vecuronium 0.1 mg/kg. The children were ventilated with 30% oxygen and 0.2% isoflurane. Expiratory carbondioxide was measured continuously and kept constant by adjusting inspiratory minute flow. Right heart and pulmonary artery pressures were obtained with fluid-filled catheters. Cardiac output was determined with the dye-dilution method. The pulmonary valve area was calculated from the

pressure gradient and the flow, using the simplified Gorlin and Gorlin formula. In addition, a right ventriculogram was made to measure the diameter of the valve annulus. To record left ventricular pressure and volume continuously, a custom-made 8 F combined micromanometer-conductance pigtail catheter with 10 electrodes (Dräger Medical Electronics, Best, The Netherlands) was carefully positioned in the left ventricle along the long axis with its tip in the apex (Figure 1). The method to obtain volume from conductance has been previously described (17, 18). Briefly, the method is based on measuring the time-varying electrical conductance of five segments of blood in the left ventricle, from which total left ventricular volume is calculated. A constant alternating current (20 kHz, 0.03 mA) is applied between the electrode in the apex and the one just above the aortic valve. Generally this was electrode 8, but electrode 9 or 10 could be used alternatively to adapt the size of the electrical field to the left ventricular axis length. Left ventricular volume (V) was derived from the five conductances measured between adjacent pairs of electrodes situated between the two current carrying electrodes, using the formula:

$$V(t) = (\frac{1}{\alpha})(\frac{L^2}{\sigma})G(t) - Vc$$

in which $V(t)$ is the instantaneous total volume, α a dimensionless slope constant, L the interelectrode distance, σ the specific resistance of the blood, and $G(t)$ the sum of the five instantaneous conductances. Vc is a volume correction term caused by the conductance of surrounding structures. To apply the current and to measure conductance-derived volume, a Leycom Sigma-5 signal conditioner-processor was used (CardioDynamics, Rijnsburg, The Netherlands). To obtain absolute volume values, the term Vc was obtained by injecting a 5 ml bolus of NaCl 10% solution in the main pulmonary artery. Because of interpatient variability of the slope constant , calibration of the conductance derived stroke volume was performed using the dye-dilution obtained stroke volume. Left ventricular pressure was measured with a catheter-mounted micromanometer. Continuously recorded pressure-volume loops were displayed on-line on an X-Y oscilloscope. To obtain the ESPVR and EDPVR, preload reduction was applied by transient occlusion of the inferior vena cava, using a catheter-mounted balloon (Figures 2 and 3). For this purpose, in the smaller children a Fogarty atrioseptostomy catheter was used (Baxter-Edwards Laboratories, Santa Ana, CA, USA), in the larger children a custom-made balloon occlusion catheter (Cordis, Miami, FL, USA) using balloon volumes up to 20 ml. The balloon was

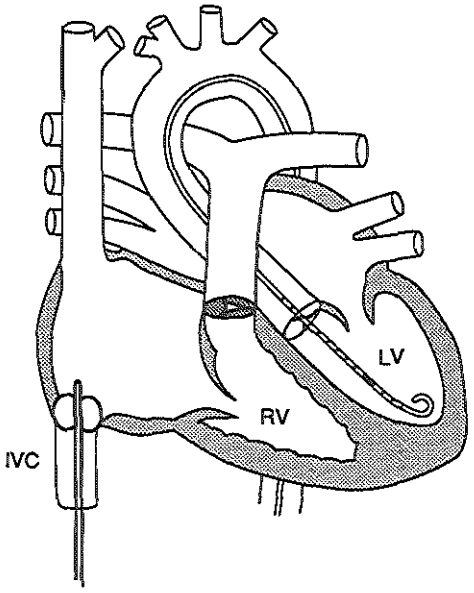

Figure 2: Scheme illustrating the position of the micromanometer-conductance catheter in the left ventricle (LV) and the occlusion catheter at the junction of the inferior vena cava (IVC) and the right atrium.

inflated with diluted contrast medium at the junction of the right atrium and the inferior caval vein and subsequently pulled downwards. To study the effect of increased heart rate, transoesophageal atrial pacing was performed using a booster pacer (model 2380, Medtronic, Minneapolis, MN, USA).

Pressure and volume data were calibrated and analyzed on a personal computer, using the Conduct-PC software package (CardioDynamics, Rijnsburg, The Netherlands). The slope (E_{es}) and the volume intercept at 75 mmHg (V_{75}) of the ESPVR were calculated, after subjecting the end-systolic pressure-volume points to linear regression. The use of V_5 is preferred over the use of V_0, the zero pressure volume axis intercept, because the former is defined at a physiologically meaningful level and circumvents the extrapolation problem of a possible nonlinearity of the ESPVR over a large volume range (29, 30). The end-diastolic

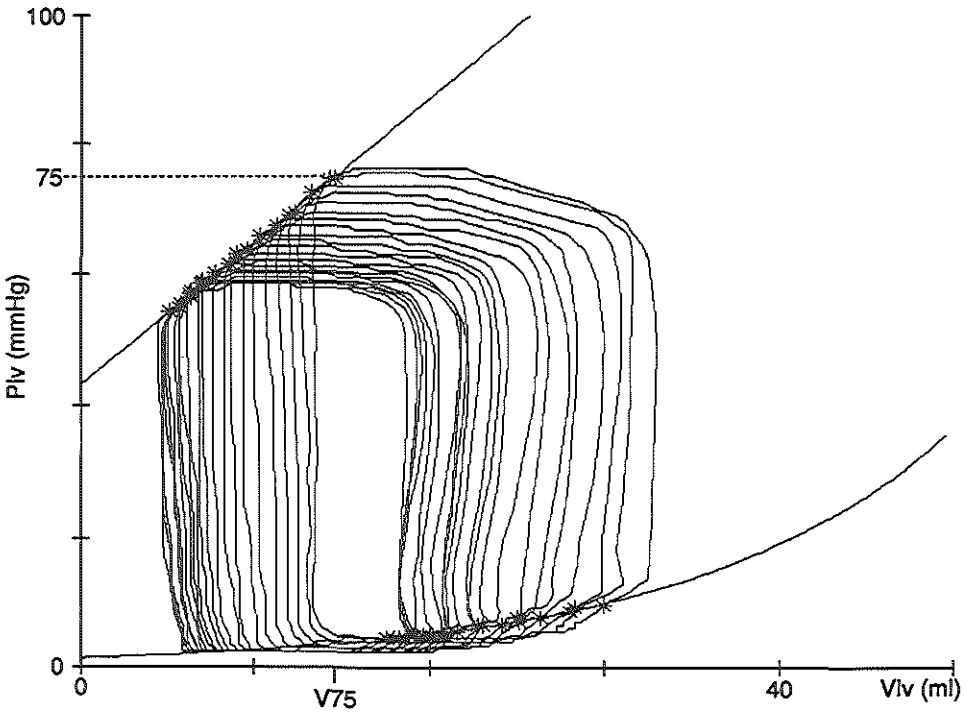

Figure 3: Representive series of pressure-volume loops obtained during inferior vena cava occlusion. The ESPVR and EDPVR are illustrated.

pressure-volume points were fitted to a simple mono-exponential function:

$$P_{ed} = a \cdot e^{\beta V_{ed}}$$

where a is pressure at zero volume, and β the diastolic chamber stiffness (28).

During the pulmonary valvuloplasty the inspiratory oxygen concentration was temporarily increased to 100%. After the valvuloplasty the structures surrounding the left ventricle (such as right ventricular blood volume) may have changed, thereby also changing the value of the volume correction term Vc. Therefore this quantity was measured again after the valvoplasty and subsequently all haemodynamic measurements were repeated.

Statistical analysis

Data are expressed as mean ± SD, unless stated otherwise. Statistical analysis on routine haemodynamic data was performed using Student's paired t-test. To

Pt	PSRV (mmHg)		PSLV (mmHg)		PSG (mmHg)		EDRV (mmHg)		EDLV (mmHg)		CI ($l.min^{-1}.m^{-2}$)	
	pre	post	pre	post	pre	post	pre	post	pre	post	pre	post
1	66	44	108	90	51	24	8	5	7	5	3.0	2.8
2	80	42	95	90	63	22	11	11	8	8	2.4	3.4
3	77	25	100	84	57	10	7	5	6	5	2.4	2.0
4	48	40	105	105	28	19	8	7	8	6	2.8	3.8
5	68	30	90	92	48	10	10	7	8	9	2.5	2.7
6	63	37	98	105	46	17	7	8	8	8	3.4	3.1
7	60	27	110	116	43	10	8	6	9	9	2.8	2.5
8	40	30	90	85	26	15	8	6	8	8	3.1	3.1
mean	62.8	34.4	99.5	95.7	45.3	15.9	8.4	6.9	7.8	7.3	2.8	2.9
SD	13.5	7.3	7.7	11.4	12.9	5.6	1.4	1.9	0.9	0.6	0.4	0.6

Pt = patient number, PSRV = peak systolic right ventricular pressure, PSLV = peak systolic left ventricular pressure, PSG = peak systolic gradient, EDRV = end-diastolic right ventricular pressure, EDLV = end-diastolic left ventricular pressure, CI = cardiac index

Table I: Peak systolic right and left ventricular pressure, valvular gradient and cardiac index pre and post pulmonary valvuloplasty.

test whether the results from the end-systolic and end-diastolic pressure-volume analysis were different before and after valvuloplasty or different with or without pacing, a repeated measures analysis of variance was performed by multiple linear regression analysis with dummy variables using effects coding (32, 33). A dummy variable representing the intervention was used, being 0 prior to valvuloplasty, and 1 after valvuloplasty, and a dummy variable to code the presence of pacing (dummy variable = 1) or no pacing (dummy variable = 0). To exclude the effect of interpatient variability in the quantities studied, 7 dummy variables were used to represent the 8 patients. To determine the statistical significance of the effects, an *F*-test was performed by dividing the mean square error of the dummy variable by the mean square error of the residual error. Differences were considered statistically significant at $p < 0.05$.

RESULTS

Valvuloplasty

Pulmonary valvuloplasty resulted in a decrease of the right ventricular peak systolic pressure from 62.8 ± 13.5 to 34.4 ± 7.3 mmHg (mean ± SD, $p < 0.001$). The peak systolic pulmonary valve gradient decreased from 45.3 ± 12.9 to 15.9 ± 5.6 mmHg ($p < 0.001$). The right ventricular end-diastolic pressure decreased from 8.4 ± 1.4 to 6.9 ± 1.9 mmHg ($p < 0.02$). The left ventricular peak systolic

pressure remained unchanged (99.5 ± 7.7 vs 95.7 ± 11.4 mmHg, NS). The left ventricular end-diastolic pressure (Ped) before valvuloplasty was 7.9 ± 1.6 and after valvuloplasty 8.2 ± 2.2 mmHg (NS). There was no change in the dye-dilution derived cardiac index (2.8 ± 0.4 vs 2.9 ± 0.6 $l.min^{-1}.m^{-2}$, NS, Table I). The shapes of the dye-dilution curves did not indicate the presence of shunts.

With respect to the pressure-volume relationships, valvuloplasty did not result in a significant change in E_{es} (1.68 ± 0.99 vs 1.95 ± 1.35 $mmHg.ml^{-1}$, NS), nor of its volume intercept V_{75} (33.57 ± 21.79 vs 31.77 ± 12.74 ml, NS). No significant changes were observed in V_{ed} (62.63 ± 37.30 vs 64.32 ± 27.58 ml, NS). The non-linear regression performed to characterize the EDPVR revealed no significant changes in its pressure intercept a (1.26 ± 0.86 vs 1.08 ± 0.54, NS) and chamber stiffness constant β (0.039 ± 0.023 vs 0.037 ± 0.013, NS).

Pacing

Transoesophageal atrial pacing was applied in all except the first patient and increased mean heart rate from 81 ± 15 to 112 ± 18 $beats.min^{-1}$ ($p < 0.001$). Pacing resulted neither in significant changes of E_{es} (1.73 ± 0.96 vs 1.90 ± 1.39 $mmHg.ml^{-1}$, NS), nor of V_{75} (30.86 ± 20.49 vs 34.94 ± 14.80 ml, NS). During the pacing-induced increase in heart rate V_{ed} remained unchanged (67.34 ± 34.50 vs 59.67 ± 31.47 ml, NS). Analysis of the EDPVR revealed an increase in its pressure intercept a from 0.97 ± 0.51 to 1.37 ± 0.86 ($p < 0.05$), and a decrease in chamber stiffness constant β from 0.042 ± 0.019 to 0.034 ± 0.018 ($p < 0.05$). A concomitant decrease in P_{ed} from 8.98 ± 2.12 to 7.14 ± 1.08 mmHg was observed ($p < 0.01$).

The effects of pacing on the parameters of the ESPVR (E_{es} and V_{75}), and the EDPVR (a and β), and on P_{ed} and V_{ed}, as assessed by the multiple linear regression technique were not significantly different before and after valvuloplasty.

DISCUSSION

The use of the combined pressure-volume catheter and aquisition of data during routine cardiac catheterization in the children studied presented no major problems. However, the size of the combined micromanometer-conductance catheter (8 French) precluded its use in smaller children. Occlusion of the inferior vena cava could be performed effectively when selecting an occlusion balloon appropriate for body size. Some investigators have expressed concern regarding the reliability of the absolute volume obtained with the conductance technique (34, 35). This concern mainly regards the volume dependence of the parallel conductance term. Other reports, however, have shown that changes in parallel conductance are small or doubtful (30, 36 - 39). To exclude the possi-

bility that the observed shifts in the pressure-volume loops were caused by changes in parallel conductance, its value was measured both before and after valvuloplasty, and the two values were used for correction of the individual absolute volumes.

The use of the ESPVR to assess left ventricular contractile performance in humans has been documented in several clinical studies (19, 20, 27, 28, 41 - 44). These studies in adults mainly relate to the evaluation of heart failure and/or coronary artery disease. The obtained absolute values for the E_{es} in this study compare well to those obtained in the normal human ventricle by Winnem et al (45). In healthy young men they observed values for E_{es} of 1.27 ± 0.25 mmHg.ml^{-1}. The negative value for the volume intercept at zero pressure V_0 in their study, emphasizes the need to evaluate volume changes in the physiologically meaningful range, such as V_{75} employed by us and others (28).

Valvuloplasty

In this study balloon valvuloplasty for valvular pulmonary stenosis resulted in an acute decrease of right ventricular systolic pressure of almost 50%. This compares well with the effect of pulmonary valvuloplasty reported in the literature (15, 16). Mean values for left ventricular peak systolic pressure, left ventricular end-diastolic pressure and cardiac index remained unchanged. The major changes in right ventricular systolic pressure did not significantly affect left ventricular contractile performance, because both the slope of the ESPVR and its volume intercept at 75 mmHg remained unchanged. Whether a shift of the interventricular septum to the right, as reported both in animal and human studies, may have occurred can not be deduced from these results. However, this is not likely to affect left ventricular volume because an increase in the septum-to-free wall distance appears to be accompanied by a similar decrease in the anterior-posterior dimension, thus maintaining an unchanged cross-sectional area and, hence, volume (2).

Morphological studies in valvular pulmonary stenosis in man have revealed extension of the hypertrophy of the myocardium to the left ventricle (14). In dogs, pulmonary artery banding resulted in an increased myocardial mass of both right and left ventricle, which may also affect diastolic function due to an increase in myocardial stiffness (6). In our study however, no immediate effect on diastolic left ventricular function was found. Whether a gradual decrease of hypertrophy of the right ventricle and the septum after valvuloplasty may eventually affect left ventricular diastolic function on the longer term is unknown.

The indication for treatment of valvular pulmonary stenosis with only small gradients is still debatable. In these patients a negative effect on left ventricular

performance might be an argument in favour of treatment. However, in our study there was no evidence for such an effect.

Increased heart rate

It has been shown that an enhanced heart rate increases the slope of the ESPVR in the canine heart, which is indicative of an increased contractility (21 - 23). To some extent a comparable leftward shift of the ESPVR is observed during infusion of dobutamine, both in animals and in man (19, 26, 36). No extensive studies have been performed regarding the effect of pacing on the contractile state of the left ventricle in man, as determined by the ESPVR. Kass reported the effect of pacing on the pressure-volume loop in a single patient, but the ESPVR during pacing was not determined (19). No further studies on the effect of pacing on ESPVR in man have been reported to our knowledge. Our study demonstrates that pacing within the physiologic range does not result in significant changes in left ventricular contractile performance. The observed but not significant trend towards an increase in E_{es} at a higher heart rate is comparable with the findings of Maugham et al in the isolated dog heart (22). They observed significant changes in E_{es} due to alterations in heart rate only below the normal range. However, in conscious dogs Freeman et al observed a steady increase in E_{es} when heart rate increased from 100 to 200 beats/min (23). To elucidate these phenomena in man, further studies with a larger range of rate changes are required.

The pacing-induced increase in heart rate did result in changes in the EDPVR of the left ventricle. Left ventricular end-diastolic pressure decreased, with a concomitant but non-significant decrease of end-diastolic volume. This probably reflects the effect of the shortened diastole. The small but significant increase of the pressure at zero-volume as well as the decrease of the chamber stiffness constant cannot be easily explained. Our results indicate that the ability of the left ventricle to respond to chronotropic stimulation was not affected by the substantial changes in right ventricular haemodynamics after pulmonary valvuloplasty.

In conclusion, the simultaneous pressure-volume studies revealed no significant changes in left ventricular contractile state shortly after balloon dilatation for moderate valvular pulmonary stenosis in children. Whether an effect may occur in the longer term can not be inferred from the present data. In addition, our study did not show an effect of a moderate increase in heart rate on left ventricular contractile performance. The small changes in left ventricular diastolic performance are hard to interpret. The conductance technique we used was able to detect rather subtle changes in left ventricular function, which might have been impossible to reveal with other volume measurement techniques. The feasibility of the application of the conductance technique for on-line determi-

nation of left ventricular pressure-volume relations in children during routine cardiac catheterization holds promise for the continuous assessment of ventricular function in this age group during therapeutic interventions.

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CHAPTER 5

SHORT- AND MID-TERM RESULTS OF BALLOON VALVULOPLASTY FOR VALVULAR AORTIC STENOSIS IN CHILDREN

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SUMMARY

In a 27-months period, 21 consecutive children (aged 0.1 - 15.7 years) with isolated valvular aortic stenosis underwent percutaneous transfemoral balloon valvuloplasty. Ten children had undergone earlier surgical valvulotomy. The indication for treatment was ST-T-segment changes at rest or during bicycle-ergometry, a continuous wave Doppler-derived transvalvular gradient > 60 mmHg or syncope, or a combination. Mean peak systolic left ventricular pressure decreased from 165 ± 19 mmHg to 131 ± 19 mmHg ($p < 0.001$). Mean end diastolic left ventricular pressure did not change significantly (12 ± 3 mmHg vs 11 ± 5 mmHg). Mean peak systolic valve gradient decreased from 71 ± 23 mmHg to 22 ± 11 mmHg ($p < 0.001$). Mean cardiac index remained unchanged (2.9 ± 0.8 $l.min^{-1}.m^{-2}$ vs 3.0 ± 0.7 $l.min^{-1}.m^{-2}$). Aortic valve regurgitation on angiography appeared or increased in 9 patients (up to grade 3 in 3 children). Non-invasive follow up studies were performed for 2 to 4.2 years (mean 2.8). ST-T-changes on the electrocardiogram at rest or during exercise were present in 6 patients before balloon valvuloplasty and had disappeared in all at 6 months follow up. Reoccurrence of ST-T-changes after a longer follow up was associated with severe valve regurgitation. Syncope was not observed after balloon valvuloplasty. The continuous wave Doppler gradient decreased from 94 ± 36 mmHg to 49 ± 15 mmHg ($p < 0.001$). After a follow up of 2 to 4.2 years (mean 2.8 years) it remained unchanged (43 ± 13 mmHg, NS). Aortic regurgitation on echocardiography appeared or increased initially in 11 patients. In some patients after longer follow up, an additional increase was observed. At the latest follow up grade 3 aortic regurgitation was present in 5 patients, 3 of whom underwent valve replacement. These 3 patients had undergone earlier surgical valvulotomy. Except for age, weight and left ventricular end diastolic pressure before valvuloplasty, there were no differences between the earlier operated and non-operated patients. Aortic valvuloplasty is effective and postpones surgery in the majority of patients. Occurrence or increase of aortic valve regurgitation may be induced, leading to valve replacement in 14% of the patients within 2 years.

INTRODUCTION

The introduction of balloon valvuloplasty for valvular aortic stenosis in children prompted several investigators to use this technique as an alternative to surgical valvulotomy. Balloon valvuloplasty has been used as an initial treatment, as well as for restenosis after earlier surgical valvulotomy. Questions remain as to whether balloon valvuloplasty is the primary choice of treatment, because of the associated risks of this technique, such as the occurrence of valvu-

lar regurgitation (1, 2). In most studies data on follow up are limited to 1 to 2 years (3 - 7). In this study we describe our experience with balloon valvuloplasty for isolated valvular aortic stenosis in children (with 2 to 4.2 years of follow up data), with special emphasis on the initial indications on the basis of which the balloon valvuloplasty was performed.

PATIENTS AND METHODS

Between April 1987 and July 1989, all children presenting consecutively at our institution with isolated valvular aortic stenosis and a continuous-wave Doppler-derived transvalvular gradient > 60 mmHg or ST-T-segment changes of ≥ 2 mm on the electrocardiogram, at rest or during exercise, or both, were included in the study. Syncope was also an indication for treatment, even if the other criteria were not met. In patients with an invasive transvalvular pressure gradient < 60 mmHg, the aortic valve area had to be < 0.7 $cm^2.m^{-2}$ to proceed to treatment. Patients with more than grade 2 valve regurgitation angiographically or with multiple cardiac malformations were not included. The inclusion criteria were fulfilled in 21 children. All 21 children (5 girls and 16 boys, mean age 7.7 years, range 0.1 to 15.9) had isolated valvular aortic stenosis, except one 5-years-old boy who underwent coarctation repair at the age of 1 day. Ten patients had undergone earlier surgical valvulotomy 2.1 to 11 years (mean 5.6 years) before balloon valvuloplasty. The continuous-wave Doppler pressure gradient was > 60 mmHg in 18 patients. Of these 18 patients, 1 had syncope, 2 had ST-T-segment changes at rest and 2 had ST-T-segment changes at exercise. In the 3 patients with a Doppler pressure gradient < 60 mmHg, 1 had syncope, and 2 had a positive exercise test. The indexed aortic valve area could be calculated in 19 patients (< 0.7 $cm^2.m^{-2}$).

Non-invasive studies

Standard surface electrocardiograms were recorded. The presence of left ventricular hypertrophy on the electrocardiogram was assessed according to voltage criteria (8). Bicycle ergometry was performed in patients with Doppler gradients < 70 mmHg. The electrocardiogram and exercise tests were judged positive when ST-T-segment changes ≥ 2 mm were present.

Echocardiography included M-mode and 2-dimensional studies combined with colour-coded Doppler. Continuous-wave Doppler was used to determine pressure gradients. Aortic regurgitation was evaluated semi quantitatively by a combination of Doppler and 2-dimensional imaging. Absence of any leakage was judged as grade 0, a regurgitant jet not exceeding the level halfway the anterior mitral valve leaflet as grade 1, a jet reaching to a level between the middle

and the tip of the anterior mitral valve leaflet as grade 2. If left ventricular dilatation was present in combination with a jet deep into the left ventricular cavity, and backflow in the aortic arch, the regurgitation was classified as grade 3. Electrocardiographic and echocardiographic studies were performed before and the day after the valvuloplasty, after 6 and 12 months and then yearly. Exercise studies at follow up were performed in patients if the age was appropriate.

Invasive studies

Right- and left-sided heart catheterizations were performed under general anaesthesia, including pressure measurements with fluid-filled catheters. Cardiac index was determined by means of the dye-dilution or Fick method. Aortic valve area was calculated with the simplified Gorlin and Gorlin formula. A supravalvular aortogram was obtained to grade eventual aortic regurgitation on a scale of 0 to 4 (9). From the angiogram, annular diameter was measured. The balloon size chosen was 0.9 - 1 time the valve annulus. Only single balloons were used. From April 1989 in the older children, stiff guide wires were used to improve the stability of the balloon during inflation. Balloons were inflated 3 to 4 times, up to pressures of 3 to 4 atm. During the actual dilatation procedure, fractional inspired oxygen concentration was temporarily raised from 30% to 100%. After the procedure, pressures and cardiac index were measured again, and aortography was repeated. Bleeding from the groin after removal of the catheters was controlled by attentive local manual compression. Patients were observed for 6 to 18 hours after the procedure in the intensive care unit, with special regard to bleeding and diminished femoral artery perfusion (10).

DATA ANALYSIS

Group data are presented as mean ± SD, and range. Statistical analysis was performed using Student's paired or unpaired *t*-test. Differences were considered significant at $p < 0.05$.

RESULTS

Cardiac catheterization data (table I)

Mean peak-systolic left ventricular pressure was 165 ± 19 before and 131 ± 19 mmHg after valvuloplasty ($p < 0.001$). Mean end-diastolic left ventricular pressure was 12 ± 3 mmHg before and 11 ± 5 mmHg after the valvuloplasty (NS). Mean peak systolic pressure difference between the left ventricle and aor-

Pt	Peak syst. LV press. (mmHg)		End diast. LV press. (mmHg)		Peak syst. grad. (mmHg)		Cardiac index ($l.min^{-1}.m^{-2}$)		Aortic valve area ($cm^2.m^{-2}$)		Syst. vascular resist. ($U.m^2$)	
	pre	post	pre	post	pre	post	pre	post	pre	post	pre	post
1 *	180	110	15	12	89	14	5.0 F	3.3	0.53	0.89	14.2	20.9
2 *	166	154	15	15	60	31	—	—	—	—	—	—
3	150	158	10	8	43	36	2.0	2.7	0.30	0.45	40.0	33.7
4	158	158	15	14	53	20	3.5	3.3	0.48	0.74	24.2	30.3
5	133	134	10	6	39	26	2.7	3.5	0.43	0.69	28.2	23.4
6	117	—	11	—	35	—	3.9	—	0.66	—	17.4	—
7 *	136	140	12	12	43	12	2.3	2.4	0.35	0.69	30.4	46.2
8	183	147	14	10	69	11	2.7	3.3	0.32	1.00	26.3	28.8
9	185	113	12	11	118	24	2.3 F	2.3	0.21	0.60	16.1	23.9
10 *	178	126	10	8	78	29	3.1	2.5	0.35	0.46	19.7	22.4
11	172	106	8	7	91	27	4.2	4.0	0.44	0.87	14.8	15.0
12 *	178	128	15	15	84	28	2.8	2.9	0.30	0.55	27.1	27.9
13 *	158	143	13	25	66	36	2.7	2.4	0.30	0.44	26.7	34.6
14 *	153	132	15	8	60	14	2.0	2.0	0.26	0.53	33.5	50.5
15	147	125	7	7	58	12	2.4	2.1	0.31	0.61	29.6	44.3
16	166	150	7	15	86	48	2.9	4.6	0.32	0.65	23.8	18.5
17 *	152	145	14	8	39	21	3.0	2.3	0.48	0.50	30.0	44.4
18 *	169	113	15	18	78	15	2.8	4.0	0.32	1.03	21.4	16.8
19 *	187	124	14	10	98	14	2.5	3.2	0.25	0.81	28.4	26.9
20	201	127	9	8	113	12	2.3 F	2.9	0.22	0.84	25.2	25.2
21	138	90	14	10	61	11	3.2 F	3.0	0.41	1.13	19.1	21.7
mean	165	131	12	11	71	22	2.9	3.0	0.35	0.71	25.2	29.2
SD	19	19	8	5	23	10	0.8	0.7	0.09	0.21	6.6	10.5
	$p < 0.001$		NS		$p < 0.001$		NS		$p < 0.001$		$p < 0.05$	

* = earlier surgical valvulotomy, F = cardiac index by Fick method, diast = diastolic, grad = gradient, LV = left ventricular, pt = patient, press = pressure, resist = resistance, syst = systemic, syst = systolic.

Table I: Cardiac catheterization data before and after balloon valvuloplasty for valvular aortic stenosis.

ta was 71 ± 23 mmHg before and 22 ± 10 mmHg after the valvuloplasty ($p < 0.001$). In 19 patients, the cardiac index (15 dye, 4 Fick) was 2.9 ± 0.8 liters.$min^{-1}.m^{-2}$ before and 3.0 ± 0.7 liters.$min^{-1}.m^{-2}$ after valvuloplasty (NS). Mean aortic valve area index was 0.35 ± 0.09 $cm^2.m^{-2}$ before and 0.71 ± 0.21 $cm^2.m^{-2}$ after valvuloplasty ($p < 0.001$). Mean systemic vascular resistance index increased from 25.6 ± 6.6 $U.m^2$ to 29.2 ± 10.5 $U.m^2$ ($p < 0.05$).

Angiographic data

Because severe femoral artery spasm after the balloon valvuloplasty prevented repeat angiography in 1 five-months-old infant, 20 patients were stud-

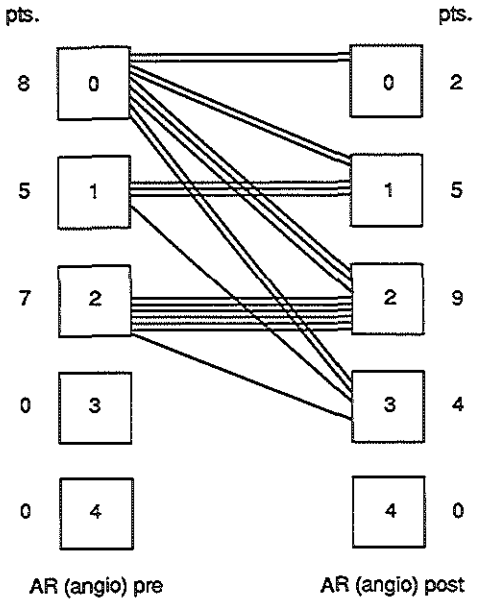

Figure 1: Angiographically (angio) determined aortic valve regurgitation (AR) before and after valvuloplasty.

ied. Aortography before balloon valvuloplasty revealed no regurgitation in 8 patients, grade 1 regurgitation in 5, and grade 2 in 7. After the balloon valvuloplasty, the aortic valve was still competent in 2 patients. Regurgitation remained unchanged in 9 patients, increased 1 grade in 4, two grades in 3, and 3 grades in 2 (Figure 1). Of the 4 patients with grade 3 regurgitation after balloon valvuloplasty, 2 did not have regurgitation before valvuloplasty, 1 had a grade 1 regurgitation and 1 had grade 2.

Electrocardiographic and exercise studies

Before balloon valvuloplasty, electrocardiography showed left ventricular hypertrophy without ST-T-changes in 16 patients, 10 of whom had no left ventricular hypertrophy anymore 6 months after balloon valvuloplasty. In 3 patients, the electrocardiogram before the valvuloplasty was normal, but showed left ventricular hypertrophy in 2 of them at 6-month follow up. Before balloon valvuloplasty the electrocardiogram at rest showed ST-T changes with signs of left ventricular hypertrophy in 2 patients; six months after balloon valvuloplasty the ST-T changes had disappeared in both patients. In one of these, who had a severe aortic regurgitation after balloon valvuloplasty, ST-T changes reappeared after 2 years. In one patient with left ventricular hypertrophy before the

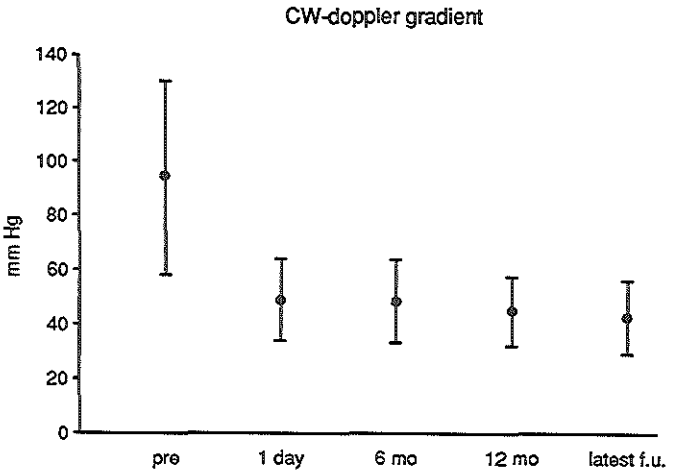

Figure 2: Transvalvular aortic gradient determined with continuous-wave (CW) Doppler before valvuloplasty, at 1 day, 6 months, 12 months and at latest follow up (f.u.).

balloon valvuloplasty, left bundle branch block occurred during balloon valvuloplasty and persisted up to 6 months, but had disappeared at 12 months. Exercise studies were performed in 4 patients before the balloon valvuloplasty and were abnormal with respect to ST-T-segment changes. The exercise-induced ST-T changes had disappeared in all 4 patients six months after the balloon valvuloplasty. Another patient with severe regurgitation after balloon valvuloplasty had short runs of ventricular tachycardia at 12 months, although there were no abnormalities at exercise at 6 months follow up.

Doppler echocardiography

The transvalvular pressure gradient determined with continuous-wave Doppler decreased from 94 ± 36 to 49 ± 15 mmHg the day after the balloon valvuloplasty ($p < 0.001$). At 6-month follow up, the pressure gradient was 48 ± 15 mmHg (NS), and at 12 months 45 ± 13 mmHg (NS). At the latest follow up (range 2 to 4.2 years, mean 2.8), the Doppler gradient was 43 ± 13 mmHg (NS; Figure 2). Aortic valve competence 1 day after balloon valvuloplasty was still present in 3 patients. Regurgitation remained unchanged in 7, and increased 1 grade in 8, two grades in 1, and 3 grades in 2. During follow up, changes also were observed (Figure 3). In 4 patients, grade 1 regurgitation increased to grade 2, and in 3, grade 2 increased to grade 3. At the latest follow up, 5 patients were judged to have grade 3 aortic regurgitation, 3 of whom underwent valve replacement.

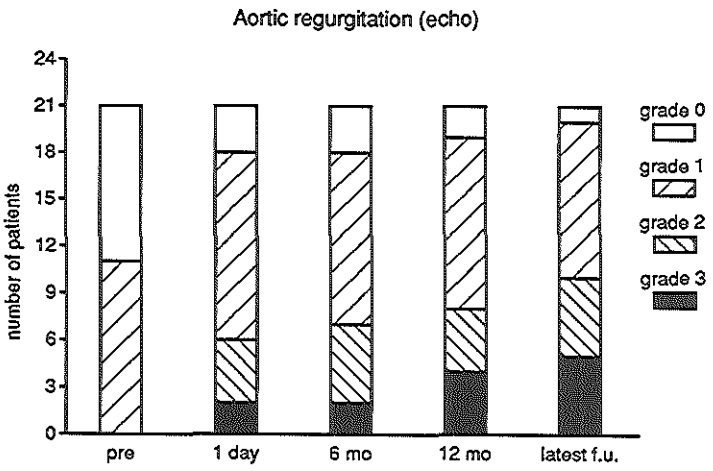

Figure 3: Aortic valve regurgitation determined with Doppler echocardiography (echo) before valvuloplasty, at 1 day, 6 months, 12 months and at latest follow up.

Short-term complications

There were no deaths. Substantial bleeding from the groin occurred in 5 patients needing transfusion. Femoral artery thrombosis occurred in 4 patients (19%), 3 of them were aged < 5 months. All 4 patients were treated with streptokinase with good results, except 1 who initially persisted to have impaired pedal pulses. However, at follow up, pulsations of both legs were equal. The increase of aortic regurgitation from grade 0 to 3 in 2 patients did not lead to acute clinical problems and both patients were discharged 2 days after balloon valvuloplasty. In 1 patient a left bundle branch block pattern on the electrocardiogram was still prominent on the day of discharge.

Clinical follow up

Syncope did not occur in any patient after balloon valvuloplasty. Clinical condition was good, even in the patients who developed substantial aortic regurgitation acutely or later. Aortic valve replacement was performed in 3 patients between 1 and 2 years after valvuloplasty. All 3 patients had undergone surgical valvulotomy before balloon valvuloplasty. The indication for valve replacement was severe aortic regurgitation and short runs of ventricular tachycardia during exercise in 1 patient (Table I, patient 13), and echocardiographically a grade 3 aortic regurgitation leading to progressive left ventricular dilatation in the 2 other patients (Table I, patient 10 and 19). In these patients the aortic root was successfully replaced by a pulmonary autograft and an allograft

Variable	Units		Surgery (n=10)	No surgery (n=11)	p
Age	year		10.6 ± 3.8	5.1 ± 4.2	< 0.01
Weight	kg		34 ± 12	19 ± 11	< 0.01
Peak syst LV press	mmHg	pre	166 ± 16	160 ± 25	NS
		post	32 ± 14	131 ± 23	NS
End-diast LV press	mmHg	pre	14 ± 2	11 ± 3	< 0.01
		post	13 ± 5	10 ± 3	NS
Peak syst gradient	mmHg	pre	70 ± 20	70 ± 29	NS
		post	21 ± 9	23 ± 12	NS
Aortic valve area	$cm^2.m^{-2}$	pre	0.35 ± 0.11	0.37 ± 0.12	NS
		post	0.64 ± 0.20	0.79 ± 0.18	NS
Cardiac index	$l.min^{-1}.m^{-2}$	pre	2.9 ± 0.8	2.9 ± 0.7	NS
		post	2.8 ± 0.6	3.2 ± 0.8	NS
Syst vasc resist	$U.m^2$	pre	25.7 ± 6.1	24.1 ± 7.3	NS
		post	32.2 ± 12.2	26.5 ± 8.4	NS
CW-Doppler gradient	mmHg	pre	92 ± 34	97 ± 39	NS
		post	47 ± 18	50 ± 12	NS
		6 mo	48 ± 21	49 ± 9	NS
		12 mo	45 ± 15	45 ± 10	NS
		latest	42 ± 17	43 ± 10	NS

diast = diastolic, LV = left ventricle, mo = months, resist = resistance, syst = systemic, syst = systolic, vasc = vascular.

Table II: Comparison of children who did or did not undergo earlier surgical valvulotomy.

was placed in the pulmonary position (11). The other 2 children with substantial regurgitation are followed at half year intervals.

Outcome related to eventual earlier surgery

A comparison was performed between the patients who had undergone earlier surgical valvulotomy and those with no previous treatment (Table II). Age and weight were significantly greater in patients who had undergone earlier surgery. Invasively determined haemodynamic parameters were not different between both groups, except for the end-diastolic left ventricular pressure before balloon valvuloplasty, which was slightly lower in the non-operated group. Doppler-derived pressure gradients were not significantly different between both groups before or after valvuloplasty. The increase in regurgitation angiographically was not significantly different between both groups. Echocardiogra-

phically, there was no difference between the groups, nor shortly after valvuloplasty nor at follow up. However, the need for valve replacement only occurred in the operated group.

DISCUSSION

The treatment of aortic valve stenosis in children aims to preserve left ventricular function and to prevent acute and chronic complications (12). To assess the severity of the stenosis the transvalvular pressure gradient is a practical measurement, especially when obtained with continuous-wave Doppler. Compared with invasively measured gradients, continuous-wave Doppler tends to overestimate the gradient owing to the difference in peak-to-peak versus a peak instantaneous measurement. In contrast, invasively measured transvalvular pressure gradients obtained under general anaesthesia may underestimate the severity of the stenosis owing to factors such as a diminished cardiac output. Therefore the cardiac output should be taken into account, and aortic valve area calculated. Furthermore, one should realize that in some patients the ventricular response (i.e. functional severity of stenosis) may not be reflected by the transvalvular gradient and aortic valve area. Changes of the ST-T-segment interpreted as a sign of subendocardial ischaemia and syncopal attacks may occur in patients with only moderate transvalvular gradients. Since this has been associated with morbidity and mortality, patients with such a presentation were also judged to have an indication for treatment (12).

In this study, balloon valvuloplasty directly resulted in a 20% reduction of peak systolic left ventricular pressure, and a 64% decrease in the transvalvular gradient. The only moderate reduction of peak systolic left ventricular pressure without changes in cardiac index must be explained by a concomitant increase in systemic vascular resistance, of which the cause is unclear. Several factors may explain this feature. The vasoconstrictive effect of an elevated inspired oxygen concentration may still be present at the time of sampling. In addition, probably due to the effect of general anaesthesia, the absolute systolic pressures are relatively low, so the effect on left ventricular systolic pressure (as measured invasively) is only limited. The follow up data only relate to non-invasive studies. This in part limits evaluation of the safety and the efficacy of the use of balloon valvuloplasty as alternative for surgical valvulotomy. The gradient reduction (as measured with continuous-wave Doppler) was not as large as that measured invasively (48% vs 64%). Restenosis at follow up was not observed. Furthermore, in the presence of significant regurgitation, continuous-wave Doppler overestimates the gradient.

Occurrence or increase of aortic regurgitation was noted in 45% of the patients after balloon valvuloplasty. Although during follow up in some patients an increase in aortic regurgitation occurred, none needed surgical intervention. The 3 patients that did need valve replacement within 1 to 2 years had a grade 3 aortic regurgitation on angiography directly after balloon valvuloplasty and 1 had a markedly elevated end-diastolic left ventricular pressure. The acute increase in aortic regurgitation was also reported by other investigators (1 - 5). The reasons for this increase are both technical and morphologic. Hazardous movements of the balloon may be prevented by using longer balloons in combination with a stiff guidewire, especially in the older children. However, in patients that underwent balloon valvuloplasty after July 1989 (not included in this study), using such a guide wire, substantial progression of aortic regurgitation was still observed.

Measurements of the valve annulus were obtained from the aortogram, which are (in our experience) comparable to those from the left ventriculogram. The measurements were obtained from the videoscreen with a calibration grid, but even the use of a grid does not warrant a completely reliable measurement. There was no relation between the relative size of the balloon used and the occurrence or progression of valve regurgitation. Transoesophageal echocardiography can elucidate the valve morphology, and the positioning of the balloon and guidewire (13). However, it remains questionable if a better knowledge of the valve morphology will provide more insight to the potential risk of inducing aortic valve regurgitation by balloon valvuloplasty. Our results confirm the findings of a recent study that a further increase in regurgitation is observed during follow up in some patients (1). Prolapse of the aortic valve, associated with rupture of the valve cusp due to valvuloplasty, is suggested to be progressive, especially when commissural support is lacking. In our patients with progressive regurgitation we have not been able to document prolapse (neither at echocardiographic examination or at surgery for valve replacement).

Except for age, weight and left ventricular end-diastolic pressure before valvuloplasty, there were no differences between the earlier operated and non-operated patients. However, the need for valve replacement occurred only in patients who had undergone earlier surgical valvulotomy.

Regarding the indication for treatment the continuous-wave Doppler gradient decreased to < 60 mmHg in all except 3 patients. Two of these patients also had substantial regurgitation that was likely to overestimate the gradient with continuous wave Doppler. In the third patient, the valve gradient after balloon valvuloplasty was slightly > 60 mmHg and remained unchanged during 2-year of follow up. However, before treatment, this patient had ST-T changes during exercise, that disappeared after balloon valvuloplasty and did not reoccur at follow up. Also all other patients with ST-T changes at rest or exercise had nor-

mal ST-T-segments shortly after the balloon valvuloplasty. Reoccurrence of these changes was clearly associated with the presence of severe aortic regurgitation with ventricular dilatation. Syncopal attacks did not occur in the few patients who presented with this complaint before balloon valvuloplasty. This study confirms the usefulness of exercise studies in these patients, also after earlier surgical valvulotomy (14).

In summary, 17 of 21 patients in this study definitely benefited from balloon valvuloplasty with regard to the initial indication for treatment. In 4 patients, the result was questionable owing to either the occurrence of severe aortic regurgitation or persistence of a substantial gradient. The immediate complications are acceptable, although femoral artery thrombosis (especially in children aged < 1 year) can prolong hospital stay and costs. Longer term follow up data are needed for a more definite evaluation of balloon valvuloplasty for valvular aortic stenosis in children.

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CHAPTER 6

BALLOON ANGIOPLASTY FOR AORTIC RECOARCTATION IN CHILDREN: INITIAL AND FOLLOW UP RESULTS AND MID-TERM EFFECT ON BLOOD PRESSURE

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(submitted for publication)

SUMMARY

Objective - To assess the direct and follow up results of balloon angioplasty for aortic recoarctation, with respect to the type of initial surgery, and to determine the mid-term effect on blood pressure.
Design - Prospective study of invasive haemodynamic and angiographic data and non-invasive data on upper body blood pressure.
Setting - Tertial referral center for paediatric cardiology.
Patients - 24 infants and children (age 0.3 - 16.2 years, mean age 5.9 years) who earlier underwent surgical correction for coarctation (14 end-to-end anastomosis, 9 subclavian flap angioplasty, 1 patch angioplasty).
Main outcome measure - Peak systolic gradient and angiographic aorta diameters over the recoarctation before, directly after and at follow up. Upper body blood pressure before, after and at latest follow up.
Results - The mean peak systolic gradient initially decreased from 35(15) to 12(9) mmHg ($p < 0.001$) and was 9 ± 10 mmHg at follow up after 1.4 ± 0.5 years. Only the patient group with a subclavian flap repair showed a further decrease of the residual gradient at follow up ($p < 0.05$). The coarctation diameter increased from 5.3 ± 2.6 to 7.7 ± 2.5 mm ($p < 0.001$) and a further increase to 9.3 ± 2.9 mm ($p < 0.01$) was present at follow up after 1.4 ± 0.5 years, without significant changes in other aortic diameters. Upper body systolic blood pressure decreased from 138 ± 24 to 115 ± 17 mmHg after balloon angioplasty and the effect on blood pressure persisted at a mean follow up of 3.7 years. The effect on bloodpressure was more pronounced in the patients with a subclavian flap angioplasty. Mortality after angioplasty for aortic recoarctation concerned 1 patient due to ventricular failure. Femoral artery thrombosis occurred in 3 patients. In 1 patient a small aneurysm occurred that had not increased at follow up. In 1 patient restenosis after angioplasty was redilated successfully. In 1 patient dilatation of a residual stenosis after angioplasty failed.
Conclusion - Balloon angioplasty for recoarctation is effective and is associated with accelerated growth of the dilated segment at follow up in most patients. The complication rate is acceptable. Follow up results point to a more pronounced effect of balloon angioplasty in patients that initially underwent a subclavian flap angioplasty. Mid-term clinical follow up reveals a persistent relief of upper body hypertension in most of the patients.

INTRODUCTION

The incidence of restenosis after surgical management of coarctation of the aorta, either end-to-end anastomosis or subclavian flap angioplasty, continues

to be a clinical problem. In particular this relates to patients that underwent surgical repair in infancy (1). The introduction of balloon angioplasty as an alternative for coarctation reoperation has gained wide acceptance. The immediate results of this treatment are satisfactory (2 - 8). Follow up after angioplasty is focussed on the incidence of restenosis and aneurysm formation. In this study we evaluated the haemodynamic and angiographic data of 24 patients with coarctation restenosis directly, and up to 2 years after the balloon angioplasty, with special regard to the type of surgery that had been performed initially. Clinical follow up to 5 years focussed on the effect on upper body systolic blood pressure.

PATIENTS AND METHODS

Patients

From October '86 to December '89 24 patients underwent balloon angioplasty for aortic recoarctation. Recoarctation was defined on the basis of absent or diminished femoral artery pulses, upper body hypertension and a substantial pressure gradient between upper and lower part of the body (8, 9). The mean age at angioplasty was 5.9 years (range 0.3 - 16.2). There were 12 boys and 12 girls. Surgical repair for coarctation had been performed 0.2 - 15.3 years earlier (mean 6.6). The type of repair was a resection of the coarctation and end-to-end anastomosis in 14 patients, a subclavian flap angioplasty in 9 and a patch angioplasty in 1. In 3 patients the end-to-end anastomosis was performed via a median sternotomy in combination with an intracardiac repair. In 5 patients there was an isolated coarctation, in 19 there were associated cardiac lesions (Table I). Mortality concerned 1 patient who died 2 days after balloon angioplasty. One patient was lost for follow up. Invasive follow up studies were performed in the remaining 22 patients after 0.4 - 2.6 years (mean 1.4). Clinical follow up studies were performed yearly up to 1.7 - 5.5 years (mean 3.7).

Technique

Cardiac catheterization was performed routinely under general anaesthesia. Peak systolic pressure differences were measured with fluid filled catheters. A biplane aortogram was made. The diameter was measured directly proximal to the coarctation site, at the level of the coarctation, just below the coarctation site and at the level of the diafragm. Heparin 100 units/kg was administered intravenously. The balloon angioplasty was performed by transfemoral approach with a single balloon. Balloon size was chosen 3 times the coarctation diameter, not exceeding the proximal aortic diameter by 120% (3). After the balloon angioplasty repeat measurements and angiography were performed. All angio-

Pt	Sex	Age surg. (year)	Type surg.	Add. diagnosis	Age BAP (year)
1	f	3.8	EE	VSD	13.3
2	m	1.3	EE	VAS	14.4
3	f	0.6	EE	VSD's	12.6
4	f	0.2	SF	VSD's	7.6
5	f	0.5	EE	VSD, SubAS, PDA	0.9
6	m	0.0	SF	ASD, VSD, PDA	0.7
7	f	0.0	EE	PDA, incompl.DA	0.3
8	m	4.4	EE	—	14.8
9	m	1.3	EE	ASD2, PAPVC	15.5
10	m	0.0	SF	VSD	5.8
11	m	0.0	SFrev.	—	3.1
12	m	2.3	EE	—	15.3
13	f	0.9	EE	VSD	16.2
14	m	0.0	SF	—	6.2
15	f	4.8	EE *	VSD, SubA	5.3
16	f	6.0	EE	—	14.6
17	m	0.2	patch	ASD, VSD'S, PDA	8.3
18	m	0.0	EE *	ASD, VSD, PDA	0.9
19	f	0.0	EE *	VSD, SubAS	0.3
20	f	0.1	SF	VSD	7.5
21	m	0.0	SFrev.	SubAS	7.8
22	f	0.0	EE	VSD, SubAS	6.6
23	f	0.0	SF	VSD, SubPS, PDA	6.2
24	f	0.0	SF	—	5.6

m = male, f = female, BAP = balloon angioplasty, EE = end-to-end, EE* = end-to-end via median sternotomy, SF = subclavian flap, SFrev. = reversed SF, incompl.DA = incomplete double arch., VSD = ventricular septal defect, ASD = atrial septal defect, SubAS = subvalvular aortic stenosis, SubPS = subvalvular pulmonary stenosis, PDA = patent ductus arteriosus.

Table I: Patient data.

grams were thouroughly reviewed for signs of intimal dissection. Complications of the procedure were listed.

At follow up the pressure withdrawal curves over the dilated site were recorded and biplane angiography was performed in projection angles equal to those at the time of balloon angioplasty. Diameters of the aorta at the four levels were measured. In case of intimal dissection biplane angiography was repeated again after one year to check further aneurysm formation.

Non-invasive studies consisted of resting bloodpressure measurements oscillometrically (Dinamap) at the right arm. Measurements were performed before, the day after balloon angioplasty and then yearly, combined with clinical examination.

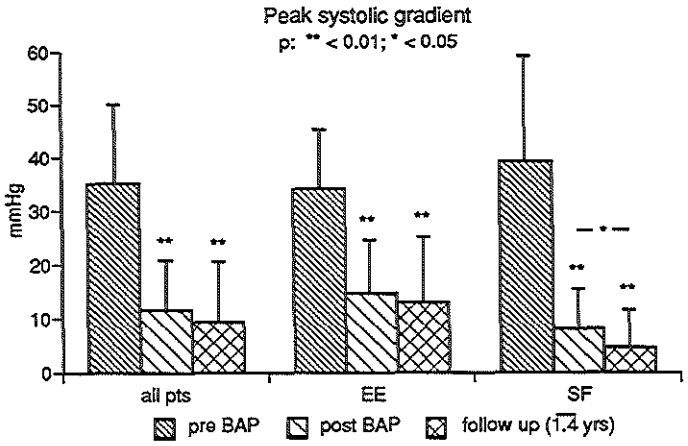

Figure 1: Invasive mean peak systolic gradient over the aortic reco-arctation before (pre) and after (post) balloon angioplasty (BAP), and at follow up (mean 1.4 years) for all patients (pts), and for those with an end-to-end (EE) anastomosis and a subclavian flap angioplasty (SF). There is a further decrease in residual gradient at follow up in the subclavian flap group.

DATA ANALYSIS

Statistical analysis of the data was performed using Student's *t*-test for paired or unpaired observations. Values are expressed as mean and standard deviation or range when appropriate. Differences were considered significant at $p < 0.05$.

RESULTS

Invasive studies

Haemodynamic data: The peak systolic gradient over the stenosis before balloon dilatation was 35 ± 15 mmHg and decreased to 12 ± 9 mmHg ($p < 0.001$) after dilatation (Figure 1). The pre-dilatation gradient in patients with an end-to-end anastomosis was not significantly different from that in patients with a subclavian flap repair (34 ± 11 vs 39 ± 19 mmHg, NS), nor was there a difference after dilatation (15 ± 10 vs 8 ± 8 mmHg, NS). For all patients the peak systolic pressure gradient at follow up after 1.4 ± 0.5 years was 9 ± 10 mmHg and not significantly different from the value directly after dilatation. The residual gradient at follow up in patients that had undergone dilatation after an end-to-end anastomosis was not significantly different from that in patients after a subcla-

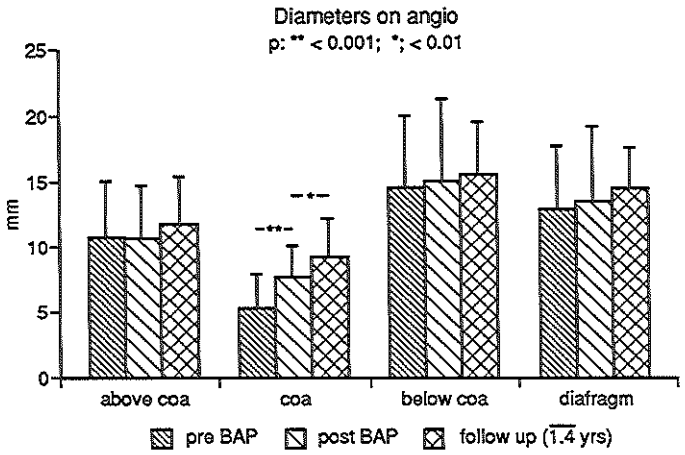

Figure 2: Angiographically determined mean aortic diameters at four levels before (pre) and after (post) balloon angioplasty (BAP) for aortic recoarctation (coa), and at follow up (mean 1.4 years).

vian flap angioplasty (13 ± 12 vs 5 ± 7 mmHg, NS). However, only the patients with a subclavian flap showed a significant further decrease in residual gradient, when compared to the result directly after dilatation (5 ± 7 vs 8 ± 8 mmHg, $p < 0.05$).

Immediately after the balloon angioplasty, in 12 patients the peak systolic pressure difference was less than 10 mmHg, in 6 between 10 and 20 mmHg and in 6 it was 20 mmHg or more. Of the 22 patients at follow-up, in 17 patients a gradient of less than 10 mmHg was present, in 1 it was between 10 and 20 and in 4 the gradient was 20 mmHg or more. In 3 of the 4 patients with a residual gradient of more than 20 mmHg at follow up an end-to-end anastomosis had been performed. In one of these 3 patients dilatation was repeated successfully. In the other 2 patients there was an elongated small segment of the distal arch not amenable for repeat balloon angioplasty. The initial result of the dilatation in these patients was disappointing too. In 1 patient with initially a subclavian flap repair in whom the peak systolic gradient had reduced from 43 to 23 mmHg and to 20 mmHg at follow up, repeat dilatation was not successful.

Coarctation diameter: The mean coarctation diameter increased from 5.3 ± 2.6 to 7.7 ± 2.5 mm ($p < 0.001$) directly after dilatation, and to 9.3 ± 2.9 mm ($p < 0.01$) at follow-up after 1.4 ± 0.5 years. Percentually the mean increase was 170% (range 106 - 369%) of the initial diameter immediately after the balloon angioplasty and 203% (range 115 - 383%) at follow up. There was no significant change of the proximal and distal aortic diameters, neither acutely nor at follow up (Figure 2). Furthermore with respect to coarctation diameter there was no

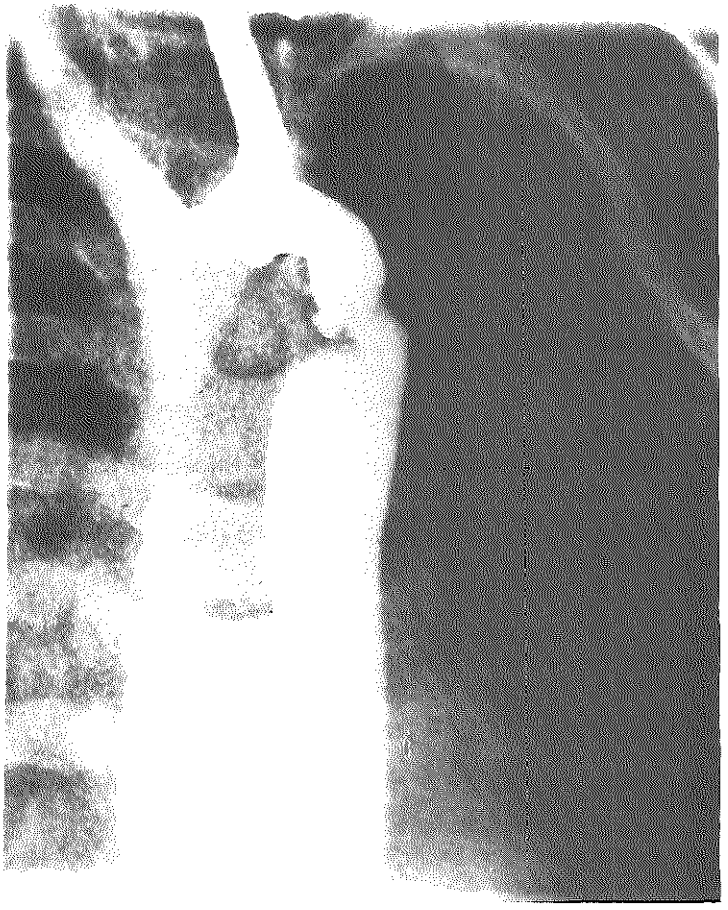

Figure 3: Aneurysm formation at the medial site after balloon angioplasty in a patient with initially a subclavian flap type repair, without enlargement at follow up. In this patient there was no residual gradient at follow up.

difference between patients with an end-to-end anastomosis and the patients with a subclavian flap repair.

Complications

One patient, who also had severe subaortic obstruction and poor left ventricular function, died 36 hours after emergency balloon angioplasty due to persistent heart failure. Angiographically the result of the balloon angioplasty was good. Post-mortem examination was not permitted. Intimal dissection leading to

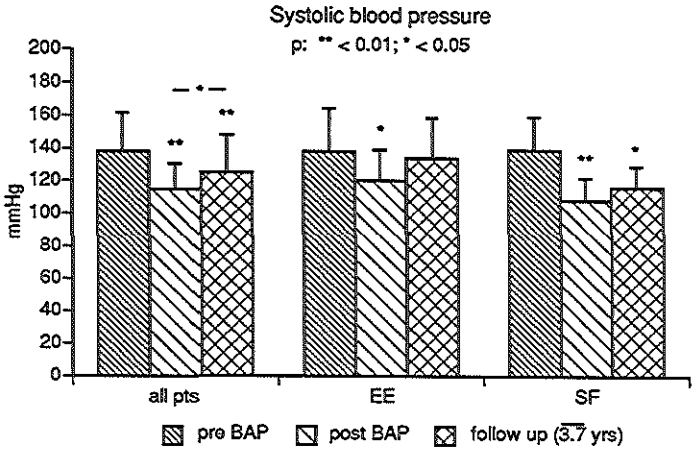

Figure 4: Right arm systolic blood pressure before (pre) and after (post) balloon angioplasty (BAP), and after a mean follow up of 3.7 years, for all patients, the end-to-end anastomosis group (EE) and the subclavian flap group (SF). The effect on blood pressure persists in the subclavian flap group.

a small aneurysm was seen in 1 patient, who had a subclavian flap type repair initially. The balloon/coarctation diameter ratio in this patient was 1.6. The aneurysm was small and had not increased in size at follow-up (Figure 3). No new aneurysms were observed at follow up in the other patients. Balloon rupture occurred in 4 patients, including the patient who presented with an aneurysm. In a 13-year-old girl a circular tear in the balloon complicated removal of the catheter, leading to femoral artery thrombosis. In contrast with our current policy she did not receive any anticoagulant or thrombolytic treatment (10). At follow-up she persisted to have diminished arterial pulsations of the leg, without any other signs of impaired circulation. Two other children developed femoral artery thrombosis. One of them, a 3 month's old girl, was treated with heparin only, without success. The third patient was successfully treated with streptokinase. In none of the patients there was excessive blood loss. One patient experienced a transient hemianopsia which had completely resolved after two days. Paradoxic hypertension after the balloon angioplasty has not been observed.

Non-invasive data

The mean peak systolic bloodpressure measured at the right arm was 138 ± 24 mmHg before and 115 ± 17 mmHg after balloon angioplasty ($p < 0.001$). Except for the patient in cardiac failure, in all patients the systolic bloodpressure was above the 95th percentile for age before dilatation (9, 10). After the inter-

vention the systolic bloodpressure was still above the 95th percentile in 4 patients. At latest follow-up (mean 3.7 years, range 1.7 - 5.5) the mean peak systolic bloodpressure was higher than that early after balloon angioplasty (125 ± 21 mmHg, $p < 0.05$, Figure 4), but still lower when compared to the value before valvuloplasty ($p < 0.01$). However, in the end-to-end anastomosis group the bloodpressure at latest follow up did not differ anymore from the value before valvuloplasty, whereas in the subclavian flap group the bloodpressure was still significantly lower (Figure 4). There were no significant differences in bloodpressure between the patients with an end-to-end anastomosis and those with a subclavian flap angioplasty before and immediately after balloon angioplasty, nor at latest follow up. The systolic bloodpressure at latest follow up was above the 95th percentile in 5 patients (3 end-to-end anastomosis, 2 subclavian flap).

Clinical signs of recurrence of coarctation after balloon angioplasty were not observed, except for the one patient that underwent a successful repeat dilatation. In this patient at follow up the effect of the second balloon angioplasty persisted.

DISCUSSION

The occurrence of restenosis after surgical repair for coarctation of the aorta remains a limited but consistent problem in clinical practice (1). Different surgical approaches have been advocated and used by the surgeons, which is reflected in this study. Initially, an end-to-end repair was favoured but then gradually the subclavian flap angioplasty was used more often in infants with reasonable results. In the last few years we expected that an extended end-to-end repair might overcome the problems of restenosis. However, especially when a combined approach of an intracardiac defect and a coarctation via a median sternotomy is performed in infants, restenosis is still observed (12).

This study confirms that balloon angioplasty for recoarctation immediately results in a substantial reduction of the invasively measured mean peak systolic gradient (67% in this study). The invasively measured gradients were obtained during general anaesthesia which may have led to underestimation of the gradient, due to factors such as diminished cardiac output and vasodilatation. Therefore changes in the peak systolic pressure in the ascending aorta are not discussed here. Our haemodynamic findings regarding the coarctation gradient however were comparable with those reported in the literature (1 - 8). After a mean follow up of 1.4 years, in most patients a considerable further decrease of the invasively obtained residual gradient was observed, especially in those after a subclavian flap angioplasty. Restenosis after the balloon dilatation was observed in only 1 patient after an end-to-end type repair. A residual stenosis with

still a gradient of 20 mmHg or more at follow up was observed in 3 patients. The mean increase of the coarctation diameter was 170% after balloon angioplasty. The follow-up results, showing a further increase in diameter, were consistent with the haemodynamic findings. In addition there proved to be an accelerated growth of the dilated segment in many patients.

After surgery for coarctation there remains an increased risk for cardiovascular complications and hypertension (13, 14). A higher probability of death in adult life is associated with persistence of high blood pressure after coarctation repair. The effect of balloon angioplasty on upper body systolic bloodpressure, one of the major reasons for treatment of recoarctation, was persistent in most of our patients, also at longer term clinical follow-up. Since absolute blood pressure values increase with age in this paediatric age group, the clinical relevance of these measurements was evaluated on the basis of blood pressure percentiles for age.

Both the persistence of the decrease in blood pressure at latest follow up, and the lower residual gradient at invasive follow up after 1.4 years in the subclavian flap group, with the absense of these phenomena in the end-to-end anastomosis group, point towards a somewhat better result of balloon dilatation for recoarctation after subclavian flap angioplasty. This difference related to the initial type of surgery has not been observed in previous studies (6, 8). In our study the patient groups are not comparable according to their age at the time balloon angioplasty was performed. However, the differences at follow up related to the type of surgery were not apparent immediately after angioplasty. This different pattern in the subclavian flap group may reflect the variation in morphological substrate. In recoarctation after a subclavian flap procedure, the obstruction in part is formed by a local residual shelf, which is likely to react better to angioplasty than a more extended circular narrowing observed after an end-to-end anastomosis. In addition there may be better growth potential in the subclavian flap patients. Another factor that may be of importance is the fact that in patients after an end-to-end anastomosis there will be discontinuity of the aortic wall elasticity and compliance.

The complications observed in our series of angioplasty are comparable with those known from other publications. In the patient that died after the angioplasty the cause of death was probably not related to the angioplasty. Femoral artery problems were observed in 14% of the patients, in two of the three patients in the first year of our experience. Although the use of low-profile balloons during balloon angioplasty and of thrombolytic agents when arterial thrombosis is suspected can reduce the incidence of femoral artery complications, it is unlikely that this problem can be eliminated completely. If possible the balloon angioplasty should be postponed until the weight of the patient is above 10 kg (11). The incidence of intimal dissection and subsequent aneurysm

formation directly or later after balloon angioplasty is a complication mainly observed in the use of this technique in primary coarctation (15). The occurrence of an aneurysm after angioplasty for recoarctation is also observed, and is confirmed in this study (6, 8). The aneurysm occurred in a patient with a subclavian flap repair and the balloon ruptured during inflation. The aneurysm occurred opposite to the site of the flap. The presence of scar tissue around the aorta, which should prevent aneurysm formation in these patients, may be less circumferential in patients after a subclavian flap than after an end-to-end type repair. Although at follow up no aneurysm enlargement was observed, the clinical importance of these aneurysms in the long-term remains unknown. The recent report on a fatal rupture during balloon angioplasty for recoarctation in a patient with initially a patch angioplasty, emphasizes the risk of this type of repair (16). Regular follow-up will be needed. Magnetic resonance imaging is suggested as an alternative for biplane angiography, however no studies comparing both techniques with respect to aneurysms have been reported yet (17).

In conclusion, this study showes that balloon angioplasty for recoarctation of the aorta can be performed with persisting results also at mid-term clinical follow-up, both in patients after an end-to-end anastomosis and more specifically in those after a subclavian flap type repair. The persistent reduction of upper body blood pressure in many patients is of major importance for diminishing long-term negative effects on cardiac function.

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CHAPTER 7

BALLOON DILATATION FOR LESS COMMON OBSTRUCTIVE CARDIOVASCULAR LESIONS IN CHILDREN

Maarten Witsenburg.

SUMMARY

Balloon dilatation in children for a variety of obstructive cardiovascular lesions other than valvular aortic stenosis, valvular pulmonary stenosis and recurrent coarctation was performed in 23 patients over a 6-year period. Indications were baffle obstruction after Mustard correction for transposition of the great arteries in 6 patients, postoperative obstruction between right ventricle and pulmonary artery in 8 patients and pulmonary artery branch stenosis in 6 patients. Dilatation of discrete subvalvular aortic stenosis, postoperative stenosis in the ascending aorta and of a stenosed modified Blalock-Taussig shunt were all performed once. Technical limitations precluded dilatation in 2 patients. In Mustard baffle obstruction dilatation resulted in a significant decrease of the mean venous gradient (9 ± 4 mmHg vs 3 ± 1 mmHg). In postoperative obstructions between the right ventricle and pulmonary artery dilatation was of very limited value, seven of the patients were subsequently operated upon. The result of dilatation of a stenosed branch pulmonary artery was successful in 2 of the 6 patients, and questionable in 2.

In this heterogenous group of stenotic lesions balloon dilatation is definitely beneficial for patients with Mustard baffle obstruction and some of the patients with a pulmonary artery branch stenosis.

INTRODUCTION

The use of interventional cardiac catheterization in the treatment of congenital heart disease was introduced by Rashkind in 1966 (1). The balloon atrial septostomy catheter he had developed was rapidly recognized as a major advance in the treatment of young infants with transposition of the great arteries, and replaced the surgical Blalock-Hanlon septectomy, with its associated risks in the cyanosed newborn. Although the introduction of the arterial switch repair in neonates reduced the use of this catheter to some extent, it continues to be of major importance in infants with inadequate mixing of pulmonary and systemic venous blood at atrial level. Incidently the septostomy catheter has been used to relief right ventricular outflow tract obstruction (2). A new breakthrough in interventional cardiac catheterization in children was the introduction of a balloon dilatation catheter for treatment of valvular pulmonary stenosis in children (3). This approach was important for the development of a wide range of balloon dilatation catheters. The dilatation technique has been applied for a variety of obstructive lesions in congenital cardiac disease, both for primary malformations as for residual or recurrent stenosis after surgical management. From the numerous reports that have been published in the recent years

some clear indications emerge. These are valvular pulmonary stenosis, valvular aortic stenosis and primary and recurrent aortic coarctation (4 - 9). Next to these indications, balloon dilatation has also been applied for many other obstructive lesions, including baffle obstruction after Mustard correction for transposition of the great arteries, subvalvular pulmonary stenosis including Fallot's tetralogy, supravalvular pulmonary stenosis, pulmonary artery branch stenosis, subvalvular aortic stenosis and stenosed systemic-to-pulmonary artery shunts (10 - 19).

In the Sophia Children's Hospital balloon dilatation was introduced in 1985. Indications most frequently used are valvular pulmonary stenosis, valvular aortic stenosis and recurrent coarctation after initial surgical repair. The results of these interventions have been discussed in the previous chapters. This study emphasizes on the use and results of balloon dilatation for other indications as they have been used in our clinic. These include baffle obstruction after Mustard correction for transposition of the great arteries, right ventricular outflow tract obstruction, branch pulmonary artery stenosis, subvalvular aortic stenosis, post surgical stenosis in the ascending aorta and stenosed systemic-to-pulmonary artery shunts.

PATIENTS AND METHODS

All 23 children that underwent balloon dilatation for stenotic lesions other than aortic valve stenosis, pulmonary valve stenosis and recurrent coarctation of the aorta, in the Sophia Children's Hospital between Januari 1985 until December 1991 were included in the study. There were 7 girls and 16 boys. Dilatations were attempted in Mustard baffle obstructions in 6 patients, postoperative obstructions between right ventricle and pulmonary artery in 8 patients and pulmonary artery branch stenosis in 6 patients. Furthermore, dilatation was performed for residual subaortic stenosis in 1 patient, post surgical stenosis in the ascending aorta in 1 patient, and for a stenosed modified Blalock-Taussig shunt in 1 patient. The initial results of the dilatation were evaluated on the basis of haemodynamic variables such as mean pressure gradients for venous connections and peak systolic gradients for ventricular and arterial pressures. Because evaluation of dilatation of pulmonary artery branch stenosis by means of pressure measurements stenosis is hampered if the contralateral pulmonary artery is normal, lung scintigraphy was used to evaluate the result whenever possible. The increase in arterial oxygen saturation was used to evaluate the result of Blalock-Taussig shunt dilatation. Follow up data of Mustard baffle obstruction after balloon dilatation was performed echocardiographically or invasively.

Stenotic site	Patients	Age (year)	Weight (kg)
Mustard baffle	6	10.3 ± 4.3	34.7 ± 15.3
RV-PA	8	7.1 ± 4.6	21.6 ± 10.7
PA-branch	6	7.1 ± 6.4	25.3 ± 21.8
Subv. aortic	1	9.1	35
Ascending aorta	1	4.3	17
B-T shunt	1	0.7	6.2

RV = right ventricle, PA = pulmonary artery, Subv = subvalvular, B-T shunt = Blalock-Taussig shunt.

Table I: Patient data.

Patient data for the different groups of patients, mean age and weight at intervention are summarized in Table I.

STATISTICS

Data are presented as mean ± SD, unless stated otherwise. Where applicable, statistical analysis was performed by Students paired or unpaired *t*-test. Differences were considered significant at $p < 0.05$.

RESULTS

Mustard baffle obstruction

Five patients had systemic venous baffle obstruction. In 3 the superior part of the baffle was narrowed. In 1 patient both superior and inferior baffle narrowing was present which were dilated at two separate sessions. In 1 patient the inferior baffle was narrowed. Another patient showed obstruction of the pulmonary venous return. In this patient a balloon dilatation catheter was advanced retrograde arterially but could not be positioned at the stenotic site. Subsequently this patient was reoperated successfully.

In the 6 dilated baffle obstructions the mean venous pressure difference between either the superior or inferior caval vein and the systemic venous atrium before angioplasty was 9 ± 4 mmHg. After angioplasty it had decreased to 3 ± 1 mmHg ($p = 0.01$).

Invasive follow up was only performed in the patient that underwent dilatation of obstructions of both the superior and the inferior baffle. Three years after the latest dilatation the residual mean gradient was 2 mmHg between the su-

perior caval vein and the systemic venous atrium and 1 mmHg between the inferior caval vein and the atrium. At follow up in all cases of superior and inferior baffle obstruction the echocardiogram showed open pathways and no substantial acceleration of Doppler flow.

Post surgical obstructions between the right ventricle and the main pulmonary artery

Attempts to dilate post surgical obstructions between the right ventricle and the main pulmonary artery were undertaken in 8 patients. Previous surgical correction of various cardiac malformations had been performed in all. In 1 patient an arterial switch operation was performed 6 months earlier and the narrowing was located at the site of the anastomosis in the main pulmonary artery. Earlier surgical correction of a tetralogy of Fallot had been performed in 5 patients. In 3 of these the stenosis was located at the distal end of the transannular patch. In 2 patients the stenosis was present at the level of proximal insertion of the patch in the right ventricular outflow tract. In 2 other patients, in whom a homograft conduit was placed between the subpulmonary ventricle and the pulmonary artery, the stenosis was located in the conduit just below the homograft valve. The mean peak systolic gradient across the stenosis before dilatation was 57 ± 19 mmHg and after dilatation 52 ± 22 mmHg (NS). Of these, in only one patient with a stenosis at the distal end of the patch the gradient was reduced to 22 mmHg and the procedure was judged to be successful. Follow up of this patient by means of Doppler flow analysis showed persistence of the gradient reduction. In the other 7 patients the obstruction was relieved surgically.

Pulmonary artery branch stenosis

Pulmonary artery branch stenosis was present in 6 patients. In 1 patient with tricuspid atresia, ventricular septal defect and transposition of the great arteries this stenosis was native and localized distally in the right pulmonary artery. In the other 5 patients the narrowing was secondary to earlier surgical intervention, being an end-to-end anastomosis in 3 patients, a Waterston shunt in 1 patient and a Blalock-Taussig shunt in 1 patient. In 3 patients lung scintigraphy was useful to evaluate the result. Of these 3 patients the dilatation resulted in a substantial increase in pulmonary artery flow in a patient with an end-to-end anastomosis and in the patient with a stenosis due to a Blalock-Taussig shunt, but had no effect in another patient with an end-to-end anastomosis. Of the other 2 post surgical patients, the one with a stenosis at the site of a prior Waterston shunt went for surgery and one patient is scheduled for invasive follow up. In the only patient with the native stenosis the procedure had no direct effect either. However, at angiography after 3 years the stenosis was less prominent.

Subvalvular aortic stenosis

One 9-year-old patient who had already undergone surgical excision and enuclation of a fixed subaortic stenosis 4 years earlier, dilatation of a recurrent subvalvular aortic stenosis was performed. The peak systolic gradient was 72 mmHg and remained unchanged after dilatation. Subsequently the patient was reoperated. Because of the disappointing result and an increasing awareness of the morphological substrate of these lesions no further patients with subvalvular aortic stenosis were listed for balloon dilatation (20).

Post surgical stenosis in the ascending aorta

A 4-year-old boy had undergone surgical correction for complex cardiac malformation including resection of a subvalvular aortic stenosis and repair of a hypoplastic aortic arch and coarctation. He was reoperated for a severe obstruction in the aortic arch but at follow up again a localized narrowing in the ascending aorta was found. An attempt to dilate this stenosis was unsuccessful because the balloon could not be positioned appropriately. Subsequently the patient was listed for surgery.

Stenosed systemic-to-pulmonary artery shunts

In one infant an attempt was undertaken to dilate a narrowed modified Blalock-Taussig shunt between the right subclavian artery and the right pulmonary artery. Dilatation was performed with a balloon with 5 mm diameter. Although initially the transcutaneous oxygen saturation increased from 0.69 to 0.80, after 3 months the saturation had dropped again and a central shunt was inserted surgically.

DISCUSSION

Interpretation of the results of balloon dilatation of these less common obstructive lesions in children with congenital heart disease is hampered by the small series of the patients treated. Also the morphological substrates vary considerably, which in this study is illustrated in the patients with an obstruction between the right ventricle and pulmonary artery. In angioplasty for coarctation the substrate is a tear in the intima and media of the vessel wall (21). Especially if part of the stenosis is formed by artificial patch material, the impact of dilatation will be mainly on the vessel wall. A recent report of fatal bleeding after balloon dilatation of recurrent coarctation in which initially a patch repair was used, emphasizes this point (22). Although this applies for several of the dilatations in this series, we did not encounter this complication. The presence

of extensive scar tissue around the stenotic site may be of importance in preventing transmural tears.

Technical limitations precluded dilatation in 2 patients. In the other patients the result of the dilatation varied.

Baffle obstruction after a Mustard procedure for transposition of the great arteries

An atrial switch operation for transposition of the great arteries, either Mustard or Senning, may be complicated by an obstruction of the venous pathways due to intra-atrial baffle hardening and shrinking at the longer term. This will result in either systemic or pulmonary venous congestion. Although this can be managed surgically, in our series the effect of dilatation was successful in all but one patient. This confirms the reports from the literature (10, 11). However the number of procedures published is very limited. The indication for treatment is not well described. A mean venous gradient of 2 - 3 mmHg between caval vein and the systemic venous atrium is a regular finding following a Mustard's procedure. We did not observe any complications but a non fatal cardiac tamponade has been observed once (Dr. M. Talsma, personal communication). Although invasive follow up was rarely performed, clinical and echocardiographic follow up data suggest persistence of the result.

Post surgical obstruction between right ventricle and main pulmonary artery

Balloon dilatation of right-sided conduit obstruction due to a stenosed prosthetic valve has been reported to be successful in 30% of the patients, postponing surgical intervention in some of them (12). Balloon dilatation of the right ventricular outflow tract in tetralogy of Fallot has been advocated to increase pulmonary bloodflow (13, 14). However, since the substrate of this palliative procedure is unclear and morbidity and mortality associated with balloon dilatation in this group of patients is substantial, in our point of view initial surgical management of such patients should be the preferred way of treatment.

Acquired obstructions between the right ventricle and the pulmonary artery may complicate surgical repair on the longer term. Hancock valved bioprostheses may obstruct due to calcification and excessive intimal proliferation. Also with the use of homografts there is a risk of obstruction, especially at the site of the proximal or distal anastomosis. If the stenosis is very localized, an attempt to dilate the stenosis may be undertaken. Our results were disappointing in most patients. During inflation of the balloon frequently the waist disappeared, but reoccurred during deflation. Other reports show a somewhat better initial result, but little is known about persistence of the gradient reduction at longer term.

Dilating pulmonary artery stenosis after an arterial switch operation is reported to be disappointing as well (15). Our experience in one patient is in line with this.

Peripheral pulmonary stenosis

The VACA-registry reported a large series of angioplasties for pulmonary artery branch stenosis (16). Native stenoses as well as branch stenoses after earlier surgery have been dilated. Balloon angioplasty results only in a moderate reduction of pressure difference and some increase of vessel diameter. Local complications such as vessel perforation and rupture have been observed. Death has been reported in 3% of the patients (16). However, one should realize that some of the more distal stenoses are not amenable for surgery. Our experience showes that the procedure was definitively beneficial in 2 patients. This is in accordance with the 50% success rate from the literature.

Recently the use of redilatable intravascular stents has been suggested for pulmonary artery branch stenosis (23, 24). This technique is currently under investigation.

Fixed subaortic stenosis

In this type of subvalvular aortic stenosis a spiralling fibrous shelf in the left ventricular outflow tract is causing the obstruction. Balloon dilatation may result in a partial relief of the gradient but also in this lesion it is likely that surgical management is more effective (17). Since the shelf is often morphologically related to the mitral valve apparatus, the dilatation procedure may result in mitral valve damage and should therefore in our opinion not be performed.

Stenosed shunts

Increasing the pulmonary bloodflow by insertion of a systemic-pulmonary shunt is useful as a temporary or definitive palliation in a variety of congenital cardiac malformations. In most institutions a modified Blalock-Taussig anastomosis is the preferred surgical procedure. During growth a stenosis may occur on either the proximal or distal site. Balloon dilatation of these stenoses may result in a substantial rise in systemic oxygen saturation, due to increased pulmonary artery bloodflow (18, 19).

In patients with congenital heart disease balloon dilatation may also be effective as a treatment for stenotic cardiovascular lesions other than pulmonary and aortic valve stenosis and coarctation. However, the eventual result is dependent on the site of the lesion, morphology and eventual surgical history. The patients with Mustard baffle obstructions and some of the patients with pulmonary artery branch stenosis will mostly benefit from this approach. Further

research on a combined treatment of balloon dilatation and stent insertion will probably result in a growing population that may be treated effectively.

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CHAPTER 8

TRANSOESOPHAGEAL ECHOCARDIOGRAPHIC MONITORING OF INTERVENTIONAL CARDIAC CATHETERIZATION IN CHILDREN

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SUMMARY

Transoesophageal echocardiography was used prospectively in 22 children scheduled for interventional cardiac catheterization (9 with pulmonary valvuloplasty, 5 with aortic valvuloplasty, 1 with pulmonary angioplasty, 2 with aortic angioplasty, 2 with patent ductus arteriosus occlusion and 3 with Mustard baffle dilatation) to determine its potential value as a monitoring technique. The patients ranged in age from 0.9 to 14.6 years (mean 5.4) and in weight from 9.5 to 49.2 kilograms (mean 21.1).

Studies were completed in all patients without complications. Pre-intervention studies provided important new information in 2 patients, leading to cancellation of the planned procedure. Major contributions of transoesophageal monitoring include 1) a real time assessment of catheter placement across either atrioventricular valve and the aortic valve during balloon valvuloplasty; 2) immediate assessment of aortic valve and aortic wall morphology during balloon dilatation; and 3) detailed morphologic and haemodynamic information together with enhanced catheter guidance during Mustard baffle dilatation. After pulmonary valvuloplasty, partial rupture of the tricuspid valve was documented in one patient. In 2 patients balloon catheter position was modified according to the transoesophageal findings. The assessment of pulmonary valve morphology and transcatheter occlusion of a patent ductus arteriosus was not enhanced by single-plane transoesophageal monitoring. Pulsed wave Doppler studies contributed additional information in the assessment of immediate haemodynamic changes after interventional procedures.

Paediatric transesophageal echocardiography is a new important guiding and monitoring technique during interventional cardiac catheterization in children. It can provide additional real time imaging information, immediate identification of complications and assessment of haemodynamic changes.

INTRODUCTION

Over the past decade, interventional cardiac catheterization has become an important new therapeutic approach to the treatment of congenital heart disease in childhood (1 - 3). Balloon dilatation has become the treatment of choice for pulmonary valve stenosis (4 - 6), and recoarctation of the aorta (7 - 9). In selected cases, umbrella closure of patent ductus arteriosus has become an alternative to surgical closure (10, 11). Clamshell occlusion of atrial or ventricular septal defects has been effected (12, 13) and is at present the subject of growing interest.

The monitoring of such interventional cardiac catheterization procedures is at present performed by a combination of radiographic screening to monitor balloon or device placement with angiocardiography and pressure recordings to evaluate the immediate results of the procedure. However, these techniques frequently prove suboptimal. Intracardiac morphology, including the acute changes in vessel wall morphology and valve leaflet structure, is not well demonstrated radiographically. Repeat angiocardiography is often impractical during the procedure. Precordial ultrasound studies have been used to monitor a variety of cardiac interventions, including the Rashkind balloon atrial septostomy (14). However, such studies may be cumbersome and interfere with the procedure.

Since the introduction of single-plane transoesophageal echocardiography into paediatric cardiology 2 years ago (15 - 17), it has rapidly gained acceptance as a diagnostic technique in the primary diagnosis of congenital heart disease (18 - 19) and a perioperative monitoring technique (20, 21) and is useful in the postsurgical follow up period (22, 23). However, to date, no study has addressed the question whether or where transoesophageal echocardiography might be helpful in monitoring and guidance over the wide range of cardiac interventional procedures currently used in paediatric cardiology.

METHODS

Study patients

To determine the value of transoesophageal echocardiography in the monitoring and guidance of interventional cardiac catheterization in the paediatric age group, 22 children were studied prospectively. Hospital ethical approval was obtained before the study and informed parental consent was obtained before individual studies were performed.

Patient age at investigation ranged from 0.9 to 14.6 years (mean 5.4), and weight from 9.5 to 49.2 kg (mean 21.1). Nine children were scheduled for pulmonary valvuloplasty, five for aortic valvuloplasty, one for pulmonary angioplasty, two for aortic angioplasty for recoarctation, two for patent ductus arteriosus occlusion and three for balloon dilatation of systemic venous pathway obstruction after a Mustard procedure (Table I).

Transoesophageal echocardiographic studies

The studies were performed in all children with use of a prototype single-plane paediatric transoesophageal probe (Department of Experimental Echocardiography, Thoraxcenter, Rotterdam) interfaced to either a Hewlett-Packard Sonos 1000 or Toshiba SSH 160 A ultrasound system. The maximal shaft diam-

Pt	Age (year)	Weight (kg)	Diagnosis	Procedure planned
1	3.6	13.1	Aortic stenosis	Balloon aortic valvuloplasty
2	0.9	9.5	Pulmonary stenosis	Balloon pulmonary valvuloplasty
3	12.7	49.2	Recoarctation	Balloon angioplasty
4	2	13.8	Pulmonary stenosis	Balloon pulmonary valvuloplasty
5	2	11.5	Patent ductus arteriosus	Ductus occlusion
6	4.2	20.6	Patent ductus arteriosus	Ductus occlusion
7	1.5	11.2	Pulmonary stenosis	Balloon pulmonary valvuloplasty
8	3.9	14.8	Pulmonary stenosis	Balloon pulmonary valvuloplasty
9	14.6	48.4	Aortic stenosis	Balloon aortic valvuloplasty
10	4.7	16.8	Pulmonary stenosis	Balloon pulmonary valvuloplasty
11	12.4	43.8	Mustard baffle obstruction	Balloon dilatation
12	4.3	16.2	Mustard baffle obstruction	Balloon dilatation
13	9.1	27	Recoarctation	Balloon angioplasty
14	12	38.4	Aortic stenosis	Balloon aortic valvuloplasty
15	7.7	24.4	Aortic stenosis	Balloon aortic valvuloplasty
16	1.9	13.6	Pulmonary stenosis	Balloon pulmonary valvuloplasty
17	5.3	18.2	Left pulmonary artery stenosis	Balloon pulmonary angioplasty
18	2.4	12.8	Aortic stenosis	Balloon aortic valvuloplasty
19	4.6	16.8	Pulmonary stenosis	Balloon pulmonary valvuloplasty
20	1.5	13	Pulmonary stenosis	Balloon pulmonary valvuloplasty
21	1.7	13.1	Pulmonary stenosis	Balloon pulmonary valvuloplasty
22	5.2	18.7	Mustard baffle dilatation	Balloon dilatation

Table I: Patient data, diagnosis and procedures in 22 cases.

eter of the probe measured 7 mm and the maximal transducer dimensions were 5 x 10 mm. Steering facilities were restricted to anterior and posterior angulation only. The transoesophageal probe allowed for 5-MHz 48-element transverse-axis cross-sectional imaging, colour flow mapping and pulsed wave Doppler sampling. The monitor of the ultrasound machine was positioned so as to provide an additional on-line monitor for the person performing the catheterization procedure. Each study was recorded in its entirety onto videotape and was analyzed both on-line and later off-line; photographs were taken from still frames.

All studies were performed with the child under general anaesthesia with endotracheal intubation. Antibiotic prophylaxis was not given in any patient in accordance with our general policy. The technique of probe insertion and the standard study protocol for the assessment of intracardiac morphology and function followed the guidelines previously described in our work (17). Particular attention was paid to demonstrating fully the morphology of any obstructive lesion and to evaluating the related haemodynamic changes with colour flow mapping techniques. Studies were completed by selective pulsed wave Doppler interrogation of atrioventricular (AV) valve flow patterns, pulmonary

venous flow patterns and the interrogation of other relevant areas of interest. The sample volume was placed within the pulmonary veins or at the level of the tip of the AV valve leaflets. Recordings were made at paper speeds of 50 or 100 mm/s during held inspiration.

This initial part of the transoesophageal investigation was completed while the operator was introducing the diagnostic catheters. The transoesophageal findings were discussed and a repeat scan was used to demonstrate in detail any suspected finding. Thereafter, the probe was withdrawn to a high oesophageal position until the initial haemodynamic and angiocardiographic study was completed. In all but the initial cases, the transoesophageal study was then recommenced while the guide wire and interventional catheter were positioned. Their intracardiac course and position were documented by imaging standard transoesophageal views (24, 25). This part of the study focused on defining the catheter position with respect to the AV valves and their subvalvular apparatus, or documenting the catheter course and position within the Mustard baffle pathways (22). When optimal positioning of the interventional catheter was achieved, combined imaging and colour flow mapping studies were carried out during the entire procedure in an attempt to assess any morphologic and haemodynamic changes.

After termination of the interventional procedure, a final transoesophageal study, which included cross-sectional imaging, colour flow mapping and pulsed wave Doppler interrogation, was performed. Transgastric short-axis scans and M-mode recordings were used to assess ventricular function and detect regional wall motion abnormalities immediately after the procedure. The probe was then removed before the final catheterization and angiocardiographic study.

RESULTS

Pre-intervention studies

Transoesophageal studies carried out before the interventional procedures documented a previously undetected moderate secundum type atrial septal defect in one patient (Case 8), who was scheduled for pulmonary valvuloplasty. Although the atrial septal defect was partially covered by a redundant tissue flap of the fossa ovalis, an unrestrictive left to right shunt was documented on both colour flow mapping and pulsed wave Doppler interrogation. Subsequent oxymetric measurements determined a Qp/Qs ratio of 2.3 : 1. Pulmonary valvuloplasty was thus cancelled and surgical correction was planned.

In a second patient with aortic stenosis (Patient 14), whose precordial study had defined mild aortic regurgitation, the transoesophageal study detected moderate regurgitation. The morphologic correlate was defined as partial pro-

lapse of the right coronary leaflet of the aortic valve. After angiocardiographic confirmation of the severity of the aortic regurgitation, aortic valvuloplasty was cancelled and the patient was scheduled for pulmonary autograft replacement.

In all three patients with systemic pathway obstruction following a Mustard procedure (Cases 11, 12 and 22), the transoesophageal study clearly defined the site, extent and morphology of the obstruction. These features could not be appreciated in such detail by either the prior precordial study or the concomitant angiocardiographic study. Angiocardiography was particularly limited in defining the length and minimal diameter of the obstruction. Transoesophageal pulsed wave Doppler assessment of the flow patterns across these narrowings revealed continuous turbulent flow patterns, which did not reach baseline values throughout the cardiac cycle. However because of malalignment to flow across these lesions, the technique failed to predict precisely the catheter-determined pressure gradient. Additional small baffle leaks were defined by transoesophageal colour flow mapping studies in two of these patients.

Pulmonary valve morphology could not be adequately demonstrated by transverse -axis transoesophageal imaging in any of the nine patients studied. In contrast, aortic valve morphology was documented in great detail in all five patients scheduled for aortic valvuloplasty. Fusion of the aortic valve commissures could be accurately defined and the presence and exact origin of aortic regurgitation (two patients) were readily defined.

In one patient with left pulmonary artery stenosis (Case 17), the interposition of the left main bronchus between the oesophagus and the lesion precluded the reliable assessment of the morphology of the obstruction. The morphology of a patent ductus arteriosus could not be defined in two patients (Cases 5 and 6). In two patients, both scheduled for angioplasty for aortic recoarctation, single plane transoesophageal studies were inadequate in the definition the extent of the recoarctation and its relation to the left subclavian artery. However, the presence of intimal changes or aneurysm could be excluded reliably by transoesophageal cross-sectional imaging before the procedure.

Interventional studies

Pulmonary valvuloplasty. In one (Case 4) of the eight patients who underwent pulmonary valvuloplasty, moderate tricuspid regurgitation was documented immediately successful dilatation. Cross-sectional transoesophageal imaging defined partial chordal rupture of the anterior tricuspid valve leaflet with prolapse into the right atrium as the underlying cause (Figure 1). Tricuspid regurgitation was confirmed at subsequent angiography and mild regurgitation persisted during the early follow up period. Guide wire and catheter placement had not been monitored by transoesophageal imaging in this patient early in the series because we were unaware of the need to monitor positioning relative

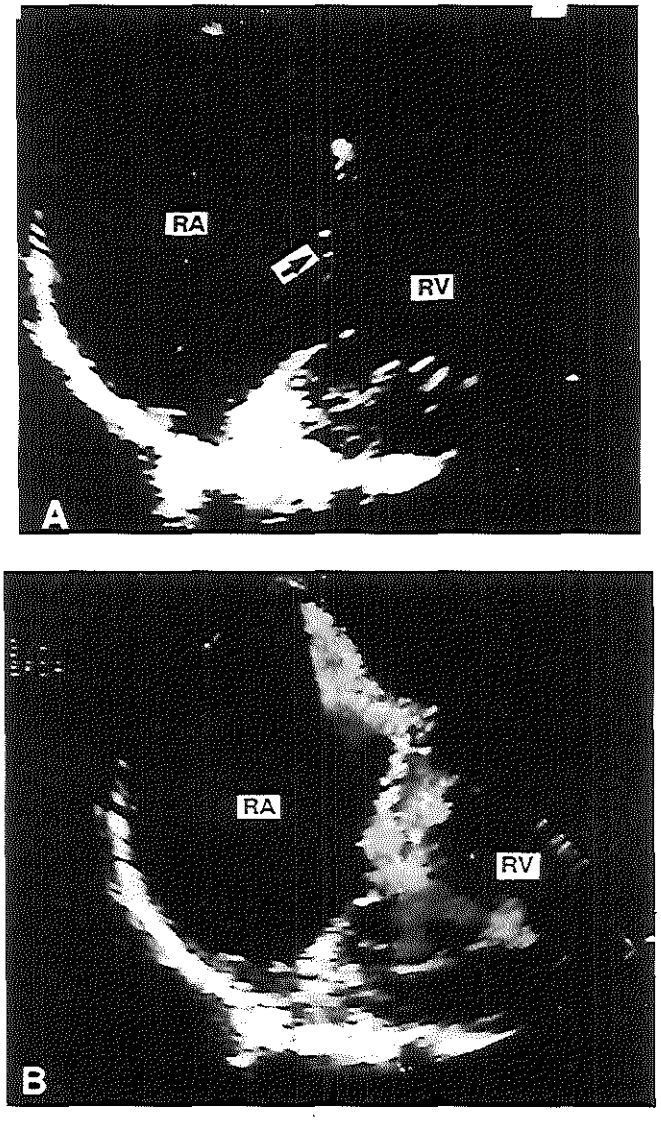

Figure 1: Case 4. A. Transoesophageal study after balloon pulmonary valvuloplasty, demonstrating partial chordal rupture of the anterior leaflet of the tricuspid valve (arrow) with prolapse into the right atrium (RA). B. The colour flow mapping study reveals a moderate tricuspid valve regurgitant jet adherent to the atrial septum.

to AV valves and their subvalvular apparatus. After this case, the study protocol was changed accordingly. In a later patient (Case 10), the balloon was demon-

strated to be localised within the tricuspid valve apparatus immediately before inflation. Subsequently, the catheter was advanced further until its position was documented to be well beyond the tricuspid valve apparatus. Postvalvuloplasty transoesophageal studies excluded tricuspid regurgitation in this and the remaining six patients. Any immediate change in either pulmonary valve morphology, residual valvular or subvalvular gradient or pulmonary incompetence could not be determined by single-plane transoesophageal studies.

Aortic valvuloplasty. The transoesophageal determined diameter of the aortic root correlated well with the angiographically derived measurement in all four patients who underwent the procedure (maximal difference in measurement ± 4%). Fusion of the aortic valve commissures and the immediate changes in valve morphology after dilatation could be assessed in detail. In all four patients, there was opening of at least one commissure with marked improvement of leaflet motility as assessed by real time imaging and M-mode studies. Partial or complete prolapse of an aortic valve leaflet could be excluded in all patients immediately after balloon inflation. Colour flow mapping studies of the left ventricular outflow tract and aortic valve performed after each balloon inflation defined trivial aortic regurgitation in two (Figure 2) and mild (central) aortic regurgitation in a third patient. Guide wire and balloon placement had been monitored before the procedure in three of these four patients. Documentation of positioning of the guide wire within the chordal apparatus of the mitral valve in one of these patients (Case 9) led to subsequent guide wire repositioning guided by real time transoesophageal imaging.

Pulmonary angioplasty. In one patient with left pulmonary artery stenosis (Case 17), the interposition of the left main bronchus between the oesophagus and this structure precluded adequate visualization of the stenosis. However, a distal segment of the left pulmonary artery could be visualised anterior to the descending aorta and turbulent flow was noted. After the procedure, colour flow mapping studies within the distal left pulmonary artery demonstrated laminar flow patterns and pulsed wave Doppler sampling excluded increased flow velocities.

Aortic angioplasty. The extent of the aortic coarctation (in two patients) was difficult to assess by transverse-axis transoesophageal imaging. Only the use of continuous M-mode interrogation of the lumen diameter while slowly withdrawing the probe allowed a rough estimation of the extent of the narrowed segment. However, the minimal cross-sectional diameter of the coarctation was accurately assessed and the intimal layers could be visualized in detail. A localized intimal dissection or aneurysm formation immediately after angioplasty was excluded in both patients. The perpendicular orientation of the descending aorta and the transoesophageal ultrasound beam precluded any meaningful pulsed wave Doppler interrogation.

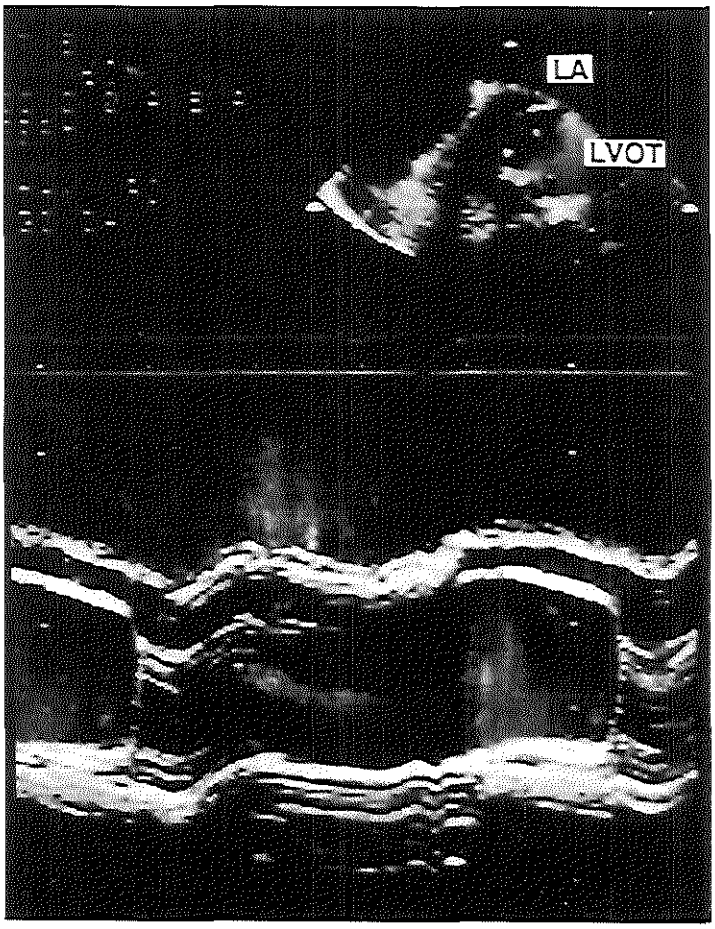

Figure 2: Case 15. Transoesophageal colour flow map (top) and colour M-mode study (bottom) in the immediate evaluation of balloon aortic valvuloplasty. From a high oesophageal position, the left ventricular outflow tract (LVOT) is visualized anterior to the left atrium (LA). The M-mode line is positioned at the level of the aortic valve. The absence of systolic turbulence across the aortic valve indicates successful gradient relief. Trivial central aortic regurgitation is noted during diastole.

Ductus occlusion. Transoesophageal studies during transcatheter occlusion of a patent ductus arteriosus in two patients failed to provide useful information on the exact position of the occluder device. However, protusion of the distal legs into the lumen of the aorta could be excluded on cross-sectional imaging and colour flow mapping studies of the descending aorta allowed us to exclude turbulent flow patterns. Pulsed wave Doppler and colour flow mapping

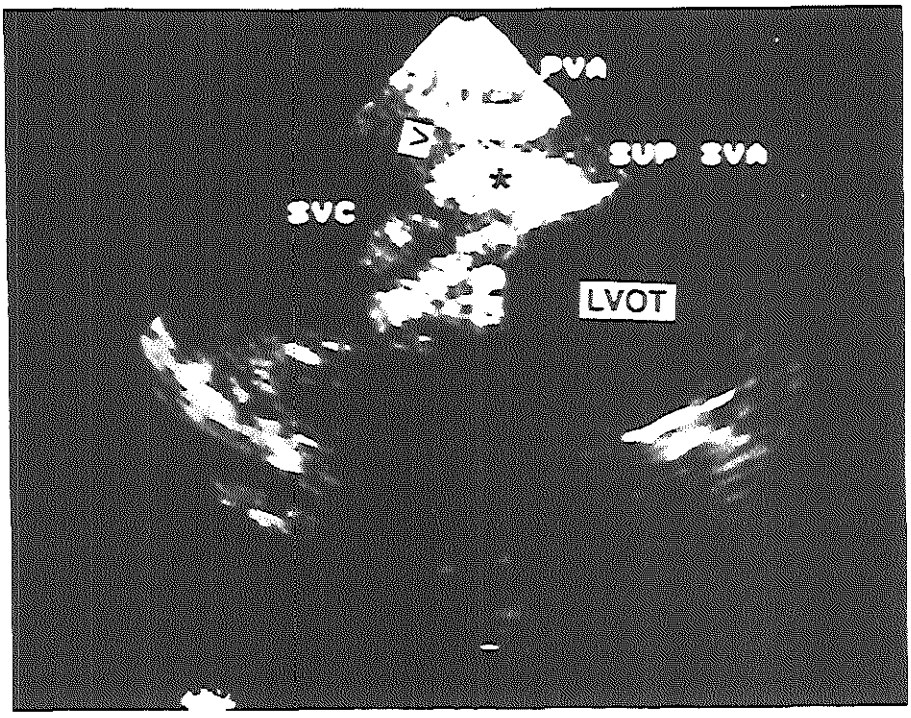

Figure 3: Case 12. Transoesophageal cross-sectional imaging of a severe obstruction in the superior limb of the systemic venous pathway after a Mustard procedure. The obstructive lesion (*) is heavily calcified, leaving only a pinhole opening of 1 mm (>). PVA = pulmonary venous atrium; SUP SVA = superior limb systemic venous atrium; SVC = superior vena cava; other abbreviation as in Figure 2.

studies of the flow patterns within the pulmonary trunk defined a minuscule residual shunt immediately after the procedure. The finding was confirmed in both by a final aortogram. In one patient (Case 6), residual shunting ceased after 10 min.

Mustard baffle dilatation. In one (Case 11) of the three patients studied, the transoesophageal cross-sectional imaging and colour flow mapping study defined a complete occlusion of the superior limb of the systemic venous pathway. No antegrade flow was recorded by pulsed wave Doppler interrogation just distal to the occlusion. Numerous attempts to cross this lesion from the femoral vein with a guide wire were unsuccessful. In the second patient (Case 12), a pinhole opening in a heavily calcified obstruction at the level of the remnant of the atrial septum was documented (Figure 3). Despite transoesophageal demonstration of the entire superior limb of the systemic venous atrium and real time monitoring of catheter manipulations, the transfemoral advancement of the

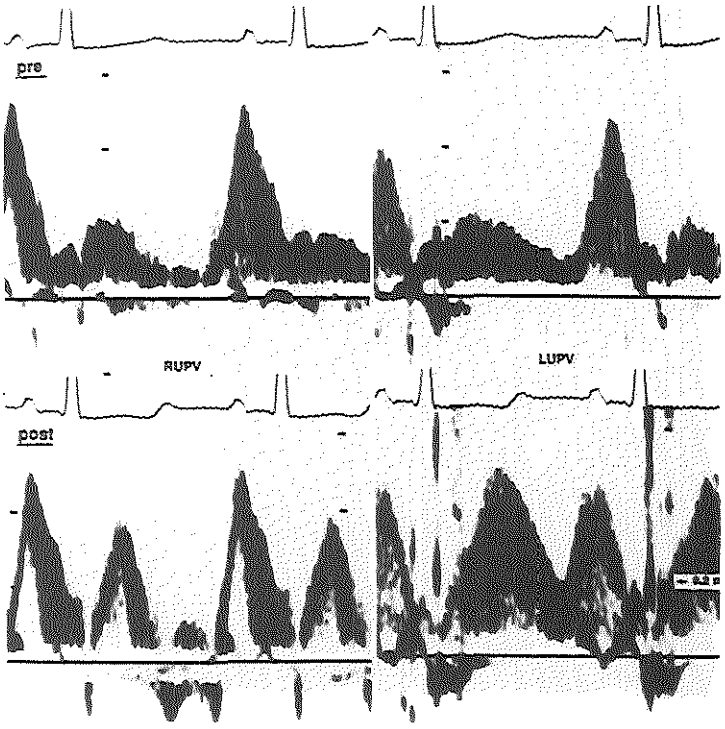

Figure 4: Transoesophageal pulsed wave Doppler interrogation of pulmonary venous flow profiles before (top) and after (bottom) pulmonary balloon valvuloplasty. Before the procedure (pre), the systolic forward flow component is decreased. After successful gradient relief (post), the systolic flow component increased markedly, whereas the diastolic flow component remained relatively unchanged. LUPV = left upper pulmonary vein; RUPV = right upper pulmonary vein.

guide wire remained unsuccessful. In the third patient (Case 22), the lesion was documented to be a long concentric narrowing with a good-sized opening (4 mm). On colour flow mapping and pulsed wave Doppler studies, continuous turbulent flow was recorded across this obstruction. Guide wire and catheter placement across the stenosis was enhanced by real time imaging of the catheter tip relative to the site of communication. After balloon dilatation of the obstruction in this patient, the maximal diameter of the narrowing had increased to 10 mm. Pulsed Doppler assessment of the flow patterns across the narrowing revealed a persistent mild increase in maximal forward flow velocity (1.6 m/s) and demonstrated a return to a typical biphasic flow pattern that reached baseline values during the cardiac cycle and thus suggested successful gradient relief. In addition, any newly aquired baffle leakage was excluded by colour flow mapping

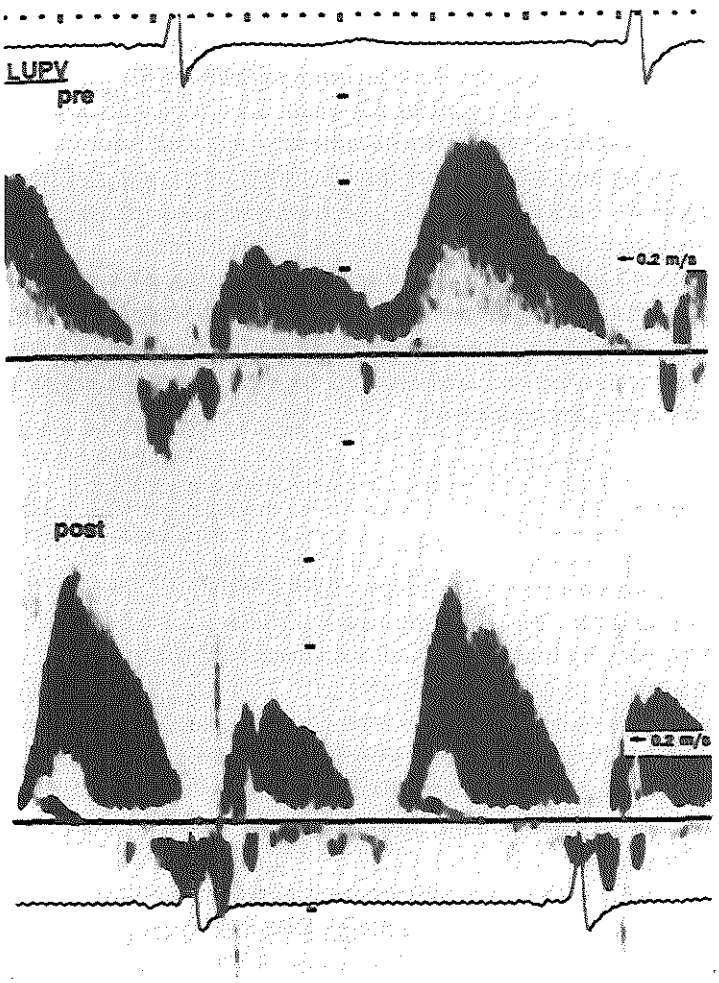

Figure 5: Case 9. Transoesophageal pulsed wave Doppler interrogation of pulmonary venous flow profiles before (top) and after (bottom) aortic balloon valvuloplasty. The pulmonary venous flow patterns within the left upper pulmonary vein (LUPV) remained essentially unchanged despite successful gradient relief. Abbreviations as in Figure 4.

studies. The findings were subsequently confirmed by the final catheterization and angiographic study.

Pulsed wave Doppler studies. Flow patterns within the pulmonary veins and across the AV valves were assessed in all patients before and after the interventional procedure to detect any immediate changes in these flow profiles. After pulmonary valvuloplasty, a marked increase in systolic forward flow com-

ponents of the pulmonary venous return was documented in five of the eight patients (Figure 4), whereas the flow patterns across the AV valves remained unchanged. There was no correlation between these changes and the pre- and post-dilatation gradients nor with the patients' age. No immediate changes in pulmonary venous and mitral valve flow patterns were noted after aortic valvuloplasty (Figure 5), aortic angioplasty and duct occlusion. In the patient who underwent pulmonary angioplasty pulmonary venous flow patterns of the left lung compared with the right lung were markedly reduced before dilatation. After successful dilatation, flow patterns of pulmonary venous return in both lungs became almost identical. During balloon inflation with complete occlusion of the pulmonary artery, only to and fro flow patterns within the left pulmonary veins were demonstrated.

DISCUSSION

Transoesophageal echocardiography using dedicated paediatric probes is a safe diagnostic and monitoring technique in children weighing > 3 kg (15 - 17). To date 268 studies have been carried out at our institutions and complications were encountered in only 4 (arrhythmias in 2, bleeding in 1 and pulmonary hypertensive crisis in 1). No death occurred. General anaesthesia together with endotracheal intubation is considered to be the optimal anaesthetic technique for such studies, although these can be performed under heavy sedation. The interventional procedure time was not prolonged and sterility was not endangered by these studies.

Early during the series, the presence of the transoesophageal probe was believed to interfere with the routine radiographic monitoring and frequently had to be removed to a high oesophageal position. However, with growing operator familiarity with the standard transoesophageal imagingplanes, the real time imaging information provided by the technique often was used specifically to monitor guide wire and balloon catheter placement. Thus, later in the series, studies no longer were believed to interfere with the procedure, but were considered to constitute an important addition to routine monitoring. Pre-intervention studies. These provided a detailed assessment of cardiac morphology and function immediately before the procedure. In this series, the information obtained led to cancellation of the procedure in two patients. In another patient, who had systemic venous pathway obstruction after a Mustard procedure, the finding of complete occlusion of the superior limb of the baffle could have led to early cancellation. In the remaining two patients with baffle obstruction, the transoesophageal imaging studies provided additional morphologic insights

into the obstructive lesions and were believed to enhance greatly the catheter placement.

Monitoring of guide wire and catheter positioning during balloon valvuloplasty and ductus occlusion. This was found to be one of the major contributions of the technique. Although in pulmonary and aortic valvuloplasty the balloon catheter is inflated only after adequate positioning is assessed by fluoroscopy, the risk of entrapment of the within the valvular or subvalvular apparatus of the AV valves cannot be excluded completely. This is especially important in neonates and infants because of relatively long balloon versus chamber dimensions. In one patient in whom tricuspid regurgitation was identified after pulmonary valvuloplasty, a stiff backup wire was used for balloon catheter placement. Tricuspid valve chordae were presumably partially sheared off. After this instance, transoesophageal studies were specifically used to monitor guidewire as well as balloon position across the AV valves in all patients. Visualization was could be achieved in great detail in all and the findings initiated catheter repositioning guided by transoesophageal imaging in two patients.

Evaluation of immediate morphologic changes. After the interventional procedures in our series of patients, the transoesophageal studies were of benefit in assessing aortic valve morphology (commissures and cusps), descending aortic wall morphology (lumen diameter and intimal integrity) and systemic pathway obstruction after the Mustard procedure (overall dimensions). However, no useful information on either pulmonary valve morphology or umbrella position within an arterial ductus was obtained by single plane transoesophageal imaging. The failure to adequately visualize the arterial ductus can be explained by interpositioning of the bronchial tree between this structure and the oesophagus. After unsuccessful studies in two patients undergoing transfemoral ductus occlusion, no more patients underwent the study. Transgastric short-axis imaging and M-mode studies allowed for the monitoring of left ventricular function during the procedure and the recovery period. In addition they made it possible to exclude left ventricular regional wall motion abnormalities, a capability that was especially important after aortic valvuloplasty.

The assessment of haemodynamic changes immediately after interventional procedures. Such assessment was found to be limited. Colour flow mapping studies together with colour M-mode recordings provided a rough indicator of residual obstructions, particularly after aortic valvuloplasty. However, residual gradients across either arterial valve could not be assessed because of the generally poor alignment of the Doppler beam with these flow patterns and the availability of pulsed wave Doppler facilities only. Similar limitations were encountered in the assessment of descending aortic flow patterns. In contrast, the assessment of flow patterns within the systemic venous pathways in patients with a Mustard procedure contributed unique additional infor-

mation. After successful dilatation, the continuous turbulent flow pattern across the obstruction became biphasic and reached baseline values during the cardiac cycle.

Exclusion of immediate complications. This was found to be an important advantage of transoesophageal monitoring during interventional catheterization. The technique provided continuous morphologic and haemodynamic information without interfering with the procedure. The immediate exclusion of aortic regurgitation after each balloon inflation for dilatation of the aortic valve proved to be of major value in this series of patients. Second or third balloon inflations were performed with much greater confidence than when they had be performed without real time transoesophageal monitoring. After Mustard baffle dilatations, the technique allowed for the immediate exclusion of baffle disruption or leakage. The sensitivity of transoesophageal colour flow mapping studies in the detection of these lesions is such that the technique may eventually obviate final angiographic studies. In addition, the majority of potential complications that may occur during the various procedures should be immediately and reliably identifiable by continuous transoesophageal monitoring.

Pulsed wave Doppler studies of AV and pulmonary venous flow patterns. These revealed several interseting insights into the immediate changes after various interventional procedures. After aortic valvuloplasty, no immediate changes in these flow patterns were observed. These observations are in agreement with the finding by Stoddard et al. (26), who excluded an immediate change in left ventricular function on the basis of unchanged mitral valve flow patterns after aortic valvuloplasty. Similar observations on pulmonary vein and AV valve flow patterns were made in the two patients who underwent successful angioplasty for recoarctation and in the two patients after ductus occlusion. In contrast, in five of the eight patients who underwent successful pulmonary valvuloplasty, marked changes in pulmonary venous flow patterns were noted immediately after the procedure. In all five patients, the systolic component of pulmonary venous forward flow was found to be largely increased after gradient relief.

Systolic forward flow is caused by both atrial relaxation and descent of the mitral valve annulus during ventricular systole (27). Improved atrial relaxation is unlikely to be the underlying cause of these observations, thus suggesting an immediate change in left ventricular geometry and function after pulmonary valvuloplasty. There was no significant difference in the changes in cardiac output between the subsets of patients who had a change in pulmonary venous flow patterns and those who did not. The diastolic flow component of pulmonary venous return and the AV valve flow patterns remained unchanged, suggesting that there are no immediate changes in diastolic right and left ventricular function after successful pulmonary valvuloplasty. Unchanged diastolic right ven-

tricular function after pulmonary valvuloplasty was recently reported by Vermilion et al. (28). More detailed studies to further elucidate these phenomena are currently under way. During pulmonary angioplasty, the comparison of pulmonary venous flow patterns in either lung may be useful in assessing the immediate result of relief of the obstruction.

Limitations of single-plane transoesophageal monitoring. These include the poor demonstration of the right ventricular outflow tract, the pulmonary valve, the precise morphology of aortic coarctation and the anatomy of a patent ductus arteriosus. It may be anticipated that several of these limitations may be overcome by the time biplane-transoesophageal imaging (29) becomes available for studies in children. The addition longitudinal-axis images that are obtained allow for an improved assessment of these cardiac structures and facilitate Doppler interrogation. In addition, the adjunct of continuous wave Doppler facilities may provide much improved insight into the immediate haemodynamic changes such as residual valvular gradients.

Further applications. Transoesophageal realtime monitoring of interventional cardiac catheterization should have a major impact on several other procedures. Monitoring of balloon septostomy appears to be particularly rewarding in patients with juxtaposition of the atrial appendages. Similarly, blade septostomy procedures are believed to be greatly enhanced by such monitoring. The monitoring of balloon dilatation of pulmonary venous obstructions would allow continuous assessment of morphologic and haemodynamic alterations. In addition, the monitoring of coil embolizations of coronary artery fistulas may be beneficial. The impact of transoesophageal monitoring of transcatheter closure of atrial septal defects was recently described by Hellenbrand et al. (31) and it appears that the technique may become a prerequisite for a high success rate. The monitoring of ventricular septal defect closure is currently under evaluation at several institutions.

Conclusions. Transoesophageal echocardiographic monitoring of interventional cardiac catheterization in children is a safe technique that does not interfere with the procedure. It provides additional important morphologic information on a wide spectrum of lesions, the immediate identification or exclusion of potential complications and the assessment of haemodynamic changes. It may be expected that in near future, the technique may become an integral part of paediatric cardiac interventions.

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CHAPTER 9

STREPTOKINASE THERAPY FOR FEMORAL ARTERY THROMBOSIS AFTER ARTERIAL CARDIAC CATHETERIZATION IN INFANTS AND CHILDREN

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SUMMARY

Data on 205 children who underwent retrograde arterial catheterization, were studied to assess the frequency of femoral artery thrombosis and the safety and efficacy of systemic streptokinase therapy for this complication. In 29 (14%) a transarterial balloon dilatation was performed. In 15 (7.3%) impaired arterial perfusion due to vascular spasm with or without thrombus formation was seen in the cannulated leg after catheterization. Despite heparinization, signs of impaired arterial circulation persisted in 9 patients (4.4% of the total). In these patients femoral artery thrombosis was strongly suspected. Six (53%) of these had undergone a balloon dilatation. Therefore in this study the risk of femoral artery thrombosis developing was 12 times greater after transarterial balloon dilatation than after arterial catheterization without dilatation (20.6 vs 1.7%).

Systemic infusion of streptokinase was started in all patients with femoral artery thrombosis. Arterial perfusion became normal in all patients, though in one this was delayed. Haematological monitoring showed lengthening of the thrombin time and a decrease of the fibrinogen concentration during streptokinase treatment. There were no serious complications.

Systemic infusion of streptokinase is a safe and useful treatment in children with persistent femoral artery thrombosis after arterial cardiac catheterization.

INTRODUCTION

Femoral artery thrombosis is the most common complication of retrograde arterial cardiac catheterization in children (1 - 3). Catheterization of infants weighing less than 10 kg and the growing use of transarterial balloon dilatation procedures increase the frequency of this complication (2, 4, 5).

In older children surgical thrombectomy has been undertaken with varying success (1, 4, 5). Because the risk of extending vascular damage is higher in neonates and infants they are less suitable for surgical intervention (2, 5).

The systemic use of thrombolytic agents seems to be a safe and effective alternative to surgical treatment (4, 5). We studied a group of children treated with streptokinase because of femoral artery thrombosis after cardiac catheterization.

Patient no	Age (year)	Weight (kg)	Diagnosis	Transarterial balloon dilatation	Interval between end of catheterization and start of streptokinase (h)
1	5.4	17.7	RECOA	+	144
2	1.6	8.8	TA	–	51
3	1.2	7.0	VSD	–	48
4	9.6	22.4	AVS	+	48
5	0.4	6.6	AVS	+	122
6	11.0	25.4	AVS	+	24
7	0.08	5.2	AVS	+	24
8	6.6	17.2	MPPS	+	19
9	0.02	3.2	PA, VSD	–	56
mean	3.9	12.6	59.7		
SD	4.3	8.1	44.0		

RECOA = aortic recoarctation, TA = tricuspid valve atresia, VSD = ventricular septal defect, AVS = aortic valve stenosis, MPPS = multiple peripheral pulmonary stenoses, PA = pulmonary atresia.

Table I: Data of patients with femoral artery thrombosis, treated with systemic infusion of streptokinase.

PATIENTS AND METHODS

Between 1 January 1987 and 1 December 1988 retrograde arterial cardiac catheterization was performed in 205 children. Of these, 29 children (14%) underwent transarterial balloon dilatation. These children received an extra intravenous bolus of heparin (100 U/kg) during the procedure as well as the heparin solution used routinely in every child to flush catheters. Thirty four (16%) children weighed less than 10 kg.

Before and after catheterization the arterial perfusion of both legs was assessed by examination of arterial pulses, bloodpressure, colour and temperature. Patients with absent or reduced arterial pulsations, substantially decreased bloodpressure, pallor, and diminished skin temperature of the cannulated leg shortly after the end of the procedure were considered to have impaired arterial perfusion due to arterial spasm with or without thrombus formation. We studied data on these patients.

In all these patients heparin was administered for different times and monitored by the activated partial thromboplastin time. In patients with persistent signs of impaired arterial circulation despite heparinization a tentative diagnosis of arterial thrombosis was made and streptokinase was used for systemic thrombolytic treatment.

The distribution of age and weight (mean ± SD) and also the time interval (mean ± SD) between the end of the catheterization and the start of streptoki-

Patient no	Loading dose in 30 min (U/kg)	Infusion dose (U/kg/h)	Duration (h)	Complications
1	1000	1000	29	None
2	1000	1000	7	None
3	1000	1000	12	None
4	2000	1000	58	Haematoma groin
5	3000	1500	8	None
6	3000	1000	24	Bleeding groin
7	3000	1000	24 *	None
	(3000)	(2000)	(45)	
8	3000	1000	120	None
9	3000	1000	72	No effect

*Because of an inadequate result after 24 hours of treatment the dose of streptokinase was increased after another loading dose. This was successful after 45 hours.

Table II: Systemic streptokinase infusion in 9 patients with femoral artery thrombosis after retrograde arterial catheterization.

nase treatment were determined. The duration of therapy (mean ± SD) was also assessed.

Before and during streptokinase therapy prothrombin time, activated partial thromboplastin time, and plasma fibrinogen concentrations were recorded in all patients; in some patients the thrombin time was also measured. Two hours after the end of streptokinase treatment heparinization was restarted in all patients to prevent re-thrombosis after successful therapy or persisting thrombus formation after treatment failure. This was continued for 12 hours.

RESULTS

Shortly after the end of the catheterization 15 (7.3%) of 205 patients showed impaired arterial perfusion of the cannulated leg. In 6 (40%) of these the arterial circulation became normal during systemic heparin treatment. Despite continued heparinization arterial perfusion remained impaired in the remaining 9 patients (60%, 4.4% of 205 patients) at 59.7 ± 44.0 hours (range 19 - 144 hours) after the procedure and femoral artery thrombosis without vascular spasm was strongly suspected (Table I). Six of these 9 patients had undergone a transarterial balloon dilatation. The median weight of these children was 12.6 ± 8.1 kg (range 3.2 - 25.4 kg); 5 of them weighed less than 10 kg. The median age was 3.9 ± 4.3 years (range 9 days - 11 years).

During systemic streptokinase treatment (Table II) arterial perfusion became normal in 8 (89%) of 9 patients after 7 - 120 hours (mean 39.6 ± 38.9

Patient no.	Thrombin time (s)		Plasma fibrinogen (g/l)	
	Before	During	Before	During
1	17	28	3.0	2.0
2	19	56	2.6	0.8
3	—	—	2.6	1.0
4	10	26	2.6	1.4
5	19	31	2.3	1.4
6	21	25	2.5	2.6
7	18	25	2.1	1.6
8	21	32	3.8	2.5
9	—	—	3.7	0.8
mean	17.9	31.9	2.8	1.6
SD	3.8	11.0	0.6	0.7

Table III: Thrombin time and plasma fibrinogen concentration before and during streptokinase treatment.

hours). Because of persisting impaired perfusion after 24 hours of treatment the streptokinase dose was increased in one patient (patient 7, Table II) after another loading dose. This resulted in normal arterial circulation after 45 hours. In the youngest patient (patient 9, Table II) absence of pulses and low systolic bloodpressure persisted despite laboratory signs of adequate fibrinolysis. After 72 hours the thrombolytic therapy in this patient was stopped. However, femoral artery perfusion was normal 5 days after the end of streptokinase treatment. There were no signs of re-thrombosis at follow up after 3 - 20 months in any patient.

During streptokinase treatment the prothrombin time and partial thromboplastin time did not change. The thrombin time increased (from 17.9 ± 3.8 s to 31.9 ± 11.0 s, mean relative increase of 0.85 ± 0.61) and the plasma fibrinogen concentration decreased (from 2.8 ± 0.6 g/l to 1.6 ± 0.7 g/l, mean relative decrease of 0.42 ± 0.24). The fibrinogen concentration did not change in patient 6, in whom streptokinase treatment resulted in a normal circulation after 45 hours (Table III).

There was no substantial bleeding during or after streptokinase treatment except for minimal bleeding at the arterial entry site that could be stopped by groin compression. No allergic reactions were seen.

DISCUSSION

Obstruction of the femoral artery by thrombus is a known complication of retrograde arterial catheterization in children. This has been confirmed by arteriography in some studies (1 - 3). Vascular spasm only contributes to femoral artery obstruction shortly after the end of the procedure (2). Spasm is unlikely to persist for more than a few hours (2). In this study we regarded persistent signs of impaired arterial circulation despite heparinization as being the result of thrombus formation without vascular spasm.

Femoral artery thrombosis is the most common complication after retrograde arterial catheterization in children (1 - 3) - it was reported in 3 - 5% of patients despite increased experience with catheterization techniques, better materials, and systemic treatment with heparin (1, 4, 5). The result in our study (4.4%) accords with earlier results. Furthermore, femoral artery thrombosis is 12 times more common after retrograde transarterial balloon dilatation than after arterial catheterization without such a procedure (20.6% vs 1.7%). The larger diameter of the balloon catheters and the irregular surface of the balloon may contribute to increased intimal damage and vascular spasm (4, 6). This is an important finding because the number of retrograde transarterial balloon dilatations has greatly increased in the past years (6 - 8). Young children, especially those weighing less than 10 kg, have a higher incidence of femoral artery thrombosis after retrograde arterial catheterization than older children and adults (2, 4, 5). We found femoral artery thrombosis in 14.7% of children weighing < 10 kg and in 2.3% of children weighing > 10 kg. Although tissue ischaemia after femoral artery thrombosis is rare, disturbance of growth and function of the leg can be impressive (2, 4, 9). Therefore, it is very important to evaluate arterial perfusion of both legs after each retrograde arterial catheterization. Absent or reduced arterial pulsations, substantially decreased bloodpressure, pallor, and diminished skin temperature of the cannulated leg after the end of the procedure are reliable criteria for femoral artery obstruction (2, 4, 5).

Persistence of impaired femoral artery perfusion indicates that treatment is needed. Surgical intervention, especially in younger children, is associated with a substantial risk of extending vascular damage (2, 5). In older children it has been undertaken with varying success (1, 4, 5). The use of thrombolytic agents seems to be a preferable alternative (4, 5). These agents act directly or indirectly as plasminogen activators. They activate plasminogen, an inactive proteolytic enzyme in plasma, to produce the fibrinolytic enzyme plasmin (10).

We treated our patients with streptokinase because this is the agent that has been most used in children for this indication. Streptokinase is a protein obtained from group C β-haemolytic streptococci (5, 10). In our study femoral artery thrombosis occurred in 9 patients after retrograde arterial catheterization

despite continued heparinization. These patients were treated with systemic infusion of streptokinase. We did not perform local arterial infusion because this requires cannulation of another artery with the attendant risk of endothelial damage and possible formation of a new thrombus (11).

In 8 (89%) of 9 patients systemic streptokinase treatment was successful. This accords with the results of two recently published studies (4, 5). The mean duration of therapy was greater in our patients compared than in these other studies (37.9 vs 13.0 hours). Older thrombi are more resistant to fibrinolysis. Peripheral arterial thromboses that are > 24 hours old need longer treatment with streptokinase (5, 10). In our study the interval between the end of catheterization and start of streptokinase treatment was not clearly related to how long treatment was needed. Despite laboratory signs of adequate fibrinolysis, streptokinase treatment was not immediately successful in one patient (11%) (the youngest in our series, 9 days old). Femoral artery perfusion was normal after 5 days, however. Recanalization after spontaneous resolution of the thrombus is highly unlikely to have occurred in such a short period. Failure of thrombolytic therapy in newborn infants may be attributed to the lower levels of plasminogen or because the functional activity of plasminogen is less than the concentrations of plasminogen inhibitors (especially α_2-antiplasmin) (12 - 14). Sometimes the use of massive amounts of thrombolytic agents may be successful in these cases (14). Activation of plasminogen by thrombolytic agents can result in haematological changes (particularly an increase of thrombin time and a decrease in plasma fibrinogen as well as an increase in plasma fibrin degradation products) (10, 15). Monitoring of the prothrombin time, partial thromboplastin time, thrombin time, plasma fibrinogen, and fibrin degradation products is a useful guide to adjusting thrombolytic treatment to avoid systemic bleeding complications (5, 10, 15). In our patients there was no lengthening of prothrombin time and partial thromboplastin time, but the thrombin time increased and there was a moderate decrease in plasma fibrinogen concentrations - both signs of fibrinolysis (Table III).

Bleeding is the most hazardous complication of systemic thrombolytic treatment. We saw no serious bleeding complications in our study. Bleeding from the arterial entry site is the most common complication - particularly in patients undergoing balloon dilatation procedures. This was seen in one of our patients. Local compression will usually stop the bleeding (4, 5).

During thrombolytic therapy invasive procedures must be avoided (10). Contraindications to thrombolytic therapy are the presence of or predisposition to intracranial hemorrhage, active internal bleeding (for example, gastrointestinal), recent major surgery (within 10 days), and pre-existing bleeding tendency (15). If serious bleeding develops thrombolysis must be stopped immediately

and coagulation changes reversed by the use of fresh frozen plasma and cryoprecipitate (10).

To avoid re-thrombosis after successful thrombolytic treatment or when thrombus formation persisted after treatment failure we treated our patients with heparin. The optimal anti-thrombotic regimen to prevent these problems still needs to be established. Heparin and/or aspirin have been recommended (16). Like other investigators we did not encounter re-thrombosis (4, 5).

Treatment with streptokinase (a bacterial product) is occasionally associated with an allergic reaction (rash, fever, nausea, a syndrome resembling serum sickness, and anaphylactic shock) especially in patients exposed to a recent streptococcal infection or streptokinase treatment (10). Urokinase, a human product, is non-antigenic and can be used instead of streptokinase (10). There were no allergic reactions in our patients.

The doses that we used and those used by others in children were not established by pharmacological investigations but were estimated from experience in adult patients. These doses were safe and effective but we do not know whether they are pharmacologically optimal.

In our study group the early use of streptokinase in the treatment of femoral artery thrombosis after percutaneous retrograde catheterization seemed to be beneficial. Because the proof of the efficacy of treatment with streptokinase cannot be drawn from this study we recommend that a randomized, controlled study should be undertaken.

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CHAPTER 10

GENERAL DISCUSSION

Interventional catheterization in children has emerged as a rapidly recognized alternative for surgery in the management of various congenital cardiac malformations. Currently both balloon dilatation for treatment of obstructive cardiovascular lesions and umbrella-closure for patent ductus arteriosus are routinely performed procedures. Including balloon septostomy, these therapeutic interventions account for 30% of all the procedures currently performed in the paediatric cardiac catheterization laboratory. The studies described in this thesis document the safe, and frequently effective use of balloon dilatation. Although the initial enthousiasm resulted in the application of balloon valvuloplasty and angioplasty for almost all possible native or post-surgical stenoses, a more balanced judgement can gradually be made. Next to an adequate relief of the stenosis and a low complication rate, such a judgement must be based on a persistence of the gradient reduction and subsequently better cardiac performance at longer term follow up.

For valvular pulmonary stenosis, performed on an elective base in the older infant and child, balloon valvuloplasty has become the preferred way of treatment. Until now, only for this diagnosis follow up studies are available including results up to 4 to 8 years.

For valvular pulmonary stenosis in the neonate and young infant balloon valvuloplasty may be successful. However, due to technical and morphological

variables, the initial failure rate is considerable and in 40% of these patients surgery is mandatory to relieve the outflow obstruction. Severity of tricuspid valve regurgitation and small pulmonary annular size are major determinants for outcome. Furthermore, restenosis and inadequate annular growth necessitate reintervention in some of these patients within one year.

The position of balloon valvuloplasty for the treatment of isolated valvular aortic stenosis is less clear. Including ourselves, several investigators documented a 50% reduction in valve gradient. Improvement of repolarization changes on the electrocardiogram at rest and exercise and a decrease of left ventricular hypertrophy have been reported. The mid-term follow up reports confirm the persistence of these results, but the occurrence or increase of aortic valve regurgitation is considerable. In 15% of our patients this resulted in valve replacement within two years. In this valvuloplasty-induced regurgitation it may be difficult to decide when valve replacement is needed. Contrary to the management of aortic valve stenosis in adulthood, in our opinion surgery should not be delayed until these patients present with signs of cardiac failure. When aortic regurgitation is substantial, this generally leads to moderate cardiac dilatation. In our experience in most of these patients this tends to stabilize six months after balloon valvuloplasty. However, if the dilatation progresses, repolarization changes occur or arrhytmias are observed the indication for surgery is clear.

Our experience of balloon valvuloplasty for valvular aortic stenosis in the neonate is rather limited, so that conclusions should not be drawn yet. Based on reports on limited series from other investigators our current policy is to apply valvuloplasty as first treatment (1, 2).

In residual or recurrent coarctation of the aorta balloon angioplasty is an attractive alternative for surgical re-intervention. The short- and mid-term follow up results are promising, especially because of the evidence for accelerated growth of the coarctation segment resulting in further gradient reduction. The complication rate is low, but the eventual delayed appearance of small aneurysms necessitates angiographic follow up. Only long-term follow up will reveal whether the decrease in upper body blood pressure persists.

In native coarctation our policy is to prefer surgery as first line treatment. The results of surgery are good, also if the operation has been performed in infancy, and the few patients that will present with recurrent coarcation can be treated with balloon angioplasty. An alternative approach is the two-stage treatment policy as recently described by Minich et al (3). In patients with a discrete coarctation, they proceeded to balloon angioplasty as primary treatment. After 6 to 9 months catheterization and angiography was repeated. If the result was insufficient (20 to 30% of their cases), defined as a residual systolic gradient of more than 20 mmHg or an aneurysm, surgery was subsequently performed. However, in our opinion it should be realized, that such an approach cannot be

justified in patients in whom aortic ductal tissue is the substrate of the coarctation. Surgical excision of at least part of this tissue should be the primary aim of treatment to prevent restenosis.

For the less common obstructive cardiovascular lesions, some emerge as objectivated indications for balloon dilatation. Although invasive follow up has not consequently be performed, in patients with Mustard baffle obstruction at the systemic venous side dilatation is feasible and effective. For post-surgical right ventricular outflow tract obstructions dilatation may be effective for a localised obstruction but will be disappointing frequently. In a setting where the primary approach for Fallot's tetralogy is correction in the first or second year of life, there are few arguments in favour of balloon dilatation of the right ventricular outflow tract obstruction. This is even more so, if the mortality and morbidity associated with this procedure in patients with Fallot's tetralogy is taken into consideration and compared with that after surgical management (4, 5). In addition, balloon dilatation of muscular stenoses cannot be based on structural data.

In pulmonary artery branch stenosis dilatation may be effective but recoil is frequently observed. This diagnosis presents a special problem, because the distal localization of some of these stenoses limits surgical therapy. The combination of balloon dilatation with implantation of redilatable stents will possibly become the more appropriate way of treatment (6, 7).

Transoesophageal echocardiography during interventional cardiac catheterization in children is helpful in the assessment of cardiac morphology and function before the procedure, in monitoring positioning of the guide wire and balloon catheter during the intervention, and in the evaluation of immediate morphologic and functional changes. Single-plane transoesophageal monitoring has its limitations, especially in the poor demonstration of the right ventricular outflow tract and pulmonary valve, the anatomy of the ductus arteriosus and coarctation. Multiplane imaging is likely to overcome this problem.

The complication rate of balloon dilatation with respect to mortality is low. Death has been observed in patients with multiple cardiac malformations, especially those presenting with cardiac failure. Infrequently technical problems may have deleterious effects. The use of oversized balloons in aortic valve stenosis may result in avulsion of valve leaflets and consequently massive regurgitation. Since balloon sizes smaller than the aortic annulus are chosen this complication has become rare. Femoral artery complications, bleeding as well as rupture and thrombosis, have contributed to the morbidity of balloon dilatation, especially in children weighing less than 10 kg. The development of smaller catheters combined with the use of small vessel introducer sheaths are important contributions to the reduction of these complications.

Evaluation of the efficacy of new treatment modalities such as balloon valvuloplasty and angioplasty for the management of stenotic cardiovascular lesions in children presents a problem. Most of the stenoses discussed in this thesis would have been treated surgically before the introduction of balloon dilatation. The results of surgical treatment of these various lesions are generally good and should be considered as the gold standard for comparison. Close collaboration with the paediatric cardiothoracic surgeons in decision making regarding the preferred way of treatment is essential. The optimal way for evaluating balloon dilatation as an alternative for surgical treatment should be a randomized prospective study. Several limitations preclude the realization of such a study. The population of children with congenital cardiac malformations is inhomogeneous. This is not only true with respect to age and weight, but there is a great variety of congenital cardiac malformations. Patients series with the same type of disorder are small. Within a group of patients with one specific malformation, there is a wide variation of severity, morphological substrate and functional implications for myocardial function. This is well illustrated in valvular aortic stenosis. A patient with valvular aortic stenosis may present as a neonate in severe cardiac failure, where systemic circulation is maintained by right-to-left shunting through a ductus arteriosus. On the other hand is the child with a bicuspid aortic valve with mild stenosis that remains mild during growth, and only eventually will show progressive calcification in adulthood.

Comparison of the result of balloon dilatation with historical controls of surgically treated patients has its own limitations. Also during the last ten years major improvements have been made in the anaesthetic and surgical management of infants and children with congenital cardiac malformations, which will not be recognized in a study with historical controls. The number of reports on the long-term follow up after surgical treatment of the three major indications for balloon dilatation (i.e. valvular pulmonary stenosis, valvular aortic stenosis and coarctation) is limited. In part this is a consequence of the limitations of noninvasive cardiological evaluation in the past. Nowadays especially two-dimensional echocardiography combined with Doppler presents more insight into morphology and to some extent into the functional implications of the specific malformation. This is especially helpful for the serial evaluation of valvular stenosis. In practice, functional noninvasive testing of the implications of exercise remains problematic in children. For some of the other malformations (i.e. baffle obstruction after a Mustard procedure, pulmonary artery branch stenosis and coarctation) other imaging modalities, such as transoesophageal echocardiography, magnetic resonance imaging or catheterization and angiography are the only tools for evaluation. For example, only in the recent years it became apparent that after repair of aortic coarctation in childhood, many individuals in adult life suffer from the consequences of an inadequate relief of the stenosis.

Immediate changes in left ventricular contractile performance as a consequence of balloon valvuloplasty for moderate valvular pulmonary stenosis were studied with a combined micromanometer-conductance catheter. Valvuloplasty neither affected the end-systolic nor the end-diastolic pressure-volume relationship. These findings disapprove impairment of left ventricular function as an argument in favour of balloon dilatation for treatment of moderate valvular pulmonary stenosis. In addition, the feasibility of on-line pressure-volume studies during routine cardiac catheterization in children was demonstrated and holds promise for the assessment of ventricular function in this age group. However, for practical reasons the application of this invasive technique for serial follow up measurements is limited.

The aim of treatment for many of the stenotic lesions described in this study is preservation of ventricular function on the long-term. Little is known about the functional response of the myocardium to pressure or volume overload in children and its determinants. Thanks to rapid developments in the recent years, varying from improved surgical techniques, better understanding of the physiology of the infant and child during the perioperative period, and smaller dilatation catheters, the moment of treatment of congenital cardiac malformations has shifted to a younger age. A tendency to treat patients with only mild-to-moderate stenosis has been observed since the introduction of balloon dilatation. A definite statement on the lowest range of pressure gradients where treatment is indicated cannot be made yet. Continued studies to get more knowledge if and when a lesion has negative effects on cardiac metabolism will help us in the optimal timing of catheter- or surgical intervention for treatment of children with congenital cardiac disease.

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CHAPTER 11

SUMMARY

In recent years balloon dilatation has become an important tool for the treatment of obstructive cardiovascular lesions in children. The aim of the studies described in this thesis, was to evaluate the initial haemodynamic changes and possible complications of balloon dilatation, and relate these findings to the longer term follow up results.

Chapter 1 summarizes the history of interventional cardiac catheterization in children. The use of balloon catheters for interventional treatment in cardiology started with the atrial septostomy catheter for infants, increased by the development of catheters for coronary angioplasty in adults and was followed by the introduction of large balloon dilatation catheters for valvuloplasty and angioplasty. The aim of the present study is described.

Chapter 2 deals with the outcome of balloon valvuloplasty for the treatment of valvular pulmonary stenosis in children over the age of 6 months. Both the initial and follow up results indicate that, in these electively treated patients, valvuloplasty is the preferred way of treatment.

Chapter 3 describes the results of balloon valvuloplasty of valvular pulmonary stenosis in neonates and infants younger than 6 months of age. In this age group treatment is non-elective. The result of balloon valvuloplasty in these patients may be adequate, but a substantial number of patients will need surgical

intervention for both technical and morphological reasons. In the longer term restenosis is observed in some patients.

Chapter 4 reports on the evaluation of changes in left ventricular function as a consequence of balloon valvuloplasty for moderate pulmonary stenosis. Left ventricular contractile performance was evaluated by means of the end-systolic and end-diastolic pressure-volume relationship, obtained with a combined micromanometer-conductance catheter. Both the effect of the acute decrease in right ventricular afterload and the effect of increased heart rate were investigated. Pulmonary valvuloplasty did not affect left ventricular systolic or diastolic function. A moderate increase in heart rate did not change the end-systolic pressure-volume relationship but resulted in small changes in the end-diastolic pressure-volume relationship. The feasibility of the clinical application of the conductance technique for on-line determination of pressure-volume relations in children is demonstrated. Although the technique has its limitations, it is an important instrument for immediate evaluation of the effect of therapeutic interventions on left ventricular performance.

Chapter 5 outlines the results of the use of balloon valvuloplasty for valvular aortic stenosis, of both native valve stenosis and recurrent stenosis after earlier surgical valvulotomy. Regarding the decrease of the valvular gradient and improvement of repolarization changes in the electrocardiogram at rest or during exercise, the initial results are promising. The major concern relates to the induction or increase of valvular regurgitation, necessitating valve replacement in a few patients within 1 to 2 years.

Chapter 6 reports the results of balloon angioplasty for recurrent or residual coarctation after initial surgical management. Follow up catheterization revealed accelerated growth of the dilated segment and further decrease of the residual gradient. Longer term clinical follow up demonstrated persistence of the decrease of upper body blood pressure.

Chapter 7 summarizes the results of balloon dilatation for less common obstructive cardiovascular lesions in children, both native and after surgical management. The technique can be safely applied, but the results of balloon dilatation for the various stenotic lesions are limited. Exceptions are the good results in baffle obstruction after Mustard operation and reasonable outcome in pulmonary artery branch stenosis.

Chapter 8 describes the application of single-plane transoesophageal echocardiography as a monitoring technique during paediatric interventional cardiac catheterization. The technique can be performed safely and is useful for immediate assessment of both morphologic and functional changes, and monitoring of catheters and guide wires. Limitations and future developments are discussed.

Chapter 9 describes the experience of the use of thrombolytic agents for management of femoral artery thrombosis, that may complicate retrograde ar-

terial catheterization. The results are satisfying but close clinical and haematological monitoring is required.

Chapter 10 discusses the value of balloon valvuloplasty and angioplasty as a treatment modality for obstructive cardiovascular lesions in the paediatric age group. Its position as an addition or an alternative to the surgical approach is outlined. The technique is safe and effective for a considerable number of patients. Based on the initial and follow up experience reported, there is a major role for balloon dilatation for the treatment of pulmonary and aortic valve stenosis, recurrent coarctation and some stenoses observed less frequently. Limitations of the technique are discussed, as well as the future developments of balloon dilatation in the paediatric cardiac catheterization laboratory.

SAMENVATTING

Ballondilatatie is in de afgelopen jaren naar voren gekomen als een behandelingsalternatief voor obstructieve cardiovasculaire afwijkingen bij kinderen. Het doel van de in deze dissertatie beschreven studies was het evalueren van de initiële haemodynamische veranderingen en mogelijke complicaties van ballondilatatie, en deze bevindingen te relateren aan het resultaat op langere termijn.

In hoofdstuk 1 wordt de ontwikkeling van hartcatheterisatie waarbij gebruik wordt gemaakt van catheter-interventietechnieken bij kinderen kort samengevat. De toepassing van balloncatheters voor behandeling in de cardiologie begon met de septostomiecatheter voor zuigelingen, breidde zich uit door de ontwikkeling van catheters voor coronaire angioplastiek bij volwassenen en werd gevolgd door de introductie van grote ballondilatatiecatheters voor valvulo- en angioplastiek. De doelstellingen van het huidige onderzoek worden uiteengezet.

In hoofdstuk 2 worden de resultaten besproken van ballonvalvuloplastiek voor pulmonalisklepstenose bij kinderen vanaf de leeftijd van 6 maanden. Uit de directe resultaten en die op termijn wordt duidelijk dat, bij deze electief behandelde patiënten, valvuloplastiek de voorkeursbehandeling is.

In hoofdstuk 3 worden de resultaten weergegeven van valvuloplastiek voor pulmonalisklepstenose bij pasgeborenen en zuigelingen jonger dan 6 maanden. Het effect van ballonvalvuloplastiek bij deze patiënten kan gunstig zijn, maar een belangrijk aantal patiënten zal chirurgisch behandeld moeten worden om

redenen van technische en morfologische aard. Op termijn treedt hernieuwde stenose op bij enkele patiënten.

Hoofdtuk 4 beschrijft de veranderingen in de functie van de linker hartkamer ten gevolge van ballonvalvuloplastiek van een matige pulmonalisstenose. Evaluatie van de functie van de linker hartkamer vond plaats door het bestuderen van de eind-systolische en de eind-diastolische druk-volume relatie, welke werd verkregen met een gecombineerde micromanometer-conductantiecatheter. Zowel het effect van een verminderde nabelasting van de rechter hartkamer als het effect van een door elektrostimulatie verhoogde hartfrequentie werden onderzocht. Noch de eind-systolische, noch de eind-diastolische druk-volume relatie veranderden als gevolg van pulmonalisklepdilatatie. Een toegenomen hartfrequentie resulteerde niet in een verandering van de eind-systolische, doch wel van de eind-diastolische druk-volume relatie. Met dit onderzoek werd tevens de praktische toepasbaarheid van de conductantietechniek voor het instantaan verkrijgen van druk-volume relaties bij kinderen aangetoond. De techniek kent weliswaar beperkingen, doch is een belangrijke methode voor het direct beoordelen van het effect van therapeutische interventies op de linker kamerfunktie.

In hoofdstuk 5 worden de resultaten besproken van ballonvalvuloplastiek voor de behandeling van aortaklepstenose, toegepast bij wel en niet eerder chirurgisch behandelde patiënten. Gezien de afname van het drukverval over de klep en de verbetering van de repolarisatie van het elektrocardiogram tijdens rust of inspanning, zijn de vroege resultaten veelbelovend. De belangrijkste zorg betreft het ontstaan of de toename van kleplekkage, welke klepvervanging binnen 1 tot 2 jaar noodzakelijk maakt bij enkele patiënten.

Hoofdstuk 6 beschrijft de resultaten van ballonangioplastiek toegepast voor een hernieuwde of reststenose bij patiënten welke reeds eerder een chirurgische behandeling van een coarctatio aortae hadden ondergaan. Bij nacatheterisatie na een jaar werd een versnelde groei van het gedilateerde segment en een verdere afname van het drukverschil aangetoond. Op langere termijn persisteerde de afname van de bloeddrukverhoging in de bovenste lichaamshelft.

Hoofdstuk 7 geeft de uitkomst weer van ballondilatatie voor minder vaak voorkomende obstructieve hart-vaat afwijkingen bij kinderen, zowel zonder als met voorafgaande chirurgische behandeling. De techniek kan veilig worden toegepast, maar het resultaat van ballondilatatie voor de verschillende vernauwingen is beperkt. Uitzonderingen hierop vormen de goede resultaten bij een vernauwing van de "baffle" na een operatie volgens Mustard en het redelijke effect bij een arteria pulmonalis takstenose.

In hoofdstuk 8 wordt de toepassing beschreven van transoesofageale echocardiografie gedurende therapeutische hartcatheterisaties bij kinderen. De techniek kan veilig worden uitgevoerd en is behulpzaam bij het direct vaststellen van zowel morfologische als functionele veranderingen, als ook voor het po-

sitioneren van catheters en voerdraden. De beperkingen en de toekomstige ontwikkelingen worden besproken.

Hoofdstuk 9 beschrijft de ervaringen met het gebruik van thrombolytica voor behandeling van arteria femoralis thrombose, welke kan optreden als complicatie na retrograde arteriële catheterisatie. De resultaten van de behandeling zijn bevredigend, doch nauwkeurige klinische en haematologische bewaking is noodzakelijk.

In hoofdstuk 10 wordt de waarde van ballonvalvulo- en angioplastiek als behandelingsmogelijkheid voor de diverse obstructieve cardiovasculaire afwijkingen bij kinderen besproken. De plaats als een toevoeging aan of een alternatief voor chirurgische therapie wordt aangegeven. De techniek is veilig, en de behandeling is voor een belangrijk aantal patiënten effectief. Op basis van de initiële resultaten, en die op termijn, wordt ballondilatatie een belangrijke rol toebedeeld bij de behandeling van pulmonalis- en aortaklepstenose, recoarctatio en enkele minder frequent voorkomende vernauwingen. De beperkingen van de techniek worden besproken, evenals de toekomstige ontwikkelingen van ballondilatatie in de kindercardiologie.

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CURRICULUM VITAE

De schrijver van dit proefschrift werd geboren op 6 oktober 1952 te Hellendoorn. In 1969 behaalde hij het eindexamen HBS-B aan het Erasmus Lyceum te Almelo, waarna in dat jaar werd begonnen met de studie geneeskunde aan de Medische Faculteit van de Rijksuniversiteit Groningen. Hij behaalde het doctoraal examen in 1974 en het artsexamen in 1976. Tot eind 1976 was hij werkzaam als arts-assistent op de afdelingen cardiologie, longziekten en urologie van het Diaconessenziekenhuis te Groningen. Van 1977 tot 1981 specialiseerde hij zich tot kinderarts in het Academisch Ziekenhuis Rotterdam/Sophia Kinderziekenhuis te Rotterdam (opleider Prof. Dr. H. K. A. Visser) in welke periode hij een half jaar werkzaam was op de afdeling kindercardiologie. Van begin 1981 tot medio 1982 was hij chef de clinique voor de afdelingen infectieziekten en intensive-care voor oudere kinderen in het zelfde ziekenhuis. Van medio 1982 tot 1984 werd hij door Prof. Jhr. V. H. de Villeneuve opgeleid tot kindercardioloog. Sindsdien werkt hij als kindercardioloog op de afdeling kindercardiologie van het Academisch Ziekenhuis Rotterdam/Sophia Kinderziekenhuis (hoofd Prof. Dr. J. Hess), waar ook de gegevens voor dit proefschrift werden bewerkt.

De schrijver is getrouwd met Machteld de Jong, arts, en heeft vier kinderen.