Endovascular balloon dilation and stent implantation in congenital cardiology: novel indications and evolving techniques.

Derize Boshoff

Doctoraal proefschrift in de medische wetenschappen

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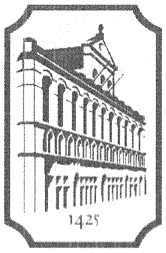

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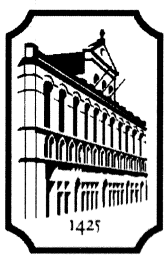

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CHAPTER 1

Introduction and General Outline

“The richness of the human experience would lose something of rewarding joy if there were no limitations to overcome.”

Helen Keller

Chapter 1

Introduction and General Outline

1.1 General introduction

1.1.1 Paediatric interventional cardiology: coming of age

Pediatric cardiology, as a subspecialty owes its origin to pediatrics and cardiology. The development of the stethoscope made it possible to establish some clinical diagnosis during life: for the first time physicians began to relate murmurs heard by auscultation to pathologic findings at autopsy (1). The past 60 years has brought unprecented progress in the diagnosis and the medical and surgical treatment of congenital heart disease. When Robert Gross, a junior pediatric surgeon, made medical history in 1938 by performing the first successful ductus arteriosus ligation in a 7 ½-year-old girl, pediatric cardiology, as a discipline, was born. The application of cardiac catheterization in the study of congenital heart disease began approximately during the same period. Forssman in 1929 was the first to show that the heart can be approached by placing a ureteral catheter via his own left antecubital vein: he walked down a flight of stairs and under fluoroscopy advanced the catheter until the tip was in his heart (2). In 1932 Cournand and Richards of New York City began performing cardiac catheterizations in patients who were in shock. With the advent of surgery for congenital cardiac defects, correct preoperative diagnosis became mandatory and shortly thereafter, Cournand and his associates, working with a pediatric cardiologist, Janet Baldwin, reported on the use of cardiac catheterizations in congenital heart disease (3). Rashkind and Miller introduced the lifesaving technique of balloon atrial septostomy in 1966 (4), creating an initial response that varied between admiration and horror but set the stage for all future intracardiac interventional procedures: the true beginning of pediatric and adult interventional cardiology (5). Dr. William Rashkind continued to develop appropriate intravascular devices to close atrial septal defects and patent ductus arteriosus nonsurgically. The end of the 1970s and the beginning of the 1980s began a dynamic and exciting period for pediatric interventional catheterization procedures. Grüntzig and Hoppf described the dilation of peripheral vessels with

an inflatable noncompliant static balloon (6). The Grüntzig balloon was a device that was small enough to be introduced percutaneously and were miniaturized even further to be applied to the coronary arteries (7). The late 1980's witnessed an exponential increase in clinical experience with balloon angioplasty for congenital stenoses. Technological advancement leading to smaller, more effective balloon catheters and guidewires, improved success rates and minimized complications even in the smallest babies. The concept of intravascular stent implantation to maintain vessel patency was first introduced by Dotter in 1969 (8). However, extensive clinical trials were not carried out until the late 1980s, after improvements in stent technology and design were made and high pressure balloons were developed. Since these early reports, enormous advances have occurred in the interventional technology for pediatric patients. The uses of the stents in congenital lesions were unique in that these were the first catheter interventional procedures that were not replacing previous "good" surgical procedure (9). Most of the results of surgical repair of pulmonary artery branch stenosis and systemic venous stenosis varied from poor to catastrophic. In 1988 Mullins reported the first use of stent implantation to treat peripheral pulmonary artery stenosis (9). New stent delivery techniques have made it possible to deliver even large stents (dilatable up to 18mm) into patients as small as 4 or 5kg (10). In paediatric patients, endovascular stents are most commonly implanted into peripheral pulmonary arterial stenosis or hypoplastic pulmonary arteries (11-16), but have also proved effective and safe for patients with systemic venous obstructions (17,18) and aortic (re)coarctation (19-26). A very exciting recent advance has been the development of percutaneous valve replacement using a biological valve (27). Currently two balloon expandable transcatheter valves are available for percutaneous pulmonary valve implantation: the Melody® valve from Medtronic (Minneapolis,MN, USA) and the SAPIEN™ THV from Edwards Lifesciences LLC (Irvine,CA, USA); experience in this new technique is growing with now more than 3500 implants world-wide. Further miniaturization of the catheter systems, refinement of the techniques and evaluation of long-term results are currently being undertaken, making these new procedures safer, more predictable and more effective. Not only has interventional cardiac catheterization replaced surgery as primary treatment for a

number of “simpler” cardiac anomalies, it is also complementary to surgery for the more complex lesions such as hypoplastic left heart syndrome and complex Tetralogy of Fallot.

1.1.2 A child is not a small adult

As interventional paediatric cardiologists, we deal with relatively small patient groups with a wide range of diagnosis and anatomical substrates to be treated. In contrast to most treatment modalities in medicine, there are very few “standardized” procedures when treating patients with congenital heart disease. As procedures are performed repeatedly, the operator can individualize techniques and modify them in a logical and safe manner extending the limits of old therapies. Very few of the materials and catheters used in paediatric/congenital catheterizations were designed or intended for use in paediatric/congenital patients. Although intravascular stents still do not have “FDA approval” for use in congenital lesions and paediatric patients, the use of these stents has been accepted as the standard of care by all centers and professional medical societies responsible for the care of patients with congenital heart disease since 1996. The “ideal” stent for use in paediatric patients should have a low profile when collapsed, have a small delivery system in order to minimize vascular trauma and should preferable be pre-mounted on appropriate balloons and balloon catheters. It should be flexible enough to negotiate the difficult turns even in a small heart, but still have good visibility under fluoroscopy for implantation and later re-evaluation. It should have sufficient wall strength to prevent rebound or collapse of the vessel over time, should have no sharp ends or tips, cause as little as possible intimal proliferation and allow further expandability over time to ultimately reach the adult diameter of the vessel in which it was implanted. In the “real” world these “ideal” stents probably will only remain a dream for such a “small” commercial market. In most instances the stents and delivery equipment that are available for adult vascular interventions in acquired (atherosclerotic) disease are modified to suit the implantation of stents in congenital lesions. When selecting the appropriate stent, the interventionalist needs to recognize and prioritize the specific features and needs of the particular vessel to be stented, taking into consideration the size of

the child and the technical aspects of the stent to be delivered to the target vessel (28). There is currently no doubt that stent implantation is a safe and effective solution for the relief of stenotic lesions, but as so elegantly stated by the late Dr. Gerd Hausdorf, "the therapeutic efficacy of stents depends exclusively on their mechanical properties, like ordinary plumbing" (29). Another matter of concern is the lifespan of these permanent implants in children with a life expectancy of 70 years or more, which is certainly a time period far beyond the scope of current interventionalists and engineers designing these stents (29).

1.2 Aims and outline of the thesis

The aim of this thesis is to describe novel indications for balloon dilation and endovascular stenting in patients with congenital heart disease and evaluate the safety and efficiency of these evolving techniques. Several studies have been done, both clinical (prospective and retrospective) and experimental (bench testing and animal experiments).

The studies will be discussed in 3 main groups:

Group 1 (Chapter 2): Growth of vessels after endovascular stenting: an animal model. An experimental study to investigate the effect of stent implantation and later surgical removal on the growth potential of juvenile vessels. The use of stents in a growing child is challenging, as ideally the final stented vessel diameter should ultimately approach the adult size. When implanting a stent in a relatively young child, serial re-dilation should be possible, unless stenting is only seen as bridge to subsequent surgery. This study originated from our clinical concern that stent removal could scar the vessel wall to the extent that further growth is limited.

Group 2 (Chapter 3): Pulmonary flow modulation – cutting balloons and stents. In this chapter different ways of pulmonary flow modulation are discussed, describing new balloon dilation- en stenting techniques in newborn (or even premature) babies up to adult patients with congenital heart disease. We discuss the treatment options of major aortopulmonary collateral arteries in the setting of Tetralogy of Fallot with pulmonary atresia, stenting of the neonatal arterial duct, techniques allowing pulmonary flow to be tailored to patient size and the off-label use of percutaneously implanted pulmonary valves.

Group 3 (Chapter 4): Stent implantation in the aortic arch. Stenting of the aortic arch in 2 extreme patient populations are presented in this chapter: the asymptomatic adolescent/adult with mild pressure gradients and arterial hypertension and the premature or critically ill neonate with severe coarctation for which urgent intervention is necessary.

Chapter 5 focuses on ways to avoid complications, the relationship between the interventional cardiologist and the cardiac surgeon and the dilemma of the pediatric cardiologist when trying to practice "evidence based medicine". Some future perspectives are mentioned followed by the conclusions of the thesis.

CHAPTER 2

Growth of vessels after endovascular stenting: an animal model

“The wise are cautious and avoid danger; fools plunge ahead with reckless confidence.”

Proverbs 14:16

In this chapter we describe an experimental study to investigate the effect of stent implantation and later surgical removal on the growth potential of juvenile vessels. This study originated from or clinical concern that stent removal could scar the vessel wall to the extent that further growth is limited.

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Preclinical research

Endovascular stenting of juvenile vessels: consequence of surgical stent removal on vessel architecture

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KEYWORDS
Stents;
Congenital heart disease;
Vessel architecture;
Stenosis

Aims To investigate the effect of stenting and later surgical removal on the architecture and therefore growth potential of juvenile vessels.
Methods and results Stents were implanted in the carotid artery and jugular vein of six 6-week-old lambs. Ten weeks later, stents were excised and the vessels closed without the use of patch material. After another 10 weeks, the vessel size (treated and untreated control side) was measured angiographically and the animals terminated for histology. All arteries were patent: treated arterial size was 9 ± 1 mm compared with 11 ± 1 mm on the control side ($P = \text{ns}$). Two veins were completely occluded and two severely stenosed; vessel size was smaller compared with the control side (8 ± 8 vs. 14 ± 5 mm; $P = 0.02$). Preserved vessel wall integrity was observed in both arteries and veins (except for local rupture of the internal elastic lamina with neointimal formation in two arteries leading to mild stenosis).
Conclusion Vessel wall architecture remains well preserved after surgical removal of stents implanted in juvenile arteries and veins. However, stenting and subsequent surgical removal results in a high risk of venous thrombosis (probably due to the lower blood velocity, lower pressure, and the absence of pulsatility in venous vessels).

Introduction

Intravascular stents are an ideal adjunct for treatment of stenosis not responsive to balloon angioplasty and have been used successfully in pediatric patients with stenosis of the pulmonary artery, stenosis of the great veins, and post-operative stenosis of Fontan anastomosis.[1] Re-expansion of stents has been shown to be feasible and safe even up to 3 years after implantation.[2,3] However, placement of stents (e.g. in pulmonary arterial lesions and aortic arch stenosis) has limitations in infants and small children due to stent inflexibility, requirement for large sheaths, and concerns about creating fixed obstructions after the placement of small diameter stents in growing patients. Smaller stents with maximal achievable diameters of 9–10 mm therefore commit the patient to future surgery to enlarge the stented area once it has been dilated to its maximal diameter.[4] The surgical removal of a stent is an aggressive procedure with possible destruction of the vessel wall.

This study originates from our clinical concern that stent removal could scar the vessel wall to the extent that further growth is limited. The objective of this experimental study was therefore to investigate the effect of stent implantation and later surgical removal on the architecture and therefore growth potential of juvenile vessels.

Methods

Experimental protocol

Institutional ethical committee (Catholic University of Leuven) approval was obtained to perform this study in sheep. Six weaned lambs (6 weeks old) were selected to undergo stent implantation in both the carotid artery and the jugular vein. A power calculation could not be performed as no information is available on incidences of the investigated subject. We therefore selected our sample size according to previous experience: a complete observation set of six animals was considered sufficient to correct for biological variability in a single endpoint, controlled prospective animal trial. The ethical restraints in the use of chronic animal experimentation had to be considered as well (each test takes 6 months).

The mean weight of the animals was 18 ± 2.2 kg. All procedures were performed under general anaesthesia. Anaesthesia was induced with ketamine hydrochloride (15 mg/kg) and maintained with fluothane. We preferred the jugular vein and carotid artery because of the surgical accessibility and the fact that the untreated side could be used for comparison as control. Between procedures, the animals were returned to the farm and no drugs were administered. The stent implantations were performed through femoral

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access. An angiogram was taken in order to identify the required stent size. The arterial stents were implanted first and the side that was first entered with the catheter was used for stent implantation (therefore leading to a random allocation: four stents left and two stents right). For practical reasons, the same side was taken for the jugular vein to allow the surgeon to retrieve the stents through one surgical incision. A total of six venous and six arterial stents were implanted. Venous stents (6 Zig CP stents, Numed, USA, manually crimped on balloon, length 28 mm) were expanded up to 12 mm (range 11–14 mm) and arterial stents (Multi-link premounted coronary stents, Guidant, Santa Clara, USA, length 15–20 mm) were expanded up to 4 or 5 mm. Stent diameter was estimated according to the vessel diameter (angiographically), therefore avoiding 'oversizing' of stents.

After 10 weeks (animal weight 43 $\pm$ 6.9 kg), a surgical cut-down was performed at the level of the stent implantation. The animals were heparinized, the vessels clamped, and longitudinally opened. The stents were removed *in toto*. The longitudinal incisions were closed with a running polypropylene suture. No patch material was used: the vessel opening was closed primary leaving only a single longitudinal surgical scar. After another 10 weeks (animal weight 55 $\pm$ 6.7 kg), angiography was performed and the affected and control sides compared with regard to vessel patency and diameter. Arterial access was obtained femorally and an aortogram performed for measurement of the carotid arteries. Venous angiography was performed via peripheral contrast injections from both ears comparing venous drainage to the treated and untreated jugular veins. Calibration for measurements was done using the angiographic catheter. The animals were subsequently terminated and the vessels dissected proximal and distal to the previously stented area. The complete segments were resected and submitted for histological analysis.

Histological analysis

The segments were transversally cut into 5 mm-thick tissue specimens and from each block a series of 4 μm sections were prepared in a standard way for histological examination. The samples were stained with haematoxylin–eosin and elastic stains to identify the integrity of the elastic lamina. The internal elastic lamina is generally more pronounced in arteries than in the corresponding veins; therefore, arterial injury was defined as destruction of the internal elastic lamina and venous injury was defined as a discontinuity of the media. The percentage of lumen patency was scored.

Data

Continuous data are presented with their mean value and standard deviation. The non-parametric Wilcoxon signed-rank test was performed (Statistica Software package, Tulsa, USA). A $P < 0.05$ was considered to indicate a significant difference.

Table 1 Angiographic diameter of control carotid artery, stented artery, and histological patency rate (10 weeks after surgical stent removal)

Carotid artery	Control artery diameter (mm) (angiographically)	Treated artery diameter (mm) (angiographically)	Treated artery patency (%) (histologically)
1	10	8	70
2	10	8	70
3	11	9	100
4	11	11	100
5	13	11	100
6	12	11	100
Mean (SD)	11 (1)	9 (1)	

Results

Arteries

Table 1 summarizes the vessel diameter (evaluated angiographically) and vessel patency (scored histological) in comparison with the control side 10 weeks after surgical stent removal. The vessel diameter is slightly smaller than the control side. There is only mild stenosis in two cases (up to 30%). Histological analysis (*Figure 1A*) illustrates preserved arterial wall architecture. There is no specific injury. The two cases with mild stenosis are due to moderate intima hyperplasia at the level of local injury of the elastic lamina (*Figure 1B*).

Veins

Table 2 summarizes the vessel diameter (evaluated angiographically) and vessel patency (scored histological) in comparison with the control side 10 weeks after surgical stent removal. Two veins proved to be completely occluded and two severely stenosed. The overall size of the veins was significantly smaller when compared with the control side ($P = 0.02$). Histological analysis shows a preserved media of the

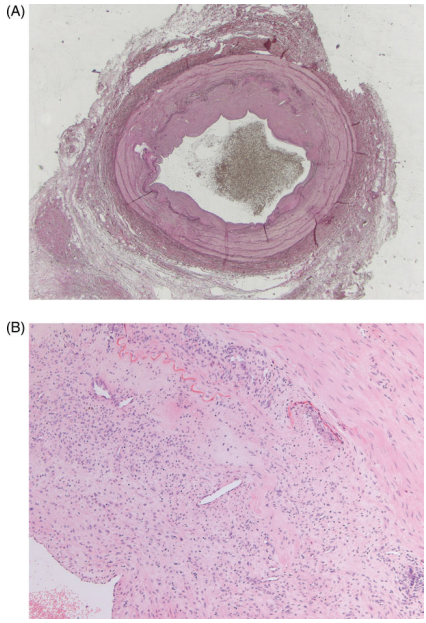

Figure 1 (*A*) Overview of a carotid artery 10 weeks after removal of stent: partial disruption of the internal elastic lamina is observed. Neointima formation results in a reduction of the lumen to 70% of its original size. (Elastic Van Gieson stain $\times$25). (*B*) Detail of the same case. Between the media (right upper corner) and the neointima, residual parts of the internal elastic lamina is seen. (haematoxylin–eosin $\times$200).

Table 2 Angiographic diameter of control jugular vein, treated vein, and histological patency rate (10 weeks after surgical stent removal)

Jugular Vein	Control vein diameter (mm) (angiographically)	Treated vein diameter (mm) (angiographically)	Treated vein patency (%) (histologically)
1	10	0	0
2	20	5	30
3	10	0	0
4	20	19	100
5	18	16	90
6	10	8	20
Mean (SD)	14 (5)	8 (8)	

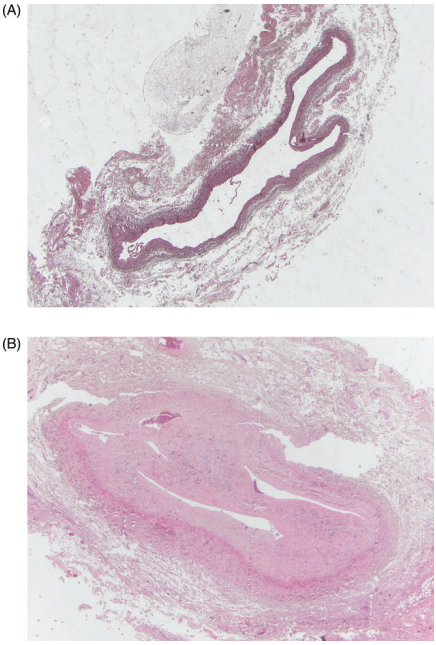

Figure 2 (*A*) Overview of a normal jugular vein. The wall architecture is well preserved. (Elastic Van Gieson stain ×12.5). (*B*) Overview of a thrombosed vein with recanalization 10 weeks after removal of stent. In the upper area, partial disruption of the entire wall is seen. (haematoxylin–eosin ×12.5).

vein wall in the four non-occluded vessels (*Figure 2A*). The two occluded vessels proved to contain thrombus. Amazingly, their vessel wall architecture was as well preserved (*Figure 2B*) as the non-occluded vessels. The lumens of the two severely stenosed vessels were filled with thrombus, but recanalization had occurred, as histologically documented by the presence of newly formed vessel lumens within the occluding thrombus.

Discussion

In the management of congenital heart disease, balloon-expandable stents have been used with success for obstructive vascular lesions that tend to recoil or collapse after dilatation.[1,3,5,6] However, stent implantation in stenotic vessels of infants and small children can be problematic because there is no ideal stent model that is small enough to be easily introduced into the infant femoral vein or artery and, at the same time, large enough to be re-dilated during growth to adult vessel diameters.[7] Such implants can be life saving, though in the immediate post-operative period and in some instances the interventional cardiologist has no other option but to commit the patient to later surgical removal of a stent.[8,9] In patients with univentricular hearts, for example, a combined surgical and interventional strategy is often needed to optimize the growth of structures. Stent implantation in hypoplastic pulmonary arteries after a bidirectional cavopulmonary connection is sometimes necessary in order to address clinical problems such as venous congestion and severe cyanosis. These stents usually have to be excised during completion of the Fontan operation.

Surgical removal of a stent is an aggressive procedure with possible destruction of the vessel wall to such an extent that the further growth potential is limited. In this experimental study, it is shown that vessel wall architecture remains remarkably well preserved on histopathological examination. All arteries were patent, but four out of six veins were thrombosed. We hypothesize that the surgical trauma caused by the endarterectomy results in a higher risk for thrombosis in a non-pulsatile, low blood velocity and low-pressure environment. The pulmonary artery has a high blood velocity in the normal circulation. After a bidirectional or total cavopulmonary connection, a non-pulsatile, low flow, and low pressure circulation is created, possibly simulating venous type flow. These findings suggest that anti-aggregate treatment and/or anticoagulation might be indicated in this clinical setting. It cannot be excluded though that the morphology of the vessel wall itself may also play a role in the increased venous thrombosis risk after stent removal.

Limitations of the study

Stents were implanted in non-stenosed vessels. Stent expansion with mild stretch of vessel (as in this series) will therefore not disrupt vessel architecture; however, such disrupture may be the case when stents are expanded in stenosed vessels.

A comparison is made between the jugular vein and the carotid artery and the response of growth of the vessel after stenting. There are no stents available that are suitable for use in both small arteries and large veins and therefore stents of different designs had to be used (CP stents in the jugular veins and multi-link premounted coronary stents in the carotid arteries). The difference in stent design and stent material introduces a variable which is difficult to evaluate, as it is theoretically possible that different metallic properties of stents may induce a different type of response in a vessel. It is our experience from clinical practice though that intimal proliferation (with in-stent stenosis) tends to develop more in smaller stents, than in larger

stents. CP stents (used in the jugular veins in this study) are often used for stenting coarctation of the aorta in adult patients and has never caused any in-stent thrombosis or significant in-stent stenosis due to intimal proliferation. However, when coronary stents are used in smaller arteries, i.e. aorto-pulmonary collaterals, in-stent stenosis due to intimal proliferation is often seen.

Conclusion

Vessel wall architecture remains well preserved after surgical removal of stents implanted in juvenile arteries and veins. However, stenting and subsequent surgical removal results in a high risk of venous thrombosis.

Anti-aggregate treatment and/or anticoagulation might therefore be indicated after stent removal in the low flow and low-pressure environment (bidirectional/total cavopulmonary connections).

Future perspectives

Surgery because of mismatch of stent size and vessel growth during development may hopefully be avoided in future with the use of biodegradable stents[10–13] and the development of the so-called breakable stents in infants and children.[14] These stents are still experimental and the biodegradable stents are currently only available up to a maximum diameter of 3.5 mm, which limits the use in older infants and children.

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Conflict of interest: none declared.

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CHAPTER 3

Pulmonary flow modulation

3.1 Treatment options of major aortopulmonary collateral arteries in the setting of Tetralogy of Fallot with pulmonary atresia.

3.2 Stenting of the neonatal arterial duct.

3.3 “Tailoring” pulmonary blood flow to accommodate somatic growth:

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3.4 Off-label use of percutaneous pulmonary valved stents.

Chapter 3

3.1 Treatment options of major aortopulmonary collateral arteries in the setting of Tetralogy of Fallot with pulmonary atresia

The principles of management are discussed, with emphasis on aiming towards normalization of the pulmonary circulatory physiology. The role of cutting balloons in successfully dilating pressure resistant stenosis and even filiform or long segment lesions are discussed in detail as well as the indications for stent implantation.

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Review Article

A review of the options for treatment of major aortopulmonary collateral arteries in the setting of tetralogy of Fallot with pulmonary atresia

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THE PULMONARY ARTERIAL SUPPLY IN PATIENTS with pulmonary atresia when combined with a ventricular septal defect is frequently unifocal via the arterial duct. In more complex cases, it can be multifocal. This can be through bilaterally patent arterial ducts, but more typically is through major aortopulmonary collateral arteries. In patients with such major aortopulmonary collateral arteries, establishing the source and arrangement of the pulmonary arterial supply is fundamental to management and prognosis.[1–3] The collateral arteries, however, show marked variability in their origin and pattern of arborisation.[4]

Definition and morphology of major aortopulmonary collateral arteries

Major aortopulmonary collateral arteries are large, congenital, systemic-to-pulmonary collateral arteries, representing remnants of the embryonic ventral splanchnic arteries. These vessels normally regress concomitant with the formation of the normal pulmonary arterial system in the first weeks of gestation. Major collateral arteries may persist, however, when there is early maldevelopment of the pulmonary valve or the central pulmonary arterial system, as occurs in pulmonary atresia in combination with a ventricular septal defect. In some patients with this malformation, the central pulmonary arterial system fails to develop proper continuity with the embryonic lung, and a normal pulmonary arterial tree is not formed. Instead, the systemic-to-pulmonary collateral arteries persist, and create a bewildering array of arterial connections to various segments of the lungs. The persisting arteries typically number between two and six, with the majority originating from the anterior wall of the descending thoracic aorta at the level of the carina. They can also take origin from the lower descending thoracic and abdominal aorta, or braciocephalic arteries.[5,6] They frequently run a retro-oesophageal course. Occasionally, the collateral arteries may arise from the left or right coronary artery[7] (Fig. 1). In most instances, it is possible to distinguish the collateral arteries from the arterial duct on the basis of their origin, course, behaviour over the neonatal period, and histological structure.[8,9] The extent of distal pulmonary vascular bed supplied by collaterals generally varies inversely to that supplied by the true pulmonary arteries, which range from being normal in size to completely absent.[10] A given lung segment may be supplied by both collateral arteries and intrapericardial pulmonary arteries, with connections between the two sources occurring centrally or peripherally, and at single or multiple sites.[11] Essential collateral arteries are those that supply exclusively the arterial bed of a given portion of the lung. Redundant collateral arteries are those which overlap with the distribution of the intrapericardial pulmonary arteries.[12] The collateral arteries are pre-programmed embryologically not to survive beyond early fetal life. Should they persist, there is a high incidence of significant stenosis, typically near the junction with the aorta or the pulmonary arteries at the hilums. These stenoses may progressively worsen due to ongoing turbulent flow,

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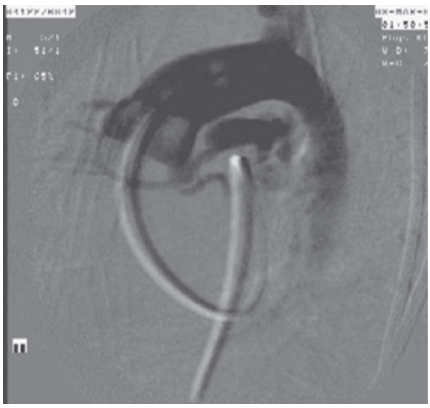

Figure 1.
The aortogram in a patient with a complex functionally univentricular heart, discordant ventriculo-arterial connections, and pulmonary atresia. The pulmonary arterial bed is perfused via a connection between the coronary arteries and the pulmonary arteries.

polycythemia, hyperviscosity, and lack of growth.[13] Due to mounds of intimal tissue containing significant amounts of collagen, the stenoses may become tough and resistant to extreme high forces beyond 20 atmospheres.

Over the past decade, surgical and interventional techniques have evolved remarkably in treating patients with complex forms of pulmonary atresia, with biventricular repair now achieved in many.[14–19] This progress has been related to the better characterization of the major collateral arteries, and their distinction from the branches of the intrapericardial pulmonary arteries, together with improvements in the interventional and surgical care of small infants.[20]

Historical review of strategies for treatment

The collateral arteries are almost always found when the pulmonary atresia itself exists in the setting of the intracardiac anatomy of tetralogy of Fallot. In this setting, the natural history is dependent on the nature of the flow of blood to the lungs. At birth, in the presence of pulmonary arteries of adequate size, cyanosis may be minimal. In the presence of hypoplastic pulmonary arteries, the flow is dependent on the presence of the aortopulmonary collateral channels.[12] Clinical presentation will depend on whether these vessels are large, moderately stenotic, or severely stenotic. A poor functional status is to be expected in those patients with excessive or inadequate pulmonary flow.

Treatment has evolved from palliative shunting, or interruption of the collateral arteries, in the 1970s, to unifocalization of the pulmonary arteries with connection to the right ventricle with or without closure of the ventricular septal defect.[21–24] The first major advances in the understanding and treatment of these lesions came with the morphologic and physiologic characterization of the extremely variable pulmonary arterial supply.[6,11,25] On the basis of these studies, Haworth et al.[26,27] postulated that the flow of blood to the lungs might be normalized by unifocalizing the individual arteries with the intrapericardial pulmonary arteries. Since these early reports, a number of programmes have been developed for the management of these challenging lesions. Early on, these strategies have been based on the concept of staged unifocalization, with the initial phase of management mostly designed to increase flow to the intrapericardial pulmonary arteries in order to stimulate their growth.[18,24,28–33] Historically, there was disagreement regarding the need for surgical intervention in patients with balanced flow to the lungs. A number of those patients had survived to adulthood without surgical intervention, or with palliative shunts alone.[12] Studies of the natural history of these patients, however, show that they develop left ventricular dysfunction as a result of chronic left-to-right shunting and left ventricular volume overload. Progressive aortic annular dilation commonly potentiates to aortic insufficiency, further impairing left ventricular function.[30] Based on these findings, operative therapy is currently recommended for all patients whose general condition and anatomic findings are amenable to surgical repair.

Present state and clinical indications

Principles of management

The principles of management of tetralogy of Fallot with pulmonary atresia and major collateral arteries are the same, despite the wide spectrum of pulmonary vascular patterns which can be found in such patients. The ultimate goal is to normalize the circulatory physiology. The key to a satisfactory surgical result is careful selection of the patient, and if required, suitable preparation. Repair should be attempted only in patients who are predicted to have a low probability of severe postoperative right ventricular hypertension. In patients with repaired tetralogy of Fallot and pulmonary atresia, the number of segments of lung supplied by the pulmonary arterial system has been found to correlate strongly with pulmonary arterial pressure and calculated pulmonary vascular resistance.[34] In patients with multifocal pulmonary arterial supply, therefore, attempts should be made to incorporate as many segments of lung as possible into the

unifocalized pulmonary vascular bed.[11] The lower the resistance in a given pulmonary segment, the better. This, in turn, is largely a function of the state of health of the microvasculature of the lung.

Description of pulmonary arterial supply

Detailed knowledge of the distribution of both the intrapericardial pulmonary and the collateral arteries is required in planning the surgical and interventional approach in each patient. Non-invasive techniques, including echocardiography and magnetic resonance imaging, may provide important information.[12] Cardiac catheterization, nonetheless, is usually essential to obtain all the necessary information. The intrapericardial pulmonary arteries may be visualized by injection of contrast through the collateral arteries that communicate with them (Fig. 2). Pulmonary venous wedge injections may be necessary if anterograde flow is insufficient. In a neonate, the collateral arteries can best be demonstrated by a descending aortogram with distal balloon occlusion (Fig. 3). Selective injections of contrast in the individual collateral arteries can then be performed. It may also be necessary to selectively inject the right or left subclavian artery, and even the coronary arteries, to define the presence and extent of so-called indirect collateral arteries.

Palliative procedures

Palliative procedures may be needed initially if primary repair appears unfeasible. Palliative procedures have a dual purpose. They not only improve the management of the immediate clinical problem, but also make the patient more suitable for later definitive surgical repair.[9] Palliation may be required in patients with patchy, unbalanced, excessive, or inadequate flow of blood to the lungs.

Issues relating to technique and equipment

Conventional staged surgical approach

As mentioned earlier, the ultimate goal of therapy in the setting of major collateral arteries is to construct separate pulmonary and systemic circulations that can function in series.[5] The conventional approach for achieving this goal is to embark on a staged surgical reconstruction to centralize the multifocal pulmonary blood supply, recruiting as many lung segments as possible, then provide egress from the right ventricle to the unifocalized pulmonary arterial system, and close the ventricular septal defect.[24,31,35] This generally requires, on average, three sequential steps, as outlined by Gupta et al[14] in their algorithm for management.

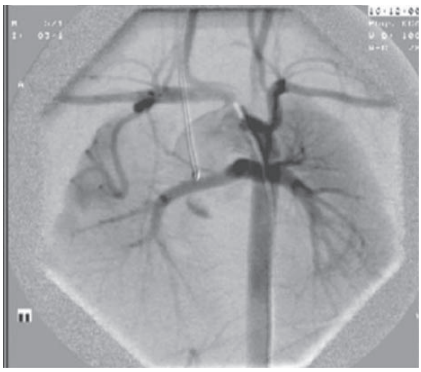

Figure 2.
The aortogram in a patient with tetralogy of Fallot, pulmonary atresia, and ventricular septal defect. The confluent pulmonary arteries are perfused via a left-sided duct, but one segment of the right upper lobe is perfused via a collateral artery originating from the right subclavian artery.

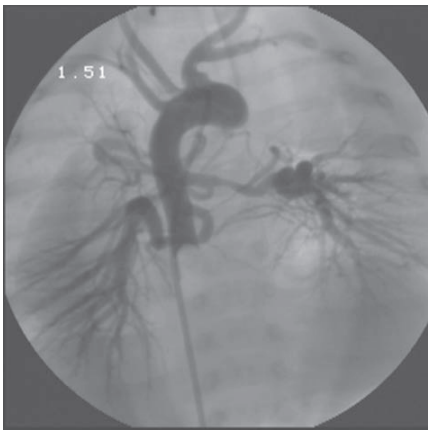

Figure 3.
Collateral arteries are demonstrated by an injection made in the descending aorta with distal balloon occlusion.

First stage: shunt or conduit from the right ventricle-to-pulmonary arteries or outflow patch

The first stage involves interventions, either surgical or by cardiac catheterization, to promote growth of the intrapericardial pulmonary arteries when present,

and to control excessive flow of blood to the lungs. In the simplest cases, the intrapericardial pulmonary arteries will be of adequate size and distribution, and the collateral vessels are redundant. Palliation by means of construction of a systemic-to-pulmonary shunt was traditionally performed in the neonatal period to maintain arterial oxygen saturation in an acceptable range, usually from 80 to 85% in room air. Currently, such patients would be considered for primary repair.

If the intrapericardial pulmonary arteries are hypoplastic, as is seen in up to one-third of patients, the options are to place a conduit from the right ventricle to the pulmonary arteries, or patch the pulmonary outflow tract without closing the ventricular septal defect[15] (Fig. 4). Some surgeons may prefer other types of shunts, such as a modified Blalock-Taussig shunt, a central shunt, or an end-to-side anastomosis of the hypoplastic pulmonary trunk to the ascending aorta. Redundant collateral arteries may be ligated surgically at the time of surgery, or embolized during cardiac catheterization before or after the surgery. In some patients, maintaining flow through redundant collateral arteries may be desirable to maintain an adequate arterial saturation.[12]

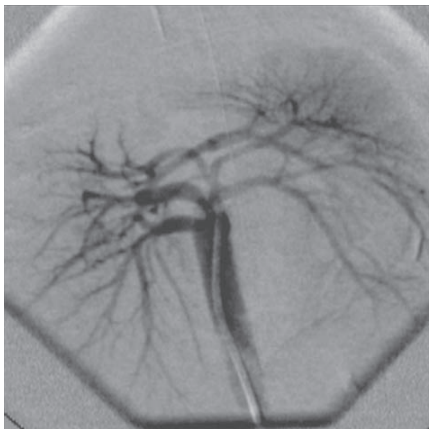

Figure 4.
The aortogram in a neonate with severely hypoplastic intrapericardial pulmonary arteries, tetralogy of Fallot, pulmonary atresia, and major aortopulmonary collaterals. In this patient, a conduit was placed from the right ventricle to the pulmonary arteries to promote growth of the intrapericardial pulmonary arteries.

Second stage: unifocalization

The second stage involves unifocalization of the major collateral arteries in both lungs. This refers broadly to procedures that join the multifocal sources of arterial supply, be they intrapericardial arteries or one or more collateral arteries, into a single source. Unifocalization should be undertaken at an age when the collateral arteries are large enough to permit construction of an anastomosis of sufficient size that is less likely to become stenotic with growth. Staged procedures may be required for bilateral and multiple collateral arteries. Many different types of procedures have been reported. These include direct anastomosis of the collateral arteries to the supply derived from intrapericardial pulmonary arteries,[24,31,36] or placement of interposition grafts between collateral arteries and the branches of the intrapericardial pulmonary arteries. These interposition grafts can be synthetic,[16,24] autologous artery or vein,[24,36] xenograft pericardium,[35] or autologous pericardium.[36]

An ideal unifocalization procedure should, first, allow incorporation of all nonredundant collateral arteries and the supply from the intrapericardial arteries to each lung without distortion. Second, conduits should be used that will either grow, or be large enough to supply adequate flow in adulthood without replacement. Third, the risk of thrombosis must be minimized, and finally, the focalized segment should be easily accessible from the mediastinum at the time of definitive repair. Unifocalization techniques using pericardial tubes are held to fulfil these criterions.[12]

Third stage: definitive repair

The third stage involves completion of the anatomic repair, with closure of the ventricular septal defect and establishment of continuity between the right ventricle and the reconstructed pulmonary vasculature. All systemic-to-pulmonary shunts, including redundant collateral arteries and surgically created shunts, should have been previously occluded, or else be retrievable from a median sternotomy incision to allow occlusion at the time of complete repair.[12] As mentioned before; successful definitive repair is dependent on the adequacy of the pulmonary vascular bed. There is now strong evidence that definitive repair is possible if 15 out of the 20 bronchopulmonary segments are connected to confluent pulmonary arteries.[9] Repair can also be achieved if 11 to 14 segments are connected to the intrapericardial pulmonary arteries, but at an increased risk of a high postoperative pressure ratio and an increased surgical mortality.[34]

Prediction of outcome after definitive repair

A number of methods have been developed to predict the outcome preoperatively based on the size of the pulmonary arteries and estimations of the pulmonary

vascular resistance.[37,38] These predictive indexes are valuable as guidelines for definitive repair, but they are not without shortcomings. Should there be reduced flow to the lungs, then the size of the pulmonary arteries may be underestimated. Measurement of distal pulmonary arterial pressure may be difficult and, as flow cannot be measured accurately, the pulmonary vascular resistance may be difficult to determine. To make acceptable the early and late morbidity and mortality for definitive repair, the predicted right ventricular pressure should be no higher than two-thirds the systemic pressure.[12]

Definitive single-stage repair in early infancy

The natural history of major collateral arteries often follows a course of progressive stenosis and occlusion. Iatrogenic occlusion can also occur when these vessels are unifocalized in stages using nonviable conduits, sometimes resulting in loss of segments.[11] Because some aortopulmonary collateral arteries do not have major stenoses, segments may be perfused by such collaterals at or near systemic pressure. This unrestricted flow can lead to early pulmonary vascular obstructive disease, which also effectively raises resistance. Injuries to the distal pulmonary vasculature due to both hypoperfusion and perfusion at systemic pressure are progressive and time-related processes. Recent publications, therefore, have advocated the normalization of the pulmonary circulation as early in life as possible, removing the pulmonary vascular bed from exposure to the inevitable haemodynamic vagaries associated with major collateral arteries.[5,11,39]

According to McElhinney et al.,[11] complete repair in early infancy allows for early normalization of cardiovascular physiology, with preservation of the pulmonary vascular bed, recruitment of all lung segments, alleviation of cyanosis, and prevention of other cardiac sequels. By performing the repair in a single stage, the number of operations required can be minimized, and the number of patients who can be completely repaired is likely to be enhanced.

Principles of one-stage unifocalization

The approach to one-stage unifocalization and complete repair follows several basic principles. Surgery is performed through a generous midline incision and median sternotomy,[5,11,39] although some investigators have described the use of a bilateral transsternal thoracotomy, also providing good exposure.[40] A variety of approaches are used to identify and dissect the collateral arteries. Both pleural spaces are opened widely just beneath the sternum and well anterior to the phrenic nerve. It is essential to control all collateral arteries before commencing cardiopulmonary bypass, and to perform reconstruction between native tissues whenever possible. Important concepts in achieving this type of unifocalization are flexibility regarding reconstruction, aggressive mobilization, maximizing the length of the major collateral arteries, and creative rerouting.[11] Avenues for rerouting the collateral arteries are developed by opening the pleura on both sides posterior to the phrenic nerves in the hilar regions, and by opening the subcarinal space through the transverse sinus.

In order to meet the objective of complete unifocalization without use of peripheral conduits, and to maximize the anastomosis of native tissues, it is possible to make side-to-side or oblique end-to-side anastomoses between collateral arteries, or between collateral arteries and the peripheral branches of intrapericardial pulmonary arteries. Alternatively, the intrapericardial pulmonary arteries can be anastomosed to an aortic button giving off multiple unobstructed collateral arteries, or a long onlay or side-to-side anastomosis made between the collateral arteries and the intrapericardial pulmonary arteries. Other options are to make an end-to-end or end-to-side anastomosis of collateral arteries to a central conduit, to augment the stenotic distal collateral arteries with an allograft patch, or to use such patches for augmentation of the reconstructed intrapericardial pulmonary arteries. In rare cases, it is possible to use allograft conduits to reconstruct the intrapericardial pulmonary arteries.[11] These techniques are used as necessary in the individual patient, and frequently combined, depending on the particular anatomy. In most patients, flow of blood to the unifocalized pulmonary arteries is provided via a valved conduit, which can be a homograft or allograft, placed from the right ventricle to the intrapericardial pulmonary arteries.

Whether or not to close the ventricular septal defect?

The decision to close the ventricular septal defect at the time of unifocalization is critical to successful repair. In contrast to staged repair, catheterization and angiographic data are not available following unifocalization. Angiographic measurements of the collateral and pulmonary arteries preoperatively can be used to estimate an index for the newly constructed pulmonary arteries, which is the sum of the indexed cross-sectional areas of all vessels unifocalized.[23] All patients with an index above 200 millimetres squared per metre squared can safely have their ventricular septal defect closed, but the index is apparently of little benefit in predicting suitability for closure in patients below this level.[11] Reddy et al.[23] therefore, developed an intraoperative technique to estimate the resistance of the unifocalized pulmonary arterial bed, showing

the method to be reliable in predicting the mean pulmonary arterial pressure when the ventricular septal defect is closed. If the mean pulmonary arterial pressure is estimated to be more than 25 millimetres of mercury in infants, the defect is typically left open.[11] Should the defect be closed, a small atrial septal defect is usually created, or else a patent oval foramen left open, to function as a "pop-off" valve for systemic venous blood in the event of right ventricular dysfunction or elevated right-sided pressures.[11,39]

Percutaneous balloon dilation of major collaterals, with or without subsequent implantation of stents

Although the current trend is towards early unifocalization or repair, some lesions are not amenable to surgical procedures. In these settings, transcatheter interventions may offer a valuable alternative or additive prior to or after surgical therapy.[41] Moreover, some patients who have previously not been considered for surgical intervention may now have reached their teens being severely cyanotic, and can be palliated by interventional techniques. Over the past ten years, increasing experience has been gained in the percutaneous treatment of major collateral arteries, improving patients clinically and facilitating further surgical procedures.[42]

Conventional balloon dilation

Some lesions can be treated with conventional balloon dilation, albeit that discrete segments are often resistant to high pressures or large balloons, with increased risk of complications such as dissection, aneurysmal formation, disruption of the adjacent vessel wall, or loss of segmental lung perfusion (Fig. 5). The choice of the size of the balloon is made according to the severity of the stenosis and the size of the vessel, but generally a non-compliant balloon not larger than one and a half times the size of the nearest normal vessel should be selected.

Dilation using cutting balloons

Cutting balloons were developed and approved for angioplasty of resistant coronary arterial obstructions.[43,44] These balloon catheters are equipped with three or four metal blades mounted on the surface of the balloon. Angioplasty produces sharp, longitudinal, incisions directed radially into the media. These microsurgical incisions result in smoother dilation, with less injury to the media or adventitia. Expansion occurs at multiple sites, and not in one tear. Elastic recoil is reduced, and there is less subsequent intimal proliferation. Despite the significant experience with such balloons for coronary angioplasty, there is limited data for their use in children. Several groups have begun to explore their safety and effectiveness in dilating peripheral pulmonary arterial stenoses resistant to conventional techniques.[45–47]

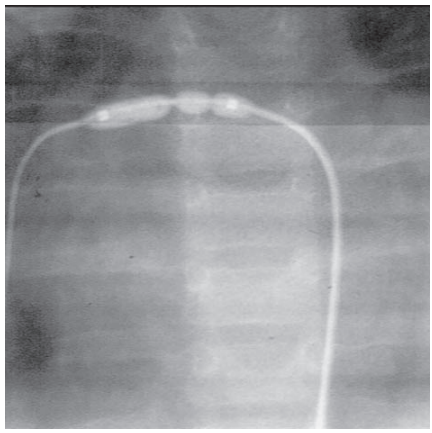

Figure 5.
Two consecutive stenoses in a collateral artery resistant to balloon dilation up to 20 atmospheres.

The balloons are currently available in sizes from 2 to 8 millimetres. Using these balloons, pressure-resistant stenoses, and even filiform or long segment lesions, can be dilated successfully and safely[42] (Fig. 6). A balloon sized approximately 1.1 times larger than the diameter of the artery is recommended. Control angiography after dilation often reveals evidence of intimal damage. This finding was described in the series of Bergersen et al.[47] in up to two-fifths of the vessels dilated. It is described as a "cobblestone" appearance, or "intimal" flap, without extravasation of contrast outside the lumen. This type of intravascular disruption is expected, and indeed is necessary for successful angioplasty.[48]

Implantation of stents

Indications for implantation of stents after dilation with either conventional or cutting balloons are significant recoil of the dilated artery, severe intimal damage with aneurysmal formation, dissection and risk of subsequent loss of patency, and critical filiform long segment narrowing. The choice of the stent will vary according to the shape, size, and length of the stenotic segment, and whether there are acute angles proximal to the stenosis. The risk for thrombosis seems to be higher in curved or long stents.[42]

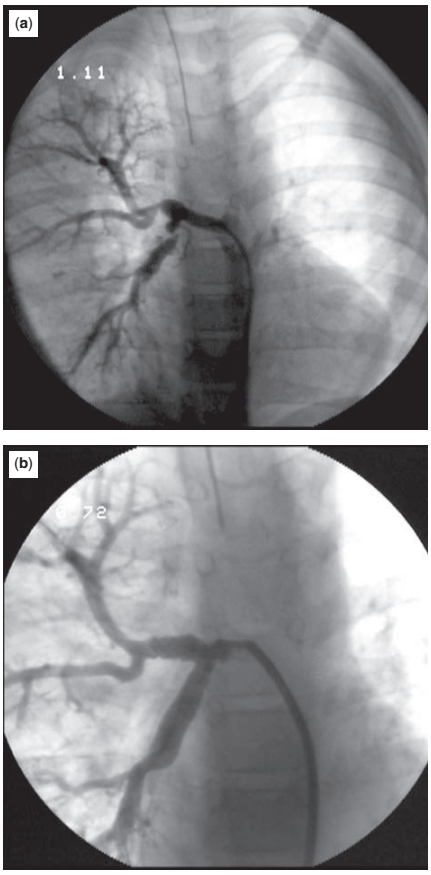

Figure 6.
*A selective injection (**a**) in a major aortopulmonary collateral artery of an 11-year-old patient with tetralogy of Fallot, pulmonary atresia, and major collateral arteries. He had become severely cyanotic due to progressive stenoses of the collateral vessels. In panel (**b**), we show the results after dilation using a cutting balloon and implantation of a stent. Arterial saturation improved from 65 to 82%.*

Transcatheter embolization of redundant collateral arteries

Patients may occasionally present with multiple, large, unobstructed aortopulmonary collateral arteries producing excessive flow of blood to the lungs, and necessitating intervention. Redundant collateral arteries may also sometimes need to be embolized before or after surgery to promote growth of the intrapericardial pulmonary arteries. A number of embolic materials have been used to occlude such collateral arteries, including tissue adhesives, detachable silicone balloons, and Gianturco coils.[49] Currently, coils are most commonly used for this purpose. The technique of embolization is similar to that used in other vessels. An alternative source of arterial supply to the lung segment supplied by the target vessel must be ensured before the collateral artery is occluded. A peculiar origin, or tortuosity of the collateral artery, may cause difficulty in positioning properly the tip of the catheter, but various guide wires and catheters, including the 3 French Target catheters are available, and may help achieve an ideal position of the catheter to ensure safe implantation of the coil.[49] A coil that is from one-third to half larger than the diameter of the target artery is recommended because of possible distention of the artery following implantation.[49] A study by Verma et al.[50] has revealed complete occlusion in nine-tenths of vessels, also demonstrating endothelialization of coils protruding into the aortic lumen. Furthermore, no episodes of stroke, embolic events, endarteritis or migration were observed. Transcatheter embolization of major aortopulmonary collateral arteries with coils, therefore, can be considered feasible, safe, and effective. The technique is of significant value in the overall management of this subset of patients.[49]

Acute and long term outcomes

Analysis of the results of surgical repair of congenital cardiac malformations associated with major collateral arteries is difficult, due to the extreme variability of the supply through the intrapericardial pulmonary arteries as opposed to the collateral arteries. Griselli et al.,[20] however, devised a classification of the pulmonary arterial supply to determine the influence of the arterial morphology on the results of surgery. Current classifications are usually based on the presence and size of the intrapericardial pulmonary arteries. Patients without intrapericardial pulmonary arteries, but with confluent intrapulmonary arteries, have a better outcome than those with nonconfluent pulmonary arteries.

The surgical techniques have evolved over the last two decades. Reddy et al.[51] reported their experience in 85 patients. Early one-stage complete unifocalization could be performed in more than nine-tenths of patients, even in those lacking intrapericardial pulmonary arteries, and yielded good functional results. Complete repair in a single stage was achieved in two-thirds of patients. Sequential unifocalization procedures are reserved for patients with multiple significant distal collateral stenoses, or those with significant co-morbid factors that contraindicate cardiopulmonary bypass. The outcome with these

strategies has been good, with early mortality of 10 percent, and 80 percent actuarial survival at 3 years. The need for reintervention, either by catheterization or surgery, to dilate or occlude vessels and to enlarge pulmonary arteries, or to change valved conduits, continues to be a problem, but as can be anticipated, patients with pulmonary arteries of small size have a 6-fold greater risk of reintervention when compared with patients having adequate-sized vasculature.[20] Actuarial survival free from reintervention was 42 percent at 5 years.[51] The natural history of this condition for purposes of comparison is difficult to elucidate. Bull et al.,[52] nonetheless, noted a mortality of 50 percent at 1 year of age in such patients. We can reasonably conclude, therefore, that a considerable improvement has been achieved for these patients.

Future outlook

Over the last decade, considerable progress has been made in the surgical and interventional treatment of patients with tetralogy of Fallot, pulmonary atresia, and major aortopulmonary collateral arteries. Despite these advances in treatment, inadequate growth of the pulmonary vasculature is seen in a fraction of patients even after optimal surgical and interventional treatment. Recent studies have implicated the Notch signalling pathway in human cardiac development by demonstrating mutations or deletions of the *JAG 1* gene as the basis for Alagille syndrome and some cases of isolated tetralogy of Fallot or pulmonary stenosis.[53] McElhinney et al.[53] demonstrated an apparently poor outcome among individuals with a *JAG 1* mutation and tetralogy of Fallot with pulmonary atresia. This observation certainly warrants additional investigation, because it may have implications for clinical decision-making in this subset of patients. The association of tetralogy of Fallot with 22q11 microdeletion is now well recognized, and is also more common in tetralogy of Fallot associated with pulmonary atresia and major collateral arteries than in tetralogy of Fallot with pulmonary stenosis. Chessa et al.[54] compared the morphology of the pulmonary arteries, and the origin, course, and connections of the major aortopulmonary collateral arteries, in patients with or without chromosome 22q11 deletion. A specific phenotype could be defined in patients with deletion. The collateral arteries mostly showed complex morphology, and the intrapericardial pulmonary arteries were smaller. Differences in the morphology of the pulmonary vessels may indicate a different timing of the faulty developmental pathway in patients with and without 22q11 deletion. Genetic information, therefore, may open the way for therapeutic strategies to enhance distal pulmonary angiogenesis, and help in planning the best surgical strategy.

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Chapter 3

3.2 Stenting the neonatal arterial duct

Ductal stenting in neonates with either duct-dependent pulmonary or systemic circulation has become a good alternative for the initial palliation of complex congenital heart disease. Changes of stent and catheter technology (low profile, flexible, premounted stents with good scaffolding), better patient selection and preparation, optimal interventional access and covering the complete length of the duct have significantly improved results. We describe our initial results using these techniques in a small group of 10 neonates with duct-dependent pulmonary circulation and a short, straight duct. This is followed by a review of ductal stenting in patients with duct-dependent pulmonary- and systemic circulation.

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Stenting the Neonatal Arterial Duct in Duct-Dependent Pulmonary Circulation: New Techniques, Better Results

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OBJECTIVES The goal of this study was to assess a new approach to stent the arterial duct in neonates with a duct-dependent pulmonary circulation.

BACKGROUND Previous attempts to stent the neonatal arterial duct were unsatisfactory. Learning from these failures, we speculated that covering the complete length of the duct with current low-profile stents might avoid previous problems.

METHODS Ten neonates with duct-dependent pulmonary circulations through a short straight duct were treated with stent implantation. The duct was crossed with an atraumatic 0.014-inch wire. A low-profile premounted coronary stent (outer diameter <4F, length 13 to 24 mm, diameter 3.0 to 4.0 mm) was positioned within the duct, not protected by a sheath; care was taken to cover the complete length of the duct from the aortaductal junction until well within the pulmonary trunk.

RESULTS All stents could safely be deployed with adequate pulmonary flow at early- and medium-term follow-up. There were no procedure-related complications; one patient died early from sepsis. All patients had adequate relief of cyanosis for at least three to four months. During follow-up, the pulmonary vasculature bed had grown without distortion. Acute occlusion of a stented duct was not observed. Ductal flow progressively decreased slowly over several months by luminal narrowing, until the stented duct had either become redundant or was dilated/restented or until elective staged surgery was performed.

CONCLUSIONS With current technology, complete stenting of a short straight duct is a safe and effective palliation, allowing adequate growth of the pulmonary arteries. (J Am Coll Cardiol 2004; 43:107–12) © 2004 by the American College of Cardiology Foundation

It has long been realized that patients with a duct-dependent pulmonary circulation would benefit if duct patency could be maintained reliably for several months (1,2). Conventional palliative treatment in neonates with such a duct-dependent circulation currently consists of treatment with prostaglandin E1 for some days, followed by the surgical creation of an aortopulmonary shunt if early repair is not feasible. Shunt-related complications such as chylothorax, phrenic and vagal nerve palsy, early or late shunt occlusion or stenosis, distortion, and differential growth of the pulmonary arteries (PAs) as well as surgical adhesions are well-recognized and may add to the complexity of subsequent surgeries (3–5).

Today, many vascular lesions are treated percutaneously, and endovascular techniques can be extended to this clinical setting. However, because of technical difficulties and unpredictable outcomes, several previous investigators have cautioned against routine placement of such stents in neonates with duct-dependent pulmonary blood flow (PBF) (6,7). Previous attempts to stent the neonatal duct with early generation, rigid, bare stents using relatively bulky, stiff wires, balloons, and sheaths frequently resulted in complications such as worsening cyanosis, bleeding, vessel rupture, duct spasm, tissue prolapse, or acute thrombosis. Additionally, incomplete covering of the duct frequently resulted in duct constriction, with inadequate pulmonary flow within hours or days after implantation. Learning from these failures, we speculated that covering the complete length of the duct with current low-profile, flexible, premounted stents with good scaffolding might avoid such problems. This report describes the experience from two university pediatric cardiac centers over a two-year period with stenting of the arterial duct in duct-dependent PBF.

METHODS

Patients. Between March 2001 and November 2002, stent implantation of the arterial duct was attempted in 10 neonates and infants with duct-dependent pulmonary circulation in two centers (University Hospital Leuven, Belgium, and the Hospital for Sick Children, University of Toronto, Canada). The procedure was offered as an alternative to surgical palliation after parental informed consent was obtained. Only patients with a short and straight duct were considered for this study; patients with a long and tortuous duct, as typically seen with pulmonary atresia and ventricular septal defect, were excluded. Early in the experience, the procedure was offered only to patients who carried a high surgical risk (premature infant, single lung) or whose pulmonary circulation was not completely duct-

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Abbreviations and Acronyms
PA = pulmonary artery
PBF = pulmonary blood flow

dependent. As experience grew, the procedure was offered to all patients fulfilling the morphologic criteria for stent implantation. All procedures were performed in agreement with the ethical guidelines of each participating center.

The age of the patients ranged between one and 42 days, median 6 days (Table 1). The body weight ranged from 2.5 to 3.7 kg, median 3.3 kg. The underlying pathology in the 10 patients was as follows: 3 had pulmonary valve atresia and intact ventricular septum, 5 had critical pulmonary valve stenosis with a hypoplastic right ventricle (1 in association with double inlet left ventricle and subvalvular pulmonary stenosis), and 2 patients had isolated PAs (1 in association with tetralogy of Fallot, right aortic arch, and left arterial duct to the left PA, and one patient with normal intracardiac anatomy, left aortic arch, and bilateral arterial ducts, with isolation of the right PA).

Cardiac catheterization and stent implantation. The initial interventional therapy in 7 of 10 patients consisted of: radiofrequency perforation and balloon dilation of pulmonary atresia in three patients and balloon dilation only of critical pulmonary valve stenosis in 4 patients. This was done on the same day in three patients, and 2, 5, 11, and 33 days before stent implantation in four patients (allowing assessment of the possibility of the pulmonary circulation not being duct-dependent). In two patients with excluded single PA and in the patient with complex univentricular heart, there was no additional procedure but implantation of the stent. The procedure was performed under general anesthesia in all patients. Angiography (typically in profile or perpendicular to the arch of the duct) was performed to demonstrate the anatomy of the arterial duct, of which the median length was 17 mm (range, 12 to 20 mm) (Fig. 1).

Stent implantation was performed from the femoral vein in eight patients (in most patients through a 5F right coronary guiding sheath) and from the femoral artery in two patients (4F sheaths). After crossing the duct with a 0.014-inch guidewire, the infusion of prostaglandin was discontinued to promote duct constriction; in patients without previous ductal constriction, prostaglandin infusion was stopped 6 h before the procedure. The duct was not crossed with a sheath; a transvenous right coronary guiding catheter ensured stability and allowed contrast flushes for accurate positioning.

Coronary stents with good scaffolding properties, premounted on low-profile balloon dilation catheters were used: Multi-link Tetra/Penta stents (Guidant, Santa Clara, California) in six patients, Express Monorail (Boston Scientific, Maple Grove, Minnesota) in two patients, and a Coroflex (B Braun Medical, Emmenbruche, Switzerland) and a Tristar stent (Guidant, Santa Clara, California) each in one patient. The mean stent diameter was 3.8 mm (range, 3.0 to 4.0 mm). We aimed to stent the complete length of the duct with a single stent. Stent length was chosen slightly longer than the duct length. When positioning the stent, care was taken to align the superior aortic end of the stent with the cranial aortoductal junction, avoiding any protrusion into the aorta; the stent therefore would protrude slightly into the pulmonary trunk (Fig. 2). We aimed not to reach the zenith of the main PA, because this may cause erosion or perforation.

After stent implantation, repeat angiography was performed to confirm the stent position and to exclude incomplete stenting of the duct (Fig. 3). In case of incomplete stenting, an additional stent was implanted to cover the whole duct.

Prophylactic antibiotic treatment (cefazolin in most patients) was given for 24 h.

During follow-up, nine patients were on antiplatelet agents (1 to 3 mg/kg acetylsalicylic acid alone in eight patients, and in combination with low-molecular-weight heparin and clopidogrel in one patient). One patient received low-molecular-weight heparin alone for two weeks.

RESULTS

In the 10 patients, a total of 13 stents were successfully implanted; a single stent was required in seven patients, and two stents were implanted in two patients at the initial procedure. In Patient 3, two procedures were required on consecutive days: the first stent covered the duct except 3 mm at the aortic end, which was widely open at that time; within 20 h the aortic end showed significant duct constriction, which was relieved by a second stent. The results are summarized in Table 1. The median fluoroscopy time was 28 min (range, 9 to 58 min) including the primary procedure when done in a single session.

The mean length of the final stent (either single stent or combination of two stents) for this group was 19 mm (range, 13 to 24 mm). There were no deaths directly related to the procedure. One patient died four days after implantation due to E. coli septicemia, where, in retrospect, the septic episode may have begun before the procedure. At autopsy, the stent was widely patent. Three patients (all with stent diameter of 4.0 mm) initially required antifailure treatment due to increased PBF. Repeat cardiac catheterization was performed in seven patients 4.7 months after implantation (range, 1.4 to 9.1 months). In all of these patients, adequate growth of the PAs was observed without distortion. Luminal narrowing within the duct had resulted in a significant reduction of the inner diameter in most patients. The aortic lumen was not affected by any implant. In Patient 1, the duct was restented 4.7 months after implantation with a 4-mm stent with a good clinical result. A bidirectional cavopulmonary shunt was subsequently performed in two patients, and is scheduled in another patient. Patients 5 and 8 underwent elective unifocalization of the PAs at 3.9 and 2.3 months; both stents were widely

Table 1. Patient Characteristics, Stent Data, and Clinical Outcome

Patient	Diagnosis	Age, days	Weight, kg	Duct Length, mm	Lungs	Stent Length, mm	Stent Diameter, mm	Immediate Result	FU Months	Reintervention/ Last Echocardiography at FU
1	PA-IVS, TS	35	3.3	18	2	20 (18 & 9)	4.0	Generous flow, mild decompensation	7.5	Restent 4 mm/18 mm after 4.7 months; then CPS at 7.5 months
2	Critical PS	1	2.8	12	2	13	3.5	Adequate flow, no decompensation	7.7	Spontaneous occlusion stent, no residual PS, PFO bidirectional shunt
3	PA-IVS, TS	4	3.2	18	2	22 (18 & 13)	4.0	Adequate flow, mild decompensation	6.2	CPS shunt, RV overhaul at 6.2 months
4	Critical PS	6	3.7	17	2	18	3.5	Adequate flow, no decompensation	14.7	Small residual ductal shunt, clinically no cyanosis
5	TOF, excluded left PA	42	3.6	15	1	18	4.0	Adequate flow, no decompensation	3.9	Repair TOF with unifocalization at 3.9 months
6	UVH, DILV, sub PS & PS	7	3.4	14	2	18	4.0	Adequate flow, slight protrusion of stent in Ao	0.1	Patient died 4 days after stenting (E coli sepsis)
7	PA-IVS, TS	2	3.5	20	2	24	4.0	Adequate flow, moderate decompensation	9.1	Adequate ductal flow, scheduled for RV overhaul
8	Excluded right PA	3	2.6	14	1	15	3.0	Generous flow, transient reperfusion edema	2.3	Implantation RAP into pulmonary trunk at 2.3 months
9	Critical PS	6	2.5	18	2	22 (18 & 13)	3.0	Adequate flow, no decompensation	4.6	Adequate growth RV, duct spontaneously closed
10	Critical PS, TS	12	2.5	16	2	20	3.0	Adequate flow, no decompensation	5.2	Adequate growth RV, duct redundant >3 months
Median		6.0	3.3	17					5.7	

Ao = aorta; CPS = cavo pulmonary shunt; DILV = double inlet left ventricle; FU = follow-up; IVS = interventricular septum; PA = pulmonary artery; PA-IVS = pulmonary atresia-intact ventricular septum; PFO = patent foramen ovale; PS = pulmonary valve stenosis; RAP = right pulmonary artery; RV = right ventricle; TOF = tetralogy of Fallot; TS = tricuspid stenosis; UVH = univentricular heart.

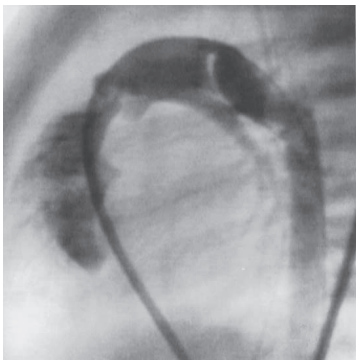

Figure 1. Angiogram (profile) in pulmonary artery through the 5F right coronary guiding sheath. Duct constriction at the pulmonary end is clearly seen; the aortic end of the duct is wide open.

patent at the time of surgery. There were no technical problems caused by the stents during the subsequent surgeries, and the stents could easily be occluded completely by simple external compression (no recoil).

Adequate right ventricular growth had occurred in four patients, making the stented ducts redundant; medication was stopped, leaving the stents to occlude spontaneously. Spontaneous ductal occlusion was documented echocardiographically in two patients 4.6 and 7.7 months after stent implantation; minimal duct flow persisted in the two remaining patients 5.2 and 14.7 months after stenting.

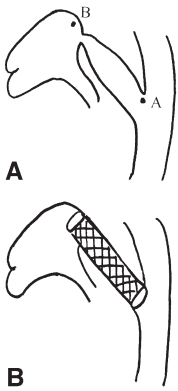

Figure 2. Schematic representation of stent sizing and positioning. **(A)** The stent should stretch from the cranial aortoductal junction **(point A)**, until halfway to the ductal constriction and the zenith of the ductal arch **(point B)**. **(B)** When positioning and deploying the stent, the distal end of the stent should be aligned with **point A** without protrusion in the aorta; the proximal end of the stent will then protrude into the pulmonary trunk.

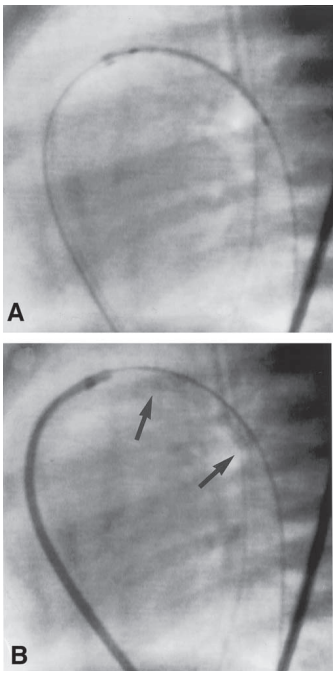

Figure 3. Cine-frames showing positioning of the stent **(A)** and final stent position after deployment **(B)**. The radio-opaque gastric tube is very useful as reference.

DISCUSSION

Several authors have highlighted technical difficulties encountered when stenting the arterial duct in duct-dependent cyanotic congenital heart disease (8–10). However, improved materials resulted in broadened indications for percutaneous intraluminal techniques, whereby many of the technical difficulties encountered in the past now can be avoided.

Current technique. Long, flexible stents, premounted on low-profile balloons are used. When choosing a stent, important features are stent length, diameter, and design.

STENT LENGTH. The most distal parts of the duct appear to have a remarkable power to constrict even when only a few millimeters are left unsupported (9). Previous animal studies revealed that placement just proximal to the duct orifice resulted in an intimal process that eventually led to complete closure within days of implantation (11). Therefore, great care must be taken to cover the duct completely from the aortic end until well within the pulmonary trunk. The stent

length is, thus, chosen slightly longer than the length of the duct.

STENT DIAMETER. Surgeons use a 4- or 5-mm interposition tube when creating a modified Blalock-Taussig shunt in neonates; however, the restriction of these shunts early after creation lies within the orifice of the subclavian artery. A stented duct is more comparable with a central shunt, which has no restriction at the aortic end; surgeons prefer in neonates for such shunts conduits from 3 up to 4 mm. The final lumen within the stent, however, will depend on the stent diameter at implantation, which will decrease within hours-days by contraction of the vessel wall leading to tissue prolapse through the stent struts, and later on will further decrease by endothelial hyperplasia. Table 1 shows the immediate result in function of stent diameter, patient weight, and single or double lung perfusion. All neonates with stent diameters of 4.0 mm initially had excessive pulmonary flow.

STENT CHARACTERISTICS. The stent design and material determine cross-sectional area, strut thickness, and radial force. Larger metallic cross-sectional areas, thicker struts, and smaller cell-areas result in good scaffolding with limited tissue prolapse, which is important when used in the arterial duct. However, these properties reduce the flexibility and conformability of the stent, and are known to enhance in-stent restenosis rate in coronary arteries. Radial force and side-branch accessibility are no issue for a stent deployed in the arterial duct.

Schneider et al. (11) observed, within days after implantation, significant stenosis within a gap articulation in the Palmaz-Schatz coronary stent; this was treated with an additional stent across the articulation. In patients with a tortuous duct, we attempted to stent with flexible stents with more conformability to follow the curves; however, stents with a larger cell area allow significant tissue prolapse, with a restrictive cobblestone appearance within hours in some cases. For the short straight duct in the patient group reported in this study, we chose stents with small cell area and good scaffolding; the somewhat reduced flexibility caused no problem when positioning these stents, and conformability is not required for this type of duct.

DUCT AND PROSTAGLANDIN. In order to grip the stent at deployment, some ductal constriction is required. If the duct has not constricted since birth, as typical in patients with fetal or very early neonatal presentations, where prostaglandins are started very early, this medication should be stopped several hours (e.g., 6 h) before the procedure. In patients presenting after duct constriction with cyanosis, prostaglandins can be stopped at the beginning of the procedure, or after the duct has been crossed with the guiding wire. Enhanced constriction during the procedure can be obtained by administering intravenous indomethacin or ibuprofen.

ANTICOAGULATION AND ANTIAGGREGATION. It is difficult to determine the role of anticoagulant and antiplatelet drugs. During the procedure, standard heparin should be given. We currently do not neutralize the heparin at the end of the procedure, but acetylsalicylic acid 1 to 3 mg/kg/day is started for as long as stent patency is required. The value of clopidogrel needs to be determined.

With growing confidence in the technique, patients are now considered for hospital discharge within 48 h after implant, provided there is no other indication for a prolonged stay.

Neointimal proliferation. Duct patency after stenting is limited by in-stent restenosis, which occurs due to neointimal proliferation and/or peal formation (8,11). The ideal stent for this procedure still needs to be defined. Stent design determines (non-)metal surface area, radial force, flexibility, conformability, scaffolding, and prevention of tissue prolapse. Drug-eluting stents or covered stents have been proposed as a means of preventing in-stent restenosis in adults (12,13). Covered stents are slightly more bulky and require larger introducer sheaths (currently +1 to 2F sizes). The drug-eluting coatings contain agents that inhibit thrombus formation (e.g., heparin), inflammation (e.g., dexamethasone), and cellular proliferation (e.g., sirolimus or paclitaxel) (14). Stents eluting antimitotic agents such as sirolimus and paclitaxel show the most promising results in coronary artery disease, with significant inhibitory effects on neointimal hyperplasia. Studies to evaluate the efficacy and safety of duct stenting with such coated stents in newborn animals will be initiated in the near future. This promising development in stent technology may prolong the duration of duct patency, rendering it an even more attractive alternative to a surgical shunt. On the other hand, in-stent stenosis can be managed by redilating or restenting the implant as a function of patient growth and/or intimal proliferation.

Comparison with the gold-standard: the surgical shunt. This enhanced technology obviously needs to be compared with the standard surgical shunt. While the stented arterial duct obviously will provide only temporary augmented pulmonary flow, as with any aortopulmonary shunt, we have been impressed by the fast recovery of the patients after stent implantation, much faster than with any surgery. The procedure is well-tolerated, even in the premature and small infants, who constitute a subgroup with higher operative risks. Without stent implantation, such premature infants would require prolonged prostinoid infusions, allowing the surgeon to operate on a larger child with more limited morbidity. In this small series, the stent strategy appears to be more cost-effective.

The lumen of a stented duct appears to narrow faster than a surgical shunt; however, all stented ducts gave adequate pulmonary flow for several months. There were no acute stent occlusions. If required, the stented duct can be redilated, which allows titration of pulmonary flow to patient size. Such redilation-restenting must be considered

Stenting the neonatal arterial duct

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Ductal stenting in neonates with either duct-dependent pulmonary or systemic circulation has become a good alternative for the initial palliation of complex congenital heart disease. Changes of stent and catheter technology (low profile, flexible, premounted stents with good scaffolding), better patient selection and preparation, optimal interventional access and covering the complete length of the duct have significantly improved results.

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It has long been realized that patients with a duct-dependent pulmonary or systemic circulation would benefit if duct patency could be maintained reliably for several months [1,2]. Conventional palliative treatment in neonates with a duct-dependent circulation currently consists of treatment with prostaglandin E1 for some days, followed by the surgical creation of an aortopulmonary shunt or surgical reconstruction of the aortic arch.

Such surgery in neonates, and even more so in premature or dysmature infants, can involve major complications, such as chylothorax, phrenic and vagal nerve palsy, early or late shunt occlusion or stenosis, distortion and differential growth of the pulmonary arteries or aorta, as well as surgical adhesions. These complications may add to the complexity of subsequent surgeries and compromise final outcome [3–6].

Previous attempts to stent the neonatal duct with early-generation, rigid, bare stents using relatively bulky, stiff wires, balloons and sheaths, frequently resulted in complications, such as worsening cyanosis or shock, bleeding, vessel rupture, duct spasm, tissue prolapse or acute thrombosis [7–10]. In addition, incomplete covering of the duct frequently resulted in ductal constriction, with inadequate pulmonary or systemic flow within hours or days following stent implantation.

By learning from these failures, using new techniques, applying a better patient selection and preparation, improved interventional access and covering the complete length of the duct with current low profile, flexible, premounted stents (with good scaffolding), the results of ductal stenting have been improved significantly [11–17]. This review discusses the stenting of different types of ducts:

- Duct-dependent pulmonary circulation
  - The short straight duct as in pulmonary atresia with intact septum
  - The long and tortuous duct as in pulmonary atresia with ventricular septal defect
  - The duct to a single lung
- Duct-dependent systemic circulation

General principles

Cardiac catheterization

Procedures should be performed under general anesthesia [12,13] or under conscious sedation [11,14,15,17,18]. Access is mostly obtained through a 5–6-Fr venous sheath and/or a 4-Fr (long) arterial sheath. Prophylactic antibiotic treatment (cefazolin in most patients) is usually recommended. Attention to hemostasis during catheter and wire manipulation is extremely important in neonates.

Angiography for ductal morphology

As with any complex interventional procedure in neonates, biplane fluoroscopy is recommended. Angiography is typically performed in the lateral projection or lateral-cranial (left anterior oblique 30° and cranial 20–30°).

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However, in newborns with duct-dependent systemic blood flow, 30° right anterior oblique demonstrates the ductal anatomy very well, especially its junction with the distal aortic arch. Contrast injections are usually performed through a transvenously placed right coronary guiding catheter [12], arterially placed multipurpose catheter [14], the 4-Fr arterial sheath or Berman angiographic catheter within the duct (or with balloon occlusion of the descending aorta below the duct) [18]. Useful landmarks during the catheterization for the aortic end of the duct are the arterially advanced multipurpose catheter [11,14], or an esophageal thermometer or gastric probe.

Management of prostaglandin infusion

Duct-dependent pulmonary circulation

The management of prostaglandin infusion depends on the morphology of the duct. In patients with pulmonary atresia with intact ventricular septum, the duct is short and straight, and ductal constriction is required in order to grip the stent at deployment. Ideally the patient should arrive in the catheterization laboratory with the smallest acceptable patent duct. If the duct has not constricted since birth (typically in patients with fetal or early neonatal diagnosis where prostaglandin was started early), some constriction should be allowed by stopping the prostaglandin infusion for several hours or days and restarting when some constriction has occurred. In patients presenting after ductal constriction with cyanosis, prostaglandin can be stopped at the beginning of the procedure or after the duct has been crossed with the guiding wire. In patients with pulmonary atresia and ventricular septum defect, no ductal constriction is required as this duct is long and tortuous.

A route for reinitiation or increase of the dose of prostaglandin during the procedure should always be available; in case of acute constriction, local application of a small dose of prostaglandin (taken from the infusion) can be performed. Enhanced constriction during the procedure can be obtained by administering intravenous ibuprofen (10-mg/kg bolus).

Duct-dependent systemic circulation

Since self-expandable and balloon-expandable stents are available for stenting ducts with a diameter ranging between 5 and 10 mm, the infusion can be stopped immediately before the catheterization in most patients, or even after the stent has been implanted.

Ductal morphology

The morphology of the arterial duct predicts the technical difficulty of stenting and the risk of restenosis and necessity for reintervention [14,19,20]. In the normal heart with a left-sided aortic arch (also usually in left-sided obstructive lesions), the arterial duct connects the left pulmonary artery to the descending aorta just distal to the origin of the left subclavian artery and has a short, straight course (as seen on the lateral projection). Such duct is also typically observed in patients who develop pulmonary stenosis or atresia late in fetal life (FIGURE 1).

The arterial duct in neonates with severe right heart obstructive lesions early in fetal life has a very different anatomy: the duct in these patients is longer, considerably more tortuous in different planes (typically cumulated angulation of 270–360° in frontal plane and 360° in lateral plane) and mostly has a vertical origin from the aortic arch (FIGURE 2) [15,20]. The pulmonary trunk and pulmonary trifurcation may have a variable size; if small to hypoplastic, ductal tissue in the wall of the pulmonary arteries can account for early or late stenosis of a branch pulmonary artery (primarily left) [21].

The duct can be left-sided, right-sided or bilateral. When ipsilateral to the arch, the duct connects at the inner curve of the arch just distal to the ipsilateral subclavian artery; when the duct is contralateral to the arch it originates from the innominate or subclavian artery. The pulmonary arteries can be confluent or nonconfluent.

In patients with hypoplastic left heart syndrome (HLHS), the morphology of the duct can be classified into three categories depending on the orientation from the vertical plane, as described by Boucek *et al*

leftward loop at a mean orientation of 18° from the vertical plane. Type 2 ductal anatomy is mesoverted, with a mean orientation of 7.1° from the vertical plane and type 3 ductal anatomy has a rightward axis, with a mean of -4° rightward. Type 1 ductal anatomy is observed in more than two-thirds of the patients with HLHS [18].

Choice of stent: length, diameter & type

When choosing a stent, important features are stent length, diameter and design. The most distal parts of the duct appear to have a remarkable power to constrict, even when only a few millimeters are left unsupported [19,22]. Therefore, great care must be taken to cover the duct completely from the aortic end

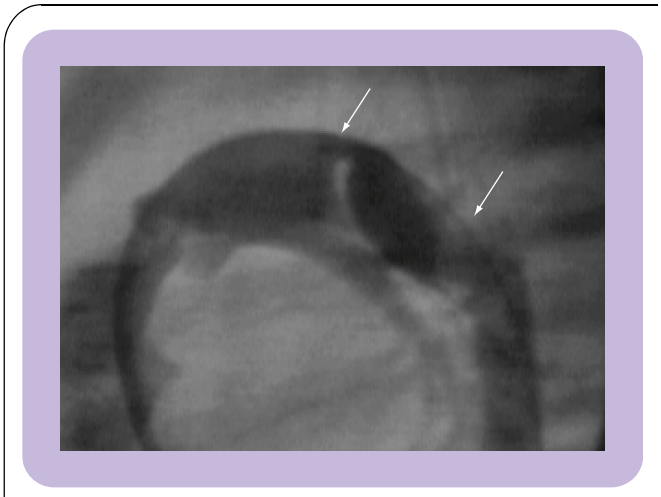

Figure 1. Angiogram through 5-Fr guiding sheath advanced into the pulmonary trunk after pulmonary valve fulguration and balloon dilation. A 0.014-inch coronary wire was advanced through the duct into the descending aorta. Important landmarks are the pulmonary end of the duct, which shows a narrow constriction, and the cranial aorto–ductal junction (arrows).

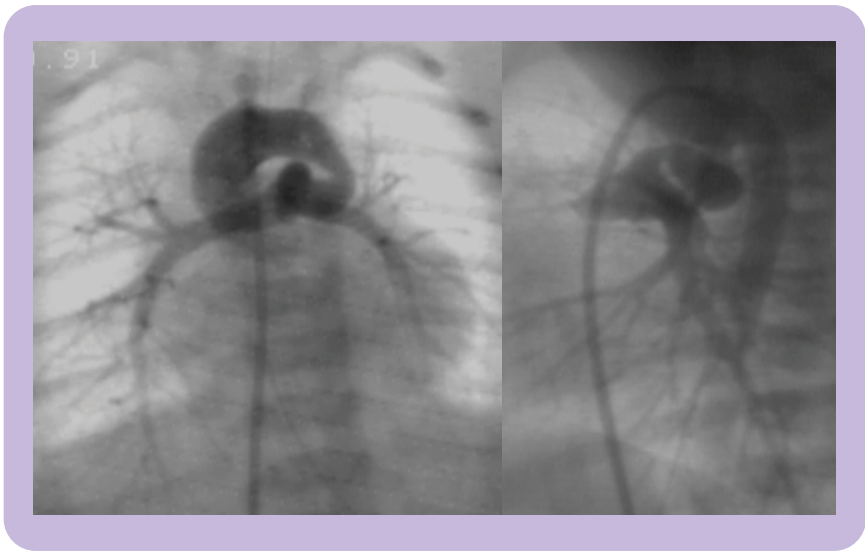

Figure 2. Aortagram of patient with pulmonary atresia–ventricular septal defect. The duct is long and tortuous, covering in the different planes 270 + 360° of angulation. Note the vertical take-off from the aorta.

until well within the pulmonary trunk, without covering the orifice of the pulmonary arteries. Ideally the complete duct should be covered by a single stent. In cases of incomplete stenting or significant prolapse of tissue through the stent cells, an additional stent should be implanted to cover and open the whole duct. The chosen stent length is thus slightly longer than the length of the duct. Determining stent length is usually relatively easy in cases with short, straight ducts, but it may be a challenge in patients with long and tortuous ducts. In a tortuous vertical duct in which the length is not exactly predictable, particularly when the advanced guiding wire will change the ductal shape, ductal stenting should be started at the pulmonary end to be sure that this part of the duct is at least covered. It is often preferable to implant two short stents in telescope technique than to confront problems when advancing a too long stent.

In patients with duct-dependent systemic circulation, crossing the isthmus is an important issue. The location of the distal end of such stent, either proximal at the ductal ampulla, or more distal in the descending aorta, may result in either the potential for late coarctation following prostaglandin discontinuation, or insufficient retrograde aortic perfusion by isthmic jailing and narrowing, resulting in brain and myocardial hypoperfusion.

Stent diameter will depend on the indication for ductal stenting (duct-dependent pulmonary flow: bilateral vs single lung or duct-dependent systemic flow), the ductal length and anatomy, and, of course, the weight of the baby. The stent design and material determine the cross-sectional area, strut thickness and radial force. Larger metallic cross-sectional areas, thicker struts and smaller cell areas result in good scaffolding with limited tissue prolapse, which is important when used in the arterial duct. However, these properties reduce the flexibility and conformability of the stent. Radial force is no issue for use in the arterial duct. Side-branch accessibility is usually not required, but might be beneficial if additional stenting is considered in case of a significant aortic coarctation or a stenotic pulmonary artery bifurcation.

Stent implantation

Duct-dependent pulmonary circulation

The short straight duct

Flexible coronary stents, premounted on low-profile balloons are used (i.e., Multilink Vision™, Tetra/Penta/Zeta stents [Guidant, CA, USA], Liberté™ [Boston Scientific, MA, USA], Driver® [Medtronic, MN, USA]). These stents can be implanted through a 5-Fr (transvenous) guiding catheter or 4-Fr (transarterial) sheath. When positioning the stent, care should be taken to have minimal protrusion in the aorta. The superior aortic end of the stent is therefore aligned with the cranial aorto–ductal junction. Some protrusion into the aorta is acceptable, as long as the other side of the aortic wall is not touched, as this might lead to a fixed obstruction with coarctation. Excessive protrusion can complicate future stent reentry for redilation (if necessary). The stent should protrude slightly into the pulmonary trunk. Typically an 18-mm stent will be used in a mature neonate.

A stented duct is comparable with a central shunt where all the restriction lies within the shunt itself. Surgical experience has taught us that in neonates such shunts should be made of conduits between 3 and 4 mm. In practice, the duct is stented to a diameter of 3.5–4 mm for a normal-term baby [12,13]. In babies weighing less than 2.5 kg, the stent diameter should not exceed 3 mm, especially if the ductal length is less than 10 mm.

The final stent lumen will however not only depend on the stent diameter at implantation, but will also decrease within hours to days due to contraction of the vessel and tissue prolapse through the stent struts, and will further decrease within weeks to months due to endothelial hyperplasia or peal formation. Patients with a stent diameter of 4.0 mm will often initially require antifailure treatment due to increased pulmonary blood flow.

Long tortuous duct, vertical duct

When these types of ducts are accessed from the femoral artery, it is often difficult (and sometimes impossible) to obtain a stable wire position for ductal stenting. It may be possible to access the aorta anterograde from the femoral vein through the heart, but this route makes catheter control more difficult and may cause hemodynamic instability in small neonates by keeping the atrioventricular and semilunar valves open. A so-called 'coaxial catheter system' may allow access to the duct: a 2.9-Fr Progreat™ microcatheter system (Terumo®, Haasrode, Belgium), which contains a 0.021-inch wire, is placed in a 4-Fr

Judkins right coronary catheter, through a cut-off 6-Fr guiding catheter (right coronary or mammary), with a short 6-Fr sheath over the cut-off end (hemostatic valve, also allowing contrast injections). The guiding catheter (with the right coronary catheter at its tip) is placed at the origin of the duct to ensure maximal stability. The duct is then gently probed by the soft 0.021-inch wire; as the wire is advanced more distally into the duct, the microcatheter is also advanced as distal as possible, followed somewhat by the right coronary catheter (if possible). Care should be taken not to induce vessel trauma or ductal spasm when trying to advance a stiff catheter into the tortuous duct. The floppy 0.021-inch wire is then exchanged for a 0.014-inch coronary wire (not too stiff), the coronary catheter removed and the stent implanted through the 6-Fr guiding sheath.

Access via the axillary artery may be the preferred route in selected patients [15,23]. Depending on the position of the duct at the inner curve of the aortic arch in relation to the subclavian arteries, the ipsi- or contralateral subclavian is used. Direct puncture of the axillary artery is preferred for placing a 'long' 4-Fr sheath within the subclavian artery; the sheath is advanced to the origin of the duct. Contrast medium can be administered easily by small hand injections during stent positioning.

In patients with a long, tortuous duct, flexible stents with more conformability to follow the curves are theoretically a better choice; however, stents with a larger cell area allow significant tissue prolapse, with the risk of a restrictive cobble stone appearance within hours. Such stents should therefore be inflated to a slightly larger diameter. Patients with this type of duct frequently have a hypoplastic pulmonary trunk and a small trifurcation, with ductal tissue extending into the pulmonary arteries; this will result in stenosis early after discontinuation of prostaglandin. These patients were classically treated with bilateral shunts, or a single shunt after plasty of the bifurcation on bypass. If stenting is chosen, the stent should preferably be advanced into the stenotic pulmonary artery, allowing perfusion of the other lung through the stent struts, or alternatively have a stented duct to one lung and a surgical shunt to the other lung.

Despite all these techniques, some of these complex, severely tortuous ducts remain very challenging and cannot be stented safely. This subgroup might remain the domain of surgical shunting.

The duct to a single lung

The term 'discontinuous pulmonary arteries', 'isolated' or 'excluded' pulmonary artery identifies a rare cardiovascular malformation in which one pulmonary artery is not connected to the main pulmonary artery but arises from an arterial duct. Isolated right pulmonary artery is found mostly in a normal heart (FIGURE 3), whereas an isolated left pulmonary artery is commonly associated with a right-sided aortic arch or with tetralogy of Fallot, in particular with pulmonary atresia and duct-dependent pulmonary circulation.

Neonatal surgical repair frequently leads to uneven distribution of the pulmonary blood [3], significant distortion [24], and residual or recurrent stenosis due to any residual ductal tissue [24,25]. Ductal stenting is therefore an attractive alternative to a surgical shunt. In addition, stent angioplasty enables the adaptation of shunt size to pulmonary artery growth by serial stent dilations, whereby corrective surgery can be postponed until the patient is older. Stent diameter in a duct to a single lung should, however, not be oversized: 3 mm is generally recommended, depending on the ductal length and weight of the baby. Larger stents can cause unilateral pulmonary overflow with the possibility of pulmonary hypertension and can even cause significant steal from the systemic circulation inducing low cardiac output [26].

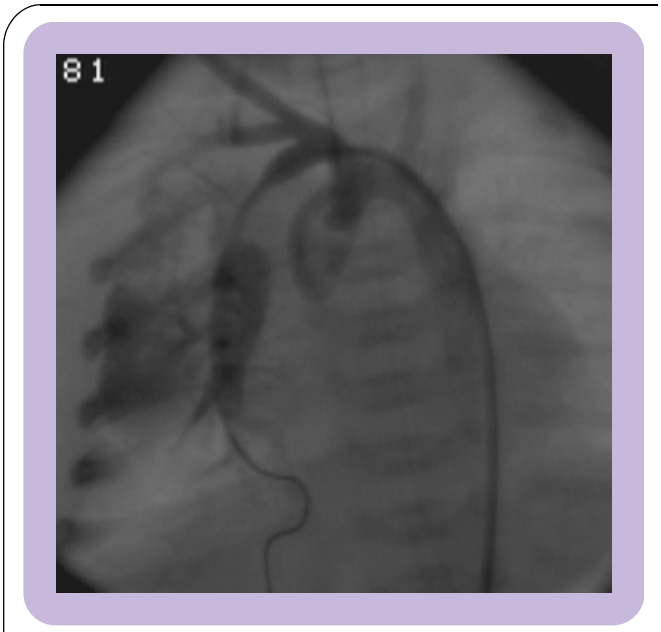

Figure 3. Aortagram of a patient with left aortic arch, bilateral duct, right pulmonary artery connected by the right duct to the right-sided brachiocephalic trunk. The right lung was 'excluded' after closure of the duct. The closed duct has been probed with a 0.014-inch coronary wire; ready for stent implantation.

Duct-dependent systemic circulation

Balloon-expandable versus self-expandable stents

Balloon- [27] or self-expandable [28] stents can be used for this indication. Balloon-expandable stents are more difficult to advance over the wire, and retrieval of the deflated balloon can cause stent slipping in an unconstricted duct. The self-expandable stents can conform to the anatomy of the arterial duct; by contrast, balloon-expandable stents are rigid and force the ductal anatomy to conform to the stent, thereby narrowing the orificium of the isthmus and impeding retrograde aortic arch flow. The balloon-expandable stent briefly interrupts systemic and myocardial perfusion during placement, which can be critical in infants with marginal ventricular function. Self-expandable stents (SinusRepo™ nitinol stents [OptiMed, Karlsruhe, Germany], Zilver stent [COOK, Denmark]) are therefore preferred for ductal stenting, especially in large ducts without any constriction. Such stents can currently be advanced through a short 5-Fr venous sheath over a 0.014-inch guiding wire, but these

modern self-expandable stents are not available worldwide. Most self-expandable stents need a 6- or even 7-Fr sheath for delivering stents, with minimum lengths of 20 mm and widths between 6 and 10 mm [18,27]. An advantage of the Sinus-Repo design is its 'anti-jump' mechanism, which allows stent retrieval after almost 80% of stent expansion and facilitates repositioning if necessary. The diameter of the utilized stents is chosen to be at least 1–2 mm above the minimal ductal diameter and even larger than the diameter of the descending aorta. This last recommendation is of particular importance when stenting the duct of newborns with interrupted aortic arch.

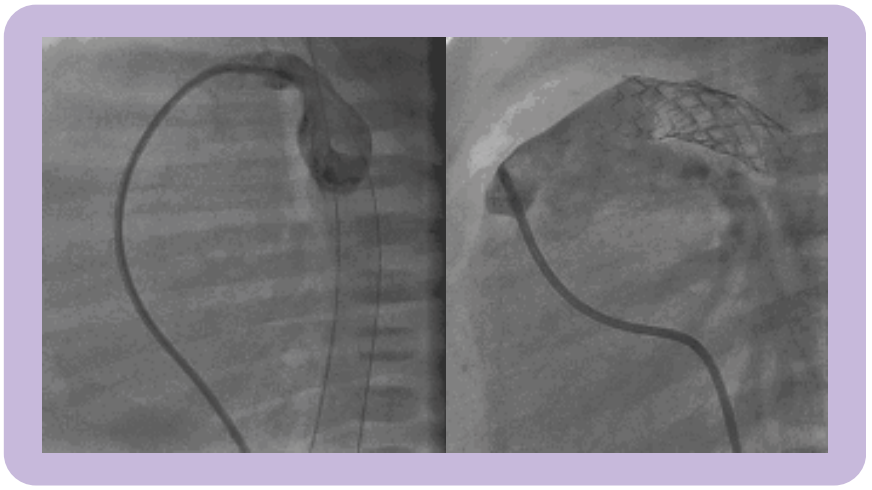

Figure 4. (A) Angiogram of a constricted, as aneurysmatic dilated duct in a newborn with hypoplastic left heart syndrome before ductal stenting (90° lateral view). (B) Shows the stented duct utilizing two balloon expandable stents (Genesis) placed in telescope technique.

This results in the implantation of stents with a diameter of 7 mm in most cases, particularly in newborns with a birth weight of less than 2.5 kg and even in prematures less than 1.5 kg. In patients where the ductal diameter measures 8–9 mm without any constriction, a 9- or 10-mm self-expandable stent should be implanted (also in patients with ductal aneurysms).

Premounted Genesis™ stents (Cordis) should be used when urgent stenting of a prostaglandin-resistant constricted duct in neonatal shock is performed, or if some ductal constriction is observed either at the pulmonary or aortic end (FIGURE 4). In an asymmetrically constricted or very short duct, a self-expandable stent may slip to the descending aorta or pulmonary trunk due to the still active working of the nitinol material after release. Premounted Genesis stents are available in different lengths of 12, 15, 18, 19 and 20 mm, they are premounted on 7-, 8- or 9–10-mm balloons, and can be advanced through a short 6–7 Fr venous sheath over a 0.035-inch guiding wire (FIGURE 4). Advancing through a long sheath is not necessary because of the tightly fixed stent.

Orientation of the arterial duct

The length of the duct, number of stents required for complete coverage, and technical and procedural complications are significantly related to the orientation of the arterial duct [18]. As described by Boucek *et al.*, the majority of the ducts take a leftward orientation (type 1: 65%) with an average length of 17.4 mm [18]. The second most common ductal anatomy is a direct front-to-back orientation (type 2: 27.5%). These ducts are shorter, averaging 15.3 mm. The ducts that take a rightward course are uncommon (type 3: 7.5%) and are short (mean: 10.9 mm). The diameters of the ducts in all three categories are usually similar, with a mean of 6.6 mm. Ducts with a front-to-back and rightward orientation may pose additional difficulty in manipulating the catheter from the right ventricle to the pulmonary artery. Placement of the stent delivery system across the right ventricle in these patients may cause tension on the tricuspid valve and right ventricle, resulting in transient bradycardia and hypotension. Such rightward morphological duct stenting can also be performed from the aortic side using modern self-expandable stents through a 5-Fr sheath.

Restrictive aortic isthmus

Retrograde aortic arch perfusion through the isthmus can be problematic after stent implantation.

The obstruction can occur immediately at stent implantation as a result of stretching the orifice in one direction, thereby narrowing it in the perpendicular direction; this is more likely to happen with a rigid, balloon-expandable stent. Stent placement is précised by positioning a multipurpose catheter within the isthmus of the aortic arch. The multipurpose catheter delineates the duct–aortic junction, and small amounts of contrast medium can be given by hand injection during stent placement to avoid overstenting of the duct causing distortion of the isthmus. In addition, access to the isthmus is preserved by the multipurpose catheter guiding. The obstruction can also occur a few hours after ductal constriction, or later as a result of tissue ingrowth or peal formation around the stent struts. The prestent echocardiographic evaluation may identify patients at risk: a very narrow or hypoplastic aortic arch appears to predispose for this complication. Patients with severe stenosis of the aortic isthmus may require either simultaneous stenting of the isthmus, or creation of a 'reversed shunt' between the pulmonary trunk and the aortic arch at the time of the sternotomy for bilateral banding [14,17,27,28,29].

Timing of ductal stenting

Duct-dependent pulmonary circulation

After radiofrequency valvotomy or balloon dilation of critical pulmonary valve stenosis has been performed, the decision needs to be made whether to proceed with ductal stenting. Technically, it is easy to stent the duct at the same procedure

while the arteriovenous guide wire circuit is established. If the right ventricle is of normal size with a normal *z*-score of the tricuspid valve (>-2) there is usually no need to stent the duct. If the right ventricle is moderately or severely hypoplastic, the tricuspid valve has a *z*-score of less than -2, the tricuspid valve is stenotic or when significant residual subvalvar stenosis persists, additional blood flow to the lungs may be required for weeks or months. The duct may then be stented at the same procedure [13]. In case of doubt, we would proceed to carry out ductal stenting, avoiding the costs and risks of maintaining the baby on a prostaglandin infusion for days or weeks (waiting for the right ventricular stroke volume to increase), and avoiding the cost and burden of a second procedure. In other centers, patients with borderline right ventricles would be continued on prostaglandin infusion until an acceptable saturation (>80%) can be maintained without ductal flow [13].

In newborns with pulmonary atresia and ventricular septal defect, ductal stenting should be considered whenever a shunt is indicated, preferably after a postnatal adaptation time of 3–5 days.

Duct-dependent systemic circulation

Early in the experience of hybrid procedures, ductal stenting was performed mostly in advance of surgical bilateral banding. However, most centers now recommend that ductal stenting is undertaken after banding due to the (theoretical) risk of stent dislocation during intraoperative manipulation [11,14,18]. In the setting of a surgical–interventional hybrid procedure, the stent can be deployed through a direct arteriotomy of the pulmonary trunk through the sternotomy [27,30]. The restriction of the atrial septum is addressed after the bilateral banding and stenting of the duct [27].

In newborns and infants with low cardiac output caused by duct constriction despite continuous prostaglandin infusion, urgent percutaneous duct stenting utilizing premounted balloon-expandable stents is an effective high-urgency therapy.

Anticoagulation – antiaggregation

The role of anticoagulant and antiplatelet drugs remains unclear. During the procedure, standard intravenous heparin should be administered. Heparin is not routinely neutralized at the end of the procedure, but acetylsalicylic acid 1–3 mg/kg/day is often given for as long as stent patency is required [12,18,23,29], although this is certainly not evidence based. The efficacy and safety of clopidogrel 0.2 mg/kg/day in this setting still needs to be determined [23].

Neointimal proliferation

Duct patency after stenting is limited by in-stent restenosis, which occurs due to neointimal proliferation and/or peal formation. The ideal stent for this procedure still needs to be defined. Stent design determines (non)metal surface area, radial force, flexibility, conformability, scaffolding and prevention of tissue prolapse. Drug-eluting stents or covered stents have been proposed as a means of preventing instent restenosis in adults. Covered stents are slightly more bulky and require larger introducer sheaths (currently +1–2 Fr sizes) and can obviously not be used in the duct-dependent systemic circulation. The drug-eluting coatings contain agents that inhibit thrombus formation (e.g., heparin), inflammation (e.g., dexamethasone) and cellular proliferation (e.g., sirolimus or paclitaxel). The efficacy and safety of ductal stenting with such coated stents in newborn babies still needs to be established; significant liberation of immune suppressive drugs in the systemic circulation can be anticipated and has been documented.

In-stent stenosis can be managed by redilating or preferably by restenting the duct, thereby also accounting for patient growth.

Discussion

Duct-dependent pulmonary circulation

Ductal stenting obviously needs to be compared with the standard surgical shunt. The interventional approach performed, with the goal to be a minimally invasive alternative to a surgical shunt, cannot yet be proposed as 'a must approach'. In experienced hands, ductal stenting appears to be feasible in approximately 80–90% of cases, the most challenging ducts being the long tortuous ones in pulmonary atresia and ventricular septal defect (VSD). In addition, such a minimally invasive alternative may only be possible by using the best currently available material and by choosing a variable arterial/venous access depending on the ductal morphology and origin. Only then is this approach less invasive than primary surgery and offers the possibility to adapt to the clinical needs of the individual patient. Compared with long term prostaglandin infusions, early ductal stenting shortens hospitalization significantly and reduces treatment costs. The lumen of a stented duct appears to narrow faster than a surgical shunt, necessitating redilation and restenting. This, however, allows titration of pulmonary flow to patient size and growth. Such redilation restenting must obviously be considered when assessing the cost–effectiveness of each strategy.

The stented arterial duct fulfils its function as a surrogate for an aortopulmonary shunt, augmenting the pulmonary blood flow until a definitive surgical procedure can be performed or until the ductal flow becomes redundant. During follow-up, no distortion of the pulmonary arteries has been observed and technical problems due to the stent are not encountered at subsequent surgeries, as the stent can easily be occluded by simple external compression (surgeons be aware: no recoil!).

Duct-dependent systemic circulation

Neonates with heart defects suitable for univentricular repair can benefit from this hybrid transcatheter-surgical palliation, having the Norwood type of aortic reconstruction carried out beyond the neonatal period at the same time of the bidirectional superior caval anastomosis [11]. Particularly in patients presenting with neonatal cardiogenic shock or other high-risk factors, percutaneous ductal stenting as part of a hybrid approach can significantly improve early survival [11,17,18,31–34]. In addition, patients with variants of the hypoplastic left heart complex, in whom the immediate postnatal decision regarding a uni- or biventricular

approach is ambiguous, or who carry a high risk when biventricular repair is performed in the neonatal period, may have a major benefit from primary hybrid transcatheter-surgical palliation, postponing definitive decisions and surgery until later [14,17].

As experience has been increasing worldwide, the technique and material used for ductal stenting in this specific patient population have been adapted. Since the use of self-expandable Sinus-Repo nitinol stents and balloon-expandable Genesis stents, the results have improved significantly. Self-expandable stents are probably the stent of choice in most patients as they can conform to the anatomy of the arterial duct without significant obstructon of the istmus. By contrast, balloon-expandable stents are more rigid and force the ductal anatomy to conform to the stent. Such stents should, therefore, be reserved for patients in shock irresponsive to prostaglandin infusion, and in patients with an asymmetrically constricted or a very short duct, in which case a self-expandable stent may slip to the descending aorta or pulmonary trunk due to the still active working of the nitinol material after release.

Expert commentary

The worldwide experience of ductal stenting in patients with either duct-dependent pulmonary or systemic circulation has significantly increased over the past few years. This can largely be attributed to the improvement of stent and catheter technology (low profile, flexible, premounted stents with good scaffolding), but also to improve patient selection and preparation, optimization of interventional access and covering the complete length of the duct. In an ideal world, stents should be specifically designed for use in the neonatal arterial duct, meeting all the requirements necessary for ductal stenting. Realistically, however, the number of patients treated each year will remain small, necessitating the use of stents originally designed for other purposes. A downside of this technique is that surgeons might gradually lose their expertise in creating a neonatal shunt, theoretically increasing the surgical risk in the rare patient who will still need a surgical shunt.

Five–year view

Ductal stenting has come to stay. In well-selected patients, the interventional results are comparable to surgery and morbidity and costs are probably lower. However, currently, this procedure is still performed in only a few centers. More widespread use is remains limited, probably due to previously reported poor results, the lack of comparison studies and larger long-term outcome studies, the veto of surgeons in many teams and the complexity of some interventions that need to be embedded in a treatment strategy supported by the whole team. As surgeons and interventional cardiologists become more partners than competitors in the treatment of congenital heart disease, the obstruction within centers will slowly fade away. Due to the limited number of patients, specific stents for this indication will not be made. The interventionalist, therefore, needs to accept the compromise by using stents designed for other (coronary or renal) applications, keeping some key issues in mind when selecting a stent (size of the delivery sheath, stent flexibility and adequate scaffolding).

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Key issues

- Ductal stenting has evolved from dangerous and unpredictable to a safe and well-controlled procedure in selected patients.
- The short and straight duct, as observed in patients with pulmonary atresia with intact ventricular septum (PA/IVS) and hypoplastic left heart syndrome, are at the 'easy' end of the therapeutic spectrum; the long and tortuous duct can be very difficult and even impossible to stent with current technology.
- Adequate patient selection and preparation (prostaglandin management) and individualized vessel access are essential for success.
- The duct needs to be stented over its complete length.
- Stents designed for other applications are used for ductal stenting.
- Stent selection depends on the indication for stenting (pulmonary vs systemic flow), patient weight, ductal morphology, size of delivery sheath, stent flexibility and adequate scaffolding.

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Chapter 3

3.3 "Tailoring" pulmonary artery blood flow to accommodate somatic growth

Introduction

Patients with decreased pulmonary blood flow often need neonatal palliation (ductal stenting, surgically created systemic to pulmonary shunts) due to severe cyanosis. In patients with increased or unprotected pulmonary flow, pulmonary artery banding during the first weeks of life is mandatory to protect the pulmonary vascular bed. These interventions are unavoidable, though have the disadvantage that pulmonary flow has to be manipulated at a very early age (low weight). During somatic growth these shunts and bands are soon outgrown, necessitating new interventions. Increasing flow percutaneously can postpone or sometimes even avoid surgery, by "buying" time until the patient is older and pulmonary artery size and resistance are better or an "adult" sized graft can be implanted.

Substrates for flow manipulation

Pulmonary blood flow usually decreases gradually over time after creation of surgical shunts (modified Blalock-Taussig shunt, central shunt, and Sano shunt) or ductal stenting. In other patients balloon dilation of the pulmonary valve may be insufficient to relieve cyanosis due to residual subvalvular stenosis or pulmonary artery hypoplasia. Stenting of the right ventricular outflow tract could be considered depending on the underlying morphology. Pulmonary flow through a surgically created band can be increased by balloon dilation, provided that a dilatable banding technique was used. This section will focus on transcatheter enlargement of surgical shunts, stenting of the atretic right ventricular outflow tract and balloon dilatable pulmonary artery bands.

Surgical shunts

Gazzaniga and co-workers introduced the use of polytetrafluoroethylene (PTFE) for creation of surgical shunts in 1976 (30). High procedural success rates and low procedural morbidity have been reported (31 - 34). Shunts are mostly created during neonatal life or early infancy at a relatively low weight, allowing no compensation for growth [except for the modified Blalock-Taussig shunt, where the orifice of the subclavian artery grows and a relative increase in shunt flow may be expected (35)].

Thin walled stretch Gore-Tex® PTFE vascular grafts (W.L. Gore & Associates, Flagstaff, AZ) are extensively used in our centre. The thin-wall stretch configuration provides longitudinal extensibility, superior anastomotic conformability and is relatively kink resistant, allowing good patency and easier tailoring and sizing during surgical implantation (36). Shunt flow decreases gradually due to somatic growth (relative decrease in shunt size), scar formation at the shunt anastomosis, or fibrous neointimal peel formation and/or thrombosis (37). Sudden occlusion can occur due to thrombosis or kinking (38).

Balloon dilation and stenting of stenosed or occluded shunts have been described by several authors using different balloon/stent to shunt ratio and different inflation pressures (ranging from 3 to 10 atm) (32 – 34, 37, 39 – 41). Some authors recommended caution when using oversized balloons for shunt dilation, due to the risk of aneurysm formation, rupture of sutures, vessel and graft (41, 42).

Verbelen et al studied the mechanical properties of Gore-Tex® vascular grafts, gaining insight into the extent that shunts can be dilated (38). The axial extensibility of thin-walled stretch grafts was superior to that of regular Gore-Tex® vascular grafts, implying that axial stress (and therefore loading on the anastomosis sites) due to circumferential expansion will be significantly higher in the case of the regular (non-stretchable) graft. The failure strain and stress of stretchable grafts in the circumferential direction were also proven to be significantly higher than those of the regular graft in the same direction, implying that a stretchable graft will be able to withstand higher dilations than a non-stretchable graft (38).

These results correlate well to the clinical experience in our unit, where thin walled stretch Gore-Tex® grafts are extensively used. Patients who had undergone stenting of a stretchable vascular graft with the aim of increasing the nominal shunt diameter were retrospectively analyzed (section 3.3.1 of this chapter) (43). We used much higher inflation pressures (up to 18 atm) than described in previous studies without any complications. Fourteen stents were implanted in 11 stretch grafts a median of 18.9 months (3.2; 21.6 months) after shunt surgery. There was a median increase in diameter of 1.4 mm (0.9; 1.7 mm) [P 5 0.001, 95% CI: 0.47; 1.7) from original nominal to final stented diameter of the shunts with a median gain of 28%. A simultaneous improvement in saturations from a median of 73% (66; 77%) to 87% (84; 89%) [P 5 0.015; 95% CI: 3; 22] was observed.

Restenting the arterial duct

Arterial duct stenting is now widely accepted as feasible, safe and effective palliation in selected patients with duct-dependent pulmonary circulation (44, 45). Neonatal arterial ducts are mostly stented using 3.0 – 4.0mm coronary stents, depending on patient weight and whether ductal flow provides single- or double lung perfusion. Flow restriction can be the result of decreased shunt size relative to increased patient size and weight and/or tissue ingrowth causing shunt stenosis. Most coronary stents can be dilated up to a maximal diameter of 5mm. Restenting of the duct often give better results than balloon dilation alone, especially in case of tissue ingrowth.

The right ventricular outflow tract as a shunt

In some patients with severe pulmonary artery hypoplasia, anatomical conditions may restrict surgical treatment and systemic to pulmonary artery shunting may not be technically feasible during early infancy. Right ventricle outflow tract balloon dilation and stent implantation can provide excellent relief of stenoses, and increases vessel size in the short term (46 – 48). Although many of these stents cannot be dilated to adult size, their efficacy in small infants and children in whom further surgery will ultimately be required makes them an attractive alternative in these patients (49). Hybrid

intervention in the operating room allows balloon dilation and stenting even in case of complex pulmonary atresia (long distance atresia; puncture across atretic valve) with the additional advantage that stents can be implanted that can theoretically be dilated up to adult size. An article describing our experience with hybrid stenting of the atretic right ventricular outflow tract in 3 small infants is discussed in section 3.3.2 of this chapter.

Balloon-dilatable pulmonary artery bands

Pulmonary artery banding is primarily used as a palliative measure in a strategy of staged cardiac repair and can be especially beneficial in patients with prematurity and/or low birth weight (50 – 52). Hybrid palliation procedures for hypoplastic left heart syndrome using bilateral pulmonary artery bands are currently also performed in many centers. Traditional bands consist of non-stretchable Gore-Tex, nylon or tape and have to be surgically removed when becoming restrictive. The benefit of an adjustable pulmonary artery band (potentially postponing surgery to a more desirable weight or age) has been highlighted by several authors (53 – 61). A system of dilatable handmade pulmonary artery bands has been developed in our unit and results have been published (section 3.3.3 of this chapter) (62). Placement of a dilatable band has now become our procedure of choice when faced with complex cardiopathies or in small, low-birth-weight infants with large shunts in order to allow us to manipulate pulmonary blood flow during follow-up when indicated. The dilatable concept also allows the surgeon to make a tighter band at the time of first palliation; traditional, non-dilatable bands are typically made larger to allow for growth, often resulting in initial pulmonary overflow.

Conclusion

Care for patients born with complex congenital heart defects is becoming increasingly challenging due to the improved neonatal survival of even the smallest and most premature infants. Palliative interventions (surgical, transcatheter or hybrid) are often needed within the first few days of life to increase or decrease pulmonary flow (with/without increasing systemic

flow). Flows may rapidly become “unbalanced” due to somatic growth, necessitating re-intervention. Manipulation or “tailoring” of pulmonary flow during growth is possible, provided that excellent cooperation exists between the interventionalist and the surgeon.

Chapter 3

3.3 “Tailoring” pulmonary blood flow to accommodate somatic growth

3.3.1 Stent expansion of shunts

Brown SC, Boshoff DE, Heying R, Gorenflo M, Rega F, Eyskens B, Meyns B, Gewillig M. Stent expansion of stretch Gore-Tex grafts in children with congenital heart lesions. Catheter Cardiovasc Interv. 2010 May 1;75(6):843-8. PubMed PMID: 20146322.

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PEDIATRIC AND CONGENITAL HEART DISEASE

Original Studies

Stent Expansion of Stretch Gore-Tex® Grafts in Children With Congenital Heart Lesions

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Objective: To evaluate the efficacy and safety of expanding vascular shunt grafts beyond original nominal diameter using stents. Methods: Bench testing confirmed the expandability of 3.5 mm and 4.0 mm vascular Gore-Tex® stretch grafts. A retrospective analysis included eleven systemic to pulmonary artery shunts with diminished flow which were stented with the aim of increasing the original nominal diameter of the shunts. Results: During bench testing, the grafts could be expanded to 4.5 mm and 5.8 mm, respectively. Fourteen stents were implanted in 11 stretch grafts a median of 18.9 months (3.2; 21.6 months) after shunt surgery. There was a median increase in diameter of 1.4 mm (0.9; 1.7 mm) [*P* = 0.001, 95% CI: 0.47; 1.7) from original nominal to final stented diameter of the shunts with a median gain of 28%. A simultaneous improvement in saturations from a median of 73% (66; 77%) to 87% (84; 89%) [*P* = 0.015; 95% CI: 3; 22] was observed. No complications were experienced during the procedures. Conclusion: In our limited experience, stretch Gore-Tex vascular grafts can be safely expanded beyond nominal diameters using high pressure vascular stents. This leads to improvement in saturation and pulmonary blood flow. It allows the clinician to tailor pulmonary flow in relation to pulmonary artery size and growth, ensuring best possible timing for the next surgical procedure. © 2010 Wiley-Liss, Inc.

Key words: shunt; dilatable shunt; stent; palliative-expansion

INTRODUCTION

Systemic to pulmonary artery shunts are effective palliation for infants with congenital heart disease associated with critical reduction of pulmonary artery blood flow [1–3]. Most shunts allow no compensation or increase in flow associated with growth. A modified Blalock-Taussig shunt allows some flow control: the orifice of the subclavian artery acts as the initial limitation and later as the child grows, the diameter of the shunt itself becomes the limiting factor [4].

When creating a shunt, the surgeon has the choice of several grafts made of different materials. Thin walled stretch Gore-Tex® vascular grafts (W.L. Gore & Associates, Flagstaff, AZ) are made of polytetrafluoroethylene (PTFE) and are extensively used in our centre. These grafts offer benefits such as ease of implantation and takedown during surgery and are purportedly more forgiving for length mismatch during implantation; they are

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relatively kink resistant and have superior anastomotic conformability whilst maintaining good patency. Stretch is available longitudinally but no radial stretch is claimed.

Stenoses and occlusions of shunts can be safely and effectively managed by balloon angioplasty and stenting [5–13]. It would be advantageous if the size of a shunt could be increased beyond the nominal diameter at initial implantation, allowing manipulation of pulmonary blood flow. The aim of this study was to determine whether the original nominal diameter of stretchable vascular grafts could be increased effectively and safely by means of percutaneous stent implantation and whether this would lead to an improvement in systemic saturation.

METHODS

During the study period, bench testing was performed to prove that increase in original nominal diameter of Gore-Tex stretch grafts was possible and to determine the limits of expansion. A 4.0 mm and a 5.0 mm stent were inflated in two pieces of 3.5 mm and 4.0 mm stretch Gore-Tex grafts respectively, at 8–10 atmospheres of pressure to obtain complete expansion. Both stents were subsequently further dilated using a 6 mm balloon at 12 atmospheres.

A retrospective analysis of our institutional pediatric cardiology database was performed to identify all children who had undergone stenting of a stretchable vascular graft with the aim of increasing the shunt diameter beyond the original nominal diameter at surgery. Eleven stretch grafts were stented with the intention of increasing diameter during a period ranging from December 2001 to June 2009. The predominant indications for interventions were arterial desaturation, inadequate pulmonary arterial flow or insufficient pulmonary artery growth, increasing the risk (and sometimes even excluding the possibility) of corrective surgery. Patient records were used to obtain catheterization and follow-up data. Digital measurements of catheterization data were performed using an IMPAX viewer (Agfa Heartlab®). The study was conducted in accordance with local ethical committee guidelines.

TECHNIQUE

All procedures were performed under general anesthesia. A retrograde femoral arterial approach, using size 4–6F guiding sheaths, was used in the case of systemic to pulmonary artery shunts, whilst the femoral vein (7F) was used for cannulation in one case of a right ventricle to pulmonary artery conduit. Standard methods and techniques were employed. In short, once the shunt was identified, it was crossed using a 0.014 inch guidewire. Angiography was subsequently carried out and appropriate measurements were performed. Some shunts were difficult to cross, and maintaining stable guidewire position was problematic; in these cases, we often used a co-axial system as previously described [14]. If possible, a 6F guiding catheter was preferred for stent delivery. However, if patient size proved to be problematic, only a 4F short femoral introducer sheath was used. Only premounted stents were used. Once the stent was in position, it was completely expanded using a pressure manometer. The balloon was inflated at least up to recommended nominal pressure. Depending on the clinical result, the delivery balloon was overinflated or a larger, high pressure balloon was used. Antibiotics and heparin (50–100 U/kg) were administrated intravenously during the procedure, followed up by oral aspirin (2 mg/kg/day) at discharge. Success was defined as any increase above the nominal diameter of the original shunt at implantation. Improvements in percutaneous saturations in room air before and after the procedures were also recorded where possible.

STATISTICAL ANALYSIS

Data was captured using excel spreadsheets, and statistical analyses were performed using Graph Pad Prism version 5.00 for Windows (Graph Pad Software, San Diego, CA). A P value <0.05 was considered statistically significant. Results were given as median with quartiles (25th; 75th) and 95% confidence intervals (non-parametric for median change).

RESULTS

Bench Test

Results of bench testing showed that after full expansion with a 6 mm balloon at 18 atmospheres, a 3.5 mm graft could be expanded up to 4.9 mm (40%),

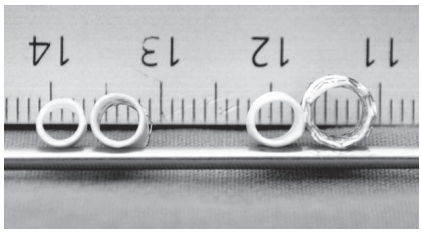

Fig. 1. Bench test of 3.5 and 4.0 stretch Gore-Tex® vascular graft. Left: 3.5 mm stretch Gore-Tex vascular graft expanded up to 4.9 mm diameter; right: a 4.0 mm stretch Gore-Tex vascular graft expanded up to 5.8 mm. See text for details.

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TABLE I. Patient Characteristics

Diagnosis	Type shunt	Original nominal diameter shunt	Stent diameter	No stents	Stent length	Type of stent	Max ball	Diameter post	Percentage increase[a]
TGA-PS	MBT	3.5	4.5	2	18, 12	Driver®	6	4.9	41
PA-VSD	Sano	6	7	1	18	Herculink®	8	7.7	28
PA-VSD	c	3.5	4	1	8	Coroflex Blue®	4	4.9	40
TA	MBT	6	7	1	18	Herculink®	7	7.7	28
PA-VSD	MBT	3.5	4.5	1	24	Driver®	4.5	3.9	11
	c	3.5	5	1	16	Liberté®	5	4.8	36
DORV-PA	c	3.5	4.5	1	16	Liberté®	4.5	4.4	25
PA-VSD	MBT	5	7	2	18, 18	Herculink®	7	6.0	20
Tet	c	3	3.5	2	18, 12	Driver®	7	3.5	16
UVH	c	4	6	1	40	Cordis Precise®	6	5.5	38
UVH	c	4	5	1	18	Multi-link Visionr®	5	5.7	43

Diameter and lengths in mm.

Manufacturers: Driver®, Medtronic Inc., Minneapolis, MN; Herculink®, Abbott Lab, IL; Coroflex Blue®, B. Braun, Netherlands; Liberté®, Boston Scientific, Natick, MA; Cordis Precise®, Cordis, Warren, NJ; Multi-Link Vision®, Abbott Lab, IL.

Max ball, maximum diameter of balloon used to expand stent; TGA-PS, transposition with sub pulmonary stenosis; PA-VSD, pulmonary atresia with ventricular septal defect; TA, tricuspid atresia; DORV, double outlet right ventricle; PA, pulmonary atresia; TOF, tetralogy of Fallot; UVH, univentricular heart complex; MBT, modified Blalock-Taussig shunt; c, central shunt.

[a]Percentage increase from original shunt (nominal) diameter.

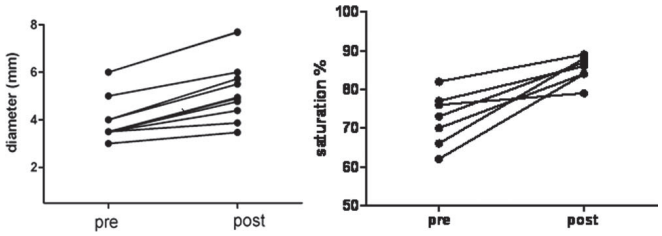

Fig. 2. Diameters and oxygen saturations before (pre) and after (post) stent implantation.

and a 4.0 mm graft up to 5.8 mm (45%) (Fig. 1). No rupture or tear occurred.

Patients

In 11 stretch grafts, 14 stents were implanted in 10 patients a median of 18.9 months (3.2; 21.6 months) after shunt surgery. Median age and weight at the time of the procedure was 1.7 years (0.3; 5.3 years) and 9.4 kg (3.8; 15.1 kg), respectively. Stented grafts consisted of modified Blalock-Taussig ($n = 4$), central ($n = 6$), and one Sano shunt. Further details can be viewed in Table I.

There was a median increase in diameter of 1.4 mm (0.9; 1.7 mm) [$P = 0.001$, 95% CI: 0.47; 1.7) from original nominal to final stented diameter of the grafts representing a median gain of 28% (Fig. 2). A noteworthy improvement in saturations from a median of 73% (66; 77%) to 87% (84; 89%) [$P = 0.015$; 95% CI: 3; 22] was also observed (Fig. 2). In two patients, the increase in diameter was obtained only after a second dilatation with high pressure balloons: 6 mm Maverick® (Boston Scientific, Waterton, MA) and 8 mm UDT® (Boston Scientific, Waterton, MA) for patients 1 and 2, respectively. One virtually occluded shunt was recanalized during the procedure. Angiographic examples can be viewed in Fig. 3. Some narrowing at the proximal anastomosis was observed in six shunts, at the distal anastomosis in nine shunts and at the mid area of one shunt before stent implantation. No complications were experienced during the procedures.

Follow-Up

The median follow-up time since last visit was 10.2 months (4.4; 41.9 months). During this period four patients were re-catheterized: three required re-stenting and one required angioplasty of the stents because of stenoses and/or peel formation. In the latter the shunt completely thrombosed eleven months later, but the patient proceeded uneventfully to surgery since there was a patent cavopulmonary connection. Five children proceeded to surgical repair, 6 months to 5 years after graft expansion. Two are still being followed up with

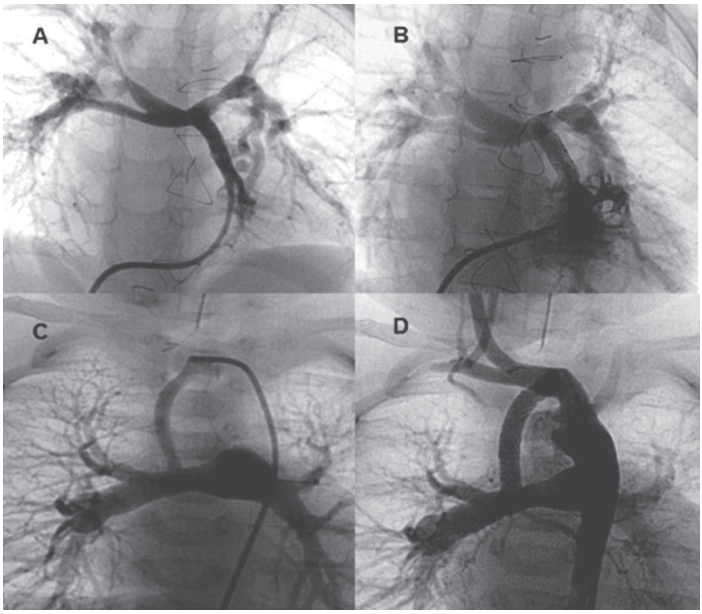

Fig. 3. Stent placement of stretch Gore-Tex® vascular graft. A and B: 6 mm Sano shunt before (A) and after stent expansion (B) up to 7.7 mm. C and D: 3.5 mm central shunt pre (C) and post (D) stent expansion up to 4.9 mm.

good saturations, and three died from problems related to co-morbidities. The deaths occurred two, four, and eleven months after shunt expansion in patients with Alagille, Kartageners, and right atrial isomerism syndromes, respectively. All shunts were patent at the time of death.

DISCUSSION

In patients with shunt dependant pulmonary flow, "premature" dysfunction of the shunt may occur during somatic growth. The clinician is faced with the following options: perform a second shunt, proceed to surgical correction accepting the risk of small pulmonary arteries and low body mass, or maintain the status quo (risking progressive cyanosis, poor pulmonary artery growth, and shunt thrombosis). Stent expansion of a stretchable graft becomes an attractive alternative in this scenario. The possibility of elective percutaneous graft enlargement broadens treatment options: lifespan of a shunt could be prolonged until satisfactory weight gain and/or pulmonary size are reached. A second surgical systemic to pulmonary artery shunt can be avoided and could allow the surgeon to create a smaller shunt at birth, especially in low birth weight infants and certain types of univentricular hearts where protection from volume overloading is important (hypoplastic left heart syndrome, unbalanced atrioventricular septal defect with right ventricle dominance). The shunt can electively be expanded in the first weeks or months after placement to manage pulmonary blood flow and keep track with growth. Furthermore, access to a catheterization laboratory is quick and easy, should the patient suddenly or unexpectedly become progressively cyanosed (especially in units where long waiting lists for surgery exist).

Results of this study show that the nominal diameter of stretch Gore-Tex vascular grafts can be significantly and safely increased with stents by means of transcatheter techniques. This was associated with a clinically significant 14% median increase in arterial oxygen saturations. Surgery could be delayed for a minimum of 6 months and for two patients not yet operated, satisfactory saturations

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were present during follow-up of 10 and 60 months. Percutaneous stent implantation allows a relatively predictable, durable, and safe expansion of vascular grafts.

Some aspects regarding the intervention need to be highlighted:

- Guidewire stability cannot be overemphasized: a coaxial system was frequently needed not only for shunt access, but also to achieve stable guidewire position. The intervention often required more than two pairs of experienced hands to maintain catheter positions and guidewire positions [14].
- A 6F arterial sheath is preferred since it will allow a 6F guiding catheter (right coronary guiding catheter or internal mammary guiding catheter in case of central shunts with acute angles). The guiding catheter also allows for hand injection angiography to facilitate perfect stent positioning.
- Premounted stents and, for smaller shunts, coronary stents were almost exclusively used (Table I). The great variety of stents were due to the fact that the review spanned a period of almost 8 years—coronary balloons available in the catheterization laboratory at the time were selected on the basis of diameter and high pressure tolerance. On average, we chose stents with a diameter 1 mm (range: 0.5–2 mm) larger than the nominal diameter of the original shunt. If required, an additional increase could be obtained using the delivery balloon or another larger, high pressure balloon. Although stent foreshortening was not observed in our patients, it remains a theoretical possibility especially if oversized balloons are used. No distortion of the pulmonary arteries was noticed on angiography.
- As reported in the literature [6], stenoses occur frequently at the anastomotic sites of the shunts and should be managed simultaneously. In general, the whole graft was stented up to the anastomoses; some protrusion into the lumen of surrounding vessels is not important, as long as there is no contact with the opposite side, except for the proximal end, especially if later re-entry is anticipated.
- We also stent expanded three larger grafts (based on our experience with the smaller diameter grafts) with a favorable increase in diameter. In these we used balloon pressures aiming for at least a 1 mm increase in diameter.

Some older children were included, consisting of complex lesions where early repair was not possible. Adequate pulmonary growth was obtained, and two patients with pulmonary atresia with ventricular septal defect (PA-VSD) proceeded to complete repair. One patient, not amenable to repair, is still being followed up with acceptable saturations.

Studies have shown that risk factors for stent thrombosis are longer length, smaller diameter, and wall abnormalities [15–17]. In this small series, low dose oral aspirin seemed to be effective in preventing stent (shunt) occlusion, as thrombosis occurred in only one stent expanded graft 11 months after intervention. No complications occurred, although dissection or aneurysm formation has been described during transcatheter management of shunts [18].

STUDY LIMITATIONS

This is a small, retrospective study and comparisons with other treatment regimens were not made. However, the primary aim of the study was to ascertain whether successful graft expansion was possible. Follow-up studies are indicated and should focus on pulmonary arterial growth.

CONCLUSION

In our limited experience, stretch Gore-Tex® vascular grafts can be safely expanded beyond original nominal diameters by percutaneous stents implantation, enhancing pulmonary blood flow as well as improving oxygen saturations. This may potentially allow the clinician to tailor shunt size to growth and pulmonary flow requirements, adding new management options.

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Chapter 3

3.3 Tailoring" pulmonary blood flow to accommodate somatic growth

3.3.2 Stenting of the right ventricular outflow tract

Cools BLM, Boshoff DE, Heying R, Eyskens B, Rega F, Meyns B, Gewillig M. Transventricular Balloon Dilation and Stenting of the RVOT in Small Infants with Tetralogy of Fallot and Pulmonary Atresia. Catheter Cardiovasc Interv, in press.

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Original Studies

Transventricular Balloon Dilation and Stenting of the RVOT in Small Infants With Tetralogy of Fallot With Pulmonary Atresia

B.L.M. Cools,[1] D.E. Boshoff,[1] R. Heying,[1] F. Rega,[2] B. Meyns,[2] and M. Gewillig,[1*]

Introduction: The management of small infants with tetralogy of Fallot (TOF) with pulmonary atresia (PA) and hypoplastic pulmonary arteries can be very challenging. **Methods:** In three small infants (weight range 2,200–3,600 g, pulmonary trunk 2.0–3.2 mm), initial palliation consisted of sternotomy, transventricular puncture of the right ventricular outflow tract, and atretic pulmonary valve, followed by balloon dilation (n = 1) or stent deployment (n = 2) from the right ventricle into the pulmonary trunk (stent diameter 5–6 mm, length 16 mm). **Results:** The procedure resulted in adequate palliation with good anterograde flow to the pulmonary arteries and near normal saturations in all three patients (>92%); there was no associated morbidity. Additional transvenous stenting was required in all patients because of progressive muscular infundibular stenosis after a median of 3 months. Two patients evolved to full repair at the age of 5 months and one patient with multiple hilar stenoses requires additional percutaneous procedures through the stented RV outflow tract. **Conclusion:** Transventricular balloon dilation and stenting of the RVOT through medial sternotomy as initial palliation strategy appears a safe and well tolerated alternative treatment in small infants with TOF with PA and a hypoplastic pulmonary trunk.

Key words: congenital heart disease; hybrid procedure; palliation; stenting; transventricular; perventricular; tetralogy of Fallot; pulmonary atresia; premature infant; small infant

INTRODUCTION

Patients with tetralogy of Fallot (TOF) with pulmonary atresia (PA) and severely hypoplastic pulmonary arteries need an intervention in the neonatal period to relieve cyanosis and to enhance catch-up growth of the pulmonary arteries. In case of an adequate weight and pulmonary artery size, primary surgical correction is the preferred option [1–6]. Neonatal surgical correction with a transannular patch or a right ventricular to pulmonary artery conduit can be associated with high morbidity [7–9]. These techniques require cardiopulmonary bypass which is poorly tolerated by premature and very small infants.

In many cases, the pulmonary arteries are diminutive and therefore a staged approach is preferable [1–6]. For years, a surgical aorto-pulmonary shunt was the first palliative step in these patients [10]. Stenting of the arterial duct and radiofrequency perforation of the atretic segment are non-surgical alternatives, but may be particularly challenging [11–13].

The evolvement of hybrid techniques has broadened the horizon in treating patients with complex congenital heart disease. We report hybrid interventions in three small infants using a combination of two techniques: a controlled and safe perforation of the atretic outflow tract by transventricular puncture, followed by

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Conflict of interest: Nothing to report.

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transluminal balloon dilation in 1 patient and stenting of the RVOT in two patients.

PATIENTS

Three low birth weight infants with TOF, PA, and severely hypoplastic pulmonary arteries were selected for hybrid intervention (Table I). Patient 1 (2,660 g, gestation 37 weeks) underwent catheterization postnatally on day 3. Angiography revealed absence of any arterial duct, complex pulmonary perfusion via atypical aorto-pulmonary collaterals and minute, but confluent central pulmonary arteries (trunk: 2 mm). Patient 2 (1,620 g, gestation 33 weeks) and 3 (2,190 g, gestation 39 weeks) presented with duct dependent flow to hypoplastic, confluent central pulmonary arteries (trunk 2.5 and 3.2 mm measured on echography). Prostaglandines were maintained for 43 and 22 days, respectively. In all three patients, the infundibular atresia was discrete and theoretically allowed direct "intracardiac" connection between the RV infundibulum and the pulmonary trunk. The weight at procedure varied from 2,200 to 3,600 g.

TABLE I. • • •

	Patient 1	Patient 2	Patient 3
Birth weight (g)	2630	1620	2190
Gestational age (weeks)	37	33	39
Saturation (%)	85	80	90
No. days prostaglandin	–	43	22
Pulmonary trunc diameter (mm)	2,0	2,5	3,2
PA branches diameter L–R (mm)	2–2	3–3	3.0–3.5
distance RVOT	5	6	5
Age at procedure (days)	59	43	22
Weight at procedure (g)	3,600	2,460	2,200
Fluoro time (min)	4	4	4
Radiation dose (cGy/cm^2)	220	250	200
stent diameter/length	7/19	5.5/16	5.3/16
age at 2nd stent (days)	184	57	99
2nd stent type	12/29 mm	5/16 mm	7/18 mm
Age at full repair (months)	–	5	5
Weight at full repair (g)	–	5.4	5.6

METHODS

All procedures were performed according to the guidelines of the local ethics committee; informed consent was obtained from the parents. The procedures were performed in a hybrid surgical suite with high resolution single plane fluoroscopy. Access was provided through medial sternotomy. In order to minimize the intravascular procedure time, all materials were prepared: a 4 French (F) introducer sheath, 2 identical needles: 21 Gauge, 4 cm length (COOK® Medical Europe, Denmark), a 0.014″ short tipped stiff coronary guide wire shortened to about 100 cm, a coronary stent (2 mm larger than the pulmonary trunk, length from 2 mm above the valve until well within the right ventricular lumen), an indeflator, 10 cc syringes with flush-saline and contrast, vascular clips, 6.0 prolene. The puncture site on the right ventricular anterior wall was determined by laying the premounted stent on the epicardium (Fig. 1A); a purse string with 6.0 prolene was created as apical as possible in order to deploy the stent from just above the pulmonary valve until well within the right ventricle; options are however limited due to the coronary anatomy. Two vascular clips were placed: one at the pulmonary valve annulus, and one at the puncture site within the purse string.

Three operators or five coordinated hands are required to perform the procedure: one hand (with radioprotective glove) must stabilize the sheath throughout the procedure, the second pair of hands performs the puncture and leads the manipulations at the level of the sheath and contrast hand injections, and the third pair controls the wire, mounts the stent on the wire and inflates the balloon.

Two identical 21 gauge needles were used. One needle was used as a reference adjacent on the surface of the RVOT to determine precise puncture depth and direction; the other needle was used to perform the puncture. The puncture was performed under direct vision in two motions: first access perpendicular to the surface for 10–15 mm into the right ventricular cavity with free blood, second angulation of the needle toward and advancement through the atretic outflow tract into the pulmonary trunk. A 0.014″ coronary guide wire was advanced blindly through the needle into the pulmonary artery. At that point, the C-arm was positioned above the thorax, and wire position was confirmed with fluoroscopy; the wire was repositioned if required (Fig. 1B). The C-arm was tilted about 20° cranially to "open" the surgical field and to create a view perpendicular to the RV outflow tract. The needle was exchanged for a 4 French introducer sheath. The dilator of the sheath was used to further dilate the valve (position revealed by the vascular clip), with subsequent advancement of the sheath just into the pulmonary arterial trunk. The dilator was removed, and a hand angiogram was performed through the sheath (Fig. 1C) to confirm wire position distally in the pulmonary artery and to determine the exact projection relationship of the vascular clip to the atretic pulmonary valve (clip typically just cranial of the atretic valve). The stent was subsequently advanced with the distal end just reaching the pulmonary trunk (typically projecting at the level of the vascular clip), leaving most of the stent in the right ventricle (Fig. 1D). When uncovering the stent, the 2nd vascular clip at the entry

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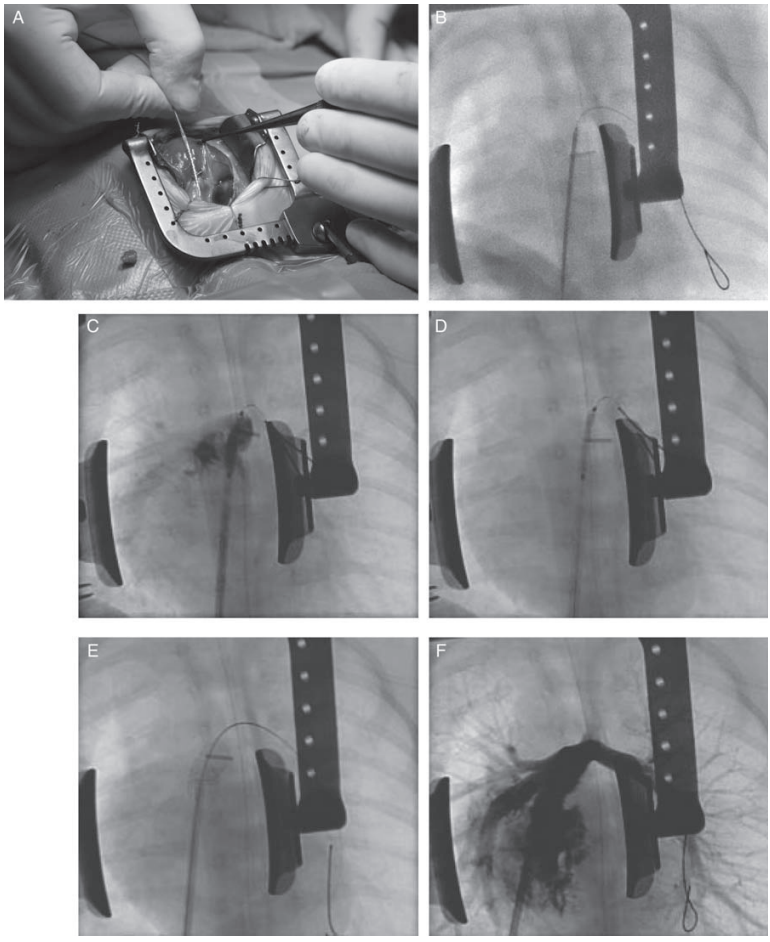

Fig. 1. A: Open sternum, vascular clip at PV annulus. Premounted stent projecting along the RVOT for determining entry point in the RV cavity. B: Radioscopic view, mild cranial tilt. Vascular clip at level of atretic pulmonary valve. Needle in RVOT with 0.014″ wire into the left pulmonary artery. C: 4 Fr sheath in RVOT over 0.014″ wire, positioning premounted coronary stent. Observe relationship between clip and atretic valve. D: Withdrawal of sheath to uncover stent, distal end of stent at the vascular clip; stent too distal and was withdrawn before inflation. E: Stent deployed in RVOT with distal part just across the pulmonary valve (vascular clip). F: Angiogram through 4Fr sheath in RV outflow: nice antregrade flow to pulmonary branches.

point allowed assessment of residual sheath depth within the right ventricle. The stent was dilated up to at least nominal pressure using an indeflator (Fig. 1E). In case of insufficient increase of arterial saturation or suboptimal stenting angiographically (Fig. 1F), additional dilation or stenting could be performed. The AQ4

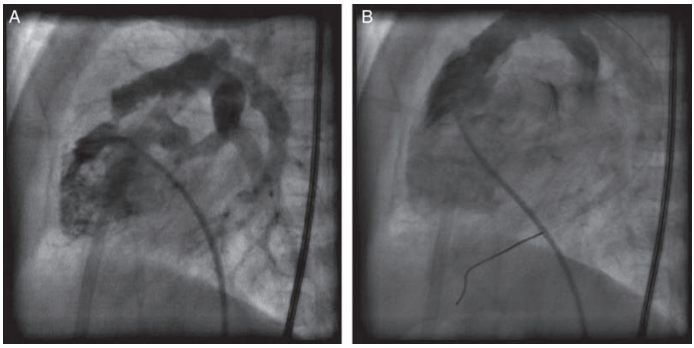

Fig. 2. Percutaneous restent procedure in patient 3 at 3 months. A: RV angiogram showing severe dynamic muscular stenosis proximal of stent in RVOT; (B) RV angiogram showing relief of the infundibular stenosis after restenting.

sheath was removed and the purse string closed. Prostaglandin infusion was discontinued, if given. The vascular clips were removed and the sternum was closed.

RESULTS

All punctures from the right ventricle into the pulmonary trunk were successful from a single ventricular puncture; no "fausse route" was created in any patient. In the first patient we initially only performed a balloon dilation (4mm Tyshak® Mini, NuMed, USA) as this was believed to be sufficient (type Brock procedure). However, restenosis occurred and a PG1910 Cordis Genesis® stent (Europe, Roden, The Netherlands) was implanted transvenously through a 6F sheath 4 months later. In patients 2 and 3, a 5/16 mm coronary stent (Liberté Monorail®, Nanterre Cedex, France) was successfully implanted. Time from puncture to sheath withdrawal was less than 10 min. Blood loss was minimal; none of the patients required a transfusion. No ECG changes suggestive for coronary compression were observed. All patients had an increase in saturation above 92%.

The patients remained hemodynamically stable throughout the procedure and could be extubated within 48 hr.

Complications: Early

Patient 2 suffered a sudden desaturation while advancing the needle; immediate completion of the procedure with deployment of stent resolved the problem (lowest saturation level was 55%, comparable to that of a difficult surgical shunt). An angiogram showed spasm of the arterial duct and the proximal left pulmonary artery, probably triggered by the needle which in retrospect was inserted too deep; this illustrates the need for the "double needle technique."

Complications: Late

No stent fracture or stent recompression was observed. All three patients developed a progressive infundibular (muscular) stenosis at the proximal end of the stent for which reintervention was indicated (15 months after transvenous stent implantation in patient 1; 1 week and 2 months after stent implantation in patients 2 and 3, respectively). The muscular stenosis was treated by restenting the outflow tract, with the stent covering the muscular band proximally and extending telescopically well into the prior stent [patient 1: Advanta® 12/29 mm covered stent inflated manually at valvular level up to 9 mm (Atrium Europe, Mijdrecht, The Netherlands); patient 2: 5/16 mm Liberté Monorail® (Nanterre Cedex, France); patient 3: 7/18 mm (Cordis® Europe, Roden, The Netherlands)]. In all three patients saturations increased to above 92%.

Late Outcome

The central pulmonary arteries in patient 1 have shown substantial growth since birth, but peripheral multiple hilar stenoses persist, despite good pulsatile anterograde flow. This patient is planned in due course for multiple transvenous interventions with high pressure balloons, cutting balloons and stenting if indicated. The muscular stenosis was treated with a covered stent as "tearing" of the pulmonary annulus by a

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future balloon dilation was expected. Patients 2 and 3 underwent surgical repair at the age of 5 months. The RVOT was opened and the stents were cut longitudinally with regular scissors. The stents were firmly attached to the outflow tract according to the surgeon, but could be removed completely, followed by infundibular resection and repair with a transannular patch.

DISCUSSION

The management of infants with TOF with pulmonary valve atresia remains challenging. Neonatal intervention at a very early age and/or a low weight is usually unavoidable. In case of severely hypoplastic pulmonary arteries a staged approach is preferred to allow pulmonary arterial growth [2,9]. Prolonged intravenous administration of prostaglandin is not without morbidity. Ductal stenting has become a good alternative for the initial palliation, but unfavorable ductal anatomy (long and tortuous; vertical origin from the inner arch) is rather the rule than the exception in this subgroup of patients, often necessitating unusual arterial access and multiple manipulations, increasing procedural time and complications (ductal spasm, incomplete stenting, and access problems) [11,12]. Percutaneous radiofrequency perforation of the pulmonary valve has been reported, but the risk of perforation is particularly high in case of long segment (muscular) atresia and in very small infants [13]. Conventional palliative treatment consists of the surgical creation of a systemic-to-pulmonary shunt (modified Blalock–Taussig or central shunt) [8–10]. Such surgery in low birth weight infants with diminutive pulmonary arteries can involve major complications such as early or late shunt occlusion, kinking or stenosis, distortion and differential growth of the pulmonary arteries, pulmonary overcirculation, chylothorax, phrenic, and vagal nerve palsy [3,7]. Other surgical options are creating a ventricular-arterial connection using a Sano-shunt or a transannular patch. Both procedures however require cardiopulmonary bypass which is poorly tolerated in the very small and premature infants [1–9,13].

We report on hybrid interventions to get adequate palliation: the surgeon provided access for accurate and safe transventricular puncture of the atretic valve without cardiopulmonary bypass, followed by transluminal stenting of the outflow tract, allowing adequate pulsatile anterograde flow with desaturated blood. This procedure can be considered a combination of an "upgraded" Brock procedure with an intracardiac Sano-type shunt (without cardiopulmonary bypass). A duct-shunted patient is thereby converted into a more "conventional" Fallot with pulmonary stenosis allowing antegrade pulsatile flow of desaturated blood into the pulmonary artery ("the better" shunt) [14,15].

The transluminal stent delineates an end-to-end anastomosis with minimal distortion. Such stent can be dilated to augment pulmonary flow during somatic growth, and provides easy access for transcatheter interventions if indicated.

We applied this technique in three high risk patients (low birth weight, diminutive pulmonary arteries) in whom significant morbidity could be anticipated using conventional strategies. The puncture of the atretic outflow tract from ventricular access is the most critical maneuver of the procedure due to the risk of creating a "fausse route." In all three patients the pulmonary trunk could easily be entered. If a "fausse route" had been created, the surgeon would probably be able to control any hemorrhage. This would certainly not be the case if the same complication occurred during a transluminal radiofrequency ablation or closed puncture technique.

The sternotomy proved to be a safe and well tolerated maneuver even in premature infants avoiding problems with adequate vascular access (axillary or carotid). A sternotomy is better tolerated than a thoracotomy, as this involves a preoperative collapse of the lung which can be problematic in an already cyanotic patient.

Performing transluminal procedures in a hybrid suite in an open chest creates a new environment with new challenges but also new opportunities. Problems are extreme proximity of the interventionalist's hands to radiation, less stability of the sheath with a "crowded" operation field, loss of typical radiologic landmarks. Advantages are the much higher limit of sheath size, the possibility to control a perforation or tear of the cardiovascular wall, the possibility to re-crimp a stent if required, the use of vascular clips as landmarks making the procedure safer and faster, and limiting the use of fluoroscopy and contrast.

Deployment of a stent in the right ventricular outflow tract might compress a coronary artery; this is a known complication in older patients during percutaneous stenting [7,16–18]. These two stenting techniques however are distinctively different: stents used in neonates are small and expansion in the surrounding tissues is more symmetrical and therefore minimal in any direction; in contrast, stents used during percutaneous revalvulation are larger and expansion (tear of the graft) typically occurs asymmetrically and excessively in one direction. If coronary compression would happen during the procedure, the interventionalist can re-crimp the stent if necessary. Covered stents were not used as there was tissue continuity from the right ventricle to the pulmonary artery [19].

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The chosen stent diameter was 2 mm larger than the pulmonary trunk as the risk of "overstretching" and tearing such neonatal pulmonary artery is small [20].

In all three patients a reconfiguration of the RVOT with progressive subpulmonary stenosis occurred with a wide range of time intervals from 5 days up to 13 months. The trend of the infundibulum to gradually "close off" (fetally and postnatally) in this type of congenital malformation has also been reported by other investigators [7]; it may be part of the natural course, but may also be related to the technique. The need for a second stent to treat the infundibular stenosis might be prevented or postponed by adapting the puncture technique (two motions thereby orientating the stent away from anterior wall), or by using a longer stent initially with maximal protrusion into the RV cavity.

This procedure was in all three patients well tolerated and safe with futile morbidity. We expect this technique to compare very well with more "conventional" shunts, and we now will consider this technique also for larger infants who require a palliative procedure.

CONCLUSION

In this small group of patients, transventricular stenting of the RVOT through medial sternotomy appears to be a safe and well tolerated initial palliation. This technique might in future compare well with conventional strategies as initial palliation in infants with TOF with PA and hypoplastic pulmonary arteries.

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Chapter 3

3.3 Tailoring" pulmonary blood flow to accommodate somatic growth

3.3.3 Balloon dilatable bands

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Dilatable pulmonary artery banding in infants with low birth weight or complex congenital heart disease allows avoidance or postponement of subsequent surgery☆

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Abstract

Objective: This study evaluated the efficiency and feasibility of dilatable bands in selected patients. **Methods:** Two types of dilatable handmade bands were retrospectively evaluated and divided into two groups: main pulmonary artery bands and bilateral branch pulmonary artery bands (hybrid stage I palliation). Stepwise balloon angioplasty (BA) was performed, increasing the diameter either to completely dilate with total release of the band, or in others, to partially dilate the bands in order to improve flow and/or saturation. **Patients and results:** Balloon angioplasty was performed in 20 patients (median birth weight 2.9 kg, range: 1.3–4.5 kg). *Main pulmonary artery: Partial dilation*: Six patients: Large ventricular septal defects (VSDs) and complex lesions requiring additional surgery. Progressive dilation allowed postponement of surgery in four children and allowed percutaneous VSD closure in one. *Complete dilation*: Eight patients: Spontaneous restriction of VSDs occurred in six patients; the bands were subsequently percutaneously completely released after a median of 39 weeks (7–91 weeks). The median gradient decreased from 90 to 38 mmHg ($p < 0.0001$). *Bilateral branch pulmonary artery:* An average 8.5% increase in saturations was achieved in five patients, and in one patient, a hybrid procedure with borderline left ventricle, complete dilation allowed successful percutaneous biventricular repair. **Conclusions:** Dilation of both main and bilateral branch pulmonary artery bands is possible, effective and safe. Dilatable main pulmonary artery bands allow for progressive dilation with postponement of surgery or complete release of the bands. Bilateral dilatable branch pulmonary bands offer palliative benefit, especially in hybrid cases where pulmonary blood flow may be limited by the bands before the ideal conditions for a stage II procedure exist.

Keywords: Pulmonary banding; Palliation; Balloon angioplasty; Clips

1. Introduction

Pulmonary artery banding (PAB) is primarily used as a palliative measure in a strategy of staged cardiac repair due to the fact that definitive repair has become the treatment of choice for most children presenting with congenital cardiac defects. Although the use of PAB has decreased markedly, it continues to maintain a therapeutic role in the management of some congenital cardiac defects. (PAB is still performed in up to 2% of congenital cardiac cases in current surgical databases [1]) New indications for PAB have also arisen, for example, hybrid palliation procedures for hypoplastic left heart syndrome using bilateral pulmonary artery bands [2,3].

Improvements in neonatal services have increased the number of low birth weight, sick neonates presenting with serious cardiac lesions. These present specific surgical challenges, especially the sick premature infant with associated problems. Recent literature [4,5] indicates that more of these children are being banded. Traditional bands are placed using non-stretchable Gore-Tex, nylon or tape and have to be surgically removed when required. Subsequent to rapid growth, a band may become too tight and needs removal and re-banding or repair of the primary lesion. Such surgical procedures are not without risk and frequently still need to be done at a relatively young age or low weight [4]. A dilatable band could potentially enable surgery to be postponed to a more desirable weight or age. This need for an adjustable band is highlighted by different publications in which dilatable [6–11], resorbable [12,13] and restrictable [14–16] bands have been attempted, but few are simple, affordable or practical and are therefore rarely used.

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We developed a system of dilatable handmade pulmonary artery bands. The aim of this study was to evaluate the efficacy and feasibility of using a dilatable band.

2. Methods

2.1. Patients

This was a retrospective review of children in whom dilatable pulmonary artery bands were placed. From April 2003 to January 2009, balloon angioplasty (BA) of a dilatable band was performed in 20 cases through standard routes of percutaneous access. Patients were divided into two main groups: group I in whom a main pulmonary artery band was placed and group II in which bilateral branch pulmonary artery (left and right pulmonary artery) bands were placed. Due to vessel anatomy, construction differed for each group. Groups were then subdivided into (1) those in whom the band was partially dilated in order to increase flow or oxygen saturation to allow further growth and thus postpone or delay surgical repair (partial dilation group) and (2) those in whom angioplasty was used to fully dilate and therefore effect complete relief (release group) of the band.

2.2. Construction of the dilatable bands

2.2.1. Main pulmonary artery (MPA) band

A non-resorbable nylon cord of 2 mm is placed around the main pulmonary artery and the desired diameter achieved according to the Trusler formula [17] without using a knot; the ends are sewn together at the preferred tension with polypropylene 6/0; the ends of the nylon cord are then folded back and fixed with two to four vascular clips (Fig. 1A). If early dilation is anticipated, the distance between the stitch and first staple should be short, as this will determine the first increase in diameter after dilation. If complete release of the band is anticipated during follow-up, the total length of the band and distance between staples should reflect at what size complete release will be desired. The band is fixed to the pulmonary artery trunk with two separate polypropylene 7/0 sutures. This design allows a progressively dilatable restriction. Depending on the desired length and number of staples, the band can thus be dilated stepwise until completely released, if required.

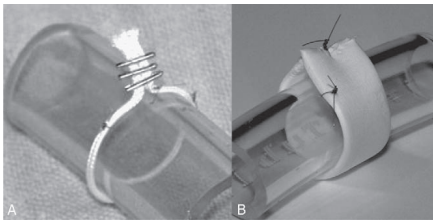

Fig. 1. (A) Dilatable band for main pulmonary artery: non-resorbable 2 mm nylon approximated and fixed with 6/0 prolene, three vascular clips. (B) Dilatable band for bilateral branch pulmonary arteries: open ring 3.0—4.0 mm Gore-Tex. Re-closed with 1 polypropylene 7/0 stitch and fixed to branch pulmonary artery with one 7/0 stitch.

2.2.2. Bilateral branch pulmonary artery bands

All were placed as a component of a stage I palliative hybrid procedure (stent ductus and bilateral banding) as suggested by Galantowicz et al. [2]. A ring of 3.0—4.0 mm Gore-Tex is cut through and re-closed with only one 7/0 polypropylene stitch (Fig. 1B). The ring is then fixed to the pulmonary artery branch artery with a polypropylene 7/0 suture.

2.3. Balloon angioplasty

Standard methods were used for BA of the bands. High-pressure, non-compliant balloons were preferred to open up the bands without exerting unnecessary tension on the adjacent tissues. Coronary angioplasty balloons were usually adequate for dilation of branch pulmonary artery bands. We preferred a strategy of sequential dilatation mostly due to safety considerations, starting with a smaller size and then dilated up to the desired result, using an average of two balloons. This would potentially also result in a more predictable final diameter.

2.4. Statistics

Data was captured using Microsoft Excel spreadsheets and statistical analyses were performed using a commercially available software package GraphPad Prism version 4.00 (GraphPad, San Diego, CA, USA). A p value less than 0.05 was considered statistically significant. Where applicable, results are given as median with range and 95% confidence intervals. The study was performed in accordance with local ethical committee guidelines; informed consent was obtained from all patients.

3. Results

The group consisted of 11 males and 9 females with a median birth weight of 2.9 kg (1.2—4.5 kg). A dilatable PAB was placed at a median age of 3.7 weeks (range: 0.3—28.3 weeks). Patient characteristics are summarised in Table 1.

3.1. Balloon angioplasty

3.1.1. Group I (main pulmonary artery bands)

3.1.1.1. Partial dilation ($n = 6$). BA was performed at a median age of 32.9 weeks (range: 13.1—99.3 weeks). The median gradient was reduced from 94 (range: 68—140 mmHg) to 61 mmHg (range: 40—80 mmHg) ($p < 0.001$). The maximal balloon diameter used was 12 mm with a median ratio of 0.5 (range: 0.3—1.0) to the adjacent normal pulmonary artery trunk and a median ratio of 2.5 (range: 1.8—3.8) to the narrowing caused by the band. We have been able to postpone surgery for 13, 19 and 2 months in patients 1, 4 and 5, respectively, at the time of writing the article. In patient 6, the surgeon could only close a large perimembranous ventricular septal defect (VSD) and some muscular VSDs at the age of 6 weeks, leaving many residual apical VSDs at that time; after bypass, the surgeon left a dilatable band on the main pulmonary artery. In the following months, five apical

Table 1
General patient characteristics.

	Diagnosis	Weight (g)	Age at banding (w)	Age BA (w)	Ratio b:nl	Outcomes
Group I						
Partial dilation						
1	UVH	1350	11.9	15.0	0.5	Awaiting surgery (13 mo post-BD)
2	Multiple VSD	2100	8.1	67.3	0.5	Surgery delayed for 13 mo
3	unb AVSD, CoA	2950	5.1	13.1	0.5	Died
4	VSD, CoA	2800	0.3	17.0	0.3	Awaiting surgery (19 mo post-BD)
5	unb AVSD, CoA	3450	9.4	48.9	1.0	Awaiting surgery (2 mo post-BD)
6	Multiple VSD	3740	5.7	99.3	0.6	1 VSD surgical closure, 5 Amplatzer devices IVS
Full dilation						
1	VSD	3850	5.7	81.3	–	Repair 19 mo
2	VSD	2350	3.1	41.0	1.0	haem. insignificant
3	VSD	3530	3.4	9.6	1.1	Repair 3 mo, died
4	VSD, CoA	3100	1.6	21.1	1.2	haem. insignificant
5	Swiss VSD, CoA	2670	28.3	109.1	1.2	haem. insignificant
6	Multiple VSD	2400	14.6	106.3	0.7	Spontaneous closure
7	VSD, CoA	3520	3.1	37.0	1.1	haem. insignificant
8	Multiple VSD, CoA	4500	0.9	11.7	–	Spontaneous closure
Group II						
1	HLHS	2300	1.0	13.7		BDG – 202 d
2	UVH, CoA	3400	0.9	10.9		BDG – 146 d
3	UVH DILV, CoA	2900	0.6	20.1		BDG – 210 d
4	HLHS	1600	4.6	13.3		BDG – 134 d
5	HLHS	2490	1.1	16.1		Biventricular repair 6 mo
6	Critical AS	4260	4.0	35.0		Percutaneous biventricular repair 8 mo

Group I: main pulmonary artery bands, Group II: bilateral (left and right) pulmonary artery bands, w, weeks; mo, months; b:nl, balloon diameter to nearest normal vessel ratio; BA, balloon angioplasty; diam, diameter; UVH, univentricular heart; VSD, ventricular septal defect; unb, unbalanced; AVSD, atrioventricular septal defect; CoA, coarctation of the aorta; HLHS, hypoplastic left heart syndrome; DILV, double inlet left ventricle; AS, aortic stenosis; IVS, interventricular septum; haem, haemodynamically; ( ), at time of writing.

VSDs were closed percutaneously before partial release of the band (still residual VSDs) after 93 weeks (Fig. 2).

3.1.1.2. Full dilation with release of band ($n = 8$). Results of BA for this group may be viewed in Fig. 3. BA was performed at a median time of 36 weeks (range: 6.1–44.6 weeks) after placement of PAB. The median gradient in the main pulmonary artery was reduced from 90 to 38 mmHg ($p < 0.0001$; 95% CI: 38–68) (Fig. 3) and the median diameter increased from 1 to 4 mm ($p = 0.0035$; 95% CI: 1.8–4.7). The median ratio of balloon diameter to nearest normal diameter of the pulmonary trunk was 1.1:1 with a maximum of 1.2:1 (in two patients the original angiographic data were irreparably damaged and could not be measured). Only two children required surgical repair (band released preoperatively at the time of catheterisation) and in the other six, the VSD either closed spontaneously or became haemodynamically insignificant. Interestingly, after a median follow-up period of 22.5 months (range: 1.5–63.4 months), the small residual gradient present immediately after dilatation decreased even further from a median of 38 mmHg (range: 12–40 mmHg) to 14 mmHg (range: 0–27 mmHg; $p = 0.0017$; 95% CI: 11.1–31.6; Fig. 3).

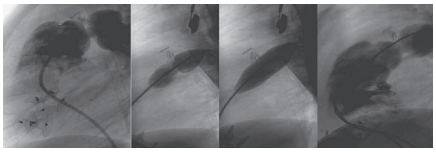

Fig. 2. RV angiogram in patient 6 (group I) after closure of several VSDs, both by surgery and percutaneous Amplatzer devices. The band is progressively dilated (12 mm balloon shown) with partial release of the band (still residual VSD's). See text for further details.

3.1.2. Group II (bilateral branch pulmonary artery bands)

BA was performed a median of 12.7 weeks (range: 9.0–20.0 weeks) following band placement. The main indication for the children in this group was early desaturation during follow-up and the need to delay surgery due to low body weight. Percutaneous saturations increased on average 8.5% after dilatation. The diameter of the initial band was used as a guide to select size of the balloon, and we mostly used coronary balloons with diameters of 100–130% of the original

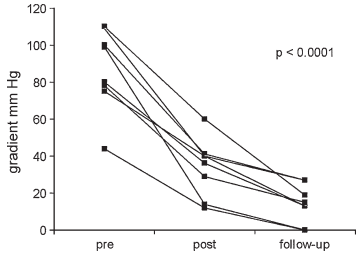

Fig. 3. Echo-Doppler pulmonary artery peak instantaneous gradient: before, immediately after balloon angioplasty and on follow-up.

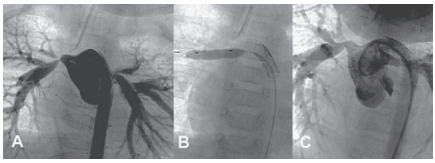

Fig. 4. (A) Pulmonary angiogram 5 months after 3.0 mm Gore-Tex rings were implanted during a hybrid procedure in a 2000 g premature infant with variant hypoplastic left heart syndrome: the bands caused critical narrowing. (B) Progressive balloon dilation with final size 4 mm balloon. (C) Angiogram after balloon dilation.

band (Fig. 4). Four children proceeded to stage II surgery with bidirectional Glenn anastomosis performed at an average age of 173 ± 38 days. Patient 5 in this group was born with a very small left heart (birth weight 2490 g: mitral valve 4 mm, aortic valve 4 mm, left ventricle 9 mm × 24 mm, all dimensions z score were less than − 3.5, coarctation evolving to interrupted arch). With the hybrid procedure, we aimed to buy time for the left heart for catch-up growth; partial BA of the bands was required to buy additional time to boost left ventricular preload, resulting in a biventricular repair at the age of 6 months. Another infant with critical aortic stenosis and a borderline left ventricle showed spontaneous improvement in left ventricular development and could proceed to a biventricular circulation; the stented duct and bands therefore became redundant. The bands (4 mm) were completely released at age 8 months using sequential dilatation with a 6-mm followed by an 8-mm balloon; no residual gradient was present on follow-up 2.7 years after dilation [18].

3.2. Complications

In one patient (birth weight 1.6 kg) dilation of a 3.0-mm band after 8.7 weeks with a 3.5-mm balloon resulted in high flow, requiring re-banding. One patient in group II (palliative) needed re-banding due to distortion of the right pulmonary artery because of a migrated band. There were three deaths. In group I, one child died 2 months after angioplasty – a child with trisomy 21 who developed chronic respiratory insufficiency. The two other deaths were unrelated to the banding or angioplasty procedures.

4. Discussion

Results of this study show that the strategy of a dilatable PAB is feasible and effective, and that BA of such a band is safe. BA of a dilatable band could bring about a significant increase in vessel diameter and/or pulmonary blood flow; alternatively, the band could be completely released by angioplasty alone, if required. No complication related to BA of the banding occurred except in one patient where early dilatation of a Gore-Tex band on a branch pulmonary artery resulted in pulmonary overflow and required re-banding. There were no deaths related to either band placement or angioplasty of a dilatable band.

In children where the main pulmonary artery was banded, the band could safely be partially dilated to improve saturations during phases of rapid somatic growth, thereby postponing surgical repair if required. MPA bands could also still be completely released for as long as 99 weeks after placement. We used stepwise, progressive dilatation with the nearest normal pulmonary trunk diameter as reference and mostly chose a balloon with a ratio of 1.0:1 when complete release of the band was required whilst a much smaller ratio was used for partial dilation (Table 1). In this study, we did not exceed a ratio of 120% and had the desired results as well as no complications using these guidelines. It also seems that, if complete release is required, the size of the adjacent normal vessel should probably dictate selection of balloon diameter. The concept of the surgical clips is that the band can be opened up with distal displacement in order to attain progressive stop–start dilation for palliative use as demonstrated in the group I (partial dilation) patients. The combined use of the clips and length of the nylon cord may thus potentially allow one to serially dilate the band, and it can be adjusted for complete dilatation at any age by adjusting the length of the cord and distance between clips, provided it is properly planned at the time of initial surgery. The distances between clips were about 2–3 mm and the length of the nylon cord should not exceed anticipated pulmonary artery diameter at the time of complete release.

The progression of mid-sized, large and multiple VSDs is difficult to predict at birth and a significant number may become smaller and even close spontaneously [19–22]. In group I (release), six VSDs either spontaneously closed or became as small as to have no haemodynamic significance and thus, by percutaneous abolishment of the gradient, further surgery was avoided. Clinically, we found dilatable bands especially useful in seriously ill small children where VSDs were associated with coarctation of the aorta and a borderline left ventricle.

None of our patients required further angioplasty to relieve a significant gradient in the main pulmonary artery during a median follow-up period of 22.5 months. Interestingly, in the group of MPA banding going on to complete release, the initial residual gradient after angioplasty over the pulmonary artery trunk steadily diminished over time, indicating that once the band is disrupted, pulmonary artery growth resumes with minimal distortion.

Balloon dilatation of bilateral pulmonary branch bands in group II in order to improve saturation is possible and seems to be safe after 9 weeks. The authors hypothesise that by this time adequate scar tissue should have developed around the vessel wall and band to maintain some of the effect of the banding even after opening the band. We did not exceed the Gore-Tex ring diameter by more than 130% for fear of opening up the band totally and allowing excessive pulmonary blood flow. Complete release of these bands was possible in one patient who after a hybrid procedure evolved to a biventricular circulation. The construction of these bands follows the normal guidelines for palliative stage I hybrid procedures [2] with some modification. By cutting through the band and reclosing it with one suture, one probably breaks open the band during angioplasty by tearing out the suture between the two ends and we were therefore very careful not to exceed the initial recommended diameter by a lot. The fact that an average improvement of 8.5% in percutaneous saturation was obtained, indicates that our

hypothesis is probably accurate. The exact increase in oxygen saturation due to the increase in diameter of branch pulmonary arteries is difficult to predict; however, it has also been demonstrated in a report of a different type of adjustable band [23].

No complications were experienced during BA. Three children died, two after repair and unrelated to dilatation or placement of the band. In group I children undergoing repair, no distortion of the pulmonary artery trunk had to be augmented during surgery (personal communication, surgeon). Two patients needed early re-banding; in one the initial band was too tight and in another it was inadequate. This compares favourably with the published results of standard, traditional PAB [24,25].

This form of dilatable band is simple and cheap, with the material readily available in all cardiothoracic theatres. The dilatable concept allows the surgeon to make a tighter band at the time of operation; traditional, non-dilatable bands are typically made larger to allow for growth, often resulting in persistent cardiac failure after the procedure. Other advantages are demonstrated in the study. In small or sick neonates with large left-to-right shunts, especially those with associated coarctation and a borderline left ventricle, a dilatable PAB can be used to avoid early major open heart surgery with bypass and also to buy time to observe the natural progression of a shunt lesion, or alternatively buy enough time to treat ventricular septal defects percutaneously. Pulmonary blood flow can be progressively increased for improvements in saturation and allow growth of the patient and especially the left heart. This may allow some children to gain weight or to permit possible biventricular repair as demonstrated in one of our patients. In developing countries with limited resources and limited access to cardiothoracic services, a dilatable band may also be a reasonable option for young, malnourished children with large shunts. However, it is important to recognise that these types of bands can only be opened and not tightened.

Limitations of this study include the retrospective, cross-sectional design of study, the fact that patients were not randomised, an absence of a control group and the relatively small number of patients. It is also important to recognise the fact that long-term follow-up will be necessary.

Of note is that it is not standard practise in our unit to dilate dilatable bands, but placement of a dilatable band is our procedure of choice when faced with complex cardiopathies or in small, low-birth-weight infants with large shunts in order to allow us to manipulate pulmonary blood flow during follow-up when indicated.

5. Conclusion

A dilatable band is an attractive alternative in certain selected patients. Surgery may be avoided or delayed. Dilatable main pulmonary artery bands with clips allow for progressive dilatation with postponement of surgery or complete release with avoidance of further surgery. Bilateral dilatable branch pulmonary bands may offer palliative benefit especially in hybrid stage I cases where pulmonary blood flow may be limited by the band before the ideal conditions for a stage II procedure exist. Dilation of both main and bilateral branch pulmonary artery bands is possible, effective and safe.

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Chapter 3

3.4 Off-label use of percutaneous pulmonary valved stents.

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Off-label use of percutaneous pulmonary valved stents in the right ventricular outflow tract: time to rewrite the label ?

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Introduction: Percutaneous pulmonary valve implantation is now considered feasible and safe. The "native" RVOT, smaller conduits (less than 16mm) and the relatively large RVOT with dynamic outflow aneurysms are currently considered off-label use. Extending indications creates concerns on safety, ethics, reimbursement and liability.

Aim of study: To report the safety and feasibility of off-label application.

Design: Retrospective analysis of prospectively collected data.

Patients and Methods: Off-label indications: conduit-free RVOT or in patients with an existing but undersized conduit.

Results: Twenty-one Melody® valves and 2 Sapien® valves were successfully implanted in 23 patients (16.9 years; range 6.1-80.5years). Pre-stenting was performed in 22 patients 4.8 months (range 0-69.2) before valve implantation (15 covered and 13 bare stents). The stent was allowed for at least 2 months ingrowth prior to implantation of the valved stent if stent stability or sealing by the covering was presumed to be insufficient. Group 1 (n=8) had a "conduit-free" RVOT after transannular/infundibular patch; after presenting in all a valve was implanted at 21.5mm [range 16-26]. Group 2 consisted of 2 elderly patients with pulmonary valve stenosis and severe RVOT calcifications. Group 3 (n=13) had an existing conduit (nominal 15.9±3.2mm, 10-20mm). The conduit was augmented from 14.7±3.5mm to 20±1.6mm (18-22mm; increase 5.3±2.6mm (2-11mm)]. The RVOT preparation and valve implantations were uneventful.

Conclusions: Percutaneous pulmonary valve implantation is safe and feasible in selected patients with off-label indication. Creating an adequate "landing zone" by pre-stenting makes the procedure safe and predictable. Labels of medical devices need to be updated.

Keywords: Right ventricular outflow tract, Pulmonary stenosis/regurgitation, Percutaneous pulmonary valve, stenting.

Abbreviations: PPVI: Percutaneous Pulmonary Valve Implantation**;** PR: Pulmonary valve Regurgitation PS: Pulmonary valve Stenosis; RVOT: Right Ventricular Outflow Tract; PIG: Peak Instantaneous Gradient; (Doppler) PTP: Peak to Peak gradient (catheterization).

INTRODUCTION

The first successful percutaneous pulmonary valve implantation (PPVI) was described in 2000 with a device comprising a valved segment of bovine jugular vein sewn within a balloon-expandable stent [1]. Currently two balloon expandable transcatheter valves are available for PPVI: the Melody® valve from Medtronic (Minneapolis,MN, USA) and the SAPIEN™ THV from Edwards Lifesciences LLC (Irvine,CA, USA). The label of both valves describes the "official" substrate for PPVI: a dysfunctional surgical conduit in the right ventricular outflow tract (RVOT) with some limitations on conduit size [2 3]. This indeed describes the ideal patient to undergo PPVI, but growing experience with now more than 3.500 implants world-wide, has shown that these criteria are often too narrow. Off-label indications such as the "native" RVOT, small conduits (absolute size less than 16 mm, or relative small nominal conduit size for the patient), and the large RVOT with aneurysms after transannular patch repair, constitute the majority of patients with a dysfunctional RVOT. Techniques have been developed allowing to extend the indications for PPVI beyond the current recommendations, so that more patients can benefit from this elegant technology in off-label indications. The issues that arise with off-label use of devices are concerns about safety, ethics, reimbursement and liability. However, a decision-making strategy that severely restricts clinical choice to "on-label" use may deprive patients of a beneficial treatment [4]. In this article we report our early experience with the off-label application of PPVI in patients with RVOT dysfunction.

METHODS

Study subjects

A retrospective analysis of our institutional congenital cardiology database was performed to identify patients who underwent off-label PPVI. Off-label indications were defined as valve implantation in patients with a native or "conduit-free" RVOT (pulmonary valve or patch), conduits smaller than 16mm, or final percutaneous implanted valve diameter ≥ 2mm larger than the original nominal diameter of the surgical conduit. Indications for

revalvulation were based on data previously published [5]. Patient records were used to obtain catheterization and follow-up data. Patients were selected on the basis of noninvasive screening including clinical assessment, transthoracic echocardiography and cardiovascular magnetic resonance imaging in most cases. Valve dysfunction was categorized echocardiographically as predominantly stenotic [RVOT peak instantaneous gradient (PIG) > 50mmHg with less than moderate pulmonary regurgitation (PR)]; predominantly regurgitant (more than moderate PR with RVOT PIG < 50mmHg); or mixed (RVOT PIG > 50mmHg and more than moderate PR). The severity of PR was classified on color flow Doppler as 0 = none, < 1 = trivial, 1-2 = mild (no retrograde diastolic flow in pulmonary trunk), 3 = moderate (retrograde diastolic flow in main pulmonary artery) and 4 = severe (additional retrograde diastolic flow in branch pulmonary artery). Patients were divided into 3 groups: group I with a "conduit-free" RVOT after transannular/infundibular patch or pulmonary valvoplasty, group 2 with native stenotic pulmonary valves, and group 3 in whom valve implantation was performed in an existing conduit which would be too small for the patient even when re-expanded to its nominal value. Digital measurements of catheterization data were performed using an IMPAX® viewer (Agfa Heartlab®,Mortsel, Belgium). The study was conducted in accordance with local ethical committee guidelines.

Cardiac catheterization and PPVI

All procedures were performed under general anesthesia with biplane fluoroscopic guidance. The catheterization procedure and valve implantation were similar to that previously described [3 6 7]. Conduit or pulmonary valve calcifications were assessed on pre-procedural chest X-rays and on fluoroscopy images during the implantation. Hemodynamic and angiographic assessment was performed and the minimum RVOT diameter estimated.

Group 1: conduit-free RVOT

In patients with a conduit-free RVOT, balloon-interrogation at low-pressure was performed using a flexible, little compliant, mildly oversized balloon

(typically Tyshak® balloon; Numed, NY, USA) to delineate the potential zone of retention (careful observation of the balloon during submaximal inflation and deflation). Simultaneous coronary angiography was performed to exclude coronary compression (8). Pre-stenting was performed in all patients; in the large outflow tract we typically used a bare stent with an hybrid open cell design to provide sufficient anchoring at the retention zone. The stents were delivered on a Balloon in Balloon® BIB dilatation catheter (NuMED, NY, USA) with diameters 2 – 4mm larger than the retention zone. Stents were deployed using hand inflation, allowing maximal control during deployment, aiming for full deployment of the proximal and distal ends, but only approximation to the wall at the retention zone, typically leaving some indentation centrally (Fig 1).

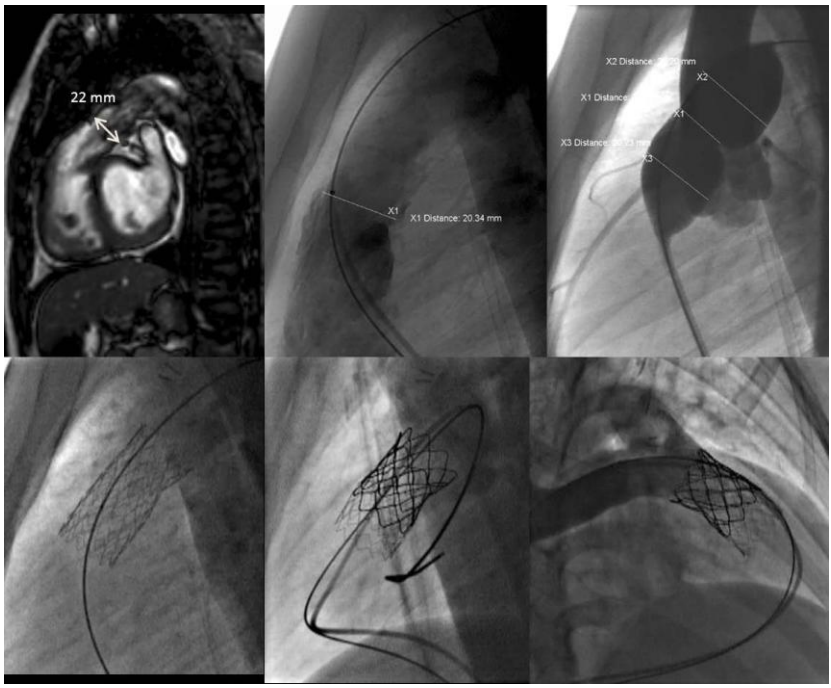

Figure 1: 12 year old symptomatic boy after infant repair of tetralogy of Fallot with a transannular patch: a/ MR showing dilated infundibulum estimated at 22 mm; PR 31%; b/ angiogram of RV: the annular region is estimated at 20 mm; b/ balloon interrogation of RVOT with 25 mm balloon shows indentation at valvular level down to 18 mm; c/ a 39 mm Andramed stent (open cells) was deployed with a 22 mm BIB; the hybrid open cell design provides multiple "hooks" to anchor; end of first procedure; d/ 2 months later a Melody valve was implanted with a 22 mm Ensemble; e/ pulmonary angiogram shows no pulmonary regurgitation.

When stent stability was presumed insufficient to withstand additional pushing and pulling, valve implantation was postponed for about 2 months to allow endothelial tissue ingrowth to fix the stent to the heart and vessel wall. Care was taken at the redo catheterization to cross the stent through the central lumen opening, either by using a J-tipped guiding wire or a balloon-catheter. If we anticipated difficulty directing the PPVI delivery system through the pre-stented RVOT, the proximal stent end was flared with a balloon, or a second "smooth" covered stent was implanted to facilitate valve positioning.

Group 2: Native pulmonary valve stenosis

This group consisted of patients with native pulmonary valve stenosis resistant to balloon dilation: the lesion was stretchable but with significant recoil, or showed extravasation due to fracture of a calcified annulus.

Group 3: dysfunctional conduit; small for patient size

In patients with an existing undersized conduit in the RVOT, we anticipated the need for significant expansion of the conduit beyond nominal value in order to get an adequate gradient relief. Balloon interrogation was done using moderate inflation pressures to determine the extensibility of the conduit without causing graft rupture. Inflation was typically done by hand using a 20 ml syringe; this automatically limits the inflation pressure. As in group 1, a standard coronary angiography with simultaneous balloon inflation at the target implantation site was performed to assess the danger for coronary artery compression; full dilation to the final anticipated size was typically not performed as graft tearing or rupture was expected [8]. In order to allow a sage and controlled expansion without blood extravasation, pre-stenting was performed typically with covered Cheatham Platinum stents™ (CCP stent™, Numed, NY, USA); we aimed to cover the full length of the conduit overlapping the proximal and distal anastomosis. Early in our experience 2 stents were deployed telescopically when required, but later we obtained longer (55 and 65 mm) covered stents. As in group 1, stents were deployed using mildly oversized BIB dilatation catheters and hand inflation; we

concentrated on stent delivery and flaring of the stent against the wall to provide maximal sealing at both ends; this delivery balloon was not used for full deployment of the stent (fig 2).

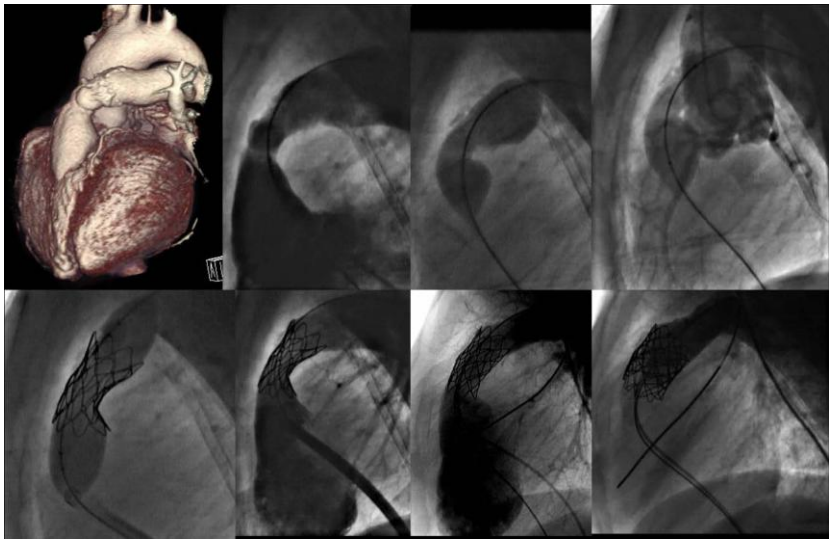

Figure 2: 12 year old patient after neonatal repair of truncus with an 13 mm bicuspidized homograft. a/ 3D reconstruction demonstrating the small homograft; the LAD is not at risk for external compression; b/ RV angiogram demonstrates the small graft between ventricle and pulmonary artery; c/ balloon interrogation with 20 mm balloon at low pressure to determine compliance of RV outflow and graft; d/ aortogram during balloon of RVOT: confirmation of safe distance of coronary arteries; e/ delivery of 20 mm Covered CP stent by 18 mm BIB balloon, handinflation; the stent is apposed to the wall; f/ RV angiogram shows the stent 15 > 11 < 18 mm; end of first procedure to allow maximal adhesion as significant fracture is anticipated; g/ 2 months later, the stent is first dilated with a 16 mm high pressure balloon, then with an 18 mm balloon; no extravasation of contrast h/ pulmonary angiogram after implantation of a Melody valve on a 20 mm Ensemble; dilation of stented graft up to 20 mm; no residual stenosis, no regurgitation.

When we anticipated a large conduit tear or rupture that would require tight sealing to avoid blood extravasation, further dilation was postponed for 2 months to allow maximal fixation and thus sealing of the stent tissue to the wall. Further dilation was performed with high pressure non-compliant balloons; angiograms and pressure recordings were done as indicated. If the coronary arteries were at risk for external compression, progressive dilation in small 2 mm steps was performed with intermittent coronarography. In the presence of significant recoil, additional bare stents were implanted until no

recoil or wringing motion was observed. The valved stent was subsequently implanted in the non-restrictive, stiff stented tube.

Statistical Analysis

Data was captured using excel spreadsheets. Results are presented as mean ± SD; the median and range are also given when the distribution is non-normal. Changes were statistically evaluated with student's *t*-test and a P value < 0.05 was considered significant.

RESULTS

Baseline Characteristics

During a period ranging from November 2006 to February 2012, 81 valves were implanted percutaneously in the RVOT; 23 (28%) patients fulfilled the criteria for off-label PPVI (group 1: n = 8; group 2: n = 2; group 3: n = 13). Diagnosis and baseline characteristics are summarized in Table 1.

Tetralogy of Fallot or one of its variants was the most common intracardiac lesion (14/23, 61%). Four patients had conduits following Rastelli type repair of TGA-PS-VSD, 2 patients had the Ross procedure for significant aortic valve regurgitation/stenosis, 1 patient had a homograft after truncus arteriosus repair and 2 patients had pulmonary valve stenosis. The mean age at PPVI was 16.9 ± 19.7 years (median 10.6 years, range 6.1 - 80.5 years) and mean weight 42.3 ± 20.4 kg (range 20 – 99 kg). The primary indication for valve implantation was PR in 9 patients (39%), RVOT obstruction in 11 (48%) and mixed disease in 3 (13%). Valve implantations were performed through the femoral vein in 21 patients, through the jugular vein in 1 patient (no femoral access possible) and via subxyphoid hybrid approach in 1 patient due to the unfavorable angle of the pre-stent in the RVOT. Two Sapien valves (1 each in group 1 and group 2) and 21 Melody valves were implanted; the choice of the valve was based predominantly on RVOT size and reimbursement issues.

Group 1

Group 1 consisted of 8 patients with tetralogy of Fallot after transannular or infundibular patch repair. None of these patients had RVOT calcifications on

fluoroscopy. In a 15 month old patient a Palmaz P128 (J&J,NJ, USA) stent was implanted on a 14 mm balloon for residual stenosis 13 months after surgical repair with an infundibular patch; 5 years later the stent was dilated to its maximal size of 18 mm, followed by implantation of a valved stent. The other 7 patients presented at the age of 11.0 ± 4.4 years with unrestrictive pulmonary regurgitation in 6 and stenosis in 1; the mean narrowest diameter of the RVOT diameter was 17.5 ± 2.0mm (range 14 – 20mm). Pre-stenting was performed in all 7 patients (6 bare hybrid open cell (Andrastent; Andramed, Germany) and 2 covered stents (Covered CP Stent, NuMED, NY, USA)) up to 20.0 ± 3.7 mm (range 14 – 24mm). A valved stent was implanted subsequently in the patient with original stenosis, and in the other 6 patients 2.3 ± 0.6 months later; final valve diameter (narrowest segment) measured 21.5 ± 2.8mm (range 16 – 26mm).

Group 2

The two patients in group 2 were both elderly patients with pulmonary valve stenosis and severe RVOT calcifications on fluoroscopy. Patient 9 (age 73.4 years) underwent a redo pulmonary balloon dilatation 31.2 years after a previous open valvotomy for severe native pulmonary stenosis. The procedure was complicated by rupture of the calcified annulus and urgent bailout stenting with a 34mm CCP stent was necessary. Subsequent PPVI 4.8 months later was uneventful. Patient 10 (age 80.5 years) had a PPVI after a failed balloon dilatation; this is the only patient in this series without prestenting.

Group 3

Group 3 consisted of 13 patients with a conduit (8 homografts (European Homograft Bank, Brussels, Belgium); 5 Contegra conduits (Medtronic, MN, USA); mean nominal conduit diameter 15.9 ± 3.2mm (range 10 – 20mm). RVOT calcifications were seen on fluoroscopy in 7 patients. The narrowest diameter of the conduit was 14.7 ± 3.5 mm. Pre-stenting was performed in all patients: 12 covered stents (CCP Stent, NuMED, NY, USA) and 4 bare metal stents (3 Andrastent, Andramed, Germany; 1 Intrastent, ev3, USA) were

implanted; 3 patients received 2 stents. In 6 patients the valved stent was implanted subsequently at the initial procedure; in 7 patients we preferred to wait 2.3 ± 0.5 months to obtain more sealing by the covering before expanding the conduit. The mean final valve diameter was 20.0 ± 1.6mm (range 18 – 22mm). The mean true increase in RVOT size (difference between narrowest angiographic baseline diameter and final valve diameter) was 5.3 ± 2.6mm (range 2 – 11mm; P < 0.001).

RVOT Gradient reduction

In all patients with significant PS (n = 14), a decrease in peak Doppler gradient across the conduit was observed from 70.6 ± 15.0 mmHg (range 55 - 110mmHg) before the procedure to 20.7 ± 9.3mmHg (range 5 – 30mmHg) on the day following the valve implantation (P <0.001). Patient 1 developed after regression of RV dilation a progressive stenosis due to a muscular band well below the valve, necessitating surgical intervention 3.4 years after valve implantation. In patient 19 the PIG across the RVOT initially decreased from 65mmHg to 37mmHg when dilated up to 18mm, but gradually increased due to patient growth and a relatively small valve size. Further dilatation of the valve 2 years after the PPVI (PTP 46mmHg) was aborted due to the risk of coronary compression.

Pulmonary valve competence

A near abolishment of PR was documented on echocardiography within 24h after valve implantation and remained stable during follow-up. The PR was graded as 0/4 in 8 patients, trivial (< ¼) in 14 patients and ¼ in 1 patient due to a small paravalvular leak (patient 9; 26mm Sapien valve in a bare stent).

Table 1: Abbreviations: Standard Deviation SD; Andra: Andrastent; AR: aortic valve regurgitation; AS: aortic valve stenosis; AVSD: Atrio Ventricular Septal Defect; CCP; Covered Cheatham Platinum stent; PA: Pulmonary valve atresia; PR: pulmonary valve regurgitation; PS: pulmonary valve stenosis; TF: tetralogy of Fallot; TGA: Transposition of Great Arteries; VSD: Ventricular Septal Defect. *: outlier, not included for mean.

GROUP 1	Patient	Diagnosis	previous	Indication	conduit	age	RVOT	Type prestent	prestent	Age	Weight	valve	size	Echo gradient		Cath gradient		PR
			intervention		size	prestent	min		to valve	at valve	at valve	size	increase	pre	post	pre	post	post
			patch		mm	years	mm		months	years	kg	mm	mm	mmHg	mmHg	mmHg	mmHg	0 - 4 /4
	1	TF DORV	infundibular	PS		1,1	4	P128 + 34CP	69,2*	6,9	30	22	18	90	10	31	13	< 1
	2	TF	transannular	PR		12,1	17	39 Andra	1,6	12,2	36	22	5	27	20	14	8	< 1
	3	TF	transannular	PR		7,1	16	39 Andra	2,4	7,3	21	22	6	10	10	4	2	< 1
	4	TF	transannular	PS		12,0	14	34 CCP	0*	12,0	36	16	2	75	30	24	10	< 1
	5	TF	transannular	PR		5,9	18,5	39 Andra	2,3	6,1	23	22	3,5	28	20	3	5	0
	6	TF	transannular	PR		7,2	18	39 Andra	1,8	7,3	20	20	2	30	15	12	5	0
	7	TF AVSD	infundibular	PR		16,5	19	39 Andra	2,1	16,7	67	22	3	45	25	15	13	< 1
	8	TF	transannular	PR		16,3	20	43 Andra + 39CCP	3,4	16,6	99	26	6	10	10	12	0	< 1
		mean	mean			9,8	16		2,3	11,2	42	21,5	5,69	32,1	18,6	12,0	6,1	
		SD	SD			5,4	5		0,6	4,4	28	2,8	2,2	22,5	7,5	7,1	4,5	
GROUP 2	9	PS	valvotomy	PS		73,0	valve 24	34 CCP + 43 Andra	4,8	73,4	66	26	2	80	5	62	0	1
	10	PS supra PS	balloon dilation	PS		-	valve 22		-	80,5	84	22	0	70	10	47	20	< 1
GROUP 3	11	AR	Ross Contegra	PS + PR	20	13,0	18	39CCP	0	13,0	40	22	4	55	19	21	9	< 1
	12	TF PA VSD	repair homograft	PR	13	15,1	13	45 CCP + 43 Andra	1,8	15,2	42	20	7	25	12	12	0	0
	13	TGA VSD PS	Rastelli Contegra	PS	14	10,6	14	39 CCP	0	10,6	43	18	4	65	26	27	9	0
	14	L-TGA DORV VSD PS	Rastelli homograft	PS	18	8,9	14	34 CCP	0	8,9	26	20	6	75	23	32	6	0
	15	TF PA VSD	repair homograft	PR	16	6,1	15	39 CCP	3,2	6,4	27	20	5	40	10	20	15	< 1
	16	AS	Ross, homograft	PS	10	8,6	10	45 CCP	2,7	8,8	26	18	8	58	25	41	6	< 1
	17	TF PA VSD	redo Contegra	PS+PR	20	13,8	20	45 + 39 CCP	0	13,8	57	22	2	60	30	17	13	0
	18	DORV TGA VSD PS	Rastelli homograft	PS	20	10,4	20	45 CCP + 43 Andra	1,9	10,6	42	22	2	110	13	32	8	< 1
	19	TF	repair Contegra	PS	14	10,4	14	Intrastent 26	0	10,4	36	18	4	65	37	28	10	0
	20	TGA VSD PS	Rastelli Contegra	PS	14	10,6	11	39 CCP	0	10,6	43	18	7	65	26	32	9	0
	21	TF	repair homograft	PR	18	8,0	16	39 Andra	2,2	8,2	27	22	6	25	16	8	0	< 1
	22	TF	repair homograft	PS + PR	17	10,4	17	55 CCP	2,4	10,6	50	20	3	65	23	30	8	< 1
	23	Truncus	repair homograft	PS	13	11,8	9	34CCP	1,8	11,9	31	20	11	55	10	14	5	< 1
		mean			15,9	10,6	14,7		2,3	10,7	37,7	20,0	5,3	58,7	20,8	24,2	7,5	
		SD			3,2	2,4	3,5		0,5	2,4	9,9	1,6	2,6	21,8	8,3	9,6	4,3	

Procedure related problems and complications

Final valve implantation was successful in all patients with no serious complications. Mean fluoroscopy duration was 16.3 ± 12 min (range 5 – 53.7 min). In patient 8 pre-stenting of the large RVOT had to be performed via the right jugular vein due to an abnormal course of the inferior caval vein. Sapien valve implantation 2 months later via jugular approach proved to be technically impossible due to the unfavorable position of the Andrastent in the angulated RVOT: when trying to advance a sheath through the stented RVOT, the proximal struts were crumpled. A 26mm Sapien valve could be implanted successfully 1 month later from a different angle via hybrid subxyphoid approach. No vascular access site complications occurred. We observed no device-related adverse events (no stent fractures, no migration, no stent recompression) during follow up of 1.2 ± 1.2 years (range 0.1 – 4.5 years).

DISCUSSION

Transcatheter pulmonary valve replacement is a promising and evolving technique, but is currently limited to patients with existing conduits between 16 and 26mm in the RVOT, if adequate for patient size [2 9]. When these selection criteria are strictly applied, less than 20% of patients with congenital heart disease who develop postoperative RVOT dysfunction (PR and obstruction) will be eligible for PPVI. In the current study, we describe the successful off-label PPVI in patients with unfavorable anatomy according to product labeling and manufacturer guidelines. Not only sufficient relief of RVOT obstruction and valve competence were obtained in all patients, but the RVOT size could be increased significantly when indicated. The valve implantations were uneventful and all patients were hemodynamically stable throughout the procedure. In our opinion, adequate pre-stenting is essential for successful outcome.

PPVI in aneurismal RVOT

A valved stent can safely be implanted in a RVOT without conduit, even after an infundibular or transannular patch repair [10]. Key point for successful

revalvulation is adequate preparation of the landing zone for the valved stent. In patients with some residual stenosis, a stent can be implanted and sufficiently secured across the stenosis, allowing immediate revalvulation. In a large aneurismal RVOT, stent migration may occur during or after valved stent implantation. We chose to deploy a bare stent with hybrid open cells; a bare stent will minimize the impact of blood flow throughout the cardiac cycle, the open cells will maximize the grip of the stent on the wall at deployment (open cells hook like scales) and will allow fast and efficient endothelial overgrowth; we typically allowed a period of about 2 months to obtain such endothelial fixation [11]. In this small series the bare stent did withstand 2 months later the manipulations of pulling and pushing as typically occurs when delivering the valved stent. In 1 patient we even crumpled the proximal struts of the stent while trying to cross it with a sheath, illustrating the stent was well fixed. While the open cell design is advantageous to anchore the stent in the RVOT, it is a disadvantage when positioning the valved stent as it might hook to the stent. Moreover, if the covering of the valved stent does not seal the retention band, a paravalvar leak may persist after valve deployment. When expected, both problems can be avoided by implanting a covered stent into the bare stent just prior to insertion of the valved stent.

After transannular patch repair of Tetralogy of Fallot, severe RVOT failure with marked anatomic distortion and progressive aneurismal dilation of that region frequently develops. Typically such large aneurismal RVOT's require surgery with an adapted technique: reconstruction to reduce the size and shape of the outflow, and implantation of a valve. Percutaneous devices designed for large aneurismal RVOT are being explored [12] [13] but clinical reports are so far limited. Such devices will address the issue of revalvulation, but not the issue of adequate reconstruction and resizing of the outflow tract which is probably important for long term RV function. Avoiding excessive dilation of the outflow tract can be achieved by fixing the progressively dilating outflow tract at a reasonable size; this can be done with a stent. Such open stent will not significantly deteriorate the hemodynamics as PR is typically already maximal, but will stabilize the outflow tract and

prevent further dilation. Such stent in the outflow tract then can become in due course the landing zone for safe and adequate revalvulation with currently available valved stents.

With the current upper outer limit of PPVI valves of 26 mm, a mildly stretched RVOT with a retention zone of about 24 mm is now the upper limit; this RVOT diameter is usually reached by the age of 10 to 12 years. Pre-stenting should therefore ideally be performed prior to this age. Revalvulation can be performed once the stent is fixed by ingrowth or later when indicated. The optimal timing of the "RVOT preparation" has to be determined and the outcome should be evaluated in comparison with surgical pulmonary valve replacement and RVOT reconstruction.

Expansion of surgical conduits

Current official indications for percutaneous revalvulation are deployment in a conduit larger than 16 mm for the Melody valve, and larger than 22 mm for the Sapien valve; the conduit should not be dilated beyond nominal value. These restrictions disqualify many patients from PPVI: either the current conduit is too small in absolute value, or the nominal conduit size is, or will be too small for the anticipated body size, leaving a residual gradient. Current techniques allow for expanding many surgical conduits well beyond nominal values. In the first decade of this century, interventionalists concentrated on the feasibility and safety of percutaneous valve delivery; this has now been proven. We now need to concentrate on adequate and optimal gradient relief, which frequently implies significant augmenting of the conduit. Use of covered stents is essential for safety: "conservative" expansion of shrunken conduits up to nominal value may result in conduit fracture, extravascular leakage and significant bleeding in 1 - 5% of cases, despite the fact that a valved stent serves as a "covered stent", as the valved stent typically will not cover the ends of the conduit [14 15]. A much higher incidence of extravasation can be expected when expanding the conduit well beyond nominal size. Our series is small but in some patients we obtained significant expansion: increase in diameter from 9 to 20 mm implies a diameter or circumference

increase of 222%, or a surface increase of 493% ! Such increase undoubtedly would be associated with a major conduit tear or fracture, which in the absence of significant mediastinal and pericardial adhesions would result in significant, if not lethal bleeding if a covered stent was not used. In our opinion it is important to cover the full conduit length, overlapping the proximal and distal anastomosis. This allows safe and adequate dilation at the initial implanting procedure, but also subsequently if further dilation is required to accommodate for somatic growth or re-re-valvulation in time. The discussion is still open whether stent flaring and tissue ingrowth is required for safe overdilation of a shrunken and calcified conduit, both up to and beyond nominal conduit size. A 2-step procedure appears safer when significant fracture or expansion of a conduit is anticipated.

Off-label use of devices

Off-label use in an informed consent case is a common and legal practice in most countries, frequently used in pediatrics in general, and in pediatric cardiology in up to 50% of interventions [16]. Physicians and patients are more and more caught in a cross-fire on a regulatory battlefield: there is an evolution in medicine from a situation where "anything reasonable" was allowed, to almost the other extreme where procedures are accepted only if allowed by labels which are based on evidence based medicine only. Issues that arise in off-label use are concerns about safety, ethics, reimbursement and liability [17] [18] [19] [20] [21]. If not allowed by label, authorization by the ethical committee is more and more requested; reimbursement is more prone to be refused; if the patient develops unfavorable side effects or outcome, even when not related to the off-label indication, the treating physician may have difficulty to withstand a legal process. It is therefore desirable that labels are re-evaluated and updated. The basic responsibility of regulatory boards (CE, FDA) is to establish reasonable assurance of the safety and effectiveness of medical devices and to regulate their approval, marketing and package labelling [4] [22]. Device manufacturers design initial pivotal trials to maximize the chances of demonstrating efficacy

and safety in order to improve the likelihood of initial approval, thereby restricting the initial labeling. The later expansion of the "indications for use" for already approved devices is very slow if not absent, because the regulatory process is expensive and lengthy.

A small case series as described in this manuscript does not qualify to change labelling of medical devices, but experience is accumulating world-wide. Not only efficacy and safety of the device for the expanded indications has to be demonstrated, but moreover the patient's benefit in comparison to the standard therapy must be evaluated both in short, medium and long term studies. Although the growing experience with PPVI and the good initial and midterm results are promising, clinical studies comparing the long-term outcome with surgical pulmonary valve replacement are still lacking.

Proposal for label adaption

The "conditio sine qua non" for safe and efficient percutaneous valve implantation is the existence of an adequate landing zone. Valves are now being implanted in many locations, provided this basic condition is met [232425]. If the label were rewritten with current knowledge, a good proposal would be: "PPVI can be performed in a RVOT if an adequate landing zone is available. A landing zone is adequate if it is sufficiently stiff to allow adequate anchoring of the valved stent, and is large enough to be and remain a non restrictive connection between the ventricle and the pulmonary artery after revalvulation, without any interference to coronary flow. Ideally the landing zone should be free of relative motion or wringing (to avoid metal fatigue predisposing for late compression or collapse), with the possibility for subsequent dilatation over its full length to accommodate for somatic growth or future re-revalvulation." Such definition will avoid excluding patients from this patient-friendly technology based on outdated concepts.

Limitations of study

The study is retrospective and suffers the biases of such investigations. The sample size is relatively small and the follow-up period short. Mid- and long-term outcomes remain to be investigated but there is no reason to expect that once implanted in a stiff tube, these valves would behave differently than in on-label indications.

CONCLUSION

PPVI is safe and feasible even in patients with "unfavorable anatomy" according to current device labeling. Creating an adequate "landing zone" by pre-stenting is crucial; the technique of pre-stenting differs depending on anatomical features. Labels of medical devices need to be updated; this role should not be left to the companies or regulatory boards only, but experience and common sense from the field should have an appropriate input.

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CHAPTER 4

Stenting the aortic arch

In chapter 4 stenting of the aortic arch in 2 extreme patient populations are described.

Boshoff D, Budts W, Mertens L, Eyskens B, Delhaas T, Meyns B, Daenen W, Gewillig M. Stenting of hypoplastic aortic segments with mild pressure gradients and arterial hypertension. Heart. 2006 Nov;92(11):1661-6. Epub 2006 Apr 27. PubMed PMID: 16644857; PubMed Central PMCID: PMC1861222.

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INTERVENTIONAL CARDIOLOGY AND SURGERY

Stenting of hypoplastic aortic segments with mild pressure gradients and arterial hypertension

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Objective: To determine the safety, feasibility and effectiveness of stent expansion of hypoplastic aortic segments with pressure gradients in patients with arterial hypertension.
Design: Non-randomised prospective clinical trial.
Setting: Tertiary referral centre, congenital cardiac unit.
Patient selection: 20 consecutive patients (median age 14.5 years, range 11.6–38.8 years) with arterial hypertension and a hypoplastic segment of the aorta. Seventeen patients had successful previous arch interventions in a coarctation site.
Interventions: Stent deployment in hypoplastic arch segments.
Main outcome measures: Gradient across the aortic arch; complications early and during follow up; residual hypertension.
Results: 23 stents were deployed: 13 in the cross and 10 in the isthmus. The mean gradient across the aortic arch decreased from 16 (SD 6) (median 17) to 3 (4) (median 1) mm Hg ($p < 0.001$). In a few patients a mild gradient persisted just distal to the left carotid artery due to residual orificial narrowing or acute angulation. No complications occurred during or after the procedure. During follow up of 2.2 years (range 0.2–4.8 years) arterial hypertension resolved in 10 patients and 10 required residual drug treatment with better control of blood pressures.
Conclusions: Pressure loss due to residual hypoplastic aortic segments can be treated effectively and safely with stent expansion. Some patients remain mildly hypertensive and require additional drug treatment.

Hypoplasia of the aortic cross or isthmus can be an isolated lesion or may persist even after adequate coarctectomy.[1 2] Such a hypoplastic segment may cause a gradient over the arch, leading to arterial hypertension.[2] Even mild residual aortic arch narrowing in post-coarctectomy patients predisposes to increased daytime blood pressure and carotid intima–media thickness.[3] Long-term follow-up studies after coarctectomy have shown significant morbidity and mortality beyond the fourth decade, usually secondary to or associated with arterial hypertension.[4 5] These data suggest that the clinician should aim for an aortic arch free of any gradient in the hope of improving long-term outcome in these patients.

Surgical options to treat residual hypoplasia of the aortic cross or isthmus are aortic arch reconstruction or a crossover operation, both of which are extensive operations that can be associated with significant morbidity. Suggesting this option for mild aortic arch narrowing with residual arterial hypertension can be regarded as a very aggressive approach. Balloon angioplasty alone is mostly unsuccessful in these lesions due to elastic recoil of the vessel or to unfavourable anatomy, such as long tubular narrowing, hypoplasia, angulation or only mild obstruction.[6]

Over the past decade, endovascular stents have become available and have been shown to effectively treat vascular stenosis in patients with congenital heart defects. Several experimental studies and early clinical reports have shown the feasibility and immediate effectiveness of balloon-expandable stent implantation in patients with coarctation or re-coarctation.[7–12] We report our early experience of stent expansion of hypoplastic aortic segments with or without previous coarctectomy.

PATIENTS AND METHODS

Between February 2001 and August 2005, 20 consecutive patients (median age 14.5 years; range 11.6–38.8 years) with hypoplasia of the aortic cross or the isthmus and arterial hypertension were treated with stent expansion of the hypoplastic segment (table 1).

Seventeen of the 20 patients previously underwent an intervention for coarctation of the aorta at the mean age of 4.2 years (range 0.0–14.9 years, median 2.4 years). End-to-end coarctectomy had been performed in eight patients, extended end-to-end coarctectomy in one patient, Waldhausen subclavian plasty in four patients, graft interposition in one patient, repair of interrupted aortic arch in one patient, balloon dilatation in one patient and covered stent implantation in one patient. Current stents were implanted 12.9 (7.9) (range 0.3–35.0, median 13.0) years after the initial aortic arch intervention.

All patients had at referral ambulatory arterial hypertension (blood pressure measured in the right arm after 5 min of rest in the supine position; no patient had an arteria lusoria). Arterial hypertension was defined as systolic or diastolic pressure above the 95th centile for age (typically post-adolescence systolic pressure > 140 mm Hg or diastolic pressure > 90 mm Hg). Seven patients were taking long-term hypertension drugs, although some had insufficient control of blood pressure (table 1).

The stent procedure was delayed until the stent could be deployed up to a (near) adult size. Informed consent was obtained from all patients and parents where appropriate. All studies were performed in accordance with local ethics committee guidelines. The procedures were performed under general anaesthesia. Heparin 100 U/kg was given once vascular access was obtained by a femoral artery puncture. Standard left catheterisation was performed, followed by an angiogram as perpendicular to the hypoplastic segment as possible (mostly mid-left anterior oblique view). A long and stiff guidewire was advanced into the ascending aorta or the left ventricle. The diameter of the balloon was chosen to

Table 1 Patient characteristics, stent data and results

Patient number	Previous arch intervention	Age (years) At coarctectomy	Age (years) At stenting	Gradient (mm Hg) Before	Gradient (mm Hg) After	Diameter (mm) Before	Diameter (mm) After	Residual waist location (mm)	Stent length (mm)	Stent position Cross BT-LC	Stent position Cross LC-LSA	Stent position Isthmus	Before stenting SBP (mm Hg)	Before stenting DBP (mm Hg)	Before stenting Drugs*	1 month after stenting SBP (mm Hg)	1 month after stenting DBP (mm Hg)	1 month after stenting Drugs*
1	BD	11.3	11.6	4	0	15	20		28			1	136	80		124	80	
2	ETE + reconstruction	0.0	23.0	15	0	11	20		28		1		138	80	Atenolol 50	124	82	Atenolol 25
3	WH	0.0	13	28	8	8	16	15	34		1		130	70		130	78	
4			14.8	14	4	10	14		28			1	132	68		122	76	
5	ETE, transection LSA	0.0	13.5	16	0	8	16		39		1		138	80		130	76	Carvedilol 6.25 candesartan 8
6	ETE	8.9	13.8	26	10	11	18		17		1		145	70	Atenolol 50 lisinopril 10	132	68	Atenolol 25 lisinopril 5 amlodipine 5
7	ETE	2.4	13.7	18	4	8	16	11	34		1		132	92		125	80	
8	WH	0.3	15.2	15	0	11	18		22	1			130	85	Bisoprolol 5 lisinopril 5	126	82	Lisinopril 5
9	ETE	6.1	16.7	20	10	11	18		56	1		1	152	90		120	82	Propranolol 80
10	Graft	14.9	24.4	23	4	12	18	15	22	1			180	90	Lacidipine 4	140	86	Bisoprolol 5
11	ETE	3.8	38.8	3	0	9	16		36			1	142	70		134	74	
12	ETE	6.2	19.2	20	13	7	14		36		1		140	90		136	84	Bisoprolol 5
13	WH	0.2	12.6	9	3	8	20		39			1	136	72		122	82	
14	WH	0.0	14.2	10	0	11	16		55		1	1	146	80		120	78	
15	Covered stent	12.9	13.3	16	0	10	18		28		1		130	90	Atenolol 25	130	84	
16	ETE	0.2	15.9	19	0	11	16		39			1	150	68		130	84	
17	ETE	3.6	17.4	18	9	10	16		28+34		1	1	150	85	Atenolol 50	140	82	Atenolol 50
18			16.3	17	1	10	16		28			1	138	90		135	86	
19	IAA ETE	0.0	14.0	18	0	10	18	17	28		1		130	90	Atenolol 25	126	76	
20			13.1	17	2	15	18		28			1	135	80		122	74	
Min		0.0	11.6	3	0	7	14		17				130	68		120	68	
Max		14.9	38.8	28	13	15	20		56				180	92		140	86	
Mean		4.2	16.7	15.7	3.4	10.3	17.1		32.7				141	81		128	80	
SD		5.1	6.2	6.2	4.3	2.1	1.8		9.8				12	9		6	5	
Median		2.4	14.5	16.5	1.5	10.0	17.0		28				138	80		128	81	

*Generic name with daily dose in mg.
BD, balloon dilatation; BT, brachiocephalic trunk; DBP, diastolic blood pressure; ETE, end-to-end coarctectomy; IAA, interrupted aortic arch; LC, left carotid artery; LSA, left subclavian artery; Max, maximum; Min, minimum; SBP, systolic blood pressure; WH, Waldhausen subclavian plasty.

equal the aortic diameter proximal to the hypoplastic segment, not exceeding the diameter of the descending aorta at the level of the diaphragm. Stents were delivered through an 11 or 12 French Mullins sheath (Cook, Bjaeverskov, Denmark) on a balloon-in-balloon (NuMED, Hopkinton, New York, USA). The stent was manually crimped on a vacuumised balloon. A cut-off sheath of an 11 or 12 French size was used to protect the stent while it was advanced through the haemostatic valve of the Mullins sheath. The stents used were Cheatham platinum (CP) stents (NuMED; n = 15) and covered CP stents (n = 5) (used only distal to the left subclavian artery), Genesis stents (Johnson & Johnson, USA; n = 1) and Intrastent (EV3, Irvine, California, USA; n = 2). CP stents were preferred when the ends of the stent might protrude over the origin of a neck vessel—due to the structure of this stent, the distal end struts can separately be opened or flared if necessary. All stents were inflated manually, leaving full control to the operator during expansion in deciding whether to dilate pressure-resistant waists.

Test angiograms were done through the Mullins sheath during positioning of the stent and after inflation of the inner balloon. Pressure measurements and aortic angiograms were repeated after stent implantation. Cephazolin (50 mg/kg, maximum 2 g) was given 1 h before the procedure and at eight-hourly intervals (total of three doses). Post-procedure haemostasis of the femoral artery was obtained with local compression in 15 patients and a Prostar XL (Biomedicon, Mumbai, India) occlusion device in the last five patients. Heparin sulfate was neutralised when activated clotting time exceeded 250 ms. Patients were discharged the day after the procedure after transthoracic echocardiography and chest roentgenography. No long-term drugs (coagulation or aggregation drugs) were given except hypertension drugs when indicated. Follow up at the referring outpatient clinic was scheduled after 1–2 months and thereafter every 6–12 months. Catheterisation or computed tomography was repeated only when indicated.

Statistical analysis

Continuous data are presented as mean (SD); the median is also given when the distribution is non-normal. Changes were statistically evaluated with paired Student's t test, and $p < 0.05$ was considered significant.

RESULTS

Immediate results at stent implantation

A total of 23 stents were implanted in 20 patients: 13 stents in the aortic cross (three between the brachiocephalic trunk and left carotid artery, 10 between the left carotid and left subclavian arteries) and 10 stents in the isthmus; three of the patients required stenting of the cross and isthmus. Figure 1 shows an aortogram before and after stent implantation in the cross. The stents were dilated up to a mean diameter of 17 (2) mm. The origin of the left subclavian artery was electively completely crossed with the stent in four patients, without any clinical complications in short-term follow up (0.6–3.3 years). The left carotid artery was partially crossed in three patients, where the stent was additionally opened and flared (fig 2). The systolic gradient across the aortic arch decreased from 16 (6) (median 17) mm Hg to 3 (4) (median 1) mm Hg ($p < 0.001$) (fig 3A) and the mean diameter of the segment increased from 10 (2) mm to 17 (2) mm ($p<0.001$) (fig 3B). In five patients a mild gradient persisted, often just distal to the left carotid artery due to residual orificial narrowing or due to acute angulation. No major complications occurred during or after the procedure; however, two patients had a moderate groin haematoma before the use of the transpuncture closing device.

Short-term follow-up data

When reassessed after one month, systolic blood pressure had decreased from 141 (12) mm Hg to 128 (6) mm Hg ($p < 0.001$). Arterial hypertension had resolved in 12 patients (below 95th centile for age) and eight required residual drugs (β blocker with or without angiotensin converting enzyme inhibitor) (table 1). However, patients treated with drugs either had better control of their arterial pressures or were taking a significantly lower dose. The follow-up has been 2.2 (1.4) years (range 0.2–4.8 years). Two more patients started taking hypertension drugs to adequately control arterial pressures.

DISCUSSION

Coarctation of the aorta often is a generalised disease of the aorta and, some authors even suggest, of the global arterial bed. Even after successful surgical repair of a coarctation, residual aortic arch abnormalities such as a narrowed arch segment, a high cervical arch, or an abnormal winding or acute angled cross may persist. Tubular hypoplasia of the

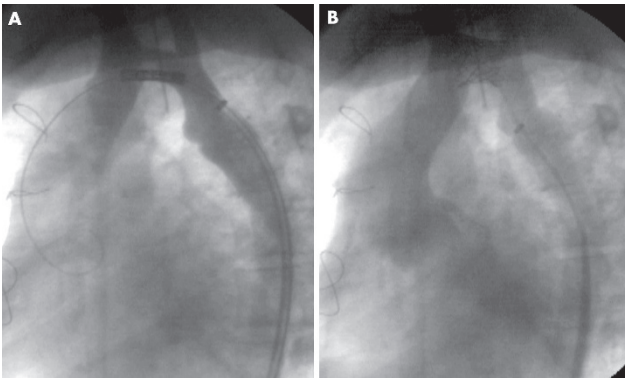

Figure 1 (A) Aortogram 15 years after neonatal Waldhausen subclavian aortoplasty combined with open aorta valvotomy (patient no 8). The coarctation site is well repaired without residual stenosis or gradient. However, the cross between the brachiocephalic trunk and the left carotid artery is hypoplastic (11 mm) with a 15 mm Hg systolic gradient. A 22 mm eight-zig Cheatham platinum stent is ready for deployment. (B) After implantation of the 22 mm stent on an 18 mm balloon, the segment had expanded up to 18 mm without a residual pressure gradient.

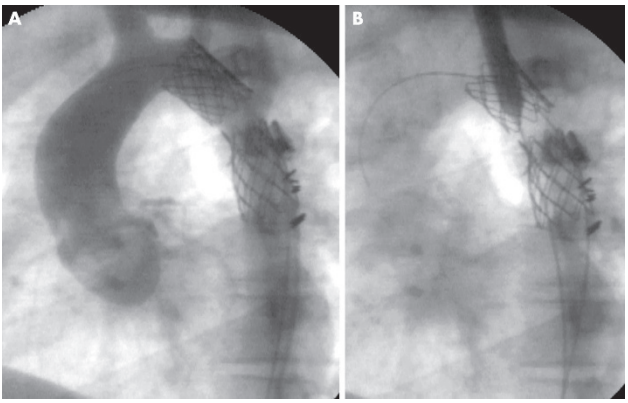

Figure 2 (A) Aortogram in a 17-year-old boy after implantation of a 28 mm eight-zig Cheatham platinum (CP) stent in the cross (between the left carotid and left subclavian arteries) and a 34 mm eight-zig covered CP stent in the isthmus (patient no 17). Both stents were dilated up to 16 mm. (B) Opening and flaring of the proximal end of the CP stent in the cross, partially crossing the origin of the left carotid artery (7 mm balloon). The flow to the left carotid artery was unrestricted.

aorta is a combination of a small diameter and an abnormal length; it can involve the transverse aorta and isthmus and does not invariably produce obstruction.[13] Long-term follow up after surgical repair of coarctation has shown that early repair during infancy optimises arch growth and that late repair increases the risk for residual hypoplasia and late arterial hypertension.[5] The incidence of re-coarctation or arch hypoplasia after surgical repair is related to the age at repair, the type of repair and how re-coarctation is defined.[1 5] Neonatal surgical repair now aims at treating hypoplastic segments by extended end-to-end repair.

Rationale for the stent implantation

Recent guidelines define significant (re)coarctation in adults as resting or exercise-induced hypertension and a resting arm–leg blood pressure gradient $\geqslant$ 30 mm Hg.[14] Patients with mild residual gradients at rest, like those in our study, would not be considered for (re)intervention on the basis of these guidelines but may still have raised blood pressures, exposing them to increased cardiovascular risk with premature morbidity and mortality.[2 4 5] Coronary artery disease is the most common cause of late death after successful coarctation repair, and late systemic hypertension is largely held responsible for this premature coronary atherosclerosis.[5 15] One can speculate that any gradient across the aortic arch will enhance arterial hypertension, among other factors such as increased stiffness of the upper vascular tree and altered pressure wave transduction.

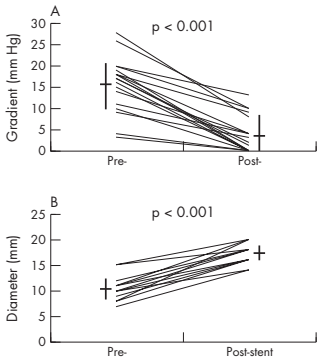

Figure 3 (A) Systolic gradient across the aortic arch and (B) diameter of the hypoplastic segment before and after stent implantation. Mean (SD).

Surgical options to treat residual hypoplasia of the aortic cross or isthmus are extensive aortic arch reconstruction under complex cardiorespiratory bypass, ascending aorta to thoracic aorta crossover or placement of an ascending aorta to abdominal aorta conduit. These surgical procedures confer some morbidity and mortality and, when compared with interventional catheterisations, longer hospitalisation, a longer rehabilitation period and relatively higher costs. Suggesting these major operations for only mild residual aortic arch narrowing may be considered excessive, and for many patients the early discomfort and risks exceed the late potential benefits. Drug treatment alone usually decreases blood pressure, but often very high doses of hypertension drugs are needed, not infrequently associated with significant side effects during long-term follow up.

In view of the high effectiveness and safety profile of transcatheter techniques and the possible benefits of complete resolution of any gradient, stenting of residual hypoplastic segments seemed to be an elegant alternative treatment option.

Results of stent implantation and follow-up

In this paper we report our early experience of stent expansion of hypoplastic aortic segments in patients with arterial hypertension, mostly after previous coarctectomy. All patients had significant and relevant gradient reduction and half had normalisation of upper limb blood pressure. Ten patients still needed hypertension treatment but with better control or at a significantly lower dose than before the intervention. It is known, however, that many patients, even without a residual gradient across the aortic arch, will develop arterial hypertension during follow-up.[2 3] Life-long follow-up remains mandatory.

All stents were inflated manually, allowing gentle and gradual expansion not exceeding 3–5 atm. This leaves full control to the operator in deciding whether to dilate

pressure-resistant waists. We speculated that overdistension of such pressure-resistant hypoplastic segments can severely damage the vessel wall, with a higher risk for transmural aortic tear or rupture. The segments that were treated with stent expansion were usually free of post-surgical scars or adhesions. Therefore, even a small tear can be catastrophic, which is unacceptable, especially when a procedure is done for prognostic reasons. Emergency deployment of a covered stent as a bailout is not safely applicable because of the proximity of the origin of the neck vessels. This strategy resulted in some residual narrowing with minimal gradient in some of the patients; we thought that the potential late benefits did not outweigh the possible early risks. Additional experience is required to determine whether these pressure-resistant waists can be dilated at the initial or later catheter intervention if indicated.

No major complications (stent migration or fracture, aortic wall dissection, rupture or aneurysm formation) were seen at stent placement and during follow up. Late aneurysm, forming unexpectedly and silently after stent implantation, has been described.[16] Close follow up of these patients is therefore mandatory. Routine imaging techniques other than transthoracic echocardiography have been advocated after stent implantation for treatment of (re-)coarctation to avoid silent complications. However, in this series we performed in most patients only a transthoracic echocardiography at follow up, as a stent in the cross or isthmus can be adequately evaluated by echocardiography (because of the short distance, and the stent more perpendicular to echocardiograph beam).

The concern that the stent can cross important branch vessels arising from the aorta has previously been discussed.[17 18] Crossing a vessel may theoretically lead to thromboembolism, vessel narrowing and branch occlusion. Patency of side branches from small coronary arteries, larger pulmonary arteries and branch vessels of the aorta, even after prolonged stent placement, has been described.[19] The left subclavian artery was electively crossed with the stent in four patients, without any complications in short-term follow up.

In our patient group we opted to treat mild residual hypoplasia only at an age when an (near) adult-sized stent could be implanted, thereby avoiding the necessity for later redilatation. Late redilatation may be associated with aortic dissection at the distal end of the stent,[20] dehiscence of the endothelium or in-stent peel into the side branch, with the risk of embolic events if any head vessel is crossed.

Increased stiffness and altered vascular relaxation reserve in the upper body vessels have been implicated in the aetiology of hypertension at rest and during exercise after coarctation repair.[21–23] After stent placement patients may theoretically develop exercise-induced gradients across the stent, as it is a rigid, metallic structure. However, preserved overall aortic compliance has been documented in animal models after stent implantation in the aorta.[24] Similarly, many surgical techniques leave the vascular tree with stiff segments.

Study limitations

The final goal of these procedures is to prolong survival without vascular complications in patients with aortic arch abnormalities. Only long-term follow up in three or four decades will determine whether this objective will be met. The observation that arterial hypertension regressed or became easier to treat suggests a more favourable outcome. Ideally, future studies should have 24 h blood pressure monitoring before and at regular intervals after the procedure, comparing different treatment strategies in patients with various degrees of hypertension (ambulatory hypertension, daytime hypertension on 24 h monitoring and exercise-induced hypertension).

Conclusion

Pressure loss due to hypoplastic aortic segments can be treated effectively and safely with stent implantation.

Many patients remain mildly hypertensive and will require additional drug treatment, with increasing incidence during follow up. The risks and benefits of intervention for even mild hypoplastic segments are favourable; the late morbidity of residual hypertension may be decreased, delayed or even avoided. Our limited experience confirms that the subclavian artery can be safely crossed with a stent, at least during short- and medium-term follow up. Lifelong follow up of these patients remains mandatory.

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IMAGES IN CARDIOLOGY

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Severe hypothermia showing Osborn waves associated with transient atrial fibrillation and ST segment depression

An 80-year-old woman with no known cardiovascular risk factors was found unconscious at home with a body temperature < 30°C (< 86°F). On arriving at the emergency department, her ECG (panel A) showed an atrial fibrillation (AF) with ST segment depression from V3 to V6. In leads V5 and V6 there was a terminal extra QRS deflection formed by the junction between the J point and the ST segment, consistent with the so-called Osborn waves (panel C). Serum electrolytes and cranial computed tomography (CT) were normal. After re-warming to a body temperature of 36.7°C (98°F), the patient recovered sinus rhythm (panel B) and the ST segment depression and the Osborn waves disappeared.

Hypothermia (body temperature < 35°C (< 95°F)) is initially associated with sinus tachycardia, but with temperatures < 32.2°C (< 90°F) sinus bradycardia supervenes, associated with a progressive prolongation of the PR interval, QRS complex, and QT interval. At temperatures ⩽ 30°C (⩽ 86°F), atrial ectopic activity can be triggered, eventually progressing into atrial fibrillation (AF). At this level of hypothermia, 80% of the patients have Osborn waves consisting of an extra deflection at the end of the QRS complex best depicted on the inferior and lateral leads. Osborn waves become more prominent as the temperature drops, and they disappear gradually with re-warming. The combination of transient Osborn waves and AF in the hypothermia setting, with the recovery of sinus rhythm after re-warming, has been rarely described. Although several ECG alterations have been described in accidental hypothermia, this is the first report of asymptomatic transient ST segment depression with recovery after re-warming.

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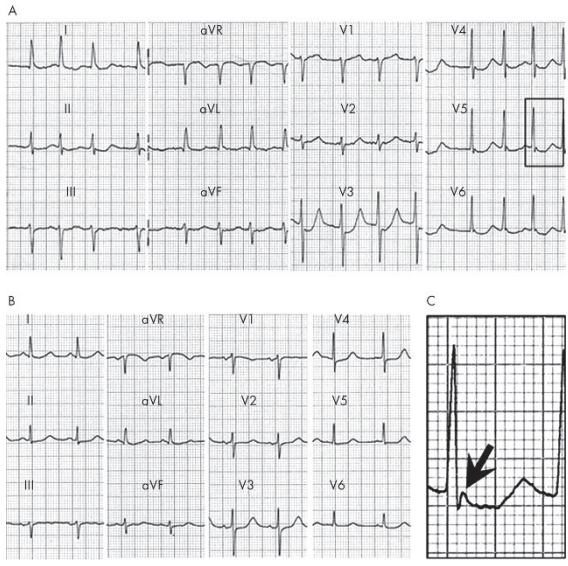

(A) Emergency department 12 lead ECG obtained at core body temperature < 30°C (<86°F) showing atrial fibrillation (AF) with ST segment depression from V3 to V6. In leads V5 and V6 there was a terminal extra QRS deflection formed by the junction between the J point and the ST segment, consistent with the so-called Osborn waves. (B) 12 lead ECG obtained after patient had been re-warmed to 36.7°C (98°F); the patient recovered sinus rhythm and the ST segment depression and the Osborn waves had disappeared. (C) Detail of the Osborn wave, also known as J waves, camel-hump waves or hypothermic waves.

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Bailout Stenting for Critical Coarctation in Premature/Critical/Complex/Early Recoarcted Neonates

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Background: Surgical repair of critical coarctation can be problematic in premature, critical, complex, or early postoperative neonates. Objectives: We aimed to review our experience with stent implantation to defer urgent surgery to an elective time. Methods: Fifteen neonates with severe aortic coarctation: five premature-hypotrophic (1,400–2,000 g), six critical and complex cardiac malformation, four early (1 day [0–2 days]; median [range]) after surgical coarctectomy or complex arch reconstruction. Bare coronary stents (diameter 4.0 [3.5–5.0] mm; length 10 [8–16] mm) were used. Stents were removed surgically depending on clinical needs. Results: Adequate aortic flow was obtained in 15 patients. The femoral artery was preserved in 13/15 patients. Two deaths occurred before stent removal and were nonprocedure related. In patients with simple stented coarctation, the stent was removed after 2.8 [0.2–5.0] months. In complex cardiac malformation, stents were finally removed 3.0 [0.2–78] months after implantation. Surgical technique: simple coarctectomy end-to-end in eight, extensive arch patch reconstruction in four. One patient is awaiting stent removal. The final maximum systolic velocity (cw-Doppler) across the aortic arch was 1.7 [1.2–2.5] m/sec. Conclusions: In premature/critical/complex neonates with severe coarctation, bailout stenting followed by early or late surgical coarctectomy appears a promising concept. © 2009 Wiley-Liss, Inc.

Key words: congenital heart disease; coarctation; intervention; neonate

INTRODUCTION

When confronted with significant arch obstruction in a critically ill neonate, the clinician has several options. The final treatment for these small malformed arches is surgical; however, there are different options of how and when to proceed the surgery.

Prostaglandin infusion is the standard treatment to maintain or regain systemic perfusion by opening the arterial duct and relaxing the coarcted isthmus [1]. However, prostin therapy may sometimes only slowly or incompletely reverse ventricular dysfunction and multiorgan failure due to slow and incomplete opening of the duct and residual constriction at the isthmus [2]. In the very small premature infant, aortic arch repair can be performed [3,4], but is frequently complicated by a residual gradient, increased perioperative morbidity due to operative hypoperfusion on top of pre-existing shock, atelectasis of the lung, injury to the phrenic or vagal nerve, and chylothorax. Surgical techniques that require deep hypothermic circulatory arrest are not easily applicable in this group of patients.

Stenting a coarcted arch can be performed on short notice and acutely improve the patient, and defer surgery to a safer period with adequate weight or stabilized hemodynamics. We reviewed our experience with this strategy in the preterm or critically ill neonate, and

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in neonates with early restenosis after surgical coarctectomy.

METHODS

Patient Selection

We screened our database for stent implantation in the aorta in infants (<2 months) between January 1, 1998 and March 30, 2009. We identified two groups: group 1 consisted of patients with a native coarctation where surgery was not considered the best option (very low-birth-weight, critically ill neonates not responding to medical treatment, complex cardiac, and noncardiac disease); a second group consisted of patients with significant early restenosis after primary surgical coarctectomy or arch repair.

The catheterization reports, angiographic data, medical, and surgical records were reviewed in all patients. The studies complies with the Declaration of Helsinki. Approval for review of patient charts was obtained from the Institutional Review Board and informed consent was obtained from the parents (guardians).

Catheterization

The data obtained from cardiac catheterization reports included sites of access, sheath sizes, catheter selection, balloon or stent size in relation to lesion, haemodynamic data, and complications of the procedures. Medical records were reviewed for complications that occurred during or after the procedure, presence of recoarctation, presence or absence of femoral artery pulse after the procedure, and need for blood transfusion. In addition, the time interval to operation and—on echocardiography—the final morphology as well as cw-Doppler profile of the isthmus were recorded. Criteria for a good final result was systolic peak velocity over the arch of $\leq$2.5 m/sec on cw-Doppler [5]. Complications were classified as major or minor as depicted in previous series [6].

Catheterization Technique and Materials Used

Before the procedure, all therapeutic options had been discussed with the parents; informed consent had been obtained as requested by institutional regulations. All procedures were performed under general anesthesia. Care was taken to position the patient with moderate hyperextension of the groin; the position of both femoral arteries was identified with a Doppler probe. Puncture of the artery was performed with a butterfly 21 Gauge needle (Surflo® SV*21 BLS, Terumo®) allowing a 0.014" wire to be introduced into the artery. A 4F short tapered introducer sheath (RCFN-4.0-18-5.5-RA1.5, Cook®) was placed in the right or left femoral artery. The sheath was introduced for only about 1–2 cm into the artery with wide tissue support to prevent vascular damage. Typically, two pairs of experienced and coordinated hands were required. Heparin was given at a reduced dosage of 50 U/kg body weight; the sheath and catheter were flushed as required with saline 2 U heparin/ml (half of usual dose). A 4F end hole vertebralis catheter was advanced up to the coarctation site where a small (1–2 cc) hand injection was made. The coarctation was crossed using a 0.014" wire ("Ironman," Boston Scientific®); if the isthmus could not be entered retrograde, a transvenous anterograde approach was used [7]. A new hand injection was made in the distal arch to delineate the distal arch and origin of the left subclavian artery (Fig. 1). The diameter of the aorta at various levels could thus be assessed. A stent was then implanted (off label use for any coronary stent). As our experience grew, stent length was chosen as the shortest length covering the distal arch from just beyond the left subclavian artery until beyond the coarctation; stent diameter 1 mm larger than the proximal isthmus at the origin of the left subclavian artery. In patients early after a failed coarctectomy, a smaller stent size was deployed not to

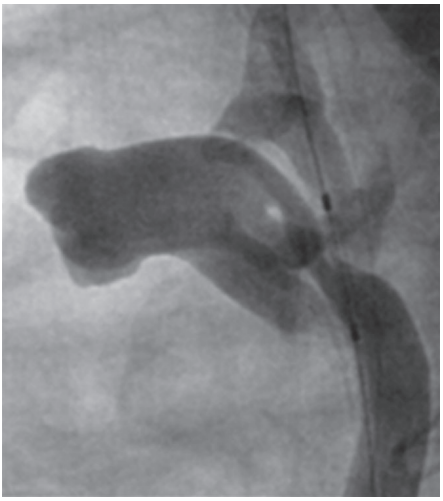

Fig. 1. Retrograde aortogram in patient 11, a 1,500 g premature infant under IV prostaglandin. Hand injection of layered contrast-saline through the 4F sheath. A 4/8 mm coronary stent is ready for deployment. Points of reference are as follows: cranial end just beyond take-off of left subclavian artery, caudal end beyond coarctation site within the thoracic aorta.

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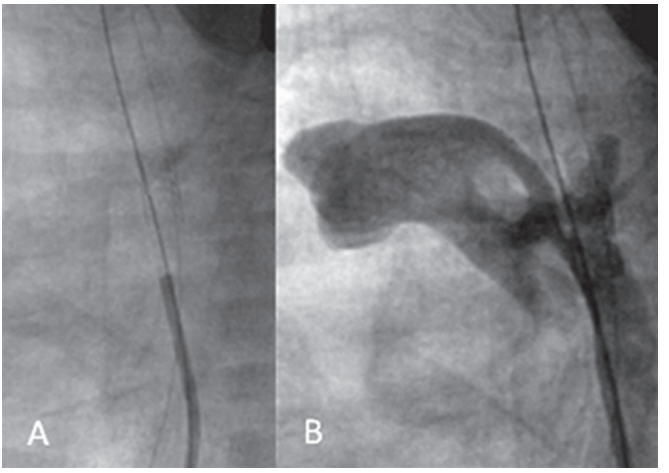

Fig. 2. A and B: Patient 11: after deployment of the 4/8 mm stent, the narrowing has disappeared. The distal aortic arch is less visualized due to good antegrade flow.

tear the "fresh" anastomosis. If required an additional stent was implanted in hypoplastic segments.

The stent was passed "unprotected" through the valve of the sheath. Stent position was controlled with a retrograde aortogram hand injection through the sheath (sequential gentle aspiration in a vertical 10 cc syringe of 5 cc saline followed by 1 cc contrast keeping contrast and saline layered and separated) (Fig. 1). The stent was deployed using an in-deflator at a pressure as recommended by the stent manufacturer (allows opening the stent within a range of 0.6 mm). In prematures and neonates with primary coarctation, the prostaglandin E-1 infusion was stopped immediately after deployment of the stent. If useful and not contraindicated (renal function), stent position was assessed with an aortogram through the 4F catheter below the stent (Fig. 2); no attempt was made to recross the stent, as the "free-hanging" stent in the thoracic aorta can easily be kinked; the wire was carefully withdrawn. After control of clotting time, the sheath was withdrawn applying ample support to the surrounding tissues in the groin. Heparin was not neutralized if ACT was not above 250 sec. Anesthesia was maintained at least until the groin had "dried" up. If no feet pulses were palpable, heparin was restarted after 1 hr for 24–48 hr.

The decision when to surgically remove the stent was taken for every patient individually: criteria were hemodynamic stability after the cardiogenic shock, adequate body weight to safely perform coarctectomy, or when additional surgery was planned (Glenn, VSD closure, etc.). If more time was needed, an additional balloon dilation or additional stent implantation was performed.

Statistics

Data were recorded using Excel spreadsheets and descriptive statistical analyses were performed using the SigmaStat software (SPSS). Where applicable, results are given as mean with range.

RESULTS

Study Population and Catheterization Procedures

Fifteen patients fulfilled the entry criteria. The patients were 36 (30–41) weeks of gestation, 8 out of 15 were premature (<37 weeks of gestation). At cardiac catheterization, the weight of the patients was 2.5 (1.5–3.8) kg and their age was 12 (3–61) days. Demographic data with respect to the two groups are given in Table I.

Group 1 consisted of very small premature–dysmature infants where the neonatologist and the surgeon felt uncomfortable to proceed with surgery at that time. This group further included more mature infants but

TABLE I. Clinical Data of Patients

Pt. no	Diagnosis	Age at stent (days)	Weight at stent (kg)	Diameter × length of stent (mm)	Age at surgery (months)	Weight at surgery (kg)	Type of definitive surgical repair
Group I: Patients with primary stent implantation							
1	Shone complex, hypopl. Ao-Arch, CoA, MS, VSD's	12	3.8	5 × 12	1.0	3.5	Ao-Arch patch angioplasty (Norwood-like)
2	TGA, VSD, subAS, hypopl. Ao-Arch, CoA	61	3.2	4 × 10	2.2	3.2	Ao-Arch patch angioplasty (Norwood-like), arterial switch, resection of subAs
3	crit. CoA, musc. VSDs	29	1.8	4 × 9	3.8	2.4	stent removal, ETE
4	crit. CoA, hypopl. Ao-Arch, bic. AoV	17	3.3	4 × 15	3.5	4.8	stent removal, ETE
5	crit. CoA, incomplete AVSD; CHARGE syndrome	8	2.7	5 × 15	–	–	–
6	crit. CoA, hypopl. Ao-Arch, bic. AoV	15	2.2	3.5 × 12	3	4.2	aortic arch patch angioplasty (Norwood-like)
7	crit. CoA, hypopl. Ao-Arch, VSD	9	1.9	4 × 8	3.3	4.9	stent removal, ETE
8	crit. CoA, hypopl Ao-Arch, bic. AoV, VSD	5	2.5	3.5 × 12	2.2	3.8	stent removal, ETE
9	crit. CoA, hypopl Ao-Arch, VSD, bic. AoV, PAPVD	3	2.6	4.5 × 16	–	–	–
10	crit. CoA, bic. AoV, VSD, borderline LV	5	1.8	4 × 9	4.2	4.9	stent removal, ETE
11	crit. CoA, bic. AoV, VSD	5	1.5	4 × 8	4.3	5.2	stent removal, ETE
Group II: Patients with primary surgical repair (in brackets type of primary repair)							
12	crit. CoA, hypopl. Ao-Arch, VSD (ETE, reversed Waldhausen plasty)	19	2.7	4 x 10	78	21	stent removal, ETE
13	CoA, hypopl. Ao-Arch, VSD (extended ETE)	15	2.2	4 x 8	69.6	16.2	stent removal, ETE
14	crit. CoA, UVH (dominant RV) (aortic arch patch reconstruction (Norwood-like))	6	3.6	5 x 11	–	–	
15	crit. CoA, VSD (ETE, reversed Waldhausen plasty)	10	2.1	4 x 8	20.4	6.3	stent removal, ETE

Ao-Arch, aortic arch; AoV, aortic valve; AVSD, atrioventricular septal defect; bic, bicuspid; crit, critical; CoA, coarctation; ETE, end-to-end anastomosis; hypopl., hypoplastic; MS, mitral valve stenosis; musc., muscular; PAPVD, partial anomalous pulmonary venous drainage; Pt-No, patient number; RV, right ventricle; subAS, subaortic stenosis; TGA, transposition of great arteries; UVH, univentricular heart; VSD, ventricular septal defect.

with poor hemodynamics (poor flow with limited effect of prostin, evolving necrotising enterocolitis, recovery from renal failure-tubulus necrosis), where the clinician felt that coarctectomy with even a short cross clamp at this time would not be well tolerated, or where percutaneous intervention was immediately available for faster relief to buy time for further surgery.

Group 2 consisted of four patients with a surgically failed arch repair in complex coarctation. In 3/4 patients, residual arch dysfunction compromised renal function early (<48 hr) after surgery; one patient was stented in the PICU using a mobile C-arm.

Catheterization

The arch was probed retrograde in 14/15 patients. In one patient, anterograde catheterization was required: this patient had a critical coarctation and a lusoria right subclavian artery (the preferred route for the wire!). From the femoral vein, a 4F mammary catheter was advanced into the left atrium; from there a Progreat coaxial system was advanced into the left ventricle, out the aorta and around the arch; the inner wire was snared in the descending aorta allowing retrograde passing of the coarctation [7].

The diameter of the presubclavian aortic arch was measured planimetrically as 3.6 (2.3–5.5) mm, the diameter of the descending aorta at the diaphragm was 5.6 (4.4–7.2) mm. The angiograms in standard profile did not allow to accurately measure the narrowest coarctation diameter.

The fluoroscopy time was 9.4 (3.5–21) min, and the amount of contrast needed was 1–2 ml/angiography.

Stent Implantation

Bare coronary stents (diameter 4.0 [3.5–5.0] mm; length 10 [8–16] mm) were used in this series. Given the time span of more than 10 years that is covered by our study, stents from various manufacturers were used (e.g., Guident Multi-Link Ultra®, Medtronic Driver Sprint RX®, and Abbott Multi-Link Vision®). We preferred stents with small cell size, thereby providing good scaffolding and impeding ductal tissue to prolapse through the cells in the days following the procedure (see discussion). In two patients after surgical

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repair, an additional stent was put in the distal cross over the extended anastomosis.

Adequate aortic flow was obtained in 14 patients. In the first patient of this series with stenting early after surgery, we implanted a stent which was rather small, because we were afraid to tear the suture line; it was redilated 6 days later uneventfully using a bigger balloon with adequate relief of arch obstruction. As our experience grew, we chose a stent as short as possible covering the isthmus from beyond the subclavian takeoff until the descending aorta (Fig. 2). As fetal-neonatal tissue allows for significant stretch, we would slightly oversize the stent in native coarctation (size of distal arch, not beyond 5 mm), and slightly undersize early postop not to tear any recent suture line.

No blood transfusion was required because of the catheterization: all procedures were performed with minimal blood loss.

The arterial duct closed within hours in all patients after discontinuation of prostaglandin E1 infusion.

Complications of the Percutaneous Intervention

There were no major complications (e.g., procedure related death, cardiac arrest, and arrhythmia) in this series. Arterial hypotension requiring a short term catecholamine treatment was observed in one patient immediately after placement of stent due to reduced systolic left ventricular function. Loss of sheath out of the femoral artery accidentally occurred in one patient during the procedure after stent insertion but before stent positioning; no retrograde angiogram was made before stent deployment.

Femoral artery patency was preserved in 13/15 patients. Many patients had transient hypoperfusion of the cannulated leg, but pulsations resumed within hours, frequently under heparin infusion. Femoral pulses had disappeared in two patients with echographic demonstrated thrombosis. The leg was pale with slow capillary refill for several hours; at no point was the viability of the leg at risk. At follow-up at 7 months and 4.3 years, respectively, these two patients did not show abnormal growth of the leg.

Interval Follow-Up

Most patients with simple coarctation could easily be weaned from supportive therapy as systemic output had adequately resumed.

All patients were given acetylic salicylic acid 1–2 mg/kg BW/d (off label use for this application).

Some patients are described in detail. In patient no. 2 (Table I), a mature 3.2 kg infant with complex dTGA presenting in shock, we first deployed a stent in the coarctation. Intracardiac repair and aortic arch repair was performed 6 days later with good outcome. In patient no 11 (Table I) presenting with low birth weight (1,500 g) and necrotizing enterocolitis, the lesion was stented primarily to 4 mm (Figs. 1–3) and a second stent (5 mm) was placed 55 days later for restenosis due to ingrowth of intimal tissue (Fig. 3). Aortic surgery could thus be postponed to 5 months of age (Fig. 4).

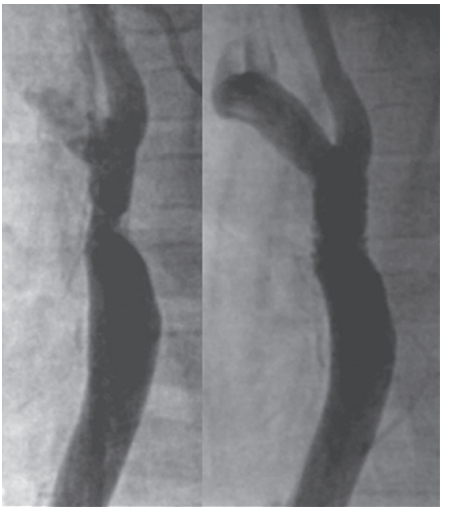

Fig. 3. A and B: A: Aortogram in patient 11, 2 months after implantation of the 4/8 mm stent: the isthmus is nice open, but there is prolapse-ingrowth of tissue at the ductal level. B: implantation of an additional 5/9 mm stent reopened the aorta adequately. Note that the distal arch has shown some catch-up growth as shown in Figs. 1 and 2.

Management of the stent (dilation, removal) was tuned to the individual needs of the patient. Surgical removal was performed if concomitant surgery was performed (e.g., Glenn, VSD closure), or if a coarctectomy could be performed at an adequate weight in stable conditions with the expectation for optimal outcome.

In two patients with stenting early after coarctectomy, the surgeon preferred a rather "late" reintervention as the dissection planes had healed. A second balloon dilation was performed in patients no. 12 after 13 months, and in patient no. 13 (Table I) after 38 months, allowing to defer redo-surgery until the age of 78 and 69 months (Table I).

Mortality during interval stent–stent removal. Two deaths were observed during follow-up: one syndromic

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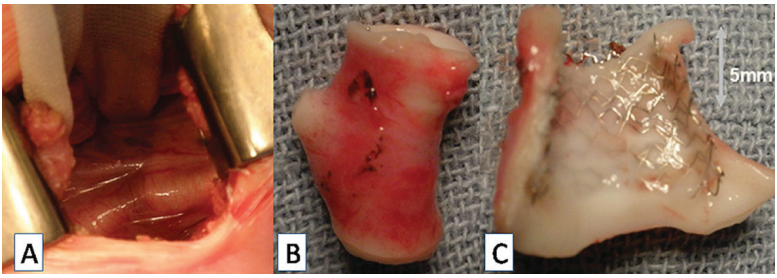

Fig. 4. Patient 11. A: Surgeons view at thoracotomy: the coarctation site is nicely exposed without trauma of the media or adventitia. B: Resected coarctation site removing the stent in whole. C: Resection piece has longitudinally been opened; the stent-in-stent has completely been covered by endothelium. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

term infant (patient no 5, Table I), with the CHARGE syndrome and perinatal asphyxia presented with incomplete AVSD, small left ventricle and critical coarctation. She was treated with a 5/15 mm stent at postnatal age of 8 days, but died 4 months later from sequelae of perinatal asphyxia. Another term infant with univentricular heart (patient no. 14, Table I) dominant right ventricle with significant tricuspid valve regurgitation) and coarctation was first surgically treated (Norwood variant with Sano shunt) and residual coarctation was stented at day 6; she died 3 weeks later from nonprocedure-related problems.

Surgical Resection and Arch Repair

Stent removal and arch reconstruction has been performed in 12 patients. One patient (number 9 in Table I) is now 7 months after stenting still awaiting final repair. The peak Doppler gradient across the arch before stent removal was 30 [25–60] mm Hg. In patients with primary surgical approach, the stent was removed after 69 [21–78] months and in patients with primary stent implantation after 2.8 [0.2–5] months. Upon inspection, the surgeon never saw any damage to the adventitia caused by the stent. The arch was carefully dissected taking care not to compress the stent as a balloon expandable stent has no elastic recoil. The stent was completely removed: if surgery occurred within days after implantation the stent was simply "picked" after arteriotomy; if surgery occurred after a few weeks the short stented segment was resected if possible, otherwise an endarterectomy was performed. The arch was reconstructed with end-to-end anastomosis in nine, and extensive arch patch reconstruction in three (Norwood-like repair). The surgeon felt the procedure was not complicated by the presence of the stent; on the contrary, the procedure at this time yielded no risk to leave any residual active ductal tissue in the anastomosis. The surgery was considered to be easier as all structures had grown, with some catch-up growth of the distal arch (Fig. 3).

After completion of the surgical repair, the final gradient (Doppler) across the arch was 0–20 mm Hg. Control chest roentgenogram showed no residual metal threads in the arch (however, these stents are little radio opaque).

Late Follow-Up

All patients have regularly been seen at our outpatient clinic for 9 months [0.4 months–5.2 years] after stent removal. On cw-Doppler echocardiography, the peak velocity over the aortic isthmus at last follow up was 1.7 [1.2–2.5] m/sec.

DISCUSSION

Significant arch obstruction in a critically ill neonate currently does require a surgical intervention; however, there are different options of how and when to proceed the surgery. Any therapeutic strategy in such patients must be judged by efficacy, time to establish adequate perfusion, complications early and late, number of procedures, hospitalization time(s), and last but not least final outcome of the arch and the patient.

This study shows that in critically ill neonates early stenting (of both native coarctation or early recoarctation post surgical coarctectomy) followed by later coarctectomy can be performed safely and with good results.

Treatment Options

Prolonged prostin infusion. Prostaglandin E1 infusion is nowadays the standard treatment to recover or maintain systemic flow in a neonate with critical coarctation, while scheduling him for elective surgical repair. However, this treatment can be associated with

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considerable side effects such as pulmonary overflow, haemodynamic instability with low diastolic blood pressure, increased vulnerability for renal failure, sepsis, and necrotizing enterocolitis. Other common side effects include apnea, hyperthermia, diarrhea, skin flushing, edema, and cortical hyperostosis [5,8,9]. Prostaglandin E1infusion may only result in incomplete ductal reopening and partial istmal relaxation, leaving insufficient systemic flow for a prolonged time [10].

Early surgical repair. In our hands, surgical coarctectomy is the procedure of choice for isolated coarctation in neonates, infants, and young children. Primary surgical coarctectomy has been performed successfully in low birth weight infants, but mortality and morbidity in this age group is increased when compared with mature neonates [11]. Such surgery is associated with an elevated incidence of early recoarctation in up to 30% [3,12]. Early failure after aortic arch repair may be due to inadequate surgical technique (e.g., kinking of a Norwood-patch, excessive tension on the anastomosis), oedema formation of the anastomosis, or constriction of residual ductal tissue.

Mortality rates in the best series have been reported to be as low as 5.5%, but remain clearly higher than in full term neonates and infants [4,12]. If surgery could safely be deferred to a later age or bigger size, it would most likely be reflected in a better final result.

Percutaneous interventions: Balloon-stent. Balloon dilatation of coarctation yields varying but usually unsatisfactory results when performed in low-birth-weight infants because of early recoil, or tear and aneurysm formation when overdilated [13–15].

Stent implantation in low-birth-weight infants with coarctation has been reported in isolated cases [16]. Stenting of early recoarctation after primary surgical coarctectomy clearly has the advantage of postponing redo-surgery thus reducing perioperative morbidity.

The series of stented primary coarctation or early recoarctation represents a small subset of the 218 surgical coarctectomies performed in infants <3 months of age within the same time period in our institution. Stenting of the coarctation such as presented here was performed with the aim to provide the surgeon with a bigger and better patient. We feel that this strategy in this highly vulnerable subset of patients has clear advantages compared with alternative concepts such as prolonged prostin infusion followed by surgical coarctectomy or primary surgical coarctectomy.

Stent Choice

Coronary stents are available in different length and diameters. Nearly all coronary bare stents can be delivered through a 6F guiding sheath or a 4F introducer sheath. Given the time span of more than 10 years that is covered by our study, stents from various manufacturers were used. The differences in stent design and material determine the cross-sectional area, the strut thickness, and the radial force. Larger metallic cross-sectional areas, thicker struts, and smaller cell-areas result in good scaffolding with limited tissue prolapse [17]. These scaffolding properties reduce the flexibility and conformability of the stent which, however, is no issue for this application (nearly straight course from groin to coarctation). Radial force is also no issue for a stent deployed in this soft fetal–neonatal tissue. Side branch accessibility might be an issue when crossing the (lusoria) subclavian artery, but priority should be given to adequate arch flow; moreover, experience from Waldhausen plasty has learned that even total occlusion of the subclavian artery is nearly always well tolerated. Depending on the design, most stents can be overdilated by 1–3 mm when using bigger balloons.

Clearly, stenting is not a definitive treatment: eventually, all stents need to be excised surgically as the materials used do not allow for redilatation to adult vessel size. In the future, resorbable stents [18] or "breakable" stents [19] may address this issue.

Vascular Damage

The biggest complication in this series was thrombosis of the femoral artery in 2/15 patients. Occlusion of the femoral artery after vascular access for cardiac catheterization may present in any age group [6]. In neonates and infants, it is usually tolerated without threatening perfusion of the leg, as they have more and develop faster collateral flow. Lee et al. have shown that transfemoral artery balloon dilatation may cause superficial femoral artery compromise, but in their series, there was no significant limb growth retardation at a 3.5-year mean follow-up [20]. The problem may persist as chronic femoral ischemia with claudicatio and limb-length discrepancy. Limb-length discrepancy exceeding 2 cm is known to be associated with gait disturbance [21]. So, every effort should be taken to avoid this complication.

The lower limit whereby a 4F sheath can be introduced "safely" into and removed from a femoral artery still needs to be determined. For obvious reasons, a trial cannot be performed. Some interventionalists advocate the use of long 4F sheaths in neonatal procedures: such sheaths give very nice support for balloon and stent manipulations, and allow small hand injections to be made during the procedure [22]. Especially in the preterm infants, we preferred to use the short 4F sheats with minimal entry into the artery, thereby theoretically limiting the damage to the artery. Other

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arterial access may be useful such as the brachial artery [22] or carotid arteries via surgical cut-down [23]. Percutaneous interventions through an umbilical artery have been reported [24]. However, in a typical patient, the umbilical artery is thrombosed and no longer available for intervention by the time the coarctation needs attention. In addition, de novo development of critical stenosis of the abdominal aorta has been reported after less invasive procedures such as placement of an umbilical artery catheter [25]. Thus, each method of percutaneous arterial access has its advantages and disadvantages. Our data show that femoral arterial access can be performed with low morbidity.

LIMITATIONS

This is a retrospective study over a long-time period, trying to determine feasibility, efficacy, and safety. Patients were not randomized to compare treatment strategies, as results of each strategy may differ in each centre over time.

We cannot provide data on long-term growth of the aortic vessel wall after stenting and stent removal. In most patients, the stent and vessel wall were resected in toto with end-to-end anastomosis; in this subgroup, we anticipate long-term results as in patients after primary repair. In some patients, the stent was removed in toto but partially with endarterectomy, whereby the surgeon still used some vessel wall in the final arch reconstruction. It is known that stenting of the aorta may result in morphological changes of vessel wall, with good early growth but with unknown long-term effects [26]. When last seen at echocardiographic evaluation, the arches were free of aneurysm formation; however, aneurysms may form several decades after the initial coarctectomy [27]. The arch of these patients should, therefore, be followed probably lifelong to detect timely late aneurysm formation (as should any patient after coarctation repair).

CONCLUSIONS

In infants with critical coarctation, bailout stenting and later surgical stent removal and arch repair can be performed safely and effectively with low morbidity. This strategy when applied in selected patients such as in the very premature, critical, or complex neonate, compares competitive with current treatment strategies on overall mortality and morbidity. Long-term studies are needed to define the impact of stenting and stent removal on growth of the aortic vessel wall.

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CHAPTER 5

General discussion and conclusion

“Pay careful attention to your own work, for then you will get the satisfaction of a job well done, and you won’t need to compare yourself to anyone else. For we are each responsible for our own conduct.”

Galatians 6:4-5

Chapter 5

5.1 General discussion and conclusion

5.1.1 Avoiding complications

The field of interventional cardiac catheterization for congenital heart disease has gone through a period of rapid expansion and diversification. Higher standards, more demanding technical skills and an awareness of learning curves for complex procedures has made the occasional operator an endangered species. Most complications can be avoided by careful patient and lesion selection, meticulous technique and sufficient operator and team experience. Even more important when dealing with relatively small patient groups with a wide range of diagnosis is commitment to rigorous self-criticism and unbiased analysis. With such tremendous ability to effectively treat even the most complex lesions in the smallest of patients comes an equal responsibility to use ionizing radiation responsibly (63). Children with complex cardiac anomalies are at greater risk because of the need for frequent catheterizations at a young age, coupled with the increased duration of complex interventional procedures (63). In addition, due to the improved survival of these patients, they now have a longer lifespan ahead of them in which to develop potential neoplasms. As paediatric interventionalists we should pay attention to the simple rules of radiation safety and use the appropriate tactics to produce adequate-quality images at low radiation cost to the patient.

5.1.2 Interventional cardiology and the surgeon

Innovations in interventional catheterization techniques have significantly altered the management of congenital heart disease over the past 2 to 3 decades. From the perspective of a cardiac surgeon, these new techniques could be interpreted as a threat to the practices of congenital heart surgeons and may even create a competitive atmosphere between surgeons and interventional cardiologists. This perspective would be very short-sighted though and is certainly not the case in our institution!. Thanks to a open

intellectual atmosphere and a willingness on the side of both surgeons and cardiologists, surgical and interventional catheterization techniques are complementary rather than competitive therapies, improving the outcome of even the most critically ill patients with the most complex cardiac anomalies. Percutaneous interventions in the paediatric population may be limited by patient size or cardiac anatomy. Hybrid procedures involving both interventional and surgical techniques have been developed to overcome these limitations, creating an even more exciting collaboration between the interventional cardiologist and the cardiac surgeon.

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5.1.3 Evidence based medicine

"Is medicine science or art? The obvious answer is that it is both – as it has always been – and that the real question is how to find the right balance between them…." (64).

In medical school we are taught to seek new knowledge and to question common wisdom; we are encouraged to practice evidence based medicine. This so-called evidence based medicine, whose philosophical origins extend back to the mid-19th century Paris and earlier, remains a hot topic for clinicians, public health practitioners, purchasers, planners and the public (65). The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research (65). While virtually everybody agrees that the ideal evidence comes in the form of randomized placebo-controlled double-blinded clinical trials, we will inevitably encounter serious problems if this kind of evidence is to be our only guide. The field of congenital heart disease with its many variations does not lend itself well to prospective double blinded studies compared to adult heart disease, where thousands of patients exist with coronary artery disease or valve abnormalities with an otherwise normal cardiac anatomy (66). Especially in pediatric cardiac surgery and interventional catheterization techniques, almost all of the advances have come from innovation rather than prospective long-term outcome studies. In spite of these obstacles, we should strive to expand the evidence based aspects of decision-making in pediatric cardiology by performing clinical

trials whenever possible (and appropriate) and developing international databases that can track anonymized patient information and outcomes as to identify risks and successes of new treatment modalities. The application of evidence based medicine to clinical practice should not occur in isolation from, but in conjunction with, critical thinking and clinical judgment (67).

5.1.4 Future perspectives

Where will the next decade take the pediatric/congenital interventionalist? We will certainly see a consolidation of the present techniques, with incremental improvements in devices, refinement of indications and patient selection and hopefully more follow-up data on previous therapies. We can expect further miniaturization of catheter systems and improvement of stent design, with emphasis on coating and biogradability. We might even use catheters to implant pulmonary valves made from the patient's own tissue or percutaneously deliver gene therapy to treat inherited cardiomyopathies or vasculopathies.

5.1.5 Conclusions

In this thesis manuscript we evaluated novel indications for balloon dilation and endovascular stenting in patients with congenital heart disease. After performing several studies, both clinical and experimental, we can conclude that these new and promising techniques are safe and effective in patients with congenital heart disease ranging from the premature infant to the adult. These innovations in therapy complement surgery, allowing a better outcome for our patients. Limitations of these studies are that they were mostly retrospective, the numbers are small and the follow-up is relatively short, highlighting the typical dilemma of the pediatric cardiologist when trying to practice evidence based medicine.

As physicians working in the exciting and rapidly expanding field of interventional congenital cardiology, it is easy to become so consumed and carried away by our technical know how that we might lose sight of what we are attempting to accomplish. We should however never lose sight of the natural history of the defects we deal with, whilst investigating and learning

about the natural/unnatural history of the devices we use and procedures we perform. The development of international registries to evaluate the outcome of newer techniques is essential. As “artists” performing our act in the “interventional theatre” we should never lose sight of our twin brother “science”…..

“Fools think their own way is right, but the wise listen to others.”

Proverbs 12:15

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Summary

The concept of balloon dilatation and intravascular stent implantation to maintain vessel patency have been introduced half a century ago. However, extensive clinical trials were not carried out until the late 1980s, after improvements in stent technology and design were made and high pressure balloons were developed. Since these early reports, enormous advances have occurred in the interventional technology for pediatric patients. In this thesis manuscript we evaluated novel indications for balloon dilation and endovascular stenting in patients with congenital heart disease. The use of stents in a growing child is challenging, as ideally the final stented vessel diameter should ultimately approach the adult size. When implanting a stent at a relatively young child, serial re-dilation should be possible, unless stenting is only seen as bridge to subsequent surgery.

In **chapter 2** we describe an experimental study to investigate the effect of stent implantation and later surgical removal on the growth potential of juvenile vessels. This study originated from or clinical concern that stent removal could scar the vessel wall to the extent that further growth is limited. Stents were implanted in the carotid artery and jugular vein of six 6-week-old lambs. Ten weeks later, stents were excised and the vessels closed without the use of patch material. After another 10 weeks, the vessel size (treated and untreated control side) was measured angiographically and the animals terminated for histology. Preserved vessel wall integrity was observed in both arteries and veins (except for local rupture of the internal elastic lamina with neointimal formation in two arteries leading to mild stenosis). Two veins were completely occluded and two severely stenosed; vessel size was significantly smaller compared with the control side. We concluded that vessel wall architecture remains well preserved after surgical removal of stents implanted in juvenile arteries and veins. However, stenting and subsequent surgical removal results in a high risk of venous thrombosis (probably due to the lower blood velocity, lower pressure, and the absence of pulsatility in venous vessels).

In **chapter 3** different ways of pulmonary flow modulation are discussed:

Treatment options of major aortopulmonary collateral arteries in the setting of Tetralogy of Fallot with pulmonary atresia

The principles of management are discussed, with emphasis on aiming towards normalization of the pulmonary circulatory physiology. The role of cutting balloons in successfully dilating pressure resistant stenosis and even filiform or long segment lesions are discussed in detail as well as the indications for stent implantation.

Stenting the neonatal arterial duct

Ductal stenting in neonates with either duct-dependent pulmonary or systemic circulation has become a good alternative for the initial palliation of complex congenital heart disease. Changes of stent and catheter technology (low profile, flexible, premounted stents with good scaffolding), better patient selection and preparation, optimal interventional access and covering the complete length of the duct have significantly improved results. We describe our initial results using these techniques in a small group of 10 neonates with duct-dependent pulmonary circulation and a short, straight duct. This is followed by a review of ductal stenting in patients with duct-dependent pulmonary- and systemic circulation.

"Tailoring" pulmonary flow

Patients with decreased pulmonary blood flow often need neonatal palliation (ductal stenting, surgically created systemic to pulmonary shunts) due to severe cyanosis. In patients with increased or unprotected pulmonary flow, pulmonary artery banding during the first weeks of life is mandatory to protect the pulmonary vascular bed. Flows may rapidly become "unbalanced" due to somatic growth, necessitating re-intervention. Manipulation or "tailoring" of pulmonary flow during growth is possible, provided that excellent cooperation exists between the interventionalist and the surgeon. We discussed the substrates of pulmonary flow manipulation with emphasis on stent expansion of Gore-Tex grafts, stenting of the right ventricular

outflow tract using hybrid interventional techniques and dilatable pulmonary artery banding.

Off-label use of percutaneous pulmonary valved stents

Percutaneous pulmonary valve implantation is now considered feasible and safe in selected patients with dysfunctional RVOT conduits. The "native" RVOT, smaller conduits (less than 16mm) and the relatively large RVOT with dynamic outflow aneurysms, as commonly seen with trans-annular patch repair of the RVOT, are considered off-label use for percutaneous valve implantation. In this study we described the successful percutaneous implantation of stented pulmonary valves in 23 patients with unfavourable anatomy according to traditional protocol. We recommend that an adequate "landing zone" should be created by pre-stenting.

In **chapter 4** stenting of the aortic arch in 2 extreme patient populations were described:

Stenting of hypoplastic aortic segments with mild pressure gradients and arterial hypertension

Hypoplasia of the aortic cross and/or isthmus can be an isolated lesion, or may persist even after adequate coarctectomy. Such a hypoplastic segment may cause a gradient over the arch, leading to arterial hypertension. Long term follow-up studies after coarctectomy have shown significant morbidity and mortality beyond the fourth decade, usually secondary to or associated with arterial hypertension. These data suggest that the clinician should aim for an aortic arch free of any gradient in the hope to improve long-term outcome in these patients. Surgical options to treat residual hypoplasia of the aortic cross and/or isthmus are an aortic arch reconstruction or cross-over operation, which both are extensive operations which can be associated with significant morbidity. In this study we reported our early experience with stent expansion of hypoplastic aortic segments in 20 patients, resolving the

arterial hypertension in 10 patients and improving blood pressure control in the remaining 10 patients.

Bailout stenting for critical coarctation in premature / critical / complex / early recoarctated neonates

Surgical repair of critical coarctation can be problematic in premature, critical, complex, or early postoperative neonates. In this study we reviewed our experience with stent implantation in 15 neonates with severe coarctation, aiming to postpone urgent surgery to an elective time. We concluded that bailout stenting followed by early or late surgical coarctectomy appears to be a promising concept in this specific patient population.

In **chapter 5** a general discussion followed. We stated that most complications in the interventional catheterization laboratory can be avoided by careful patient and lesion selection, meticulous technique and sufficient operator experience and that it is our duty as paediatric interventionalists to use ionizing radiation responsibly. The relationship between the interventional cardiologist and the cardiac surgeon were discussed, concluding that our therapies are complementary and not competitive. Patients with congenital heart disease represent a relatively small population with a wide range of diagnosis, which is unique when compared to adult heart disease where thousands of patients exist with coronary artery disease or valve abnormalities with an otherwise normal cardiac anatomy. Performing randomized, placebo-controlled, double-blinded clinical trials in such a patient population is therefore unrealistic. Especially in pediatric cardiac surgery and interventional catheterization techniques, almost all of the advances have come from innovation rather than prospective long-term outcome studies. In spite of the many difficulties to practice evidence based medicine in pediatric cardiology, we should strive to expand the evidence based aspects of decision-making by performing clinical trials whenever possible and developing international databases that can provide information on outcomes and identify risks and successes of new treatment modalities. We concluded that the novel techniques and indications for balloon dilation and endovascular stenting

described in this thesis are safe and effective in patients with congenital heart disease, ranging from the premature infant to the adult.

Samenvatting

De congenitale interventionele hartkatheterisatie technieken hebben de afgelopen jaren een enorm vooruitgang gekend. Het concept van endovasculaire ballondilatatie en stenting bestaat al meer dan een halve eeuw, maar het is pas sinds eind 1980 dat uitgebreide klinische studies gepubliceerd werden (voornamelijk in volwassenen). Dankzij verkleining van kathetersystemen, verfijning van technieken en evaluatie van resultaten op termijn zijn deze procedures veiliger en meer voorspelbaar geworden in pediatrische patiënten. In deze thesis beschreven we nieuwe indicaties voor ballondilatatie en endovasculaire stenting in patiënten met congenitale hartziekte. Er werd een experimentele dierenstudie en verschillende klinische studies uitgevoerd. Stentimplantatie wordt bij kinderen meestal uitgesteld tot een stent kan geïmplanteerd worden met het potentiaal om tot volwassen maat geëxpandeerd te kunnen worden. In sommige gevallen is de interventionele cardioloog echter genoodzaakt om stents in jonge baby's met kleine bloedvaten te implanteren, met het gevolg dat de stents later chirurgisch moeten verwijderd worden.

In **hoofdstuk 2** beschrijven wij de resultaten van een gecontroleerde prospectieve dierenstudie om de vraag te beantwoorden of chirurgische verwijdering van een stent de architectuur van de bloedvaatwand zodanig kon beschadigen dat haar groeipotentiaal daardoor in gedrang zou komen. Stents werden geïmplanteerd via femorale toegang in de carotis arteries en jugulaire venen van 6 lammeren van 6 weken oud. Tien weken later werden de stents chirurgisch verwijderd en de bloedvaten primair gesloten zonder patch materiaal, met slechts een longitudinaal chirurgische litteken. Nog 10 weken later werden de behandelde en controle vaten angiografisch vergeleken betreffende hun diameter. Vervolgens werden de dieren getermineerd en de bloedvaten gereseceerd voor histologie en evaluatie van doorgankelijkheid. In zowel arteries als venes was de integriteit van de bloedvaatwand behouden buiten voor lokale ruptuur van de lamina elastica interna met neointima proliferatie in 2 arteries met milde stenoses ten gevolge. De diameter van de behandelde venen was echter significant kleiner dan de controle zijde: 2

venen waren volledig geoccludeerd en 2 belangrijk vernauwd. We concludeerden uit deze studie dat de architectuur van de bloedvaatwanden goed behouden bleef na chirurgische verwijdering van stents geïmplanteerd in juveniele arteries en venen. Er is echter een hoog risico voor veneuze trombose na stent verwijdering vermoedelijk ten gevolge van de lagere druk en bloedsnelheid en afwezigheid van pulsatiliteit.

In **hoofdstuk 3** werden enkele klinische studies beschreven waardoor de pulmonale flow kan gemoduleerd worden:

Behandelingsopties in geval van aortopulmonale collaterale bij patiënten met Tetralogie van Fallot

We rapporteerden in een overzichtsartikel onze ervaring en ook die van andere auteurs betreffende het gebruik van cutting ballonen bij aortopulmonale collaterale. We concludeerden dat stenoses resistent aan hoge druk en zelfs lang segment filiforme stenoses succesvol en veilig behandeld kunnen worden met gebruik van cutting ballonnen. Indicaties voor stentimplantatie zijn belangrijke recoil van de gedilateerde arterie, ernstige intimale schade met aneurysma formatie, dissectie met risico van bloedvaat occlusie of kritische lang segment filiforme stenose.

Stenting van de neonataal ductus arteriosus

Stenting van de neonatale ductus arteriosus werd tot ongeveer een decade geleden als een technisch zeer moeilijke procedure met een hoog risico beschouwd. Deze problemen waren vaak het gevolg van vroege generatie, rigide stents geïmplanteerd met stijve ballons over stijve voerdraden, doorheen rigide sheaths. We postuleerden echter dat ductus stenting veilig en efficiënt uitgevoerd kan worden met nieuwe interventionele technieken in geselecteerde patiënten. We beschreven onze initiële resultaten van ductus stenting in 10 geselecteerde neonaten met ductus dependente longcirculatie. Sinds deze publicatie zijn meerdere artikels van verschillende auteurs verschenen en ductus stenting wordt nu als een veilig alternatief beschouwd voor de initiële palliatie bij geselecteerde patiënten. De techniek is minimaal invasief en in tegenstelling met een chirurgische shunt is titratie van

pulmonale flow in functie van de patiënt grootte en groei mogelijk dmv ballondilatatie en restenting van ductus. In een overzichtsartikel beschreven we de huidige technieken en selectie criteria voor ductus stenting in ductus-dependente pulmonale- en systeemcirculatie.

Manipulatie van het longdebiet

Patiënten met verminderderde longdebiet hebben vaak een palliatieve ingreep nodig tijdens het neonatale tijdperk omwille van progressieve cyanose. Ook bij patiënten met verhoogde of onbeschermde pulmonale vloei is een palliatieve interventie in de vorm van een pulmonale arteriële banding nodig gedurende de eerste levensweken. Deze interventies zijn noodzakelijk maar hebben het nadeel dat pulmonale vloei reeds op een zeer jonge leeftijd en vaak bij een zeer laag gewicht moeten gemanipuleerd worden. Ten gevolge van normale somatische groei worden chirurgische shunts snel te klein en pulmonale banden te strak en zijn nieuwe interventies noodzakelijk. Met verbetering van longdoorbloeding met behulp van katheterisatie technieken kan chirurgie potentieel uitgesteld worden tot de patiënt iets ouder is, de pulmonale arteries groter zijn met een lagere weerstand of totdat een volwassen maat conduit kan geïmplanteerd worden. Substraten voor manipulatie van flow zijn chirurgische shunts, de rechter ventrikel uitstroombaan en dilateerbare pulmonale banden. We beschreven de succesvolle stent expansie van rekbare Gore-Tex shunts, stent implantatie door middel van een hybride techniek in jonge baby's met een atretische rechter ventrikel uitstroombaan en onze ervaring met dilateerbare pulmonale banden.

Uitbreiding van de indicaties voor percutane implantatie van pulmonale klepstents

De eerste succesvolle percutane klepimplantatie werd 10 jaar geleden beschreven. De Melody klepstent (Medtronic) wordt sinds enkele jaren als een veilig en efficiënt alternatief beschouwd bij geselecteerde patiënten met RV uitstroombaan obstructie of insufficiëntie. De Sapien Edward klepstent is sinds recent ook beschikbaar voor pulmonale implantatie. De huidige aanbevolen selectiecriteria zijn echter beperkt tot een bestaande conduit tussen 16 en 24mm. De natieve RV uitstroombaan, conduits kleiner dan 16

mm en relatief grote uitstroombanen zoals klassiek na een transannulair patch herstel bij TF komen niet in aanmerking voor deze procedures.
We beschreven in deze studie de succesvolle percutane implantatie van klepstents in 23 patiënten met ongunstige anatomie volgens traditionele protocollen. Pre-stenting werd echter aanbevolen om een voldoende landingzone te creëren.

In **hoofdstuk 4** beschreven we de resultaten van stent implantatie in de aortaboog bij 2 extreem patiënten populaties:

Stent implantatie in de volgroeide aortaboog ter hoogte van hypoplastische segmenten

Hypoplasie van de aorta arcus of isthmus kan een geïsoleerd letsel zijn of persisteren na coarctectomie. Een hypoplastisch segment kan verantwoordelijk zijn voor een drukgradiënt over de boog met arteriële hypertensie ten gevolg. Lange termijn studies na coarctectomie tonen een significant verhoogde morbiditeit en mortaliteit na de 4de decade, meestal in associatie met arteriële hypertensie. Deze data suggereren dat de clinicus moet streven naar een aortaboog zonder enige gradiënt in de hoop om de lange termijn uitkomst in deze patiënten te verbeteren. Chirurgische opties in geval van residuele hypoplasie zijn een aortaboog reconstructie of cross-over operatie; dit zijn allebei vrij extensieve ingrepen en te agressief bij een milde restvernauwing. In deze studie hebben wij de veiligheid en efficiëntie van stent expansie van hypoplastische segmenten met slechts een milde drukgradiënt prospectief geëvalueerd in 20 patiënten met arteriële hypertensie. Er waren geen complicaties gedurende of na de procedure. Een significante vermindering in de drukgradiënt over de boog werd bekomen en de arteriële bloeddruk kon genormaliseerd worden in 10 patiënten; de andere 10 patiënten hebben betere bloeddruk controle gehad met minder medicatie.

Stent implantatie in de aortaboog: kritische of complexe coarctatio/recoarctatio bij pasgeborenen

Soms wordt de clinicus geconfronteerd met een belangrijke aortaboogobstructie bij een kritisch zieke neonaat. De uiteindelijke behandeling is chirurgisch, maar moet soms uitgesteld worden omwille van prematuriteit of een laag geboortegewicht. In deze studie rapporteerden we onze ervaring met betrekking tot stentimplantatie bij 15 neonati met coarctatio of recoarctatio met de bedoeling om chirurgische correctie uit te stellen. Voldoende systeemperfusie werd bekomen bij alle patiënten. De stents kon uiteindelijk zonder problemen chirurgisch verwijderd worden.

In **hoofdstuk 5** sluiten we af met een algemene discussie. We kunnen de meeste complicaties in het interventionele katheterisatie laboratorium voorkomen met behulp van de juiste patiënten selectie, nauwgezette techniek en voldoende ervaring van de interventionele cardioloog. Het is verder noodzakelijk dat we verantwoordelijk omgaan met ioniserende stralen. De verhouding tussen de interventionele cardioloog en congenitale hartchirurg werd zeker niet negatief beïnvloed door de vooruitgang in interventionele technieken. Integendeel, onze therapieën zijn complementair en hebben de uiteindelijke prognose van ons patiënten positief beïnvloed. Patiënten met aangeboren hartafwijkingen verschillen duidelijk van volwassenen met verworven coronaire- en kleppathologie: de aantallen zijn veel kleiner en het type pathologie meer divers. Het is dan ook onrealistisch om bij deze groep van patiënten gerandomiseerde, placebo gecontroleerde, dubbelblinde klinische studies uit te voeren. De meeste vooruitgang in congenitale cardiale heelkunde en interventionele katheterisatie technieken worden geboekt door innovatie en niet door prospectieve langtermijn studies. We moeten echter streven om ons klinische beslissingen te baseren op bestaande evidentie en om klinische studies uit te voeren zover mogelijk. We moeten de ontwikkeling van internationale databasissen steunen met de bedoeling om informatieve te bekomen over lange termijn uitkomsten en risico's en successen van nieuwe behandelingsmodaliteiten. We concludeerden ten slotte dat de nieuwe ballondilatatie en stenting technieken zoals in dit manuscript beschreven, veilig en efficiënt kunnen zijn in een diverse groep van patiënten met congenitale hartziekte. Dankzij deze nieuwe technieken hebben we meer behandelingsopties en is een betere uitkomst voor onze patiënten mogelijk.

Curriculum Vitae

Birth Date: 29 February 1968, Pretoria, South Africa

Married to: Johan Nel, Anaesthesiologist –Intensivist, Maasland Ziekenhuis, Sittard, The Netherlands

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Postgraduate Education

Doctorate in medical science: Catholic University Leuven, Belgium: to be completed August 2012.

Paediatric cardiology training:

- 6 months rotation in Paediatric Cardiology as Paediatric Registrar at the Pretoria Academic Hospital, University of Pretoria, South Africa.
- 24 months as Fellow in Paediatric Cardiology, University Hospital, Gasthuisberg, Leuven, Belgium: January 2000 - December 2001.
- Six weeks rotation as clinical observer in the Interventional Catheterization Laboratory at the Hospital for Sick Kids, Toronto, Canada: October – November 2001 (Prof. Lee Benson).

Paediatrics training:

- FC Paed SA: April 1999 - Fellow of the College of Paediatricians of South Africa - National Paediatric specialist examination - chosen as one of the two best candidates.
- M Med Paed: April 2000 - a postgraduate masters degree in Paediatrics, attained at the University of Pretoria, South Africa (Degree awarded after submission of research report ("Clinical Predictors of Hypoxaemia in Term Newborn Infants within the First Hour of Life'. This paper was presented as a short oral presentation at the 7th World IAMANEH conference in Stellenbosch, South Africa in April 2000)

Undergraduate Education

Medical studies:

MBCHB (Bachelors in Medicine and Surgery) - Cum Laude, November 1992, University of Pretoria, South Africa**;** Distinctions in all subjects- Internal Medicine, Obstetrics and Gynaecology, Psychiatry, Paediatrics, Surgery.

Special Achievements: 1992 Academic Colours - University Student Council; 1990-92 Elected - Medical Student Council; 1990-91 Editor - Medical Student Paper; 1990 Winner of the HW Snyman Award for Community Health; 1989 Winner of the Inter-University Orator's competition; 1988 Winner of Ben Meyer Award for Physiology.

Post school: Rotary Exchange Student - Bremen, Germany 1986

School: Matriculated 1985; Afrikaans Girls Highschool - Pretoria, South Africa; All subjects passed with distinctions on higher grade; Afrikaans, English, Maths, German, Latin, Science

Achievements: Head Prefect Std 10 (Matric); Medal for Top Academic Scholar - Std 6 - 10; Prefect Std 9;Won several Orator's competitions; Gymnastics - Provincial Colours 1980-1985.

Experience

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1) Working as Consultant Paediatric Cardiologist in 2 regional hospitals in Belgium:

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List of publications

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