Pulmonary Artery Branch Stent Implantation in Congenital Heart Disease: A 10-Year Multicenter Experience

Implante de stents en ramas de arterias pulmonares en cardiopatías congenitas: experiencia multicéntrica en 10 años

ALEJANDRO PEIRONEMTSAC 1,2,3,4; ALEJANDRO CONTRERASMTSAC 2; MARCELO CABRERA1; ADOLFO FERRERO GUADAGNOLI2; ANÍBAL GENTILETTI1; ANA SCHROHMTSAC 4; LIDIA LAGHEZZA4; IGNACIO JUANEDAMTSAC 2; JUAN DÍAZ2; CHRISTIAN KREUTZERMTSAC 2

ABSTRACT

Background: Stent implant is considered the treatment of choice for most cases of congenital or postoperative pulmonary artery branch stenosis in patients with congenital heart defects. However, there are still doubts on the clinical effectiveness and the incidence of complications of this technique that need to be elucidated.

Methods: This multicenter study has a descriptive, observational and retrospective design. The procedures were performed between January 2005 and April 2015. Twenty-five patients with pulmonary artery branch stenosis underwent stent implant and were followed-up both clinically and by different imaging tests. Persistent clinical and/or anatomic improvement defined clinical effectiveness.

Results: Average age was 9.48 years (2 months-34 years), mean weight was 27.54 kg (3-104 kg) and 44% were women. The most frequent congenital heart defects in the treated cohort were tetralogy of Fallot and its variants, followed by single ventricle heart physiology after bidirectional Glenn shunt and/or Fontan-Kreutzer procedures. Right ventricular systolic and pulmonary artery pressure decreased significantly after the intervention (from 68.35 mmHg to 45.8 mmHg and from 47.4 mm Hg to 32 mm Hg, respectively) (p < 0.0001). The initial minimum diameter of the treated pulmonary artery branch increased significantly after the procedure (from 3.98 mm to 9.82 mm, p < 0.0001). The incidence of complications was 8% (n = 2) and the clinical effectiveness of the procedure was good in 22 patients (88%).

Conclusions: Stent implant in pulmonary artery branch stenosis is a safe and feasible though challenging technique, with significant clinical and anatomic improvement. The procedure represents an alternative to surgery and decreases the need for reinterventions in patients with congenital heart defects.

Key words: Pulmonary artery – Stenosis - Heart defects, Congenital – Stenting – Intraoperative complications

RESUMEN

Introducción: La angioplastia con implante de stent se considera el tratamiento de elección para la mayoría de los casos de estenosis congénita o adquirida posquirúrgica de ramas de arterias pulmonares en pacientes portadores de cardiopatías congénitas. Sin embargo, aún persisten dudas sobre la efectividad clínica y la incidencia de complicaciones de esta técnica que necesitan ser esclarecidas.

Material y métodos: Estudio multicéntrico descriptivo, retrospectivo, observacional. Los procedimientos se realizaron desde enero de 2005 hasta abril de 2015. Un total 25 pacientes fueron sometidos a angioplastia con implante de stent en ramas de arterias pulmonares, los cuales fueron seguidos evolutivamente en su estado clínico y por diferentes métodos de imágenes. Se definió buena efectividad clínica al mejoramiento clínico sintomático y/o anatómico persistente del paciente intervenido.

Resultados: La cohorte de 25 pacientes tenía una edad promedio de 9,48 años (2 meses-34 años), un peso promedio de 27,54 kg (3-104) y el 44% era de sexo femenino. Las cardiopatías congénitas de base intervenidas fueron en su mayoría tetralogía de Fallot y sus variantes, seguida por corazones con fisiología univentricular poscirugías de Glenn bidireccional y/o de Fontan-Kreutzer. La presión sistólica del ventrículo derecho y de la arteria pulmonar disminuyeron significativamente posintervención (de 68,35 mm Hg a 45,8 mm Hg y de 47,4 mm Hg a 32,08 mm Hg, respectivamente) (p < 0,0001). El diámetro mínimo de la lesión a tratar se incrementó significativamente posintervención (de 3,98 mm a 9,82 mm, p < 0,0001). La incidencia de complicaciones fue del 8% (2 pacientes) y se registró buena efectividad clínica en 22 pacientes (88%).

Conclusions: La angioplastia con colocación de stent en las ramas de arterias pulmonares resultó una técnica segura y eficaz, aunque desafiante, con una marcada mejora clínica y anatómica de las lesiones tratadas. Representa una alternativa a la cirugía, con disminución del riesgo de reintervenciones en pacientes con cardiopatías congénitas.

Palabras clave: Arteria pulmonar - Estenosis - Cardiopatías congénitas - Stenting –Complicaciones intraoperatorias
INTRODUCTION
Pulmonary artery branch stenosis (PBS) may occur congenitally as an isolated lesion or, more commonly, in association with other congenital heart defects as tetralogy of Fallot (TOF) and its variants. Surgical repair of different congenital defects may also result in acquired PPS, particularly in patients with single ventricle physiology. (1) The surgical approach of PBS is a complex problem, as it varies according to the severity of the defect and may increase right ventricular (RV) pressure in patients with biventricular physiology or lead to ventricular hypertrophy or suboptimal outcomes in patients with single ventricle physiology. Therefore, PBS is considered an independent high risk variable for morbidity and mortality in the immediate and long-term postoperative period of congenital heart defects.

Pulmonary artery branch stenosis surgery is usually technically difficult with a high tendency to early restenosis. Currently, surgery is generally reserved for patients with central defects that cannot be treated with catheter-based techniques or for those who have coexistent defects requiring surgical repair. The effectiveness of catheter balloon angioplasty without stent implant is limited, as it is usually associated with early restenosis and may have significant complications such as vessel rupture, dissection and aneurysm development. Nowadays, catheter balloon angioplasty with endovascular stenting emerges as the strategy of choice for PBS. (3) Stent implantation has significantly improved the effectiveness of the procedure and increased the success rate to over 90%. (3) This technique avoids overdistension of the pulmonary artery branch which may be associated with vessel rupture, dissection or aneurysm formation during follow-up. In addition, the radial force of the stent holds the vessel open after deployment, counteracting the natural elastic recoil of the arterial wall. (2)

Although transcatheter stenting is accepted as the treatment of choice for PBS, there are no data directly comparing this technique versus surgical repair. (4) Moreover, the clinical effectiveness and the incidence of complications of stent implant in PBS are not yet clear and need to be elucidated.

METHODS
The study has a descriptive, observational and retrospective design. The procedures were performed between January 2005 and April 2015 on 25 patients with PBS, in whom 29 interventions were carried out on pulmonary artery branch and 30 stents were implanted.

A RV systolic pressure greater than 2/3 systemic blood pressure or a difference in pulmonary perfusion scans between both lungs ≥35% was considered as indication for the intervention. (2, 3)

Patient outcome was followed-up. Persistent clinical and/or anatomic improvement (increase of initial vessel diameter >50%) were considered parameters of clinical effectiveness.

RESULTS
The study included 25 patients. Table 1 shows demographic data.

Average age was 9.48 years, ranging from 2 months to 34 years, and average weight was 27.54 kg, varying between 3 and 104 kg. The associated heart defects were TOF and its variants in 10 patients (40%), single ventricle in 8 (32%), truncus arteriosus in 2 (8%), Williams syndrome in 2 (8%), Noonan syndrome in 1 (4%), defect detected after removal of a pulmonary artery band in 1 (4%) and secondary to Jatene procedure for d-transposition of great arteries (d-TGA) in 1 patient (4%). (Table 2) The left pulmonary branch was affected in 14 patients (56%), the right branch in 7 (28%) and both pulmonary branches in 4 patients (16%). The pulmonary artery branch was accessed by femoral vein puncture in 56% of cases, by internal jugular vein puncture in 32%, via a hybrid approach (surgical plus interventional technique) in 8% and by transhepatic approach in the remaining 4% of cases.

Eight patients (32%) had previously undergone a modified Blalock Tausig (B-T) shunt to the ipsilateral treated branch and 3 patients (12%) had received pulmonary artery branch banding as part of a hybrid approach for hypoplastic left heart syndrome (HLHS). A previous intervention of the affected pulmonary artery branch had been performed in 5 patients (20%); conventional catheter balloon angioplasty in 3 (12%) and angioplasty using cutting balloon in 2 (8%). Bare metal CP™ (NuMed) stents were used in 12 patients and 2 patients received covered CP™ stents. Palmaz-Genesis™ stents were implanted in 9 patients, Express™ vascular LD (Boston Scientific) in 3, Liberte™ (Boston Scientific) in 2, Advanta V12™ (Atrium) in 1, and self-expandable Sentinol™ stent (Boston Scientific) in 1 patient.

Right ventricular systolic pressure before the in-
Systemic-to-pulmonary artery pressure before the intervention was 68.35±16.9 mmHg (40-96 mmHg) and decreased to 45.8±9.89 mmHg (27-64 mmHg) (p <0.0001) after the procedure (Figure 1, left). Systolic pulmonary artery pressure before the intervention was 47.4±21.7 mmHg (14-86 mmHg) and decreased to 32.08±12.39 mmHg (14-62 mmHg) (p<0.0001) (Figure 1, center). Distal pressure in the affected pulmonary artery branch was 21.41±10.3 mmHg before the procedure (10-66 mmHg) and increased to 24.45±8.3 mmHg (14-45 mmHg) (p=0.14) after the procedure. The initial minimum diameter of the pulmonary artery branch was 3.98±1.85 mm (1.5-8.6 mm) and increased to 9.82±3.65 mm (4-16 mm) (p <0.0001) after the procedure (Figure 1, right).

The incidence of procedure-related complications was 8% (n=2) and included stent migration requiring implantation of a new stent in 1 patient and thrombosis distal to the stenosis of the treated branch in the other patient. During follow-up, the incidence of complications was 12% (n=3): one stent fracture without integrity loss, with embolization of the distal fragment, one complete occlusion of a self-expanding stent implanted in a pulmonary artery with complex anatomy and one death during hybrid approach due to multiple organ failure in a patient with previous Fontan-Kreutzer surgery.

Five patients (20%) underwent stent redilation to accommodate somatic growth at a mean time of 34.6 months (11.3-39.5) following stent implant.

Average follow-up time was 39.2 months (1-22 months) and the clinical effectiveness of the procedure was good in 22 patients (88%).

During long-term follow-up, one patient with complex TOF required surgical removal of two tandem stents from the right pulmonary artery branch, reconstruction of the RV outflow tract and bilateral repair of the pulmonary arteries.

In 4 patients (16%), other procedures were performed at the same time of stent implantation in pulmonary artery branches: coil embolization to occlude aortopulmonary collateral vessels, B-T shunt occlusion with covered stent, occlusion of a persistent left-sided vena cava draining into the coronary sinus with a vascular occlusion device and dilation of a calcified conduit between the RV and the pulmonary artery.

**DISCUSSION**

Pulmonary artery branch stenosis may occur congenitally as an isolated lesion or in association with other congenital heart defects. (5) It may also result as sequelae of surgical interventions of congenital heart defects, (6) associated with Takayasu’s arteritis or Behcet’s disease (7, 8) or as part of Williams-Beuren, Noonan or Alagille syndromes.

This entity was initially described in 1938 (9) and

**Table 1. Demographic characteristics, venous access and treated branches.**

<table>
<thead>
<tr>
<th>Age</th>
<th>9.48 years (2 months-34 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>27.5 kg (3-104 kg)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male 56% / Female 44%</td>
</tr>
<tr>
<td>Venous access</td>
<td>Femoral vein 56% / Jugular vein 32% / Hybrid access 8% / Transhepatic vein 4%</td>
</tr>
<tr>
<td>Treated branches</td>
<td>Left 56% / Right 28% / Bilateral or kissing 16%</td>
</tr>
</tbody>
</table>

**Table 2. Underlying congenital heart defects**

<table>
<thead>
<tr>
<th>Underlying congenital heart defects</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetralogy of Fallot and its variants</td>
<td>10 patients (40%)</td>
</tr>
<tr>
<td>Single ventricle heart</td>
<td>8 patients (32%)</td>
</tr>
<tr>
<td>Truncus arteriosus</td>
<td>2 patients (8%)</td>
</tr>
<tr>
<td>Williams syndrome</td>
<td>2 patients (8%)</td>
</tr>
<tr>
<td>Noonan syndrome</td>
<td>1 patient (4%)</td>
</tr>
<tr>
<td>Stenosis after removal of pulmonary artery banding</td>
<td>1 patient (4%)</td>
</tr>
<tr>
<td>d-TGA post Jatene procedure</td>
<td>1 patient (4%)</td>
</tr>
</tbody>
</table>

Fig. 1. Right ventricular (RV) systolic pressure was 68.35±16.9 mmHg vs. 45.8±9.89 mmHg (p<0.0001). Pulmonary artery (PA) systolic pressure was 47.4±21.7 mmHg vs. 32.08±12.39 mmHg (p<0.0001). Minimal pulmonary artery branch diameter was 3.98±1.85 mm vs. 9.82±3.65 mm (p<0.0001). Baseline measurements are in pink and measurements after the intervention are in red.
is still poorly recognized. The progressive and non-uniform segmental vascular obstruction of the pulmonary arteries is typically associated with progressive dyspnea and fatigue. The segmental stenosis can be single or multiple and can be confined to the main pulmonary artery branches or affect more peripheral segmental branches. (10) Patients with symptoms and evidence of increased RV pressure should be considered candidates for the intervention. (11) Pulmonary angiography remains the gold standard for the diagnosis of PBS; yet, multi-slice computed tomography scan and magnetic resonance imaging may be useful to provide additional information before the intervention. Radionuclide pulmonary perfusion scan plays an important role to reveal segmental perfusion defects after the intervention in a minimally invasive manner. (12)

In our series, the most common defects presenting PBS needing intervention were TOF and its variants and single ventricle physiology in patients with previous bidirectional Glenn or Fontan-Kreutzer procedures. Thirty-two percent of these patients had previously undergone a modified B-T shunt to the ipsilateral treated branch and 12% had received pulmonary artery branch banding as part of a hybrid approach for HLHS.

Pulmonary artery branch stenosis treatment includes clinical follow-up in asymptomatic patients with biventricular physiology, preserved RV function and symmetric pulmonary blood flow distribution. On the other hand, patients with right heart failure symptoms, elevated RV pressures, marked pulmonary blood flow asymmetry (<25% total flow perfusion to a single lung), severe pulmonary valve regurgitation, hemodynamic impairment or RV dysfunction (5) should be considered for stent therapy. In patients with single ventricle physiology, increased pressures in the territories of bidirectional Glenn or Fontan-Kreutzer procedures, presence of pulmonary arterial branch distortion with variation in normal laminated blood flow and the development of ascitis, protein-losing enteropathy, Stokes’ collar and plastic bronchitis should be considered indications for the intervention.

Pulmonary artery branch stenosis location is crucial to determine the therapeutic approach. Surgery is generally reserved for patients with proximal central branch lesions. Distal or hilar lesions should be treated with transcatheter interventional strategies during pulmonary artery angiography (13, 14) or, less frequently, during a hybrid procedure.

Catheter-based interventions for PBS include high pressure or low pressure balloon angioplasty and cutting balloon angioplasty for resistant lesions. (15) Cutting balloons produce precise and controlled linear incisions in the lesion site, minimizing barotrauma injury compared to high pressure balloons. Twenty percent of our patients were treated with conventional balloon angioplasty and 8% of these patients with resistant lesions, defined as increase of initial minimal lumen diameter <50% with a pressure of 10 ATM, underwent cutting balloon angioplasty.

In our strategy, balloon angioplasty is reserved for young children with distal isolated stenosis at vessel bifurcation.

Angioplasty with stent implantation was first described by Mullins et al. by the end of the ‘80s (16, 17) to support the affected area and avoid restenosis due to elastic recoil. We indicated stent placement in compliant elastic lesions with significant elastic recoil after conventional balloon angioplasty, central or proximal lesions, lesions due to external compression (typically left pulmonary branch compression caused by neoaorta after Norwood surgery), resistant lesions after conventional balloon angioplasty or after the use of cutting balloon and stenosis at a surgical site in the early postoperative period. (18) Stent implant produces greater luminal diameter of the treated artery and reduces the incidence of short-and long-term complications compared with catheter balloon angioplasty. It has also been shown that stents can be redilated to adapt stent diameter to patient growth in children (19) or to treat restenosis due to neointimal proliferation. (20)

Success rates have been previously defined. (21) In our experience, there was a significant improvement in all the parameters. The diameter of the treated stenotic segment increased by ≥50%, the pressure gradient across the stenosis decreased by ≥50% and there was a significant reduction in RV systolic pressure.

The incidence of procedure-related complications was 8% and included stent migration requiring implantation of a second tandem stent in one patient and thrombosis distal to the stenosis of the treated branch in the other patient. Both patients recovered without residual lesions. During follow-up, the incidence of complications was 12% and included one stent fracture (Palmaz-Genesis™, Cordis) with embolization of the distal fragment without consequences, one complete occlusion of a self-expandable stent implanted in a pulmonary artery with complex anatomy in single ventricle physiology and one death during hybrid approach after Fontan-Kreutzer surgery that was unrelated to prior stent implantation.

We preferred to use stents delivered through small sheaths that can be redilated in the future to accompany somatic growth in pediatric patients. We chose stainless steel or platinum stents, which could also be covered with polytetrafluoroethylene in selected cases when there was risk of rupture.

We implanted a self-expandable stent in a patient who presented critical stenosis due to traction of the left pulmonary artery branch after ipsilateral B-T shunt. The decision was based on the complex anatomy and extreme angulation of the lesion in order to rectify it before the implantation of a balloon expandable stent. Unfortunately, the patient developed a complete occlusion with stent collapse during follow-up. Likewise, covered stents are selected in cases of wall vessel lesions (previous dissections or aneurysms),
very dissimilar initial and final vessel diameter, and in cases presenting associations that can be treated simultaneously with covered stent implant (simultaneous occlusion of a B-T shunt or RV outflow tract occlusion in single ventricle hearts, among others).

We used the femoral veins or the internal jugular veins to access the lesions as they are the easiest and most direct approaches. In cases of venous access obstruction due to multiple previous interventions, the transhepatic approach was successfully used. A hybrid approach was performed in young children requiring larger stents to treat complex lesions and in whom the larger sheaths were contraindicated due to patient size, or when the patient required a concomitant surgical approach.

Finally, we think that the possibility of stent placement in the pulmonary circuit has been one of the most important therapeutic advances of the last decade in interventional cardiology of congenital heart defects. The procedure requires appropriate training, a tough learning curve and a special expertise to deal with complications. Scientific discussion and teamwork between surgeons and interventional cardiologists are crucial to accomplish therapeutic success in these patients. Continuous technological advances in the development of less traumatic, more flexible and low-profile devices (not requiring large sheaths for their placement) and the introduction of biodegradable material will expand the horizon of interventional cardiology in the management of this challenging condition.

CONCLUSIONS
Stent implant in pulmonary artery branch stenosis is a safe and feasible though challenging technique in patients with congenital heart defects.

The immediate clinical and hemodynamic outcomes were adequate and persisted during mid and long-term follow-up. Pediatric patients will require future redilation to accommodate somatic growth.

Conflicts of interest
None declared. (See author’s conflicts of interest forms in the web / Supplementary Material)

REFERENCES