ORIGINAL ARTICLE

Right Ventricular Outflow Tract Stenting in Severe Tetralogy of Fallot: an Option to the Blalock-Taussig Shunt

Implante de stent en tracto de salida de ventrículo derecho en tetrología de Fallot grave: alternativa a la anastomosis de Blalock-Taussig

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ABSTRACT

Background: The initial management of patients with Tetralogy of Fallot (TOF) associated with unfavorable anatomy and significantly reduced pulmonary blood flow is controversial and still a clinical challenge.
Methods: We conducted a multicenter, retrospective and observational study in consecutive neonates and young infants with diagnosis of TOF treated at four different centers of the city of Cordoba, Argentina, who underwent (RVOT) stenting as the first approach to alleviate their congenital heart defect. The indication of a primary palliative intervention was decided by the cardiovascular surgery team in each participating center. An initial percutaneous approach was considered under the following circumstances: complex anatomy (pulmonary branches with Z score ≤ -2.5), cardiogenic shock, cyanotic spells, low weight or significant comorbidities (necrotizing enterocolitis, prematurity, kidney dysfunction or convulsions).
Results: From August 2017 to May 2018, 6 patients with symptomatic TOF underwent RVOT stenting. Mean age was 39.3 days (9-87), mean weight was 3.60 kg (2.2-5.4) and 66% were girls. Coronary or peripheral stents were used with diameter between 4.0 mm and 6.0 mm. Systemic arterial oxygen saturation was 66.4% (42-77) before the procedure and increased to 90.6% (86-96) before discharge (p <0.001) There were no complications during the procedure. Patients were hospitalized for an average of 7 days (1-13) and mean follow-up was 106.8 days (4-292). There were no deaths at 30 days.
Conclusions: Right ventricular outflow tract stenting in patients with TOF and unfavorable anatomy is a reasonable option for neonates and young infants as an alternative to the modified Blalock-Taussig shunt or initial primary corrective surgery.

Key words: Tetralogy of Fallot –Stent - Right ventricular outflow tract - Blalock-Taussig anastomosis

RESUMEN

Introducción: El manejo inicial de pacientes con tetralogía de Fallot (TOF) asociado a una anatomía desfavorable y flujo vascular pulmonar significativamente reducido es controversial y continúa siendo un desafío clínico.
Material y métodos: Estudio multicéntrico, retrospectivo, observacional. Se incluyeron pacientes consecutivos (neonatos y lactantes menores) con diagnóstico de TOF asistidos en cuatro centros diferentes de la ciudad de Córdoba, Argentina, que recibieron *stent* en tracto de salida de ventrículo derecho (TSVD) como abordaje inicial de su cardiopatía congénita. La indicación de intervención paliativa inicial fue consensuada en reunión del equipo cardiovascular en cada centro participante. Una anatomía compleja (ramas pulmonares con Z *score*≤ -2,5), presentación en *shock* cardiogénico o en crisis de cianosis, bajo peso o comorbilidades significativas (enterocolitis necrotizante, prematurez, insuficiencia renal, convulsiones) inclinaron la decisión hacia un abordaje percutáneo inicial.
Resultados: Entreagosto de 2017 hasta mayo de 2018, 6 pacientes con TOF sintomáticos recibieron stent en TSVD. La edad media fue 39,3 días (9-87), el peso medio fue 3,60 kg (2,2-5,4) y el 66% eran de sexo femenino. Los *stents* utilizados fueron coronarios o periféricos con un diámetro que varió entre 4,0 y 6,0 mm. La saturación periférica previa a la colocación del *stent* fue de 66,4% (42-77) incrementado a 90,6% (86-96) previo al alta (p<0,001). No se registraron complicaciones durante la intervención. El tiempo de internación fue de 7 días (1-13) y el tiempo de seguimiento fue de 106,8 días (4-292). No hubo mortalidad a los 30 días.
Conclusión: El implante de *stent* en TSVD en pacientes con TOF y anatomía desfavorable es una opción razonable en neonatos y lactantes menores como alternativa a la realización de una anastomosis de Blalock-Taussig modificada o corrección primaria inicial.

Palabras clave: Tetralogía de Fallot - *Stent* - Tracto de salida de ventrículo derecho -Anastomosis de Blalock-Taussig

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INTRODUCTION

The initial management of patients with Tetralogy of Fallot (TOF) associated with unfavorable anatomy and significantly reduced pulmonary blood flow is controversial and still a clinical challenge. Primary repair in neonates is uncommon due to elevated early morbidity and mortality and to the frequent need for reoperations. (1-3) Modified Blalock-Taussig shunt (MBTS) is the initial strategy in these patients, but it is also associated with elevated indices of complications as acute narrowing or distortion of the pulmonary artery branches, excessive pulmonary blood flow and, occasionally, mortality. (4)

Percutaneous right ventricular outflow tract (RVOT) balloon dilation has been described as initial palliation, but the method was abandoned because of unfavorable outcomes, including frequent technical failure and complications mainly associated with subvalvular stenosis of muscular etiology due to the anterosuperior displacement of the infundibular septum. (5, 6)

At the beginning of the 21st century, many centers have begun the publication of encouraging and reproducible experiences with RVOT stenting in neonates and young infants with symptomatic TOF, as an option to MBTS as initial strategy.

This multicenter study summarizes our initial experience in neonates and young infants with symptomatic TOF undergoing RVOT stenting as initial palliation for their cyanotic congenital heart defect.

METHODS

A multicenter, retrospective and observational study was conducted in consecutive neonates and young infants with diagnosis of TOF treated at four different centers of the city of Cordoba, Argentina, who had undergone RVOT stenting as the initial approach to alleviate their congenital heart defect. All the procedures were performed by the same interventional cardiologist (AP).

The indication of the initial palliative intervention was agreed with the cardiovascular surgery team in each participating center. An initial percutaneous approach was considered under the following circumstances: complex anatomy (pulmonary branches with a Z score ≤ -2.5), cardiogenic shock or cyanotic spells at presentation, low weight or significant comorbidities (necrotizing enterocolitis, prematurity, kidney dysfunction or convulsions).

The Z scores for each cardiac structure reported were obtained according to each patient's age, weight and height, from the Z –Scores of Cardiac Structures- Wessex Data: (http://parameterz.blogspot.com.ar/2008/09/z-scores-of-cardiac-structures-wessex.html.)

Technique

All procedures were performed under general anesthesia and orotracheal intubation. The inotropic agents and prostaglandins that the patients received in the intensive care unit were continued and adapted after stent implant. The patients were positioned on the catheterization table with the arms elevated to allow better visualization of the cardiac structures in lateral and oblique projections. All the procedures were accessed via the right femoral vein. All patients received IV heparin 50 IU/kg and antibiotic prophylaxis with IV cephalosporin 50 mg/kg.

The initial right ventricular angiogram was performed through a diagnostic catheter (Arrow-Berman^{TM}, USA) placed in the apex of the right ventricle in 45° right anterior oblique and 90° straight lateral projections. Thereafter, measurements of the main and pulmonary artery branches, pulmonary valve annulus and distal portion of the RVOT were made. Selection of stent type and dimensions (diameter and length) was guided according to the size of the patient, the dimensions of the outflow tract, the distance to cover between the RVOT and the main pulmonary artery and the anticipated duration of palliation. As a general rule, the stent diameter was chosen to approximate the distal main pulmonary artery diameter, with a length covering the distal muscular RVOT, the pulmonary valve and the proximal main pulmonary artery, trying to respect the origin of both pulmonary artery branches in its bifurcation (Figure 1).

Coronary or peripheral pre-mounted stents were used. A 4 Fr right Judkins guide catheter (Cordis^{TM}, USA) was advanced through the stenosis and a 0.014" coronary guidewire was placed in the distal right pulmonary artery as extra support (Boston Scientific^{TM}, USA). Then, the right Judkins catheter was removed and a 6 F right Judkins guide catheter (Cordis^{TM}, USA) with a Y connector hemostasis valve was introduced, through which the selected stent was advanced. With the help of the guide catheter, the stent was positioned in the ROVT, occupying the infundibulum, the pulmonary valve and part of the main pulmonary artery.

A manual pump was used for stent deployment under a nominal pressure of 10 to 14 atm. The balloon and the coronary guide catheter were removed and right ventriculography was repeated in the mentioned projections with the same guide catheter used for stent implant. In two patients, right ventriculography evidenced that the RVOT was not completed covered by the stent, and stent overlapping was required.

Those patients who remained stable were evaluated by

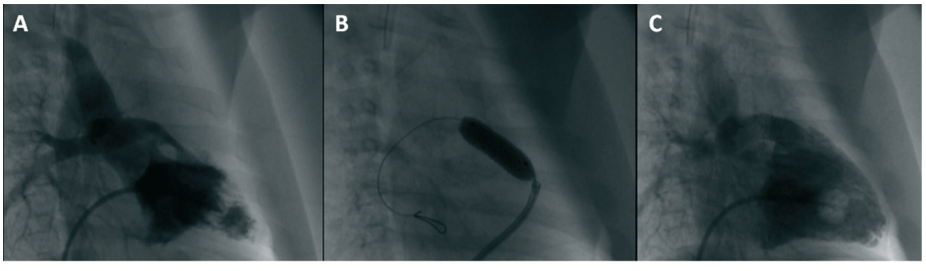

Fig. 1. (**A**) Right ventricular outflow tract angiograms in 45° right anterior oblique projection with subpulmonary stenosis due to severe anterosuperior displacement of the infundibular septum. (**B**) Balloon insuflated during stent implant. (**C**) Final result showing improved size of the right ventricular outflow tract after stent implant.

the anesthesiologists and cardiovascular intensivists, and were extubated in the catheterization laboratory before returning to the intensive care unit. In the other patients, the endotracheal tube was removed when their clinical status improved. Patients who experienced an increase of oxygen saturation in excess of 20% were treated with loop diuretics twice daily. Once oral feeding was tolerated, daily aspirin administration (5–10 mg/kg) was started and maintained until complete repair with stent removal.

Statistical analysis

Categorical variables are expressed as percentage and continuous variables as mean and range. The non-parametric Mann-Whitney test for independent variables was used to compare continuous variables. All the statistical calculations were performed using SPSS 17.0 software package.

Ethical considerations

Right ventricular outflow tract stenting as an alternative to MBTS was approved by the ethics committee of each institution and all the parents or legal guardians signed a specific consent form for the procedure. The study was conducted following the recommendations of the Declaration of Helsinki for observational studies.

RESULTS

From August 2017 to May 2018, six patients (neonates and young infants) with symptomatic TOF underwent RVOT stenting as an alternative to MBTS (Table 1). Mean age was 39.3 days (9-87), mean weight was 3.60 kg (2.2-5.4) and 66% were girls. Four patients (66%) had cyanotic spells and three (50%) received prostaglandins and required mechanical ventilation (MV). Beta blockers were administered to four patients (66%). The procedure was elective in two patients and urgent in the remaining patients. The following diastolic dimensions were obtained: infundibular region 2.2 mm (1.5-2.9) (Z score -25.05), pulmonary annulus 2.82 mm (2.4-3.5) (Z score -10.28), main pulmonary artery 3.26 mm (2.3-4.5) (Z score -7.13), right pulmonary artery 3.44 mm (2.9-4) (Z score -3.07), and left pulmonary artery 3.08 mm (2-3.8) (Z score -3.51). Systemic arterial oxygen saturation was 66.4% (42-77) before the procedure and increased to 90.6% (86-96) before discharge ($p < 0.001$) (Figure 2).

Coronary or peripheral stents were used with a diameter between 4.0 mm and 6.0 mm. Two patients required stent overlapping to cover the entire RVOT. There were no complications during the procedure. Patients were hospitalized for an average of 7 days (1-13) and mean follow-up was 106.8 days (4-292). There were no deaths at 30 days of the procedure nor until corrective surgery. Two patients were successfully operated on at the age of 7 and 10 months and required transannular patching and subtotal stent removal (Figure 3). One patient presented frequent ventricular premature beats after the intervention needing antiarrhythmic agents. Two patients hospitalized due to cyanotic spells with severe hypoxemia requiring MV presented convulsions and were medicated with phenobarbital and levetiracetam, respectively.

Brain scans did not show signs of ischemia or significant bleeding. After discharge, all the patients were followed-up by their attending cardiologist with clinical control of systemic oxygen saturation, 12-lead electrocardiogram, chest x-ray and Doppler-color echocardiography (Figure 4). Before complete corrective surgery, cardiac catheterization was performed to evaluate the RVOT, the stent implanted and the growth of the pulmonary artery branches.

DISCUSSION

Most of the asymptomatic patients with TOF, presenting large, confluent pulmonary arteries, undergo

Table 1. Demographic data, clinical status, intevention, stents used and complications

Patients	Age (days)	Sex	Weight (kg)	Cyanotic spells	MV	PG	Em	SaO2 before	SaO2 after	Stent	Surgery	Complications
#1	9	F	2.2	Yes	Yes	Yes	Yes	69	93	Rebel 4.5 x 16 (one)	Yes	IV amiodarone
#2	58	F	2.9	Yes	Yes	Yes	Yes	42	86	Express Vascular 6 x 18 (two)	Yes	Convulsions before/after Levetiracetam
#3	45	F	4.65	No	No	No	No	72	90	Integrity 4.0 x 22 (two)	No	No
#4	19	M	2.9	Yes	Yes	Yes	Yes	72	88	Rebel 4.0 x 20 (one)	No	Convulsions after Phenobarbital
#5	87	M	5.4	No	No	No	No	77	96	Express Vascular 6 x 18 (onw)	No	No
#6	18	F	3.6	Yes	No	No	Yes	74	98	Rebel 4.0 x 20 (one)	No	No

MV: Mechanical ventilation. PG: Prostaglandins. Em: Emergency. SaO2 before: Oxygen saturation before stenting. SaO2 after: Oxygen saturation after stenting.

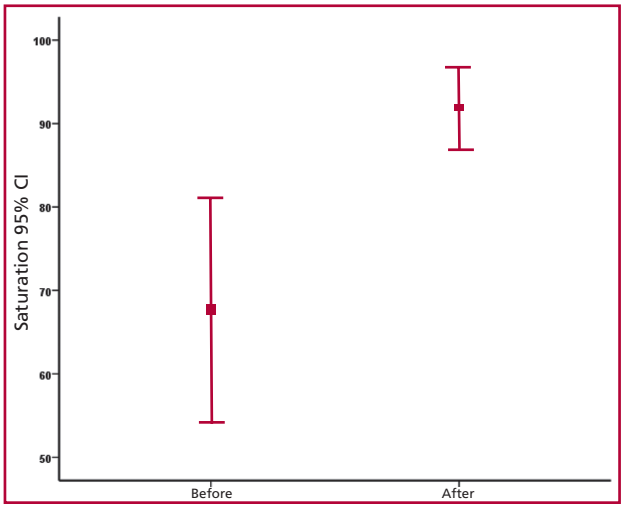

Fig. 2. Systemic oxygen saturation before and after stenting

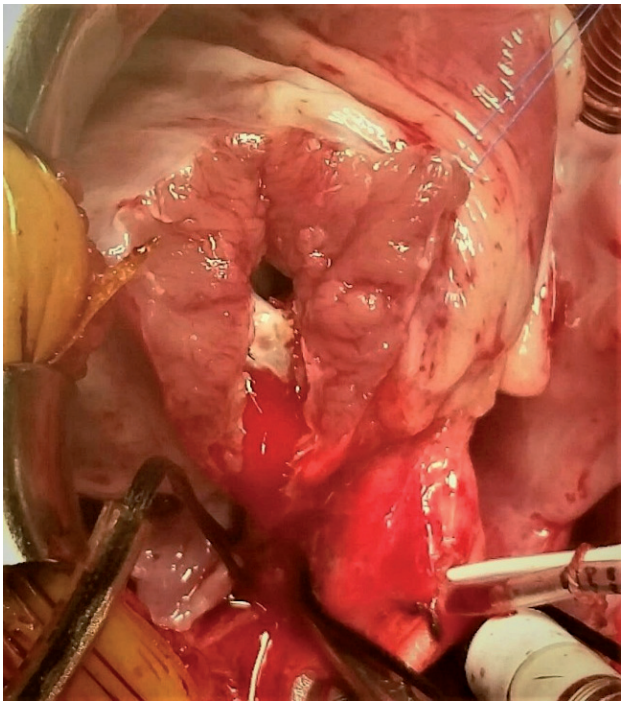

Fig. 3. Image during complete corrective surgery showing the right ventricular outflow tract with the stent partially removed.

primary surgical repair between the age of 3 and 9 months weighing approximately 5-9 kg, with excellent outcomes. (1-2) Newborns or young infants requiring early interventions usually depend on prostaglandins or have severe cyanosis with significantly reduced anterograde pulmonary flow as a result of unfavorable anatomy of the RVOT (infundibular or valvular stenosis) or of the pulmonary vascular tree (hypoplastic pulmonary artery branches or presence of collaterals). Initial MBTS is an effective strategy in symptomatic patients with inadequate anatomy or significant comorbidities (prematurity, low body weight, infections, and neurological, kidney and gastrointestinal disorders), but is associated with high short- and long-term mortality. (4) Long-term complications, as pulmonary artery branch distortion, vocal cord or diaphragmatic paralysis, excessive pulmonary blood flow and those associated with thoracotomy/sternotomy also have a long-term impact. (13)

Percutaneous interventions in congenital heart defects have evolved over the past 15 years. Consequently, premature patients and neonates with cyanosis have been treated with stent implant in patent ductus arteriosus or dysfunctional MBTS to ensure an effective pulmonary blood flow. Based on these experiences, RVOT stenting as an option to MBTS is a safe, effective and reproducible initial strategy. (11)

Our initial experience included severely compromised patients with significant cyanosis, hypoxemia requiring MV and prostaglandins, and with very small pulmonary arteries, as demonstrated by the Z score. These patients were considered at high risk for surgical treatment. With this percutaneous intervention the patients achieve better hemodynamic status and stability, as the systemic venous return is directed towards the pulmonary circulation, increasing systemic oxygen saturation, and in turn avoids a reduction in diastolic aortic perfusion pressure.

These changes improve coronary perfusion in contrast to MBTS. Thoracotomy/steronotomy, sometimes needing cardiopulmonary bypass, with the potential complications these interventions entail, are also avoided, especially in the neonatal period. According to published experiences, RVOT stenting promotes better pulmonary artery growth (angiographic Nakata and McGoon indexes and echocardiographic measurements) due to increased anterograde pulmonary blood flow, compared with the flow provided by MBTS. (14-15)

Coronary or peripheral balloon-expandable stents were used with a diameter between 4.0 mm and 6.0 mm. We usually try to use the smallest stents possible to limit pulmonary blood flow and avoid excessive pulmonary circulation or right ventricular dysfunction caused by free pulmonary valve regurgitation. The diameter of the stent was chosen to approximate that of the distal main pulmonary artery, with a length covering the distal muscular RVOT, the pulmonary valve and the main pulmonary artery before its bifurcation. As a consequence of this strategy, some patients required stent overlapping to cover the entire length of the outflow tract, avoiding the development of early subpulmonary (muscular portion) stenosis.

The decision to cover the entire RVOT, including the pulmonary valve and the main pulmonary artery, was based on the experience of other centers (8, 11) which as a result of respecting the pulmonary valve during initial stenting had a high incidence of early reinterventions owing to residual outflow tract stenosis. Due to the unfavorable anatomy of this subgroup

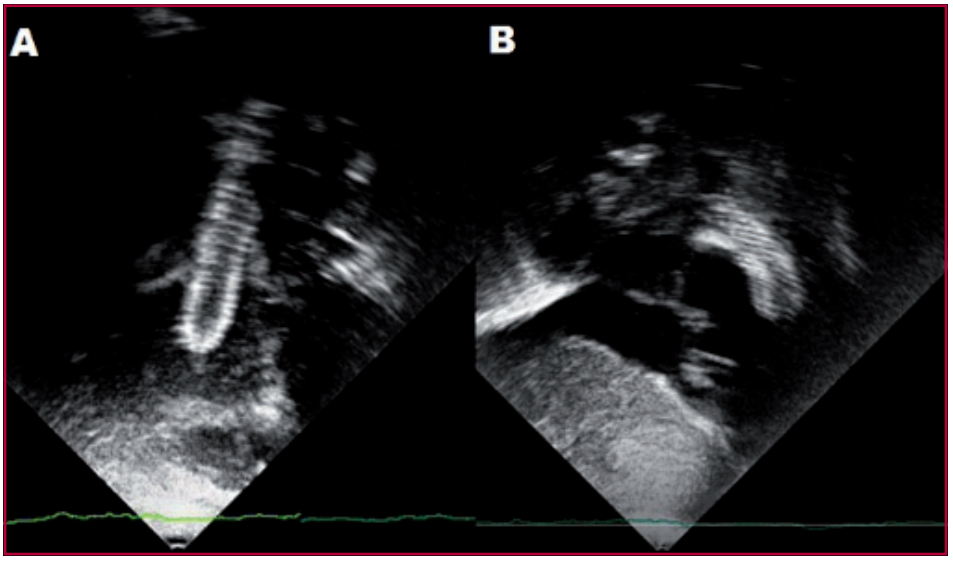

Fig. 4. Color-Doppler echocardiography illustrating subcostal long-axis view (**A**) and subcostal short-axis view (**B**) of the stent implanted in the right ventricular outflow tract.

of patients, most, if not all, will invariably require transannular patching during complete corrective surgery.

In the future, the implantation of drug eluting stents to prevent intimal neoproliferation, as well as bioabsorbable stents will play an important role in this condition.

According to published series, (11, 16) between 44% and 95% of stents are partially or completely removed during surgical correction, depending on the time since they were implanted. In centers with high volume of patients, cardiopulmonary bypass time was similar between patients with stents implanted in the RVOT, those undergoing primary corrective surgery with transannular patching or those undergoing MBTS as initial palliation. (10, 11, 16) However, in an unpublished personal communication, Dr. Marcelo Jatene from São Paulo, Brazil, found a significant difference in cardiopulmonary bypass time in patients requiring stent removal during corrective surgery compared with control patients with classic TOF.

Two of our patients developed convulsions: one of them before and the other after the procedure, with normal brain imaging studies. In both patients, body weight was <3 kg; they presented with cyanotic spells, requiring MV and infusion of prostaglandins, and the operation was performed on an urgent basis. We consider that their functional neurological disorder was mainly associated with the severity of their clinical presentation.

This study demonstrates the efficacy and safety of RVOT stenting as a bridge to corrective surgery. Future randomized clinical trials would be necessary to identify the adequate initial strategy in neonates and young infants with severe TOF presenting early symptoms. We believe that these studies should compare RVOT stenting with MBTS and initial primary corrective surgery in this subgroup of patients.

CONCLUSIONS

The initial results of our experience with RVOT stenting in patients with severe TOF, in terms of survival and improved hemodynamic parameters, reproduce the results of international series. The criteria used for selecting patients are crucial for this intervention to become a reasonable alternative to MBTS or initial primary corrective surgery for neonates and young infants.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

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