Pediatric Cardiology
https://doi.org/10.1007/s00246-020-02321-2

ORIGINAL ARTICLE

Initial Experience in Chile with Stent Implantation in the Right Ventricle Outflow Tract in High-Risk Patients with Tetralogy of Fallot

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Received: 27 September 2019 / Accepted: 17 February 2020

Abstract
Tetralogy of Fallot (ToF) treatment is difficult in patients with surgical risk factors or unfavorable anatomy. Stent implantation in the right ventricular outflow tract (RVOT) is an option for these patients. We report our initial experience in Chile with RVOT stenting in patients with ToF. Retrospective and descriptive study conducted in three pediatric cardiovascular centers in Chile between 2012 and 2015, including all ToF patients with stent in the RVOT as first procedure. Clinical records, echocardiographic, interventional, and surgical reports were reviewed for demographics and information of RVOT and pulmonary arteries. 12 newborns with ToF were included (75% female). Median age was 20 days (1–70) and mean weight was 2178 g (1400–3414). Saturations increased after the procedure from 74.3% (55–88) to 88.5% (80–98%), ($p < 0.01$). No complications or mortality were related to interventions. Follow-up was 11 months (7–36). Median right and left pulmonary arteries *Z*-score increased from −4.0 (−5.2 to −0.3) and −1.5 (−4.8 to −0.26) to +0.53 (0.0 to 2.2) and +1.1 (0.5 to 2.9), ($p < 0.05$), respectively. Nakata index increased from 63 mm^2/mm^2 (35 to 143) to 162 mm^2/mm^2 (107 to 197), ($p < 0.05$). Surgical repair was performed at a median of 4 months (2–7). Transannular patch repair was necessary in all patients and there was no surgical mortality. RVOT stenting is a safe and useful option for patients with ToF and surgical risk factors or unfavorable anatomy. It increases the pulmonary blood flow, improving saturation and pulmonary artery growth as a bridge for surgical repair.

Keywords Tetralogy of Fallot · Stent · Right ventricular outflow tract · High risk · Neonate

Introduction

Tetralogy of Fallot (ToF) is the most common cyanotic congenital heart disease. Clinical manifestations are related to the severity of right ventricle outflow tract (RVOT) obstruction, as well as the anatomy of the main pulmonary artery and the development of its branches. Nowadays, the treatment of choice is complete surgical repair in one stage during infancy when weight and anatomical key factors are favorable [1, 2]. Nevertheless, there is a high-risk subgroup of symptomatic patients (cyanotic) with low or very low birth weight, prematurity, comorbidities, or unfavorable anatomy in which one stage repair is associated with higher morbidity and mortality rates, so a delay in timing for corrective surgery is desirable in order to obtain more favorable conditions with better weight and improved pulmonary artery growth. When a staged repair strategy is preferred, Blalock-Taussig shunt (BTS) or right ventricular to pulmonary conduits with no ventricular septal defect closure are the most utilized alternatives [3–6].

Palliative procedures such as BTS, patent ductus arteriosus (PDA) stent, or RVOT stenting are all valid options in critically ill and hypoxic patients. The later is an attractive option to promote antegrade pulsatile pulmonary blood flow, thus improving and stabilizing patient's condition and allowing pulmonary artery growth, and better weight for surgery

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Published online: 27 February 2020

and without the complications observed in the BTS, such as the risk of possible distortion of the pulmonary artery branches, phrenic nerve injury, chylothorax, obstruction of shunt, or pulmonary overflow [3, 7, 8].

Since Gibbs et al. [9] reported the first cases in RVOT stenting, several authors have reported this procedure [4, 7, 8], suggesting that this approach could be an alternative, delaying the time of surgery, to avoid the high-risk factors involved when trying to repair these infants. In this paper, we review our initial experience in RVOT stenting for symptomatic ToF patients from the only three pediatric cardiac surgery centers that exist in Chile.

Patients and Methods

This is a retrospective study including all ToF patients treated with one or more stents implanted in the RVOT as initial palliative approach from April 2012 to March 2015. We included patients from the only 3 pediatric cardiac surgery centers that exist in Chile. The local Institutional Review Board at each participating institution approved the study. Written consent was obtained for every patient. We retrospectively reviewed demographics and clinical data, anatomic dimensions (RVOT obstruction degree, diameters at infundibulum, pulmonary valve annulus, main pulmonary artery and its branches), and adjusted by *Z*-score and Nakata index. Basal pulmonary artery diameters were measured in all the patients from transthoracic echocardiogram before the procedure, on pulmonary angiograms during the procedure, and then on transthoracic echocardiogram during the follow-up before the surgical repair. We also obtained hemodynamic data from cardiac catheterization, interventional procedure details, surgical reports, and medium-term follow-up. Patients were assigned for RVOT stenting on a case-to-case basis after a local multidisciplinary meeting in each center, with no external interferences.

Statistical Analysis

Data are expressed as mean ± SD or median (range). T paired student's test was used to compare before and after parameters for each patient. A value of $p < 0.05$ was considered statistically significant.

Procedure

All procedures were made at the catheterization laboratory under general anesthesia. Vascular accesses were the femoral vein or perventricular after sternotomy. Heparin 100 UI/Kg and antibiotic prophylaxis with cefazolin 100 mg/kg/day were administered in all cases. Right ventriculography was performed in different projections as needed to obtain accurate measurements of RVOT, main pulmonary artery, and pulmonary valve (Fig. 1a). Vascular 4–7 French sheaths were utilized. The pulmonary valve was crossed with a 0.018 hydrophilic or 0.014 high-support stiff coronary guidewire. Stents were selected based on measurements at the narrowest point and length of RVOT, pulmonary valve, or main pulmonary artery. Premounted stents were chosen to be at least double the narrowest point or 1–2 mm larger than pulmonary valve annulus and covering the infundibular length and pulmonary valve annulus. Multiple hand injections were made to be sure of proper stent implantation (Fig. 1b).

Results

Demographic Data

Selected patients were all symptomatic ToF infants with deep cyanosis, hypoxic spells or critically ill, presenting with severe pulmonary flow obstruction and/or pulmonary artery underdevelopment, depending on prostaglandin E1 infusion. Many of them were preterm babies and/or very low weight at birth.

During the studied period, 12 patients underwent stent implantation in the RVOT. Nine (75%) were female. In all of the cases the stents were implanted in the desired position, however, in one patient, a partial stent migration occurred 24 h after the procedure without hemodynamic detriment. Median age at the procedure was 20 days (range 1–70 days). Median gestational age was 34 weeks (range 28–40 weeks) and mean weight of 2178 g (range 1400–3414 g). Preterm newborn patients were in 58.3% (7/12) with a weight less than 2500 g and 33% of them with a significant-associated morbidity (sepsis, chronic respiratory disease, and respiratory distress syndrome).

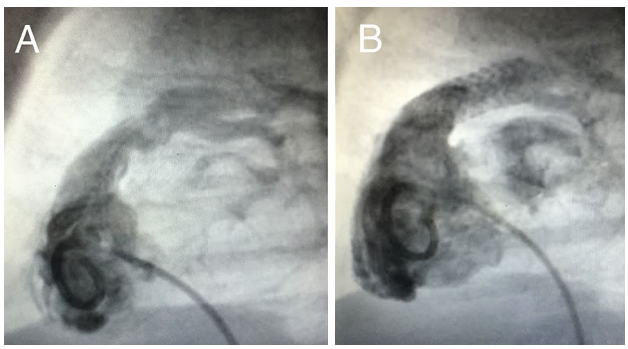

Fig. 1 Right ventriculography in lateral projection, in a patient with tetralogy of Fallot before (**a**) and after right ventricle outflow tract stent implantation (**b**). Note severe basal infundibular stenosis and small pulmonary arteries. After stent implantation, complete relief of outflow tract obstruction was demonstrated with improvement in blood flow to hypoplastic pulmonary arteries

A total of 14 stents were implanted in 12 patients (2 patients received 2 stents). The implanted stents were Palmaz Blue (Cordis®) in 9 (64.3%), Multilink (Abbott®) in 3 (21.4%), 1 Kaname (Terumo®) (7.1%), and 1 Palmaz Genesis 2420 (Cordis®) (7.1%). In 8 patients (66.7%), the procedure was performed with a perventricular hybrid approach. Median stent diameter implanted was 5.25 mm (range 3.5–8.0 mm) with a stent to RVOT diameter ratio of 1.88 ± 0.26 (range 1.2–2.1) and stent length ranged from 12 to 24 mm with a median of 15 mm. All the patients had Prostaglandin E1 infusion at the moment of the procedure and it was discontinued after demonstrating antegrade flow throughout the RVOT. Oxygen saturation before the procedure was mean of 74.3% (range 55–88%). A significant improvement in oxygen saturation was demonstrated 24 h after the procedure with a mean of 88.5% (range 80–98%) ($p < 0.01$).

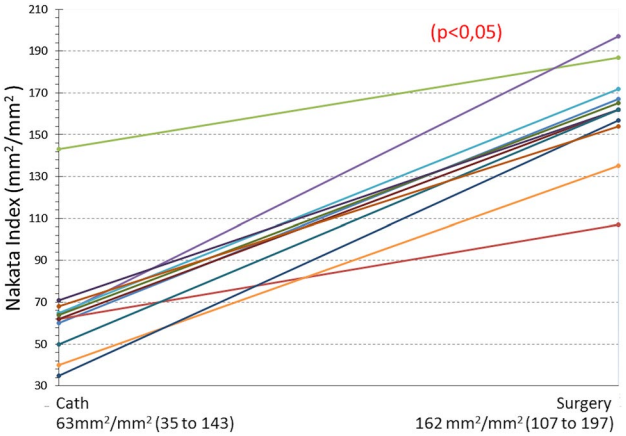

Fig. 3 Nakata index at the time of stenting procedure and before surgery, demonstrating significant growth of both branches of the pulmonary artery ($p < 0.05$)

Pulmonary Arteries Anatomy and Growth (Figs. 2 and 3)

The median basal pulmonary annulus was 3.8 mm (range 2.7–6.0 mm) with a *Z*-score of − 3.94 (range − 6.3 to − 1.6). The right pulmonary artery basal diameter was 2.1 mm (range 1.8–3.6 mm) with a *Z*-score of − 4 (range − 5.2 to − 0.3) and the left pulmonary artery basal diameter was 2.9 mm (range 1.9–3.8 mm) with a *Z*-score of − 1.5 (range − 4.8 to − 0.26). The basal Nakata index was mean of 63 mm^2/m^2 (range 35–143 mm^2/m^2). During the waiting time for surgical repair, a significant growth of pulmonary arteries was observed. The right pulmonary artery increased to a mean of 5.2 mm (range 4.2–6.7 mm) with a *Z*-score of 0.53 (range 0.0 to + 2.2) and the left pulmonary artery increased to a mean of 6.0 mm (range 3.8–6.5 mm) with a *Z*-score of 1.1 (range + 0.5 to + 2.9). The Nakata index at the moment of the surgical repair was mean of 162 mm^2/m^2 (range 107–197 mm^2/m^2).

Surgery

All patients underwent corrective surgery at median age of 4 months (range 2–7 months) with a mean weight of 5.7 ± 0.9 kg (range 3.4–7.6 kg). During the surgery in 11 patients (91.7%), the stent was completely explanted (Fig. 4). In all the patients, a transannular patch (TAP) was used as repair technique. After the surgery, the inpatient stay was a median of 7 days (range 6–32 days). One patient developed severe tricuspid regurgitation after the surgery due to tricuspid subvalvular apparatus distortion after the

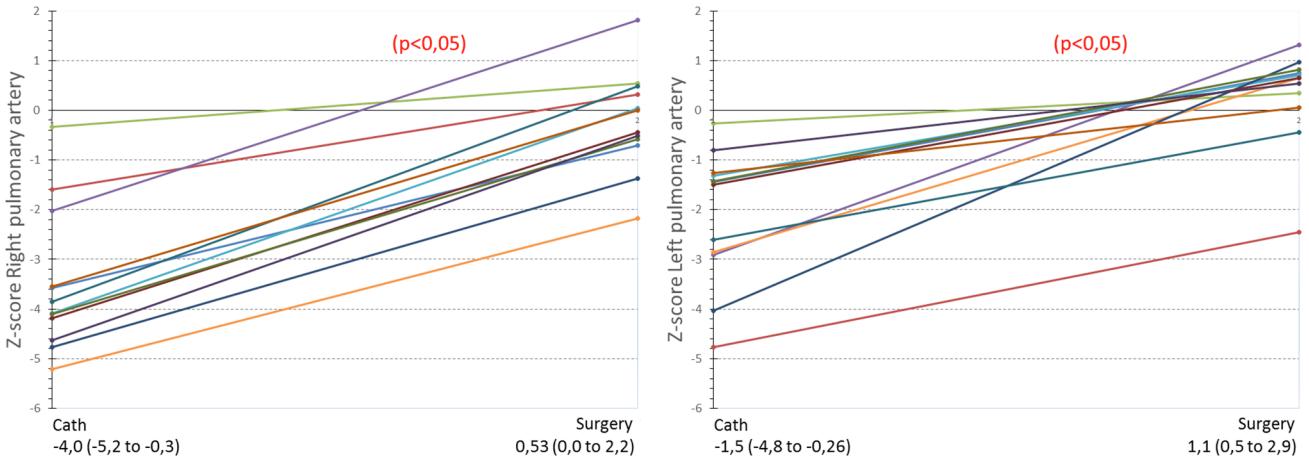

Fig. 2 Pulmonary arteries diameter *Z*-score at the time of stenting procedure and before surgery, demonstrating significant growth of both branches of the pulmonary artery ($p < 0.05$)

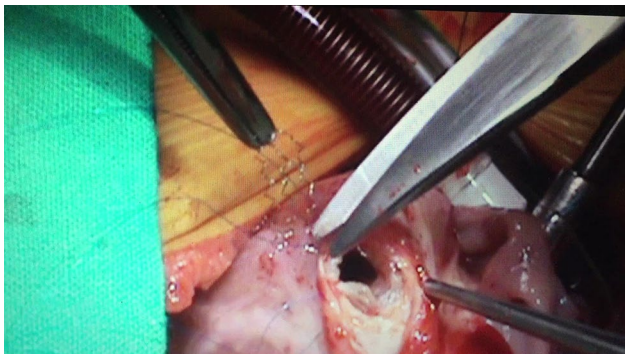

Fig. 4 Intraoperative image during the ToF surgical repair showing the moment when the stent is removed from the right ventricle outflow tract

stent explantation and subsequently underwent prosthetic valve replacement. No mortality was reported for the surgical repair.

Discussion

In symptomatic neonates and young infants with ToF and risk factors like prematurity, birth weight less than 3 kg, associated morbidities, and hypoplastic pulmonary arteries have a higher morbidity and mortality when undergo surgical palliation with BTS or early surgical repair (mortality rate of 7.3% and 7.8%, respectively) [6, 10–14]. The Society of Thoracic Surgeons has suggested that the best surgical results could be achieved when surgical repair is performed between 3 to 12 months of age [6]. Due to these results, there has been a growing interest in palliative treatment with stenting of the RVOT in high-risk patients. Initial studies have reported that the approach used in this study is a safer alternative to surgical systemic to pulmonary shunts, improving pulmonary blood flow and avoiding the risk of distortion of the pulmonary artery branches [7, 8].

Recent studies have compared the medium-term results of the RVOT stent with BTS without finding differences in survival between the strategies [15]. Intensive care and hospital stay duration, perioperative complications, and the need for re-surgery or early complete repair was minor for the RVOT stenting group [15]. On the other hand, comparisons between RVOT stenting and neonatal repair have shown comparable short-term and long-term outcomes [16].

In our study, we observed a statistically significant improvement in oxygen saturation after the procedure and also a significant improvement in the size of the pulmonary artery branches after RVOT stenting. Our patients developed normal size pulmonary arteries at the time of surgical repair measured by *Z*-score and Nakata Index values. This permitted all our patients to undergo a delayed surgical repair without mortality in spite of their original risk factors. Similar findings have been described by others [17, 18].

A key aspect of this procedure is the adequate selection of the stent length. An additional stent implantation may be necessary to cover the entire infundibular obstruction in the RVOT before leaving the catheterization laboratory. This was necessary in 2 patients in our study (16.6%), in others studies this was observed from 13.3 to 44% patients and from 2 to 4 stents implanted [15, 17, 19, 20].

The adverse event rate for this procedure has been reported to be up to 5.7% [19]. The more frequent complications include cardiac tamponade, stent fracture, arrhythmia, neointimal proliferation inside the stent, infective endocarditis of the stent and death. In our experience, we did not have any severe adverse events related to the stenting procedure. There was one patient that had distal stent migration 24 h after the implant, but did not require any reintervention or re-starting of the prostaglandin infusion. One patient had severe tricuspid regurgitation after surgical stent removal during corrective surgery, probably secondary to subvalvular tricuspid apparatus injury during surgical stent removal. In others studies, this complication has been observed more frequently at the time of stent implantation in the RVOT, probably due to alteration of the subvalvar apparatus of the tricuspid valve [15, 20]. Procedure-related morbidity occurred in our study was less frequent and less serious compared to other palliative procedures such as the PDA stent and much less than the BTS group [21]. Mortality was much higher in the PDA stent or BT shunt than in our study (6.6% or 10.4%, respectively, versus 0%) [21].

In our study, patients underwent corrective surgery at the median age and a mean weight lower than other series reported [15, 18]. Nevertheless, our results demonstrated similar good outcomes as reported by others [20].

Similar to our experience, other reports describe difficulties in removing the stent from RVOT during surgery due to fibrous tissue ingrowth around the stent in some patients. To avoid damage to surrounding structures, in some patients the posterior wall of the stent has been left in situ, and in all cases this has been well tolerated [4, 18, 20].

In all our patients a TAP was used as the repair technique, however, one could implant a stent limited only to the infundibulum thus preserving the native pulmonary valve. In other series, TAP repair was necessary in approximately 50%, promoting infundibular stenting without covering the pulmonary annulus [15, 18]. This is an interesting alternative to consider when dealing with this kind of patient.

Conclusions

Stenting of the RVOT in symptomatic and high-risk patients with ToF is a safe alternative to surgical correction or surgical systemic to pulmonary shunt and should be considered

in this high-risk population. Our experience showed excellent results in this group of patients with no serious adverse events during the initial procedure and no surgical mortality during the repair.

This procedure produced an increase in pulmonary blood flow and pulsatile antegrade flow which resulted in an increase in oxygen saturation and symmetric branch pulmonary artery growth, which allowed patient stabilization and delayed surgical repair until the patients had better weight and more favorable anatomical conditions.

Study Limitations

This report shows our early experience with stenting of the RVOT in symptomatic patients with ToF in three centers in our country, with only 3 to 4 patients per center. This could reflect different strategies, and selection criteria was used in each institution to treat these symptomatic patients. Due the limited number of patient in this report, conclusions should be considered with care. Our report has also the limitations of a retrospective study.

Funding This study was not grant funded.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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