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A case series of transcatheter Potts Shunt creation in a pediatric population affected with refractory pulmonary artery hypertension: focus on the role of ECMO

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Abstract

Purpose: Patients with suprasystemic idiopathic pulmonary hypertension (S-PAH) have a poor prognosis. Therapeutic options are limited. Reverse Potts shunt creation modifies physiology transforming patients with PAH into Eisenmenger physiology with a better outcome. Percutaneous transcatheter stent secured aortopulmonary connection (transcatheter Potts Shunt, TPS) is a feasible very high-risk procedural option in such patients. We report our experience with patients undergoing TPS at our institution requiring extracorporeal membrane oxygenation (ECMO) support.

Methods: A prospective observational study of patients with drug-refractory PAH, worsening NYHA class, and right ventricular failure undergoing TPS. Two patients required rescue ECMO for cardiac arrest during the procedure. Subsequently, "standby ECMO" was available in all the following cases and elective support was provided in patients with extremely poor conditions.

Results: Ten pediatric patients, underwent TPS at our institution. Two patients were rescued by ECMO after cardiac arrest during the shunt creation. This occurred as a result of the acute loading of the left ventricle (LV) after retrograde aortic arch filling through the Potts shunt. Following this, another two patients underwent elective ECMO after the uneventful induction of anesthesia. They all died postoperatively despite a successful TPS procedure. The causes of death were not related to the use of ECMO, but the complication of severe PAH. Six patients with successful TPS did not require ECMO and survived.

Conclusions: TPS is a pioneering procedure offering the opportunity to treat high-risk idiopathic drug-refractory PAH patients. Acute LV failure is a complication of TPS in patients with S-PAH. Elective ECMO, an option to avoid circulatory arrest and acute profound hypoxia secondary to exclusive right-to left shunt systemic perfusion by Potts shunt and LV dysfunction with resulting pulmonary edema, may be used at the early stage of the learning curve, but it does not influence the prognosis of these patients which remains poor.

Keywords
pulmonary hypertension; ECMO; children; reversed Potts shunt; cath lab

Introduction

Supra systemic pulmonary arterial hypertension (PAH) often leads to right ventricular (RV) failure due to chronically elevated afterload. When untreated, idiopathic PAH results in death within 2-3 years following the diagnosis in adults and within the first 1 year of diagnosis in children.[1–3] There are limited therapeutic options. The first line treatment is medical therapy, which includes phosphodiesterase-5 inhibitors, endothelin receptor antagonists and prostacyclin analogues. Despite maxi-

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mal medical treatment some patients fail to show improvement or even deteriorate. Atrial septostomy is an alternative treatment to improve left ventricular (LV) preload achieved at the expense of whole body desaturation.[4] Lung transplantation is a surgical option; however, an insufficient donor pool and rejection-related complications make it quite challenging. As a result, the overall mortality rate within 5 years of PAH diagnosis is reported between 25% and 60%. [5] Based on the historical observations of improved survival in Eisenmenger syndrome patients when compared with patients with isolated PAH, surgical creation of a connection between the left pulmonary artery and the descending aorta has been successfully utilized to achieve RV afterload reduction via equalization of pulmonary and systemic arterial pressures. Such a reversed Potts shunt effectively changes the natural history and improves symptoms and survival in drug-refractory PAH children to provide extra time for lung transplantation. Since thoracic surgery in patients with suprasystemic PAH and RV failure is associated with increased morbidity and mortality, transcatheter stent secured aortopulmonary connection (i.e. transcatheter Potts shunt TPS) has been proposed (Figure 1). This approach is easily performed in the presence of a tiny patent ductus arteriosus, but in its absence, the procedure requires the creation of a controlled connection. Following successful animal studies, two medical centers reported the feasibility of transcatheter Potts shunt creation in adult PAH patients.[6-13] Based on these observations, a program of TPS in children was started at our institution, involving a specific team of cardiologists, anesthesiologists and cardiac surgeons. Here we report the experience with patients undergoing TPS at our institution, and the use of extracorporeal membrane oxygenation (ECMO) for circulatory support in this fragile population.[14]

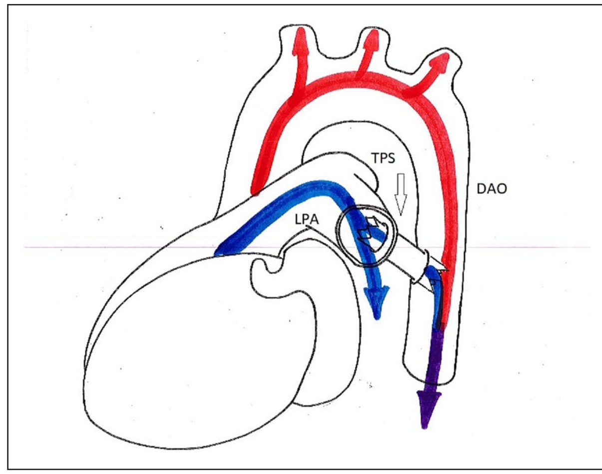

Figure 1. Transcatheter Potts shunt (TPS): connection between Descending Aorta (DAO) and Left Pulmonary Artery (LPA).

Methods

TPS was proposed for cases with suprasystemic PAH despite maximal medical treatment and worsening NYHA class, RV failure signs, increasing NT-proBNP level, decreasing 6-minute walk distance and deteriorating RV systolic function.[15,16] Criteria for inclusion in the TPS program, as well as procedural aspects are presented in a previous publication (Boudjemline et al.).[9] The study was approved by a local ethics committee. This manuscript focuses on the subgroup of patients with pre- or post-procedural ECMO.

The first two procedures were uneventful (Table 1). The third and fifth procedure were followed by cardiac arrest during the procedure, and required rescue veno-arterial ECMO.[17–22] Based on this experience it was decided to provide "standby ECMO" for all subsequent cases. Femoral and iliac vessels were studied before catheterization by angio-CT. The ECMO circuit comprised a centrifugal pump and a polymethylpentene hollow fiber oxygenator. Arterial and venous cannulae were inserted in the femoral vessels. The ECMO circuit was available for rapid setup and priming. All circuits were heparin-coated and were approved for a use over 5 days. Each ECMO system had an integrated battery pack, as well as a drive and steering units. In case of ECMO requirement, correct position of the cannulas was guided by fluoroscopy and by transesophageal echocardiography: the tip of the arterial cannula (patient inflow) was positioned in the abdominal aorta, the tip of the venous cannula (patient outflow) was placed in the inferior vena cava, close to the right atrium.[23–27] The ECMO circuit was primed with a lactate ringer solution plus 100 UI of heparin per 100 ml of priming in eight cases. Another two patients received blood-primed ECMO with 100 UI of heparin per 100 ml of priming. The patients received 30 UI/Kg unfractionated heparin prior to ECMO. The initial activating clotting time (ACT) target was $>$ 150 seconds. The postprocedural coagulation monitoring protocol employed antithrombin III levels and anti-factor Xa assays.[10,28–30]

Another two patients (patients 7 and 9) underwent elective ECMO after uneventful induction of anesthesia, and prior to the TPS procedure.

Results

Ten patients had TPS between 1st January 2016 and 1st February 2017, their characteristics are shown in Tables 1 and 2, and are detailed in a previous report.[14]

Six patients with successful Potts procedures did not require ECMO and survived (Boudjemline et al.)[9].

Table 1. Intra- and postoprocedural characteristics.

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	Mean	%
Duration of anesthesia/ procedure (mn)	280/220	140/82	250/134	140/76	270/97	140/71	260/52	200/120	280/93	160/60	212/110	
Duration of MV (d)	1	1	3	1	8	1	40	2	1	1	5.9	
Inotropes (d)	2	1	3	0	8	1	40	2	1	1	5.9	
LOS in ICU (d)	3	3	3	1	8	2	40	3	5	2	7	
ECMO	N	N	Y	N	Y	N	Y	N	Y	N		40
Mortality 1st week	N	N	Y	N	N	N	N	N	N	N		10
Mortality 30-d	N	N	Y	N	Y	N	N	N	N	N		20
In-hospital Mortality	N	N	Y	N	Y	N	Y	N	Y	Y		40
NYHA Class after Potts	I	II	UN.	I	UN.	I	UN.	III	UN.	II		

d: Day; ICU: Intensive Care Unit; LOS: Length of Stay; MV: Mechanical Ventilation; mn: minutes; N: Not; NYHA Class: New York Heart Association classification for PAH; P: Patient; UN.: Unavailable; Y: Yes.

Table 2. Baseline characteristics of the study population.

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	Mean
Age (years)	13.3	17.9	9.6	8.7	5.9	10.8	14.3	8.9	12.5	8.5	10.7
Weight (kg)	34	78	33	37	17	27	45	35	41	25	37.3
Sex	W	W	W	M	W	M	M	W	W	M	UN.
Age for diagnosis (years)	11	12	0.1	4.5	0.4	9	13.9	UN.	UN.	8	7.4
Diagnosis	PAH BMPR2	PAH BMPR2	PAH with wide ASD	PAH BMPR2	PAH BMPR2	I-PAH	I-PAH	PAH with TGA	PAH with TGA	PAH BMPR2	UN.
NYHA Class.	III	III	IV	IV	III	IV	IV	III	III	IV	UN.
Sildenafil (mg/kg/d)	1.76	0.77	3.6	1.62	3.52	4.44	0.89	1.71	1.46	2.4	2.2
Bosentan (mg/d)	3.67	3.20	3.78	3.89	3.76	4.15	5.55	1.83	3.05	3.84	3.7
Prostaglandins type and dose (n/kg/mn)	E 20	T 20	T 30	E 14	T 31	T 35	E 42	E 40	T 35	T 29	UN.
Ratio Pr. PA/Ao	1.4	1.1	1.6	1.1	1.3	1.2	1.3	1.2	1.3	1.5	1.3
PVR (Wood/m^2)	26.3	12	39.3	14.1	15	21	UN.	26	15	12	21.2
Cardiac Index (L/mn/m^2)	2.9	2.1	2.5	2.5	3.4	3.7	UN.	3.14	2.5	4.3	3

Ao: Aorta; ASD: Atrial Septal Defect; BMPR2: mutation of gene bone morphogenetic protein receptor type 2; d: day; E: epoprostenol; I-PAH: idiopathic-PAH; kg: kilograms; L: Liters; M: man; m^2: square meters; mg: milligrams; mn: minutes; n: nanograms; NYHA Class.: New York Heart Association classification for PAH; P: patient, PA: Pulmonary Artery; PAH: Pulmonary Artery Hypertension; Pr.: Pressure; PVR: Pulmonary Vascular Resistance; T: treprostinil; TGA: Transposition of Great Arteries; UN: Unavailable; W: woman.

Patient 3 had a hemodynamic collapse after anesthetic induction requiring resuscitations, inotropic support and cardioversions for atrial tachycardia. An attempt at stent placement resulted in embolization followed by stent retrieval through the vessel wall defects before the placement of a second stent. This exposed him to severe bleeding. This patient experienced cardiac arrest despite a large atrial septal defect with a massive right-to-left shunt which, unfortunately, did not protect from LV unloading. We were able to start the ECMO run about 25 minutes later. After this event, we decided to prepare and prime an ECMO machine in the cath lab before all subsequent procedures. Patient 5, the second patient, experienced cardiac arrest at induction of anesthesia, and a persistently low cardiac output state before TPS despite cardiopulmonary resuscitation and inotropic support. This patient also required multiple percutaneous perforation attempts, and the delivery sheath had to be exchanged before the successful crossing of the vascular walls. This consequently delayed the stent implantation, increased the potential for bleeding, and resulted in a second cardiac arrest during the procedure. The patient was rescued by ECMO within 15 minutes of the second cardiac arrest. Both patients recovered cardiac function at 48 hours after the procedure. Patient 3 experienced massive cerebral hemorrhage (probably secondary to prolonged low cardiac output syndrome and anticoagulation) on day 2 and the ECMO run was stopped on day 3. Patient 5 was successfully weaned from ECMO on day 2, however he experienced a multi-organ failure later on, with signs of brain damage; this patient died from irreversible brain damage on day 10. A retrospective analysis of the first cases allowed to see that echocardiographic features were worse in non-survivors compared with survivors, including dysfunctional RV and small LV volumes with reduced cardiac

Table 3. Data of patients on ECMO.

	P3	P5	P7	P9	Mean	Range	%
W (kg)	33	17.5	45	41.7	34.3	17.5–45	
H (cm)	132	108	168	160	142	108–168	
BS (m^2)	1.10	0.72	1.45	1.36	1.15	0.72–1.45	
A (years)	9.4	5.8	14.3	12.5	10.5	5.8–14.3	
I/O P.D. (inches)	3/8–3/8	1/4–1/4	3/8–3/8	3/8–3/8			
Canule Ar. (Fr.)	15	12	15	15			
Canule Ven. (Fr.)	17	14	19	19			
Priming (C-A/B)	B	C-A	B	C-A			
Indication	Cardiac arrest	Cardiac arrest	Clinical status, Echo	Echo			
Duration (d)	2	2	40	1			
Death before 30 d (Y/N)	y	Y	N	N			50
Death before HD (Y/N)	Y	Y	Y	N			75
Cause of death	Cerebral hemorrhage	MOF, irreversible brain damage	ARDS	Sudden death			

A: age; Ar.: arterial; ARDS: acute respiratory distress syndrome; B: blood; BS: body surface; C-A: crystalloids-albumin; d: days; Echo: echocardiography; Fr.: French; H: height; HD: hospital discharge; I/O P.D.: Inlet-Outlet Pump Dimension; Ind.: indications; MOF: multiorgan failure; N: not; P: patient; Ven.: venous; W: weight; Y: yes.

output. Therefore, it was decided to perform the following procedures under elective ECMO in case presenting with such echocardiographic features. Thus, patients 7 and 9, underwent TPS with elective ECMO after uneventful induction of anesthesia. Patient 7 died at day 40 following septic shock and acute viral respiratory distress syndrome, and patient 9 died at day 30 of sudden death while waiting for heart and lung transplant.

Patients who survived recovered, their echocardiographic scores for biventricular function, and right diastolic function improved.[31] At hospital discharge, clinical conditions were subjectively improved for all. Medical treatment for PAH was continued in all cases.

Discussion

Here we report our experience with TPS creation in 10 patients, out of whom four either required rescue ECMO or were placed on elective ECMO before the procedure (Table 3).

ECMO has been deployed successfully to support children of all ages, from newborn to adult-sized patients with CHD requiring cardiac surgery.[32] However, in patients submitted to cardiac procedures, the use of ECMO is mainly reported postoperatively and is rarely used electively for circulatory support during procedure.[21–27] To our knowledge, this is the first report of ECMO being used during TPS procedures. The 100% mortality of ECMO patients here may question its usefulness, however, this needs to be considered given the severity of idiopathic PAH. Nasr et al. reported a strikingly high mortality rate in a pediatric population with isolated PAH who required ECMO, suggesting ECMO should be avoided in PAH patients.[28] Other authors, on the other hand, recommend ECMO in PAH patients and highlight the need for a more timely implementation of ECMO, to effect a reduction in the mortality related to the disease.[29] TPS creation is a pioneering procedure. It offers the chance to treat very high-risk patients in whom the therapeutic options are limited. When the Potts shunt becomes effective, the LV afterload increases due to retrograde aortic arch filling through the Potts shunt, and the LV preload decreases due to a reduction of pulmonary venous blood flow. Thus, the output of the off-loaded LV may fall suddenly and result in hypoxia and cardiac arrest. We believe that elective ECMO, either provided before the procedure or rapidly in case of LV failure occurring during the procedure might play a strategic role and increase the chances of success of TPS procedures. However, several prerequisite conditions are required: (i) vascular access equipment, as well as a primed ECMO circuit for rapid setup, need to be immediately available in the catheterization laboratory; (ii) a dedicated “standby team” including a cardiac surgeon and a perfusionist need to be immediately available and functional at the time of stent insertion; (iii) transoesophageal echography needs to be available for monitoring of cardiac function, cannula placement and the assessment of LV function and aortic flow pattern. In case of acute LV failure and retrograde aortic arch filling through the Potts shunt, the communication should be occluded (e.g. by the balloon inflation within the stent) to re-establish the pre-procedural circulation. This would allow for appropriate medical treatment and set up of the extracorporeal support, to avoid profound hypoxia and cardiac arrest.

Despite our efforts, all ECMO patients died postoperatively. However, death was not due to ECMO complications, but to complications related to PAH. Therefore, it is likely that these patients were not appropriate candidates for Potts procedure, whether performed surgically or percutaneously. Further studies are needed to identify the pre-procedural factors which could help in identifying the patients who will not tolerate the transcatheter Potts shunt, in order to provide recommendations.[32]

Conclusion

TPS is a pioneering procedure that offers the opportunity to treat very high-risk idiopathic drug-refractory PAH patients. However, acute LV failure is a complication of TPS in patients with supra-systemic PAH. Elective ECMO, a potential support option to avoid circulatory arrest and acute profound hypoxia secondary to exclusive right-to-left shunt systemic perfusion by Potts shunt and LV dysfunction with resulting pulmonary edema, may be used at the early stage of the learning curve, but it does not influence the prognosis of these patients which remains poor.

Main limitations

This is a report from a single pediatric cardiac center, involving a very small sample of patients. ECMO patients died of complications unrelated to the use of ECMO, and, likely, they were not appropriate candidates for a Potts procedure. This is a potential source of bias in the interpretation of the usefulness of ECMO in this setting. However, the small sample size did not allow for the identification of the criteria for patient selection.

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