Outcomes of Surgery for Total Anomalous Pulmonary Venous Return without Total Circulatory Arrest

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Background: Recent developments in surgical techniques and hospital care have led to improved outcomes following total anomalous pulmonary venous return (TAPVR) repair. However, the surgical repair of TAPVR remains associated with a high risk of mortality and need for reoperation. We conducted this retrospective study to evaluate mid-term outcomes following *in situ* TAPVR repair without total circulatory arrest (TCA), and to identify the risk factors associated with surgical outcomes. **Methods:** We retrospectively reviewed 29 cases of surgical intervention for TAPVR conducted between April 2000 and July 2015. All patients were newborns or infants who underwent *in situ* TAPVR repair without TCA. **Results:** Four anatomic subtypes of TAPVR were included in this study: supracardiac (20 cases, 69.0%), cardiac (4 cases, 13.8%), infracardiac (4 cases, 13.8%), and mixed (1 case, 3.4%). The median follow-up period for all patients was 42.9 months. Two (6.9%) early mortalities occurred, as well as 2 (6.9%) cases of postoperative pulmonary venous obstruction (PVO). Preoperative ventilator care (p=0.027) and preoperative PVO (p=0.002) were found to be independent risk factors for mortality. **Conclusion:** *In situ* repair of TAPVR without TCA was associated with encouraging mid-term outcomes. Preoperative ventilator care and preoperative PVO were found to be independent risk factors for mortality associated with TAPVR repair.

Key words: 1. Congenital heart disease (CHD)
2. Total anomalous pulmonary venous return
3. Total circulatory arrest

Introduction

Total anomalous pulmonary venous return (TAPVR) is a rare congenital heart malformation that accounts for 1% to 3% of all congenital heart anomalies [1]. It is characterized by abnormal return of the pulmonary veins into the systemic venous system. Since 1951, when the first surgical attempt to correct this condition was reported, advancements in surgical procedures and hospital care have led to improved outcomes among patients undergoing TAPVR repair [1-4].

However, surgical intervention for TAPVR remains associated with an increased risk of early mortality, with early postoperative mortality rates of 10% to 50% [2-5]. Pulmonary venous obstruction (PVO)—the most crucial complication after TAPVR repair—has been reported to occur in 8% to 54% of cases [6-8].

We performed this retrospective study over a 16-year period at a single institution to evaluate mid-term mortality and morbidity outcomes among patients who underwent TAPVR repair with an *in situ* approach via mild to moderate cardioplegic hypothermia with-

out total circulatory arrest (TCA).

Methods

1) Patients

A review of the pediatric cardiothoracic surgical database at Kyungpook National University Hospital identified 29 newborn or infant patients who underwent surgical repair of TAPVR between April 2000 and July 2015. Patients with the following types of comorbidities were excluded from this study: functional single ventricle, ventricular septal defect, coarctation of the aorta, and interrupted aortic arch. We retrospectively reviewed patient's medical records to evaluate the operative variables, postoperative progression, and their clinical course during follow-up.

2) Definition

All cases were evaluated using echocardiography. Since 2010, preoperative chest computed tomography (CT) has been the standard method of evaluation for the detailed assessment of anatomy at our institution; however, CT was not always performed in patients whose condition was considered critical. Although 27 of the 29 patients in this study underwent chest CT before the operation, 2 patients with obstructive TAPVR proceeded to surgery with echocardiographic images alone due to their critical status.

Pulmonary veins were regarded as obstructed if a significant gradient was present between the drainage point and the pulmonary veins (flow acceleration ≥ 2.0 m/sec). Emergency surgery was defined as an immediate operation that was required within 24 hours of diagnosis. Early mortality was defined as death within a month of the operation or during primary hospitalization.

3) Surgical techniques

All operations were performed under cardiopulmonary bypass (CPB), without TCA. For cardiac TAPVR patients (n=2), coronary sinus unroofing was performed; the *in situ* technique was performed in all other patients.

The *in situ* (internal) technique is carried out transatrially and transseptally [9-11]. This approach is similar to the type II repair described by Wilson et al. [8]. With the heart in a normal anatomic position and without retracting the myocardium, we performed a right atriotomy with an extended incision through the interatrial septum into the posterior wall of the left atrium (LA). The anterior wall of the pulmonary venous confluence was then incised and connected to the LA. A continuous suture was used to form the anastomosis between the anterior wall of the pulmonary vein and the posterior incision of the LA. Next, the atrial septum was closed with an autologous pericardial patch, which enabled expansion of the volume of the small LA. Finally, the procedure was completed by direct closure of the right atriotomy.

The temperature during CPB was the lowest rectal temperature measured throughout the operation. Three categories of cardioplegic hypothermia exist: deep, moderate, and mild. In the majority of cases (22 of 29), TAPVR repairs were performed under conditions of mild hypothermic CPB. From 2000 to 2006, we performed the operation under mild or moderate hypothermia. From 2006 onwards, we performed all TAPVR repairs under conditions of mild hypothermia. After the median sternotomy, patients were heparinized and CPB were conducted by cannulation of the ascending aorta and the bicaval vein. The venting catheter was placed via the pulmonary artery, the aorta was cross-clamped, and cardiac arrest was induced by delivering cold cardioplegic solution to the aortic root. The venting catheter of the pulmonary artery and frequent use of CO_2 insufflation permitted a relatively good view of the operative field, albeit under mild hypothermic cardioplegia.

4) Statistical analysis

Data were analyzed with IBM SPSS ver. 20.0 (IBM Co., Armonk, NY, USA). All values of continuous variables were expressed as mean±standard deviation. The chi-square test or the Fisher exact test was applied for comparing and evaluating the results of the operation. All p-values< 0.05 were considered to indicate statistical significance.

Results

In total, there were 21 male patients (63.6%), and 8 female patients (24.2%). Their median age and weight at the time of surgery was 30 days (range, 1 to 133 days) and 3.6 kg (range, 1.9 to 6.3 kg), respectively. Patients had 1 of the 4 types of TAPVR:

Table 1. The preoperative demographic data

Variable	Value
Age (day)	30.8±36.7 (1–133)
Gender	
Male	21 (63.6)
Female	8 (24.2)
Weight (kg)	3.6±1.0 (1.9–6.3)
Body surface area (m^2)	0.22±0.41 (0.15–0.31)
Total anomalous pulmonary venous return type	
Supracardiac	20 (69.0)
Cardiac	4 (13.8)
Infracardiac	4 (13.8)
Mixed	1 (3.4)

Values are presented as mean±standard deviation (range) or number (%).

Table 2. Operative variables

Variable	Value
Preoperative pulmonary venous obstruction	5 (17.2)
Emergent operation	9 (29.0)
Preoperative ventilator care	7 (24.1)
Cardiopulmonary bypass time (min)	101.8±46.8 (38–281)
Aortic cross clamp time (min)	64.5±27.9 (24–152)
Lowest rectal temperature (°C)	29.2±3.77 (19–34)

Values are presented as number (%) or mean±standard deviation (range).

Table 3. Postoperative outcomes

Variable	Value
Intubation time (hr)	51.4±43.4 (19–240)
Early mortality	2 (6.9)
Postoperative pulmonary venous obstruction	2 (6.9)
Follow-up time (mo)	42.9±41.9 (0–148)
Last echocardiogram follow-up time (mo)	29.9±34.59 (0–136)

Values are presented as mean±standard deviation (range) or number (%).

29), and 2 patients (6.9%) required reoperation due to a postoperative PVO. The mean follow-up period was 42.9 months (range, 1 to 148 months), with a mean echocardiographic follow-up period of 30.0 months (range, 1 to 135 months) (Table 3). The mortality and PVO morbidity data are presented in Table 4. Cases of mortality and morbidity were independent, and there were no cases of late mortality and morbidity after discharge from the hospital.

The first case of mortality was a patient with obstructive supracardiac TAPVR. Preoperatively, the patient had a large atrial septal defect (ASD) and patent ductus arteriosus with a small vertical vein. Anastomosis between the common pulmonary venous (CPV) chamber and the LA posterior wall was performed. The CPB time and ACC time were 136 minutes and 46 minutes, respectively; no remarkable intraoperative events occurred. In postoperative echocardiography, mild flow acceleration (1.5 m/sec) was found at the anastomosis site, as well as grade I tricuspid regurgitation. Laboratory tests showed a disseminated intravascular coagulation pattern, and acute renal failure developed on postoperative day (POD) 3. It was necessary to perform peritoneal dialysis due to the patient's prolonged poor urine output. On POD 26, the patient was extubated, but the patient's condition remained precarious. On POD 50, reintubation was performed due to respiratory failure. Consequently, pneumonia with sepsis developed and we were not able to wean the patient from the ventilator; the patient finally expired due to septic shock on POD 71.

The second case of mortality, with the same type of TAPVR as the first, exhibited severe hypoxia at birth. Therefore, an emergency operation was performed without a detailed evaluation. During the operation, the CPV chamber was found to be extremely small,

supracardiac (20 patients, 69.0%), cardiac (4 patients, 13.8%), infracardiac (4 patients, 13.8%), and mixed (1 patient, 3.4%). The preoperative demographic data of the patients are summarized in Table 1.

We detected preoperative PVO in 5 patients (17.2%). Nine patients (29.0%) underwent emergency operations. All patients who had obstructive TAPVR required emergency surgery. The mean CPB time was 101.8 minutes (range, 38 to 281 minutes) and the mean aortic cross-clamping (ACC) time was 64.5 minutes (range, 24 to 152 minutes). Twenty-two operations (75.9%) were performed under mild hypothermic CPB and 7 operations (24.1%) were performed under moderate hypothermic CPB; all were performed without deep hypothermia and TCA. Seven (24.1%) patients required preoperative ventilator care. The operative variables are summarized in Table 2.

Postoperatively, the mean duration of ventilator care (intubation time) was 51.4 hours (range, 19 to 240 hours). The early mortality rate was 6.9% (2 of

Table 4. Postoperative mortality and pulmonary venous obstruction morbidity

Variable	Brief presentation of the two cases of mortality		Brief presentation of the two cases of reoperation	
	Case 1	Case 2	Case 1	Case 2
Type	Supracardiac	Supracardiac	Infracardiac	Supracardiac
Age (day)	1	1	3	20
Weight (kg)	3.6	3.0	2.5	3.4
Preoperative obstruction	Yes	Yes	No	No
Preoperative O_2 saturation (%)	98	50	90	97
Cardiopulmonary bypass time (min)	136	281	110	155
Aortic cross clamp time (min)	46	152	54	89
Echocardiography				
Preoperative	Large ASD and PDA, small vertical vein	Small common chamber	Large ASD, grade II TR	Large ASD, small PDA
Postoperative	Mild stenosis (1.5 m/sec), grade I TR	Small common chamber	Patent vertical vein, 2 m/sec at anastomosis site	2 m/sec at anastomosis
Date of death	POD #71	POD #75	-	-
Cause of death	Pneumonia, sepsis (long-term ventilator care)	Congenital lymphangiectasis, sepsis	-	-
Re-intervention date	-	-	POD #1	POD #18
Intervention	-	-	Revision of anastomosis site	Pulmonary vein angioplasty, left atrioplasty

ASD, atrial septal defect; PDA, patent ductus arteriosus; TR, tricuspid regurgitation; POD, postoperative day.

with a thickened wall. This problem meant that an excessive amount of operative time was required. The CPB time and ACC time were 281 minutes and 152 minutes, respectively. Postoperatively, extracorporeal membrane oxygenation (ECMO) was required due to low cardiac output syndrome. The day after surgery, we performed postoperative bleeding control. On POD 3, we removed the ECMO circuit, and the sternum wound was closed on POD 6. The patient had a prolonged pleural effusion, and was diagnosed with postoperative chylothorax on POD 16. We observed the patient clinically for an additional 4 days, but the patient did not show sufficient improvement to enable thoracic duct ligation surgery. On POD 30, we performed follow-up echocardiography, which revealed no postoperative PVO, but did show a right pleural effusion. The effusion persisted, waxing and waning in size. Central line infection, dehydration, and malnutrition occurred due to prolonged total parenteral nutrition. Ultimately, the patient expired due to septic shock on POD 75.

Two cases required surgical repair for postope-

rative PVO. The first case was a patient with infracardiac TAPVR. The age and birth weight of the patient were 3 days and 2.5 kg, respectively. Preoperatively, the patient had no obstructive pulmonary veins and a large ASD. Anastomosis between the CPV chamber and the left atrial posterior wall was performed with a continuous over-and-over suture. The day after the operation, we performed postoperative echocardiography due to persistent tachypnea. The flow acceleration at the anastomosis site was 2.0 to 2.5 m/sec, and we decided to perform a revision of the anastomosis site. With the patient under CPB, the previous sutures were removed and a new multiple interrupted suture was performed. The CPB time and ACC time were 198 minutes and 94 minutes, respectively. Postoperative echocardiography revealed a wide CPV-LA junction with mixed-flow turbulence (1.5 m/sec). In 2011 (5 years postoperatively), most last follow-up echocardiography results showed the same findings.

The second case of surgical repair for PVO was a patient with supracardiac TAPVR. The age and birth

Table 5. Risk factors associated with mortality in patients with total anomalous pulmonary venous return

Factors	Deaths	Survivors	p-value
Age (mo)	1.5±0.7	33.0±37.2	0.08
Body weight (kg)	3.3±0.4	3.6±1.0	0.22
Body surface area (m^2)	0.20±0.02	0.22±0.04	0.24
Preoperative ventilator care	2 (100.0)	5 (18.5)	0.027
Preoperative pulmonary venous obstruction	2 (100.0)	3 (11.1)	0.002
Emergency operation	2 (100.0)	7 (25.9)	0.089
Cardiopulmonary bypass time (min)	208.5±102.5	93.9±31.9	0.003
Aortic cross clamp time (min)	99.0±74.9	61.9±22.9	0.003

Values are presented as mean±standard deviation or number (%).

Table 6. Risk factors associated with re-operation in patients with total anomalous pulmonary venous return

Factors	Postoperative PVO (n=2)	Non-PVO (n=25)	p-value
Age (mo)	12.5±12.0	32.2±37.7	0.182
Body weight (kg)	2.9±0.6	3.7±1.0	0.394
Body surface area (m^2)	0.20±0.42	0.31±0.22	0.817
Preoperative ventilator care	2 (100.0)	7 (25.9)	0.65
Preoperative PVO	2 (100.0)	5 (18.5)	0.104
Emergency operation	2 (100.0)	7 (25.9)	0.157
Cardiopulmonary bypass time	132.5±31.8	99.5±47.4	0.774
Aortic cross clamp time	71.5±24.75	64.0±28.5	0.890

Values are presented as mean±standard deviation or number (%).
PVO, pulmonary venous obstruction.

weight of the patient were 20 days and 3.4 kg, respectively. Preoperatively, the patient had no obstructive pulmonary vein and a large ASD. An anastomosis between the CPV chamber and the left atrial posterior wall was performed. Postoperative echocardiography revealed a flow disturbance (2 m/sec) at the anastomosis site. On POD 18, we performed postoperative echocardiography due to tachypnea. The systolic gradient at the anastomosis site was 2.5 to 3.0 m/sec, and surgical repair for postoperative PVO was performed. Stenosis of the right superior and inferior pulmonary veins was identified with a Hegar dilator, and pulmonary venous angioplasty was performed with an autologous pericardial patch. Postoperatively (up to the present), no further obstruction of the pulmonary venous drainage was observed.

Both of these reoperation cases are thought to have been necessary due to technical problems and were performed in the early period of this study. The risk factors associated with mortality and morbidity are summarized in Tables 5 and 6. Overall, mortality was significantly associated with pre-operative ventilator care (p=0.027) and the presence of preoperative PVO (p=0.027). No risk factor was significantly associated with postoperative PVO.

Discussion

Over time, the surgical outcomes associated with repair of TAPVR have significantly improved, most likely as a result of appropriate diagnoses, improved surgical and anesthetic techniques, and advanced perioperative care. Like most institutions of pediatric cardiothoracic surgery, we are concerned with identifying strategies for TAPVR repair that result in improved outcomes.

Three components of the management of TAPVR repair at our institution are worth noting. First, our institution made significant efforts to ensure the accurate diagnosis of TAPVR. We performed chest CT in almost all cases of TAPVR, except in the 2 cases that were obstructive. The 2 patients with obstructive TAPVR underwent surgery with only portable echocardiographic data due to their unstable vital

signs and the life-threatening status of their conditions. Initially, chest CT was the preferred diagnostic tool for TAPVR in our institution. However, in 2010, a notable case of obstructive supracardiac TAPVR led to changes in our standard protocol. In this case, the neonate patient had severe hypoxia at birth, with O_2 saturation values that did not exceed 50% despite a fraction of expired oxygen with mechanical ventilation of 1.0, and underwent an emergency operation. Intraoperatively, the common chamber was found to be extremely small with a thickened wall; thus, the procedure required an excessive amount of time for an anastomosis to be formed between the LA and the pulmonary vein. The CPB time during surgery was 281 minutes and the ACC time was 152 minutes. The operation took more than twice as long as the average procedure (CPB time, 100.4 minutes; ACC time, 63.8 minutes) and ECMO was required postoperatively due to low cardiac output syndrome. Two months later, the infant patient died of pneumonia and sepsis. Since this case of mortality, we have performed preoperative chest CT as a standard evaluation. Even in an emergency, the 10 minutes needed to evaluate the anatomy of the important great vessels in a precise manner is now considered an appropriate and important use of time.

Second, in the majority of cases (27 of 29) we used an *in situ* (internal) technique. This technique allows the heart to be held in the pericardial well, where it is easily cooled by its surroundings. The *in situ* technique also reduces the risk of kinking or twisting of the anastomosis. In addition, it avoids the retraction of the myocardium and has the advantage of allowing improved exposure of the pulmonary veins. The favorable visibility of the operative field resulted in shorter CPB times and improved outcomes. However, this technique requires a long incision in both atria and more suture lines, which increases the risk of atrial arrhythmia. Careful suturing is required in order to avoid the sinus node. In this study, permanent atrioventricular block did not occur as a complication, although a single case of temporary arrhythmia took place.

Third, all repairs were performed under CPB without TCA. An important auxiliary method for repair of TAPVR is TCA under deep hypothermia. However, cardiac operations under TCA are associated with an increased risk of post-arrest complications. The major disadvantages of TCA include morbid neurologic sequelae, coagulopathy, pulmonary dysfunction, and acute renal failure [12]. Furthermore, TCA may extend the operative time. However, in most patients (22 of 29) in this study, TAPVR repair was performed under mild hypothermic CPB. This circumvented the need for CPB cooling and rewarming periods and reduced the operative time.

Overall, we found better mid-term outcomes (the early mortality rate and the incidence of postoperative PVO were both 6.9%) than have been reported in previous studies, which reported mortality rates of 10% to 50% [2-5] and PVO morbidity rates of 8% to 54% [6-8]. Although our study was performed in a single institution and excluded patients with complex TAPVR, we report favorable overall outcomes. We consider the 3 aforementioned components of the clinical management of TAPVR repair to have significantly contributed to these positive results.

The risk factors that were significantly associated with mortality in patients undergoing TAPVR repair were preoperative ventilator care, preoperative PVO, CPB time, and ACC time. In agreement with a previous report, preoperative PVO was found to have a significant effect on the mortality rate; however, we did not find PVO to affect the operative time [13]. This difference may be a consequence of the small number of patients and events observed in our study.

In conclusion, *in situ* repair of TAPVR without TCA is a favorable surgical option that reduces mid-term mortality and morbidity. In addition, the routine use of preoperative chest CT is valuable for the detailed assessment of anatomy. Finally, preoperative ventilator care and preoperative PVO are independent risk factors for mortality following TAPVR repair.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Acknowledgments

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