ORIGINAL RESEARCH ARTICLE

Total Anomalous Pulmonary Venous Connection

The Current Management Strategies in a Pediatric Cohort of 768 Patients

BACKGROUND: Total anomalous pulmonary venous connection (TAPVC) is a rare form of congenital heart disease. This study describes current surgical treatment strategies and experiences in a cohort of patients from 2 congenital cardiac centers in Shanghai and Guangdong in China.

METHODS: This retrospective study included 768 patients operated on between 2005 and 2014. Although most patients (n=690) underwent conventional repair, a sutureless technique was used in 10% (n=78) of cases. A multilevel mixed-effects parametric survival model and a competing-risk analysis were used to analyze associated risk factors for death and recurrent pulmonary venous obstruction (PVO), respectively. Kaplan-Meier analysis was used to analyze the overall survival. The Nelson-Aalen cumulative risk curve was used to compare distributions of time with recurrent PVO.

RESULTS: The mean surgical age and weight were 214.9±39.2 days and 5.4±3.6 kg, respectively. Obstructed TAPVC (PVO) was documented in 192 (25%) of the 768 patients. There were 38 intraoperative deaths and 13 late deaths. A younger age at the time of repair (P=0.001), mixed (P=0.004) and infracardiac (P=0.035) TAPVC, preoperative PVO (P=0.027), prolonged cardiopulmonary bypass time (P<0.001), and longer duration of ventilation (P=0.028) were associated with mortality. The median follow-up was 23.2 months (range; 1–112 months). Among the 717 survivors, recurrent PVO was observed in 111 patients (15%). Associated risk factors for recurrent PVO included preoperative PVO (P<0.001), infracardiac TAPVC (P<0.001), mixed TAPVC (P=0.013), and prolonged cardiopulmonary bypass time (P<0.001). Sutureless technique was associated with a lower restenosis rate compared with conventional repair in patients with preoperative PVO (P=0.038), except in newborn patients (P=0.443). Reintervention for restenosis was performed in 24 patients. The function of most survivors (91%) was classified according to the New York Heart Association as functional class I or II.

CONCLUSIONS: Surgical correction in patients with TAPVC with a biventricular anatomy can achieve an acceptable outcome. Risk factors such as a younger age at the time of repair, infracardiac and mixed TAPVC, and preoperative PVO were associated with a poorer prognosis.

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Clinical Perspective

What Is New?

- This is the first large, multi-institutional study describing current treatment strategies for total anomalous pulmonary venous connection (TAPVC) in Asia.
- The liberal use of computed tomography angiography as a preoperative evaluation of morphology is encouraged by this series. It helps to improve diagnostic accuracy and is helpful for surgical planning.

What Are the Clinical Implications?

- Acceptable outcomes after surgical correction for TAPVC have been achieved in recently established, specialized congenital heart centers in China.
- This study indicates that neonatal patients, infracardiac and mixed TAPVC, preoperative pulmonary venous obstruction, prolonged cardiopulmonary bypass time, and ventilation duration are associated with a poorer prognosis.
- Computed tomography angiography provides an accurate, noninvasive, economical diagnostic modality in preoperative evaluation of TAPVC.
- Restenosis after TAPVC repair poses an ongoing challenge. The sutureless technique has gained favor as a prophylactic method recently; however, its benefits over other methods require further confirmation. Its use as a surgical technique to decrease restenosis remains controversial.

Total anomalous pulmonary venous connection (TAPVC) is a rare but heterogeneous anomaly, accounting for ≈1% to 3% of congenital heart disease cases.[1] It is characterized by failure of the pulmonary venous confluence (PVC) to be absorbed into the dorsal portion of the left atrium (LA) in combination with a persistent splanchnic connection to the systemic venous systems. Historically, TAPVC has led to a high mortality rate of ≈80% in the first year of life without intervention.[2] Advances in surgical techniques, improvement in diagnostic accuracy, and changes in perioperative management have contributed to a dramatic decrease in perioperative mortality, although several factors such as neonatal surgical repair, preoperative pulmonary venous obstruction (PVO), mixed anatomic variation, single-ventricle physiology, and heterotaxy have remained important risk factors for poorer postoperative survival.[3–5] Postrepair PVO poses an ongoing surgical challenge and is associated with increased late mortality and morbidity.[6,7] In recent years, a sutureless technique has gained favor as a prophylactic method to decrease postrepair PVO. This new technique has appeared to be effective.[8]

Because of the rarity of reports on a multi-institutional comprehensive perioperative evaluation of TAPVC in the contemporary era, we conducted a retrospective study using a large cohort of patients to assess the impact of current management strategies on the outcomes of TAPVC.

METHODS

Review Methods and Definitions

The Institutional Committee on Clinical Investigation of Shanghai Children's Medical Center and Guangdong Cardiovascular Institute approved this protocol with a waiver of informed consent. Clinical data were collected from the hospital database and extracted from the medical records and from the outpatient records at the last available follow-up.

Echocardiography was performed on all patients. Computed tomography angiography (CTA) was performed in 92% of patients (706 of 768). Cardiac catheterization was required for further evaluation in 36 patients. Patients with functionally univentricular circulations were excluded. Emergency operation was defined as lifesaving surgery that required surgery within 24 hours of presentation. A diagnosis of preoperative PVO was made by a combined evaluation of oxygen saturation and echocardiography data, which indicated a nonphasic flow velocity >1.8 m/s.[9] Morphological features of preoperative PVO, which was investigated with CTA and intraoperative assessment, included intrinsic stenosis that was identified when there was pulmonary ostial stenosis, pulmonary venous hypoplasia, or both; external stenosis that was identified when obstruction occurred within the anomalous connecting vein or at its connection to the systemic circulation; and restrictive atrial septal defect (<3 mm) defined when there was obstruction at the interatrial septum. Early mortality was defined as death occurring during the hospital stay after the index operation. Postoperative PVO was diagnosed on documentation as abnormal pulmonary venous flow patterns (described above) during the follow-up.

Long-Term Follow-Up

As part of institutional standard procedures, all surgical patients who were discharged alive from hospital were required to return for outpatient follow-up visits at 6 and 12 months after the initial operation and then annually (Figure I in the online-only Data Supplement). We have 2 dedicated research staff members (1 doctor and 1 nurse) in each center. If patients miss a scheduled follow-up visit, our research staff usually contacts them by telephone or mail. Some patients were required to visit local hospitals for routine examinations. Any abnormal examination result or suspicious change in cardiac condition prompted a return visit for further evaluation at 1 of the 2 primary centers. During the follow-up period, echocardiography and electrocardiography were performed routinely. If the echocardiography Doppler finding indicated recurrent PVO, CT was further required to evaluate the obstruction.

Operative Data

TAPVC repair was performed through a median sternotomy under standard aorto-bicaval cardiopulmonary bypass (CPB) with moderate hypothermia in 735 patients (95%). In most patients, we can ensure a satisfactory intraoperative visualization by using pump suckers. In some cases, a temporal reduction of bypass flow was adopted to facilitate the exposure. Deep hypothermic circulatory arrest was used in only 33 patients in an earlier time. The ductus arteriosus was dissected and ligated before CPB was started if patent. The sutureless

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technique was used in 78 patients. Special care was taken to minimize handling of the pulmonary veins (PVs) and to avoid trauma to the pulmonary venous orifices. The ligation of the vertical vein (VV) was performed in most patients (97%). All operations were performed by senior surgeons.

Conventional Repair

Supracardiac Form

After full mobilization of the left and right pulmonary artery (PA) branches to reduce anastomotic tension, direct side-to-side anastomosis (>1–1.5 cm) between the confluence and the LA was performed through a superior approach as described by Tucker et al.[10] The atrial septal defect was directly closed or was closed with a pericardial patch to enlarge the potential small LA.

Cardiac Form

Unroofing of the coronary sinus with a baffle connection of the coronary sinus to the resulting atrial septal defect was routinely performed in cardiac patients.

Infracardiac Form

A right atriotomy was performed, and the incision was extended across the interatrial septum into the back wall of the LA. The front wall of the PVC was incised and anastomosed to the LA in a side-to-side fashion, as visualized by the surgeon through the back wall incision in the LA. For several patients, we extended the incision to the individual PVs to achieve an acceptably wide anastomosis because of the small confluence.

Mixed Form

The repair of mixed-type TAPVC involved a combination of the above approaches as dictated by the specific anatomy of the lesion. In most patients, the incision was extended to the individual PV because there was usually a lack of a distinct CPV.

Sutureless Technique

An incision was made in the venous confluence and then extended to the individual PVs. In situ pericardial flaps were anastomosed distally to the incised veins to create a neo-LA. Detailed information of the sutureless technique has been provided previously.[8]

Statistical Analysis

Data were collected and analyzed with SAS (version 9.3; SAS Institute Inc, Cary, NC) and Stata (version 14; StataCorp LP, Texas, TX). Normally distributed continuous variables are described as mean±SD. Student *t* tests were used to compare the differences between groups. For skewed continuous variables, median (range) was used to describe distributions, and the Wilcoxon-Mann-Whitney *U* test was used to compare differences between groups. Descriptive statistics for categorical variables were reported as frequency/percentage and were compared by use of the Pearson χ^2 or Fisher exact test. Kaplan-Meier analysis was used to analyze the overall survival. The Nelson-Aalen cumulative risk curve was used to compare distributions of time to restenosis because death was a competing risk for restenosis. Values of P<0.05 were considered statistically significant. After verification of proportionality assumptions, univariate and multilevel mixed-effects parametric survival models were used to assess factors associated with mortality. A competing-risk analysis was adopted to assess factors associated with restenosis. Variables significant at the 0.1 level in univariate analyses were considered. Collinearity diagnosis was performed with the Spearman correlation and the criterion of Belsley et al.[11] A multilevel mixed-effects parametric model was used to adjust for different centers and surgeons' performance differences when assessing the factors associated with mortality. To fit a multilevel mixed-effects parametric survival model, the conditional distribution of the response, given the random effects, is assumed to follow the Weibull distribution wherein the cluster subject was the surgeon group.[12]

RESULTS

From January 2005 to June 2014, 768 patients (511 male, 67%) underwent surgical repair of TAPVC. Age groups were defined as repair as neonates (age ≤30 days; n=122, 15.9%), infants (age 30–365 days; n=573, 74.6%), and children (age ≥365 days; n=73, 9.5%). TAPVC was subdivided into 4 types, according to the Darling et al[13] classification. Detailed patient characteristics are depicted in Table 1. One hundred ninety-two patients (25%, 192 of 768) had obstructed TAPVC, among whom a higher proportion of patients (17%, 33 of 192, versus 9%, 52/576; P=0.002) developed acidosis or multisystem organ dysfunction before surgery. The mean CPB time was 84.0±39.5 minutes (median, 78 minutes; range, 23–407 minutes), aortic clamping time was 44.8±22.0 minutes (median, 40 minutes;

Table 1. Preoperative Data

Patient Characteristics	
Surgical age, d, mean±SD	214.9±39.2
Surgical weight, kg, mean±SD	5.4±3.6
Length at surgery, cm, mean±SD	56.7±13.6
Prematurity, n (%)	69 (9)
Associated cardiac lesion	
Patent ductus arteriosus	568 (74)
Atrial septal defect	752 (98)
Ventricular septal defect	19 (2.5)
Coarctation of aorta	2 (0.3)
Tetralogy of Fallot	1 (0.1)
Pulmonary artery stenosis/ pulmonary artery branch stenosis	52 (6.8)
Anatomic type	
Supracardiac	348 (45.3)
Cardiac	280 (36.5)
Infracardiac	86 (11.2)
Mixed	54 (7)

range, 13–248 minutes), and cardiac arrest time was 30.8±11.0 minutes (median, 28 minutes; range, 16–61 minutes). The median cardiac care unit and hospital stay were 7 days (range, 1–93 days) and 15 days (range, 1–100 days), respectively. Median length of ventilator support was 51 hours (range, 2–1372 hours). Delayed sternal closure was performed to accommodate normalization of right ventricular work and stabilization of PA pressures in 41 patients. Diaphragmatic plication was performed in 22 patients (2.9%). Iloprost inhalation, bosentan, or phosphodiesterase-5 was used alone or in combination for postsurgical management of PA hypertension. Routine monitoring of blood platelet and liver function and ECG were performed.

Morphology

Preoperative morphological assessment, based mainly on CTA, was confirmed by intraoperative inspection.

In supracardiac TAPVC, the PVC drained into the innominate vein (n=287), the superior vena cava (n=41), or the azygous vein (n=8) via an ascending VV. The PVC directly drained into the superior vena cava in 12 patients. The VV was on the left in 308 patients, on the right in 36 patients, at the medial position in 2 patients, and on both sides in 2 patients. There were 4 kinds of external stenosis in supracardiac TAPVC: (1) The VV coursed between the left PA and ductus arteriosus and was compressed by this "circulus vasculosus"; (2) the VV was compressed by the left/right PA and left/right bronchus; (3) narrowness was found at the insertion on the VV into the superior vena cava or the innominate vein; and (4) the VV was compressed by the aortic arch. In cardiac TAPVC, the PVC drained into the coronary sinus in most patients (n=251, 89.6%). In the remaining patients, individual PVs were observed to drain directly into the right atrium. Detailed information is shown in Table I in the online-only Data Supplement. In infracardiac TAPVC, the PVC drained into a descending VV through the diaphragm. The drainage of the VV can be categorized into 3 types: direct connection to the portal vein (n=44), direct connection to the inferior vena cava (n=28), and direct connection to the hepatic vein (n=14). There was no difference in the presence of obstruction among the 3 subtypes (*P*>0.05). Mixed TAPVC was made up of a combination of supracardiac and cardiac anatomic variation in 49 patients. Two patients had a combination of infracardiac and cardiac anatomic variations. The other 3 patients had a combination of supracardiac and infracardiac anatomic variation.

Operative and Late Mortality

Early death occurred in 38 patients (5%) after the initial surgery. Four patients failed to recover from bypass: 3 patients died intraoperatively and 1 patient received extracorporeal membrane oxygenation and died 2 days later. The other causes of death included low-output failure (n=10), severe PA hypertension secondary to postrepair PVO (n=10), respiratory failure after inability to recover from ventilation (n=5), multiple organ dysfunction syndrome (n=4), intracranial hemorrhage (n=1), bacterial sepsis (n=1), and unknown (n=3). Forty-eight of the 730 living patients after discharge were lost to follow-up. There were 13 late deaths among the patients available for follow-up. Ten patients died of severe recurrent PVO (restenosis in individual PVs), among whom reintervention was performed in 6 patients. Sudden death occurred in 1 patient and was of an unknown cause. Noncardiac death occurred in another 2 patients. Significant variables associated with perioperative mortality by a univariable analysis as shown in Table 2 were entered into a multivariable analysis. Patients with a younger age at repair (*P*=0.001), infracardiac (*P*=0.035) and mixed (*P*=0.004) anatomic variation, preoperative PVO (*P*=0.027), longer duration of CPB (*P*<0.001), and ventilation (*P*=0.028) had a higher likelihood of death. In a separate analysis for neonatal patients, we found that mixed anatomic variation (*P*=0.006) and longer CPB time (*P*<0.001) were associated with mortality (Table II in the online-only Data Supplement). Mortality among the subtypes of preoperative PVO is shown in Table III in the online-only Data Supplement.

Restenosis and Reintervention

Evidence of postrepair PVO, which comprised individual PV stenosis (n=92), anastomotic restriction (n=17), or both (n=2), was observed in 111 patients. Competing-risk analysis indicated that risk factors for recurrent PVO included preoperative PVO (*P*<0.001), mixed (*P*=0.013) and infracardiac (*P*<0.001) TAPVC, and longer CPB time (*P*<0.001; Table 3). In a separate analysis for neonatal patients, we found that lower weight (*P*=0.026), preoperative PVO (*P*=0.046), and longer CPB time (*P*=0.011) were associated with recurrent PVO (Table IV in the online-only Data Supplement). Compared with conventional repair, the sutureless technique showed a propensity for a lower restenosis rate in patients presenting with preoperative PVO (*P*=0.038). No difference was observed in the restenosis rate between these 2 approaches in the neonatal patients (*P*=0.443) or patients without preoperative PVO (*P*=0.932; Figures 1 and 2).

A detailed comparison between sutureless and conventional technique is shown in Table 4. Fifty-one patients developed multi-PV or anastomotic stenosis and had clinically significant PVO after discharge, with symptoms that included hemoptysis, dyspnea, recurrent respiratory infection, or limited exercise tolerance. Among these patients, 24 underwent reintervention. The other 27 patients did not undergo a timely reintervention because of a lack of health insurance. Three of the

Table 2. Univariable and Multilevel Mixed-Effects Model of Factors Associated With Mortality

Variable	Univariable Analysis			Multilevel Mixed-Effects Model		
	P Value	c-HR	95% CI	*P* Value	a-HR	95% CI
Age	<0.001	0.984	0.977–0.991	0.001	0.989	0.982–0.996
Weight	0.683	0.995	0.973–1.018			
Sex	0.438	1.268	0.696–2.310			
Preoperative poor status	<0.001	3.099	1.679–5.719	0.832	1.803	0.520–2.255
Emergency operation	<0.001	3.071	1.783–5.292	0.190	1.594	0.810–2.907
Preoperative pulmonary venous obstruction	<0.001	3.176	1.844–5.470	0.027	2.006	1.082–3.718
Use of sutureless repair	0.860	0.920	0.366–2.314			
Infracardiac TAPVC	0.005	2.512	1.318–4.788	0.035	2.154	1.056–4.395
Mixed TAPVC	0.022	2.411	1.135–5.122	0.004	3.368	1.464–7.746
CPB time	<0.001	1.011	1.007–1.014	<0.001	1.009	1.005–1.013
AXC*	<0.001	1.015	1.008–1.023			
Duration of ventilation	<0.001	1.003	1.002–1.004	0.028	1.002	1.000–1.003
CCU stay*	<0.001	1.040	1.025–1.056			

a-HR indicates adjusted hazard ratio; AXC, aortic cross-clamping; CCU, cardiac care unit; c-HR: crude hazard ratio; CI, confidence interval; CPB, cardiopulmonary bypass; and TAPVC, total anomalous pulmonary venous connection.

*Collinearity between the variables CPB time and AXC, duration of ventilation, and CCU stay.

27 patients died. Among the remaining 24 patients, 15 required frequent in-hospital medical treatment because of respiratory infection/hemoptysis, and 9 had worsening exercise tolerance in their daily lives. Furthermore, increased velocities of the involved PVs were noted on echocardiography in 18 patients at their subsequent follow-up. Close surveillance of the 24 patients was maintained, and reintervention was performed as soon as possible. Four additional patients with significant restenosis did not undergo reintervention because of parent refusal, and they were lost to follow-up. The remaining 56 patients had narrowing around the entrance of single

Table 3. Univariable- and Cause-Specific and Subdistribution Hazard Models Associated With Recurrent PVO

Variable	Univariable Analysis			Subdistribution Hazard model			Cause-Specific Hazard Model		
	P Value	c-HR	95% CI	*P* Value	a-HR	95% CI	*P* Value	a-HR	95% CI
Age	0.003	0.997	0.996–0.999	0.421	0.999	0.995–1.002	0.067	0.999	0.997–1.000
Weight	0.018	1.013	1.002–1.024	0.987	1.000	0.986–1.014	0.578	0.996	0.982–1.001
Sex	0.438	1.268	0.696–2.310						
Preoperative poor status	0.076	1.540	0.957–2.478	0.465	0.820	0.481–1.398	0.558	0.850	0.495–1.462
Emergency operation	0.002	1.767	1.235–2.528	0.304	1.245	0.820–1.890	0.173	1.317	0.887–1.956
Preoperative PVO	<0.001	3.175	2.249–4.483	<0.001	2.240	1.527–3.288	<0.001	2.307	1.598–3.330
Use of sutureless repair	0.542	0.818	0.428–1.562						
Mixed TAPVC	0.057	1.688	0.985–2.891	0.034	1.857	1.049–3.287	0.013	2.020	1.155–3.533
Infracardiac TAPVC	<0.001	2.974	1.984–4.457	0.004	2.454	1.328–4.533	<0.001	2.900	1.632–5.151
CPB time	<0.001	1.008	1.006–1.011	0.002	1.005	1.002–1.009	<0.001	1.006	1.003–1.009
AXC*	<0.001	1.020	1.014–1.026						
Duration of ventilation	<0.001	1.002	1.001–1.003	0.308	1.001	0.999–1.002	0.113	1.001	1.000–1.002
CCU stay*	<0.001	1.024	1.012–1.037						

a-HR indicates adjusted hazard ratio; AXC, aortic cross-clamping; CCU, cardiac care unit; c-HR: crude hazard ratio; CI, confidence interval; CPB, cardiopulmonary bypass; PVO, pulmonary venous obstruction; and TAPVC, total anomalous pulmonary venous connection.

*Collinearity between the variables CPB time and AXC, duration of ventilation, and CCU stay.

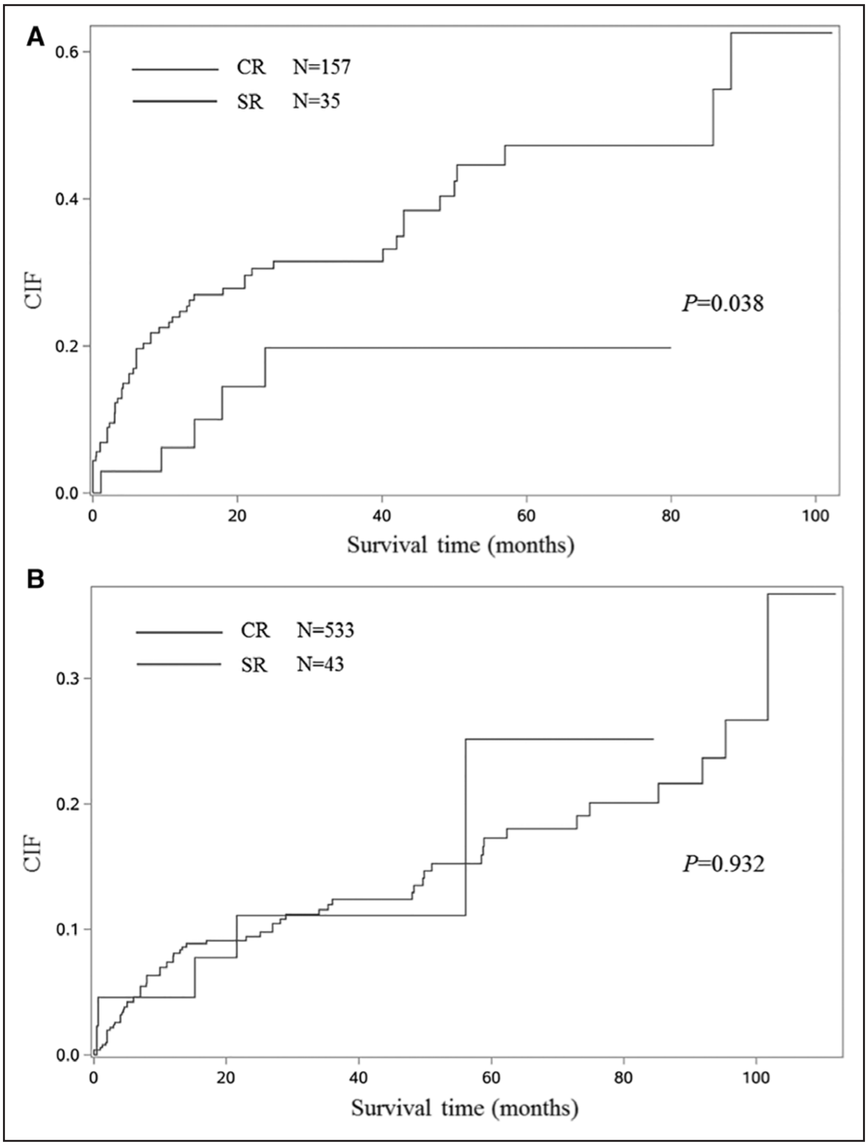

Figure 1. Cumulative incidence functions (CIFs) based on the use of the sutureless repair (SR) technique and conventional repair (CR) in this cohort of patients. CIFs based on the use of the SR technique and CR in patients (**A**) with preoperative pulmonary venous obstruction (PVO) and (**B**) without preoperative PVO.

PV and did not show any symptoms at their last follow-up. Their parents preferred to undergo ongoing follow-up instead of immediate reoperation despite our suggestion that there may be progressive deterioration as a result of recurrent PVO and symptomatology may undervalue the degree of obstruction. Surgical techniques adopted for revision of the recurrent PVO included sutureless technique in 12 cases, patch augmentation in 7 cases, and PV endarterectomy in 5 cases. Close observation was maintained for the remaining patients who experienced recurrent PVO. Five patients required balloon dilatation for stenosis of the superior vena cava (velocities >1.5 m/s) during the follow-up.

Follow-Up Data After Operation

Clinical follow-up was available for 682 survivors (93%, 682 of 730) with a median interval of 23.2 months (range, 1–112 months). Overall survival among the 4 subtypes of TAPVC is shown in Figure 3. New York Heart Association functional class was available in the survivors, and most of them (91%) were in class I or II.

DISCUSSION

Mortality

In our study cohort, the techniques adopted for TAPVC repair are associated with an acceptable survival rate, which is comparable to that reported in the Society of Thoracic Surgeons database.[1] In this study, we found that a younger age at repair, infracardiac and mixed anatomic variation, and preoperative PVO were associated with a higher mortality rate. Despite improvements achieved in the overall mortality after TAPVC correction, early mortality in younger patients has not improved in most surgery centers.[14] This subset of patients usually represent the most severe end of the TAPVC spectrum

Table 4. Comparison of Perioperative Data Between the 2 Different Surgical Strategies

	Sutureless Repair					Conventional Repair				
Variable	Overall	Supracardiac	Cardiac	Infracardiac	Mixed	Overall	Supracardiac	Cardiac	Infracardiac	Mixed
Patients, n	78	59	2	13	4	690	289	278	73	50
Age, d	323.7±23.8†	414.7±35.0	62.0±14.1	27.2±3.5†	76.0±22.5	202.6±41.0†	242.8±49.0	200.4±43.0	73.5±17.5†	171.8±49.8
Preoperative poor status, n (%)	11 (14.1)	11 (18.6)	0 (0)	0 (0)	0 (0)	74 (10.7)	33 (11.4)	21 (7.6)	13 (17.8)	7 (14)
Preoperative PVO, n (%)	35 (44.9%)	26† (44.6)	1 (50)	7 (53.8)	1 (25)	157 (22.7)	77† (26.6)	44 (15.8)	22 (30.1)	14 (28)
CPB time, min	94.6±40.6†	93.3±42.1	99.5±70.0	102.6±32.2	85.5±40.8	82.8±39.2†	94.3±39.0	66.1±36.4	87.1±31.6	103.0±31.1
AXC, min	48.5±19.4†	47.8±16.5	55.5±13.4	51.3±26.9	51.8±33.9	44.3±22.2†	49.3±20.2	36.3±23.1	47.0±19.2	56.2±17.8
CCU stay, d	11.1±5.6‡	10.6±5.6‡	19.0±5.7	10.5±3.2†	16.8±8.8	9.7±8.9‡	8.8±7.5‡	10.4±4*	9.0±6.6†	12.6±10.5
Ventilation, h	104.0±31.0†	98.4±22.0*	92.5±34.6	139.5±61.0*	77.0±22.9	87.2±29.5†	83.1±31.5*	82.9±26.8	114.9±49.0*	95.2±36.3
Mortality, n (%)	5	4	0	0	1	46	19	9	12	6
Postrepair PVO, n (%)										
With preoperative PVO	5*	4	0	1	0	53*	26	9	11	7
Without preoperative PVO	5	2	0	2	1	48	16	15	13	4

AXC indicates aortic cross-clamping; CCU, cardiac care unit; CPB, cardiopulmonary bypass; and PVO, pulmonary venous obstruction.

*Values are expressed as mean±interquartile value (mean±SD otherwise). Student *t* test or Mann-Whitney *U* test was used for comparisons of continuous variables as appropriate.

†*P*<0.05.

‡*P*<0 0.001.

and present with features that include hypoxia, hypercapnia, or acidosis. According to the previous report by Karamlou et al,[6] a younger age appears to be a surrogate for more emergency operations that are associated with a higher early rate. Patients with infracardiac TAPVC are more likely to have connections to the portal system or longer anomalous venous channels, which are prone to developing preoperative PVO. There is a high proportion of early and late death in patients with mixed anatomic variation, and this subset of patients were usually described as having a poor prognosis,[6,15,16] which might be explained by the lack of a single confluence that is reported to be a significant risk for adverse outcomes.[17] Longer CPB time may reflect the complexity of the surgical procedure or unstable patients requiring longer bypass support.

In this series, there was a statistically higher mortality rate in patients with intrinsic stenosis than in those with

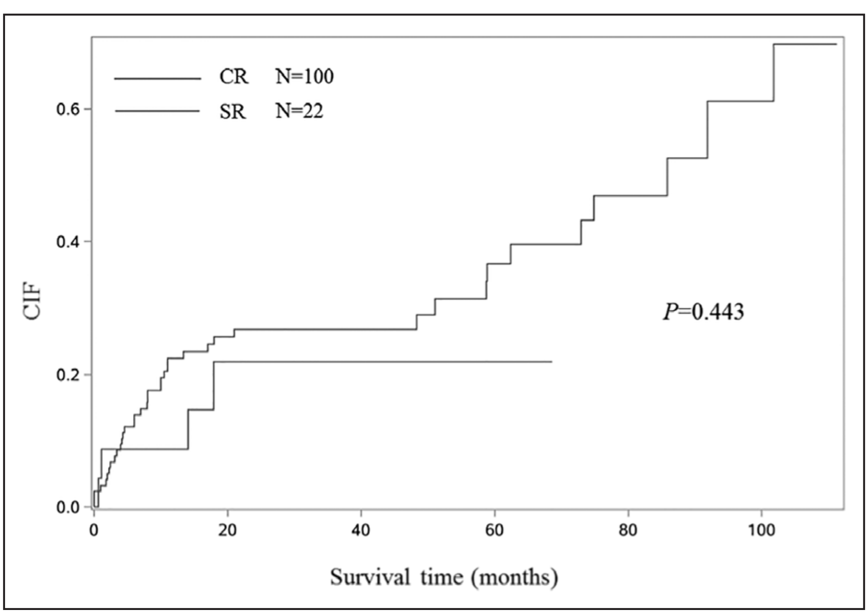

Figure 2. Cumulative incidence functions (CIFs) based on the use of the sutureless repair (SR) technique and conventional repair (CR) in neonatal patients.

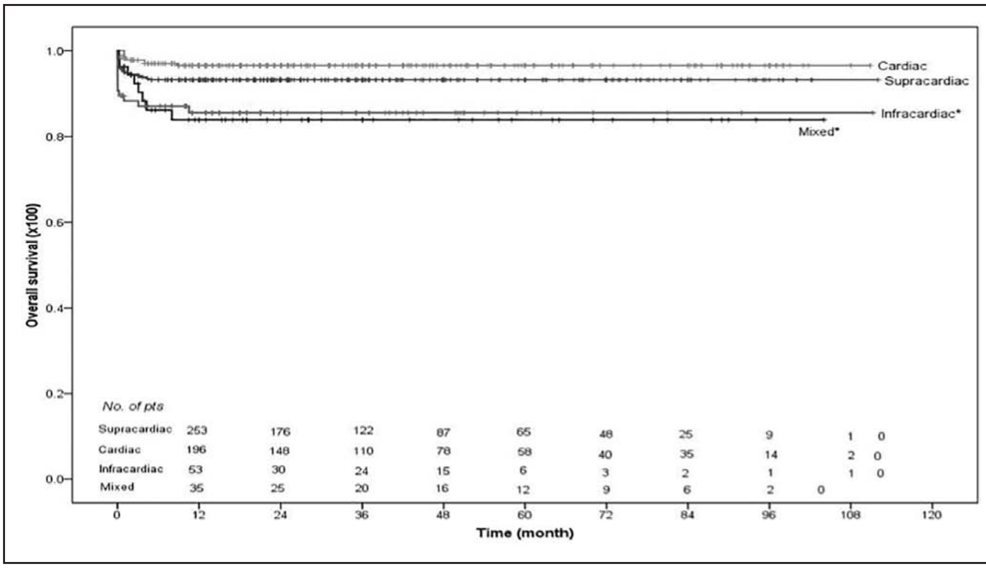

Figure 3. Kaplan-Meier analysis of overall survival among the 4 subtypes of total anomalous pulmonary venous connection (TAPVC).

*The overall survival in patients with mixed and infracardiac TAPVC is lower than in those with cardiac and supracardiac variation. *P*<0.05.

extrinsic stenosis or restrictive atrial septal defect. Intrinsic stenosis is a rare variation in obstructed TAPVC with a reported incidence of ≈6% in an international population-based study.[17] Jenkins et al[18] stated that individual PV size was an important predictor of survival in neonates with TAPVC. Bando et al[4] also found diffuse pulmonary venous narrowing to be a risk factor for death. Several published studies have shown that PV hypoplasia/stenosis probably develops early in gestation. Consequently, this in utero obstruction results in progressive hypoplasia of the pulmonary vascular bed and persistence of the lymphatic system.[19] Pulmonary lymphatic congestion in turn can cause micro-obstruction in the pulmonary vasculature. Such prenatal structural changes may predispose a patient to the progressive development of PVO that is not responsive to surgical repair.

Preoperative Diagnosis by CTA

CTA provides an alternative diagnostic modality with good spatial and temporal resolution for use in the preoperative evaluation of TAPVC. Furthermore, it is helpful in identifying airway abnormalities. CTA is superior to echocardiography in delineating the atypical vessels draining into the systemic vein because it reveals the tracts and draining site of the anomalously connected PVs and identifies the existence of VV obstruction. It is a more economical and efficient method than magnetic resonance imaging, which requires prolonged time for image acquisition and patient sedation. Cardiac catheterization may be performed for further evaluation. However, it is an invasive and an expensive method that requires general anesthesia, increases the risk of radiation exposure, and fails to provide detail information on the 3-dimensional course of the vessels. Thus, CTA plays an increasing role in TAPVC diagnosis despite its main disadvantage of radiation exposure.

Postoperative PVO

Postrepair PVO (5%–18%) results in the preponderance of reoperations after TAPVC correction.[20,21] In this cohort, the total rate of postoperative PVO was ≈15%, and there was a higher mortality rate in patients who developed recurrent PVO, although this did not reach statistical significance. By competing-risk analysis, we found that preoperative PVO and infracardiac and mixed anatomic variation were associated with recurrent PVO. Anastomotic restriction and de novo stenosis of individual PVs were 2 forms of restenosis in our series. The precise mechanisms remain unclear. Surgical traumatic manipulations or micro-obstructive changes may have a role in progressive vasoconstriction after the initial operation. In some patients, postoperative PVO began at the anastomosis site and then extended to involve the ostium or wall of the individual PVs. A possible explanation is that anastomotic obstruction may result in stenosis of upstream PVs.[22] Isolated anastomotic stricture may still develop despite adequate anastomosis in some patients. It is possible that the contractile elements in the CPV may result in constriction over time, which then contributes to an inadequate postoperative growth of the surgical anastomosis.[23] Because of the absence of a distinct CPV, individual anastomosis of PVs was usually required in most patients with mixed TAPVC. Thus, the mixed subtype is associated with an increased risk of restenosis. This finding in our patients confirms the results reported by Seale et al[17] and Karamlou et al.[6]

Surgical Technique

The contributions of different techniques to the development of subsequent PVO remain controversial.[24,25] From a single-institution experience, Hancock Friesen et al[25] demonstrated that none of the existing surgical procedures had an impact on the incidence of recurrent PVO. Recently, a sutureless technique has been reported to be a first-line therapeutic option in different subtypes of TAPVC.[26–28] This technique is favored because of its many advantages. First, it avoids any stitches in the cut edges of the PVs, which is believed to minimize the development of PVO. Second, the single suture line is geometrically simple and avoids distortion compared with the complex geometry of a suture line associated with an irregularly shaped incision in the CPV.[8] In the present study, both sutureless and conventional techniques were used in the initial operation. We found that the sutureless technique was associated with a lower restenosis rate in patients with preoperative PVO compared with the conventional repair and that no statistical difference was found in patients without preoperative PVO. However, we cannot conclude that the sutureless technique is superior to conventional repair because this study represents a combined experience of 2 centers. Therefore, technical and treatment bias may exist, as discussed below. A prospective, randomized trial is required to definitively answer the question.

Surgery for Neonates With TAPVC

Neonates remain a difficult cohort of patients in TAPVC.[15] A separate analysis of neonatal patients in this series indicated that risk factors for mortality included mixed TAPVC and longer CPB time, whereas risk factors for postoperative PVO included lower weight, preoperative PVO, and a longer CPB time. No statistical difference in postoperative PVO was observed in neonatal patients repaired by sutureless and conventional techniques. There may be several hypotheses. First, the CPB time was longer with the sutureless technique compared with conventional repair. This might affect the surgical results that may be associated with postoperative PVO. Second, the sutureless technique has been developed more recently, so a learning curve for performing this technique, especially in neonatal patients, may exist. This may also be a potential confounding factor. Third, this series consisted of a small proportion of neonates (15%). Therefore, statistical significance might be limited. Of note, this is a retrospective and consecutive study. We did not calculate the sample size prospectively or purposefully and did not have strict inclusion and exclusion criteria. Furthermore, the sutureless technique as a prophylactic method in the primary correction of TAPVC has been adopted only recently. These caused a disparity in numbers between the different study groups, which may prevent our ability to draw conclusions. To the best of our knowledge, there are only limited reports comparing sutureless and conventional techniques in repairing neonates with TAPVC.

Limitations

This series tended to include older patients, mainly because of the late presentation of some patients. The main reasons for late presentation are the relative lack of prenatal diagnosis of congenital heart disease and the lack of health insurance in some patients during the study period. The study is subject to the usual limitations of a retrospective, nonrandomized study design. Because the present study is multi-institutional, it is possible that there was variation in management protocols and surgical techniques, which complicates our ability to analyze data. The sutureless technique was performed mainly in the Guangdong Cardiovascular Institute. This may preclude meaningful comparison of outcomes between the sutureless and conventional techniques. The advancement of postoperative management may also affect the outcomes we analyzed. Reintervention for postoperative PVO is still a vexing problem, and a longer follow-up period is warranted. In contrast to the experiences in the United States or Europe, reintervention in China is somewhat conservative and is constrained mainly by the preferences of the patients' parents and financial burden, which may affect the accuracy of the late follow-up information.

Conclusions

Acceptable outcomes after surgical correction for TAPVC have been achieved in recently established, specialized congenital heart centers in China. Neonatal patients, infracardiac and mixed TAPVC, and preoperative PVO are associated with a poorer prognosis. CTA has an important role in the preoperative morphological evaluation of TAPVC and is helpful for surgical planning. The unique benefits of the sutureless technique in decreasing recurrent PVO require further study.

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FOOTNOTES

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