Rechanneling of total anomalous pulmonary venous connection with or without vertical vein ligation: Results and guidelines for candidate selection

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Objective: This study investigated whether postoperative low cardiac output and mortality in obstructed total anomalous pulmonary venous connection could be reduced by selective vertical vein patency.

Methods: Fifty-eight patients undergoing rechanneling of total anomalous pulmonary venous connection between 1997 and 2006 were studied. The vertical vein was left patent in 27 patients (group I) and ligated in 31 (group II). Mean ages were 1.49 ± 1.63 and 4.37 ± 3.38 months for groups I and II, respectively.

Results: Operative mortalities were 29.1% and 7.4% for ligated and unligated groups, respectively (relative risk 1.75, 1.16-2.64, $P = .036$). Age younger than 1 month, obstructive total anomalous pulmonary venous connection, hypoplastic pulmonary veins, pulmonary hypertensive crisis, low cardiac output, and vertical vein ligation were significant risk factors for death according to logistic regression analysis. Patients with obstructed total anomalous pulmonary venous connection undergoing vertical vein ligation demonstrated predominant right ventricular dysfunction (relative risk 2.93, 1.28-6.73, $P = .011$), pulmonary hypertensive crisis (relative risk 2.90, 1.25-6.75, $P = .013$), and 3.28 times the risk of death (95% confidence interval 1.08-9.99, $P = .032$) relative to the unligated group.

Conclusions: In a subset of patients with obstructed total anomalous pulmonary venous connection, an unligated vertical vein reduces pulmonary arterial pressure, decreases perioperative pulmonary hypertensive crises, provides a temporary pop-off valve during pulmonary hypertensive crisis, and improves survival by providing superior hemodynamics. The high mortality in the ligated group suggests that patients with obstructed total anomalous pulmonary venous connection with post-bypass moderate pulmonary hypertension possibly should not undergo vertical vein ligation. We propose routine use of an adjustable ligature around the vertical vein in all patients with more than moderate post-bypass pulmonary hypertension, allowing gradual tightening in increments without multiple reoperations.

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Abbreviations and Acronyms

ASD	= atrial septal defect
CI	= confidence interval
CPB	= cardiopulmonary bypass
LA	= left atrium
PA	= pulmonary artery
RR	= relative risk
SPAP	= systolic pulmonary arterial pressure
TAPVC	= total anomalous pulmonary venous connection

Despite improvements during the past decade in pediatric anesthesia, intensive care, and myocardial protection, repair of obstructive total anomalous pulmonary venous connection (TAPVC) continues to be associated with significant mortality, reportedly ranging from 10% to 50%.¹⁻⁵ In 1999, we reported worse outcomes of TAPVC repair as a result of delayed referral, accounting for cardiac cachexia, emergency operation, pulmonary infection, and severe pulmonary artery (PA) hypertension.⁵

Studies have documented that in the presence of obstructive pulmonary venous drainage, the left-sided chambers are smaller than those in nonobstructive cases.⁶⁻⁹ Despite innovative surgical techniques to increase the dimension of the left atrial (LA) cavity and pharmacologic manipulations to combat pulmonary hypertensive crisis, low cardiac output remains a significant problem, leading to hemodynamic instability and morbidity after surgery.¹⁻⁹

From these observations, it has been hypothesized that a patent vertical vein may function as a temporary reservoir for pulmonary venous blood after TAPVC repair, volume unloading the small, noncompliant, left-sided cardiac chambers until they are able to grow and adapt to the increased flow demands.⁸⁻¹¹ Not all investigators and surgeons have accepted these findings or used these techniques. To investigate this hypothesis, this study aimed first to ascertain whether the practice of routine ligation of vertical vein is necessary, second to examine the effects of selective patent vertical vein on postoperative hemodynamics, third to compare the outcomes of patients undergoing interruption of the vertical vein with those in whom it was left unligated, and fourth to determine the long-term fate of the unligated vertical vein.

Patients and Methods**Criteria for Decision Making and Selection of Patients**

This prospective study evaluated outcomes after selective use of vertical vein ligation in a consecutive series of patients undergoing repair of isolated TAPVC. Only patients with type I, III, or IV TAPVC with a discernible ascending or descending vertical vein were included in this study. The decision to keep the vertical vein patent was made after the occurrence of elevated PA pressure

(systemic or suprasystemic) after coming off cardiopulmonary bypass (CPB) and untoward hemodynamic effects on snaring the vertical vein. All patients with nonobstructed TAPVC without pulmonary hypertension and patients with obstructed TAPVC with moderate post-CPB pulmonary hypertension (systolic PA pressure [SPAP] 31-50 mm Hg) underwent vertical vein ligation. Thus, there were four forces driving our criteria for selection of patients in whom the vertical vein was kept patent after rechanneling of TAPVC: (1) the desire to reduce the PA pressure in the perioperative period after achievement of an adequately sized, unrestrictive anastomosis along with pharmacologic manipulations; (2) the desire to reduce pulmonary hypertensive crises, low cardiac output, and in-hospital mortality after repair of TAPVC with pulmonary hypertension; (3) the desire that the unligated vertical vein serve as a temporary pop-off valve in the event of pulmonary hypertensive crises; and (4) the desire that the unligated vertical vein function as a temporary venous reservoir for pulmonary venous blood, volume unloading the small, noncompliant left-sided cardiac chambers until they were able to grow and adapt to the requisite flow demands.

We excluded all patients with anomalous pulmonary venous drainage to the right superior vena cava, coronary sinus, or right atrium who lacked a discernible vertical vein ($n = 5$). We also excluded children with associated complex lesions, such as atrioventricular canal, transposition of the great arteries, or functionally univentricular heart ($n = 3$).

Demographics and Preoperative Evaluation

To test our postulates, we embarked on a program of not ligating the vertical vein in selected patients undergoing TAPVC repair at our institution. All patients in this study population were operated on by a single surgeon (U.K.C.), making uniformity in the surgical protocol possible. The patients were entered in the study protocol after informed consent had been obtained from their parents or guardians. Fifty-eight consecutive patients undergoing rechanneling of isolated TAPVC from January 1997 through March 2006 at All India Institute of Medical Sciences, New Delhi, were included in this prospective study (Figure E1). In this study, 27 patients (46.5%) underwent rechanneling of TAPVC without vertical vein ligation (group I), and 31 patients (53.5%) underwent vertical vein ligation (group II). Their demographic and clinical profiles are depicted in Table 1.

Patient age at operation ranged from 1 day to 8 months (mean 1.49 ± 1.63 months, median 1 month) among those who did not undergo vertical vein ligation and from 1 to 12 months (mean 4.37 ± 3.37 months, median 3 months) among those who did. Fourteen patients (24.1%) were younger than 1 month, and 9 (15.5%) patients were between 6 and 12 months (Figure E2). Because of the uses of selective ligation, there were significant differences in the baseline characteristics of the two groups (Table 1). Most patients in this study group were small for age and 53.5% weighed less than the 50th percentile of predicted weight for Indian neonates and infants.

Echocardiography was our principal diagnostic modality. Transthoracic 2-dimensional, color flow, Doppler echocardiography was performed (Sonos 5500; Hewlett-Packard Company, Palo Alto, Calif), and patients were categorized according to the site of pulmonary venous drainage. Cardiac catheterization and angiocar-

TABLE 1. Demographic, operative, and postoperative details of the study group

	Group I	Group II	P value
No. of patients (n = 58)	27 (46.5%)	31 (53.5%)	
Age (mo, mean $\pm$ SD)	1.49 $\pm$ 1.63	4.37 $\pm$ 3.38	<.001
Weight (kg, mean $\pm$ SD)	3.75 $\pm$ 1.08	5.19 $\pm$ 1.54	<.001
TAPVC (No.)			.11
Obstructive (n = 30)	17 (63)	13 (42)	
Nonobstructive (n = 28)	10 (37)	18 (58)	
Anatomy (No.)			.09
Supracardiac (n = 53)	25 (92.6%)	28 (90.3%)	
Infracardiac (n = 2)	2 (7.4%)	0	
Mixed (n = 3)	0	3 (9.7)	
Pulmonary arterial hypertension (No.)			<.001
Yes (n = 46)	27 (100%)	19 (61.3%)	
No (n = 12)	0	12 (38.7%)	
Preoperative hemodynamic data			
Systolic PAP (No.)			<.001
<18 mm Hg (n = 12)	0	12 (38.7%)	
19-30 mm Hg (n = 2)	0	2 (6.4%)	
31-50 mm Hg (n = 14)	7 (25.9%)	7 (22.6%)	
>50 mm Hg (n = 30)	20 (74.1%)	10 (32.3%)	
Mean PAP in patients with systolic PAP >18 mm Hg (No., n = 46)	58.8 $\pm$ 9.5 (n = 27)	54.8 $\pm$ 8.5 (n = 19)	.15
RVSP/LVSP (No.)			.001
1.2 $\pm$ 0.2 (n = 30)	20 (74.1%)	10 (32.2%)	
0.7 $\pm$ 0.2 (n = 28)	7 (25.9%)	21 (67.8%)	
Preoperative arterial pH (mean $\pm$ SD)	7.22 $\pm$ 0.05	7.36 $\pm$ 0.04	<.001
Preoperative Pao ₂ (mm Hg, mean $\pm$ SD)	35 $\pm$ 7	48 $\pm$ 5	<.001
Preoperative mechanical ventilation (No.)			.016
Yes (n = 9)	8 (29.6%)	1 (3.2%)	
No (n = 49)	19 (70.4%)	30 (96.8%)	
Preoperative inotropes (No.)			.004
Yes (n = 13)	11 (40.7%)	2 (6.5%)	
No (n = 45)	16 (59.3%)	29 (93.5%)	
Operation timing (No.)			.009
Emergency (n = 28)	18 (66.7%)	10 (32.2%)	
Elective (n = 30)	9 (33.3%)	21 (67.8%)	
In-hospital mortality (No.)			
Overall	2 (7.4%)	9 (29.1%)	.04
Cardiac and pulmonary hypertension related	2 (7.4%)	8 (25.8%)	.09
Pulmonary hypertensive crises (No.)			<.001
Yes (n = 23)	4 (14.8%)	19 (61.3%)	
No (n = 35)	23 (85.2%)	12 (38.7%)	
Low cardiac output (No.)			<.001
Yes (n = 25)	5 (18.5%)	20 (64.5%)	
No (n = 33)	22 (81.5%)	11 (35.5%)	
Duration of mechanical ventilation (d)			<.001
Mean $\pm$ SD	35 $\pm$ 2	6.5 $\pm$ 3	
Range	1-7	2-20	
ICU stay (d, mean $\pm$ SD)	7.26 $\pm$ 6.13	15.25 $\pm$ 8.73	<.001
Hospital stay (d, mean $\pm$ SD)	14.70 $\pm$ 4.24	23.74 $\pm$ 10.0	<.001
Postoperative hemodynamic data in patients with preoperative systolic PAP >18 mm Hg (n = 46)			
Mean PAP (mm Hg, mean $\pm$ SD)	34 $\pm$ 5	45 $\pm$ 4	<.001
Mean ABP (mm Hg, mean $\pm$ SD)	64 $\pm$ 5	48 $\pm$ 3	<.001
Mean LAP (mm Hg, mean $\pm$ SD)	12 $\pm$ 2	19 $\pm$ 3	<.001
Arterial blood pH (mean $\pm$ SD)	7.46 $\pm$ 0.05	7.27 $\pm$ 0.03	<.001

TAPVC, Total anomalous pulmonary venous connection; PAP, pulmonary arterial pressure; RVSP/LVSP, right-to-left ventricular systolic pressure ratio; ICU, intensive care unit; ABP, arterial blood pressure; LAP, left atrial pressure.

diography were performed in 9 patients in whom an accurate anatomic pattern of pulmonary venous return was not established by echocardiography and in 10 patients to evaluate the degree of PA hypertension. Of the 58 patients, 53 (91.3%) had a supracardiac connection, 2 (3.5%) had an infracardiac connection, and 3 (5.2%) had a combination of supracardiac and infracardiac pulmonary venous connections.

Obstructed pulmonary venous drainage was present in 30 patients (51.8%). Of these obstructed drainages, 28 (93.3%) were supracardiac and 2 (6.7%) were infracardiac. The level of obstruction in the supracardiac variety ($n = 28$) was located at the vertical vein–innominate vein junction. This includes 2 cases in which preoperative balloon dilation of the vertical vein was performed. The ductus arteriosus was patent in 32 patients. Nine patients (15.5%) required mechanical ventilation before surgery for respiratory distress, and 13 patients (22.4%) required inotropic support for hemodynamic instability. The PA pressure was measured in all patients before the institution of CPB (Table 1).

Definitions

Echocardiography was our principal diagnostic modality, and 39 of the 58 patients proceeded to operation with only echocardiographic data. The indications of preoperative cardiac catheterization were (1) anatomy that was unresolved by echocardiography, (2) characterization of the pulmonary venous obstruction, or (3) exclusion of major associated cardiac anomalies that required delineation or intervention.

Preoperative pulmonary venous drainage was considered obstructive if there was echocardiographic ($n = 20/58$) or angiographic ($n = 10/58$) data that indicated: (1) a significant gradient between the pulmonary veins and their point of drainage (flow acceleration >2 m/s by echocardiography or pressure gradient >4 mm Hg), (2) monophasic and continuous Doppler flow pattern in the individual pulmonary veins, the pulmonary venous confluence or the vertical vein, or (3) angiographically evident localized reduction in a single pulmonary vein diameter of 50% or more. Pulmonary hypertension was defined as a right-to-left ventricular systolic pressure ratio of 0.6. According to SPAP, as measured by cardiac catheterization or on echocardiography on the basis of the velocity of tricuspid regurgitation, pulmonary hypertension was graded as follows: none (SPAP <18 mm Hg), mild (SPAP 19–30 mm Hg), moderate (SPAP 31–50 mm Hg), or severe (SPAP >50 mm Hg). Isolated or simple TAPVC was diagnosed if the patient had TAPVC in association with a secundum atrial septal defect (ASD), a patent ductus arteriosus, or both. An operation was classified as an emergency if the patient was taken to the operating room within the first 24 hours after arrival at the hospital for hemodynamic or ventilatory compromise.

Low cardiac output syndrome in repaired TAPVC was diagnosed if the patient required inotropic support (dopamine at 4–10 $\mu\text{g}/[\text{kg} \cdot \text{min}]$), dobutamine at 5–10 $\mu\text{g}/[\text{kg} \cdot \text{min}]$, epinephrine at 0.01–0.1 $\mu\text{g}/[\text{kg} \cdot \text{min}]$, milrinone at 50 $\mu\text{g}/\text{kg}$ intravenous bolus followed by 0.375–0.75 $\mu\text{g}/[\text{kg} \cdot \text{min}]$), either isolated or in combination in the operating room or in the intensive care unit, to maintain stable hemodynamics in the absence of residual structural lesions and mechanical external compression after correction of all electrolytes or blood gas abnormalities and after adjustment of the preload to its optimal value. Low-output syndrome was also diag-

nosed if there was an increasing requirement of the previously mentioned inotropes along with afterload reduction with sodium nitroprusside. Patients who received less than 4 $\mu\text{g}/[\text{kg} \cdot \text{min}]$ dopamine to increase renal perfusion were not considered to have low output syndrome.

Invasive monitoring to measure cardiac output directly (thermodilution catheter, PA pressure line, and thermistors) is cumbersome and hazardous in children and generally avoided in our setup, except in complex cases. We generally limit intracardiac monitoring to right atrial, LA, and PA pressure lines.

Accordingly, under the definition of low output syndrome after repaired TAPVC, an integration of relevant clinical, laboratory, and bedside echocardiographic criteria was used. The criteria for diagnosis were as follows: cold extremities, absent pedal pulses, decreased toe temperature, reduced systolic pressure, impaired renal function and oliguria (<1.0 mL/[kg $\cdot$ hr]), metabolic acidosis, increased serum lactate levels (≥ 2 mmol/L for ≥ 2 hours), low mixed venous oxygen saturation ($\leq 50\%$), and blunted sensorium in the absence of residual anastomotic or pulmonary venous obstruction.

Operative and Postoperative Management

The surgical techniques and intraoperative and postoperative management protocols were uniform throughout the study period. Twenty-eight patients (48.3%) required emergency surgical intervention for hemodynamic or respiratory compromise. The operations were performed with moderately hypothermic CPB through angled venous cannulas into the superior and inferior caval veins and aortic cannulation. Cold hyperkalemic blood cardioplegia and topical hypothermia were used for myocardial protection. After routine ligation of patent ductus arteriosus at the commencement of CPB, cooling was started. During the cooling phase, the vertical vein was dissected extrapericardially and looped. In patients with supracardiac connection draining into the innominate vein and infracardiac connection, the apex of the heart was lifted cephalad and to the right, with the right pleural cavity wide open. This allowed excellent exposure.

Long, transverse incisions were made on the common pulmonary venous chamber and the LA. A large anastomosis (2.5–3 cm, or as large as the calculated mitral valve orifice area) was made between these two chambers from outside with a running 6-0 polypropylene suture (Vicryl; Ethicon Inc, Somerville, NJ). ASDs were closed either through a separate right atriotomy or through the same LA incision. For patients with large ASDs, we used Dacron polyester fabric or pericardial patches to close the atrial septum, extending it to the right of the anastomosis of the pulmonary venous sinus. This not only served to enhance the capacity of the LA but also ensured an adequately sized communication between the pulmonary vein and the LA. In the mixed type of drainage, repair was accomplished through a combination of transatrial and apical approaches.

In this series, we maintained patency of the foramen ovale or ASD in patients with obstructive supracardiac and infracardiac type of lesions with PA hypertension ($n = 30$) for decompression of the right-sided chambers in the event of pulmonary hypertensive crises. We proceeded to keep the vertical vein unligated if the PA pressure remained elevated (systemic or suprasystemic) after coming off CPB on snaring the vertical vein. LA and PA pressures

were monitored continuously after the operation. After the operation, patients were sedated and paralyzed during the first 24 to 48 hours. PA hypertension was treated with hyperventilation, sedation, phenoxybenzamine, sildenafil citrate (INN sildenafil), and inhaled nitric oxide (10-15 ppm) in varying combinations.

Eleven patients with unligated vertical veins continued to exhibit signs and symptoms of right heart failure as a result of a large left-to-right shunt. The vertical vein was subsequently ligated through a re sternotomy in 4 patients, a left anterolateral thoracotomy in 2 patients, and a percutaneously adjustable vertical vein ligation in 5 patients between 1 and 2 postoperative weeks.

The sternum was left open in 8 patients. Delayed sternal closure was done 24 to 48 hours after hemodynamic stability was achieved. Median duration of inotrope requirement was 7 days (range 5-18 days). Median duration of ventilation was 6 days (range 2-20 days). Twenty-six patients received total parenteral nutrition commencing after 48 hours of ventilation. After the operation, patients were weaned from digoxin, diuretics, phenoxybenzamine, and angiotensin-converting enzyme-inhibitors at varying intervals.

The mean CPB time was 42 minutes (range 32–70 minutes), and the mean aortic crossclamp time was 32 minutes (range 25–42 minutes). Left ventricular assist devices and extracorporeal membrane oxygenation were not used for any patient in this study group.

Statistical Analysis

Data were analyzed with STATA 9.0 (Stata Corporation, College Station, Tex). Continuous and interval-related data are presented as mean $\pm$ SD, whereas categorical variables are presented as frequency distribution and percentages. Qualitative data were analyzed with the χ^2 test, and quantitative data were analyzed with the Student *t*-test.

Mortalities were calculated depending on the total number of years of follow-up for each patient. Actuarial estimates were calculated with the Kaplan–Meier technique, and the log-rank test was performed to analyze statistically the difference in survival between patients undergoing rechanneling of TAPVC with versus without vertical vein ligation (Figure E3).

Univariate logistic regression was performed to calculate the relative risk (RR) and the 95% confidence interval (CI) for each independent variable. A multivariate forward stepwise logistic regression model was used to identify independent risk factors for in-hospital mortality. Selection of independent variables was a forward stepwise method with critical *P* values of .10 and .15 for variable inclusion and exclusion, respectively. Vertical vein ligation was used as a potential explanatory variable along with other candidate variables (Tables E1 and E2). Two-tailed probability was used in all the statistical tests.

Results

Short-term Results

The operative mortalities were 29.1% and 7.4% for the ligated and unligated groups, respectively (RR 1.75, 95% CI 1.16-2.64, *P* = .036). The deaths (*n* = 11, 18.9%) were due to persistent postoperative PA hypertension and low cardiac output (group I *n* = 2, group II *n* = 6), massive pulmonary

hemorrhage (group II *n* = 1), refractory ventricular arrhythmias (group II *n* = 1), and sepsis (group II *n* = 1).

The operative mortalities were 30% (*n* = 9/30) for patients with obstructive TAPVC and 7.2% (*n* = 2/28) with nonobstructive TAPVC (RR 1.83, 95% CI 1.2-2.79, *P* = .026). In the obstructed TAPVC group (*n* = 30), perioperative mortalities were 53.8% for patients who underwent vertical vein ligation and 11.8% for those who did not; this difference was statistically significant (χ^2_1) = 6.21, RR 2.72, 95% CI 1.27-5.83, *P* = .02).

After the operation, 54 patients exhibited an entirely satisfactory primary repair (echocardiography showing a large anastomosis, as large as or larger than mitral valve orifice area, with no gradient between the pulmonary venous confluence and LA and nonturbulent biphasic pulmonary venous flow at less than 1.2 m/s), and 4 patients demonstrated subtle echocardiographic changes with a large unrestrictive anastomosis with no gradient between common pulmonary venous chamber and LA and biphasic or nearly biphasic pulmonary venous flow with a velocity of 1.2 to 1.6 m/s.

Patients with nonobstructed venous drainage without pulmonary hypertension (supracardiac, *n* = 12) underwent vertical vein ligation without hemodynamic instability. However, 56.7% of patients (*n* = 17/30) with preoperative obstructed pulmonary venous drainage and 35.7% of patients (*n* = 10/28) with nonobstructed pulmonary venous drainage with pulmonary hypertension had varying degrees of hemodynamic deterioration after repair. Loosening of the vertical vein resulted in a significant decrease of the PA and LA pressures in all patients (*P* < .001). This was associated with a significant increase in mean arterial blood pressure and correction of metabolic acidosis in all cases (Tables 1 and E3). Although a pulmonary-to-systemic blood flow ratio greater than 0.6 remained in 15 of 27 patients with obstructed pulmonary venous drainage 12 hours after the operation, the ratio decreased significantly to less than 0.6 during a mean time of 45 ± 15 hours (range 15-60 hours) in 12 patients.

It is pertinent to state that, in this study group, the vertical vein was left unligated only in patients (*n* = 27) demonstrating systemic or suprasystemic PA pressure and unstable hemodynamics. Patients with obstructive TAPVC who exhibited moderate post-CPB PA hypertension with stable hemodynamics (*n* = 13) underwent concomitant vertical vein ligation. The SPAP in this subgroup of patients decreased to around half systemic during the operation. Subsequently, after initial 24 hours, 23 patients (group I *n* = 4; group II *n* = 19) had paroxysmal pulmonary hypertensive crises. These hypertensive episodes were more frequent and severe in patients with a ligated vertical vein. Despite institution of pulmonary vasodilators, 6 patients of the ligated group (19.4%) and 2 patients of the unligated group (7.4%)

ultimately died of these hypertensive episodes. The risk of death from pulmonary hypertensive crisis was 2.9 times higher (95% CI 1.25-6.75, $P = .013$) for patients who had obstructive TAPVC and underwent vertical vein ligation (Table E2). Serial echocardiography during these episodes demonstrated left-to-right shunting through the patent vertical vein in all cases, clearly documenting the vertical vein's role as a temporary vent.

Before the operation, of 30 patients with obstructive TAPVC, 4 patients exhibited a small indexed individual pulmonary vein size and 2 patients had a small-sized pulmonary venous confluence. Autopsy findings documented a small pulmonary venous confluence, diffuse hypoplasia, intimal hypertrophy, and increased medial thickness of the PAs and veins in 4 nonsurvivors (group I $n = 2$; group II $n = 2$). Two patients of group II who died of paroxysmal hypertensive crises exhibited pulmonary lymphangiectasia and interstitial emphysema on postmortem examination. One patient undergoing vertical vein ligation could not be weaned from CPB because of massive intrapulmonary hemorrhage. Before the operation, he was ventilated and had ventricular fibrillation and diffusely small pulmonary veins.

Eleven patients with obstructed TAPVC with unligated vertical vein continued to have tachypnea and right heart failure between 1 and 2 postoperative weeks. Postoperative echocardiograms showed unobstructed pulmonary venous return into the LA, with a distended vertical vein and a large left-to-right shunt. The vertical vein was subsequently ligated through re sternotomy in 4 cases, left anterolateral thoracotomy in 2 cases, and adjustable vertical vein ligature in 5 cases. In 6 cases, on snaring of the vertical vein, the mean LA pressure increased to 23.33 ± 1.96 mm Hg (range 21-26 mm Hg), accompanied by acute increase of PA pressure to suprasystemic levels. These patients were mechanically ventilated with an inspired oxygen fraction of 0.8 and 10 ppm nitric oxide and were administered pulmonary vasodilators (sodium nitroprusside $0.5 \mu\text{g}/[\text{kg} \cdot \text{min}]$, phenoxylbenzamine 0.5 mg/kg at 8-hour intervals) for 72 to 96 hours. Subsequently, the mean LA pressure decreased to 17.33 ± 1.63 mm Hg (range 16-20 mm Hg) in all patients, ($P < .001$), all of whom had an uneventful recovery.

By univariate analysis, age younger than 1 month, weight less than 50th percentile, obstructed drainage, diffusely hypoplastic pulmonary veins, presence of severe pulmonary hypertension, ligated vertical vein in the presence of preoperative PA hypertension, emergency surgery, postoperative pulmonary hypertensive crises, and low output syndrome were significant negative factors for survival (Table E1). Furthermore, with this strategy of selective vertical vein patency, the ligated vertical vein group with TAPVC of the obstructed variety demonstrated statistically significantly higher incidences of postoperative right ventricular dysfunction, low cardiac output (RR 2.4, 95% CI

1.48-3.9, $P = .007$] and pulmonary hypertensive crisis (RR 2.28, 95% CI 1.31-3.96, $P = .002$).

Multivariate analysis identified only seven predictors for death after TAPVC repair (Table E2). The risk of death was 3.28 times higher (95% CI 1.08-9.99) for patients with TAPVC and PA hypertension undergoing vertical vein ligation than in the unligated group.

Late Outcomes

There were no late deaths. Follow-up was 100% complete and ranged from 1 to 104 months (mean 33.34 ± 29.88 months, median 30 months). The total follow-up was 130.6 patient-years, with mean survival times of 96 ± 5 (mean $\pm$ SE) months (95% CI 86-107 months), for group I and 71 ± 8 (mean $\pm$ SE) months (95% CI 55-86 months) for group II. At 33.34 ± 29.88 months, the actuarial survivals were $92.6\% \pm 0.05\%$ in group I and $71.0\% \pm 0.08\%$ in group II. By log-rank test, the difference in survival between the two groups was statistically significant ($P = .037$; Figure E3). All survivors of groups I and II ($n = 47$) were in New York Heart Association functional class I or II at last follow-up visit. Vertical vein patency did not affect late postoperative outcome. There were no reoperations in the late postoperative period. At a mean follow-up of 33.34 ± 29.88 months, serial 2-dimensional echocardiography failed to reveal flow through the unligated ascending or descending vertical vein in the remaining 14 patients.

Discussion

Careful analysis of published series substantiates improved outcomes of TAPVC repair with time.¹⁻⁵ The management strategies leading to this improvement include aggressive preoperative stabilization, improved diagnostic accuracy (with echocardiography often obviating the need for cardiac catheterization), improvement in myocardial protection, creation of a large, tension-free anastomosis, precise geometric alignment of the pulmonary venous chamber with the body of the LA (avoiding torsion and rotation of the pulmonary veins), introduction of phenoxylbenzamine and nitric oxide in the management of pulmonary hypertensive crises, and delayed sternal closure.¹⁻⁵

Despite introduction of these management strategies, postoperative low output persists in a subset of patients undergoing repair of obstructive TAPVC.¹⁻⁵ Recurrent pulmonary hypertensive crises, rapid development of PA and pulmonary venous medial hypertrophy, and small, noncompliant LA and LV have been variously implicated as the causative factors for low output syndrome.¹⁻⁹

The important factors that may have contributed to a high overall mortality (18.9%) in this study are late presentation, failure of early recognition (and thus delayed referral), and underdeveloped infants. This is in contrast to the West, where most patients (>50%) are operated on before

1 month of age.^{1-4,8,10,11} Late referral is also responsible for the development of severe pulmonary hypertension, a prolonged period of malnutrition, and ultimately cardiac cachexia. In our earlier publication, we demonstrated that these patients are predisposed toward pulmonary infection, sepsis, and postoperative intrabronchial hemorrhage and that they react unfavorably to such stresses as CPB and postoperative events.⁵

The mechanisms causing heightened pulmonary vasoreactivity after repair of TAPVC are multifactorial and may reflect release of platelet-activating factors, endothelin, and arachidonic metabolites from pulmonary endothelial cells; decreased ratio of prostacyclin to thromboxane; and a greater decline or absence of acetylcholine responsiveness.¹⁻¹¹ Many agents have been advanced as optimal on the grounds that they selectively reduce pulmonary vascular resistance, but few do so, and no clearly superior agent has been identified. In this study, varying combinations of fentanyl, hyperventilation, correction of acidosis, inhaled nitric oxide, sodium nitroprusside, and phenoxybenzamine were therefore used to decrease the prevalence and severity of pulmonary hypertensive crises. Thirty patients in this series with obstructive supracardiac and infracardiac lesions had atrial septal fenestration. During pulmonary hypertensive crises with limited right ventricular output and elevated central venous pressure, a fenestrated ASD permitted right-to-left shunting, increasing left ventricular preload and cardiac output, albeit at the expense of some degree of systemic desaturation.

Previous investigators have concluded that there are four anatomic and physiologic issues involved in a subset of patients with obstructed TAPVC. The issues are (1) structurally smaller left-sided chambers, (2) a noncompliant and dysfunctional left ventricle, (3) transient increase in pulmonary vascular resistance (disease-related or CPB-related heightened pulmonary vasoreactivity), and (4) increased pulmonary vascular resistance as a result of increased medial thickness of the pulmonary vasculature. Such chamber abnormalities have been attributed to reduced atrial filling and chamber underloading as a result of a large left-to-right shunt and decreased left ventricular diastolic pressure volume relation related to elevated right ventricular diastolic pressure or volume.¹²⁻¹⁴ It is noteworthy that all patients with preoperative obstructive pulmonary venous drainage in this study ($n = 30$) had SPAP greater than 50 mm Hg and a mean right-to-left ventricular pressure ratio of 1.2 ± 0.02 mm Hg (Table 1). To allow the left side of the heart to adapt to and maintain adequate cardiac output, we used redundant Dacron polyester fabric or pericardial patches to close the ASD and incorporated part of the vertical vein to achieve structural alignment and augmentation of the LA cavity. Other investigators have reported a two-patch technique of LA enlargement to increase atrial compliance.^{4,15} Subse-

quently, several investigators have demonstrated increased incidence of supraventricular arrhythmias as a result of transversal right atrial incision and division of the crista supraventricularis.¹⁻⁴ We have not used this technique.

Reports addressing the issue of unligated vertical vein and postoperative hemodynamics are limited and controversial.^{10,11,16-18} As yet, there is no fool-proof formula for selection of candidates for keeping the vertical vein patent. Traditionally, most surgeons have emphasized routine ligation of the vertical vein at the time of rechanneling of TAPVC repair to prevent the perceived consequence of a residual left-to-right shunt.¹⁻⁵ Some investigators, however, have recently demonstrated that the practice of routine interruption of the vertical vein is unnecessary and may actually be undesirable for patients with small left heart chambers. It is conjectured that the unligated vertical vein may serve as a temporary pop-off valve, allowing the left heart chambers adequate time for growth and functional adaptation.^{10,11,16-18}

In this series, the decision to keep the vertical vein patent was made after the occurrence of systemic or suprasystemic PA pressure after coming off CPB on snaring the vertical vein (Table E3). In the absence of anastomotic stricture, this undesirable effect can be explained by decreased unloading of the pulmonary venous chamber caused by noncompliant left-sided chambers. Incorporation of the vertical vein resulted in increasing the size of the LA by inclusion of this venous reservoir, served to lower the PA and vertical vein pressures almost immediately, and at the same time acted as a pop-off valve to the systemic venous system during episodes of pulmonary hypertensive crisis. It is conceivable that leaving a calibrated atrial septal fenestration might also help to decompress the small LA after repair. Thus the unligated vertical vein in conjunction with a calibrated atrial septal fenestration resulted in equalization of LA and central venous pressures and was the automatic choice to avoid a dismal outcome in the perioperative period.

The unligated vertical vein group (group I) demonstrated statistically significant decrease in in-hospital mortality ($P = .04$), decreased pulmonary hypertensive crises ($P < .001$), lessened requirement for postoperative mechanical ventilation ($P < .001$), shortened intensive care unit and hospital stays ($P < .001$), and improved postoperative hemodynamics ($P < .001$; Table 1). Logistic regression analysis accounting for the effects of other factors demonstrated 3.28 times (95% CI 1.08-9.99) increased risk of death after vertical vein ligation in the setting of obstructed TAPVC with pulmonary hypertension (Table E2).

On the other hand, despite keeping the vertical vein open, 2 patients (7.4%) died early postoperatively of recurrent pulmonary hypertensive crisis and low cardiac output. Autopsy findings documented small pulmonary venous confluence, diffuse hypoplasia, intimal hypertrophy, and in-

creased medial thickness of the pulmonary vasculature in 4 nonsurvivors (group I $n = 2$, group II $n = 2$). Two patients of group II who died of paroxysmal pulmonary hypertensive crisis exhibited pulmonary lymphangiectasia and interstitial emphysema on postmortem examination. Anatomic studies by others have shown that preoperative pulmonary venous obstruction is associated with increased medial thickness in both PAs and veins that exceeds by far the degree of change observed in other lesions with pulmonary hypertension caused by left-to-right shunts alone.^{19,20}

On the basis of these observations, we speculate that the medial and intimal changes seen in preoperative obstruction may predispose toward the development of intrinsic pulmonary vein stenosis and that a patent vertical vein in this subset of patients does not exert favorable effects on morbidity and outcome after surgery, even in the presence of adequate pulmonary venous decompression. In light of the bleak prognosis for this subset of patients, alternative management strategies such as lung transplantation may perhaps be considered for them.²¹

Contrary to the report by Cope and colleagues,¹⁰ in which the patent venous pathway atrophied, 11 of 23 survivors of obstructive supracardiac TAPVC in this study showed symptoms of a large left-to-right shunt through the unligated vertical vein. Although delayed closure of the vertical vein was successful in all cases, with concomitant elevation of PA pressure, it was attended by extremely high LA pressure in 6 patients and proved a difficult postoperative challenge. These findings indicate the presence of a relatively small, noncompliant, dysfunctional left-sided chambers or of disease-related or CPB-related pulmonary vasoreactivity. Serial postoperative Doppler echocardiography (mean follow-up 33.34 ± 29.88 months) showed gradual decrease of blood flow through the vertical vein and increase of left heart volume in the remaining 14 survivors of group I. There was no flow through the unligated vertical vein in both patients with infracardiac TAPVC. We concur with the observation of Jegier and associates¹⁸ that high resistance of the hepatic capillary bed accounts for the termination of flow through the descending vertical vein. These observations support our contention that for an unligated vertical vein to undergo spontaneous closure, the left heart chambers must achieve normal size and function. As suggested by Cope and colleagues,¹⁰ the development of a persistent left-to-right shunt through an unligated vertical vein does not necessarily relegate a patient to a second operation. Such candidates may be subjected to percutaneous angiographic vertical vein embolization.

On the basis of our results, we recommend the following guidelines for candidate selection: (1) Significant elevation of PA or LA pressure on snaring or ligation of the vertical vein after achievement of an adequate unrestrictive anastomosis is a useful clinical indicator of impaired LA compli-

ance or disease-related or CPB-related pulmonary vasoreactivity. The vertical vein in such patients with obstructive TAPVC and pulmonary hypertension may be left unligated if post-CPB PA pressure remains systemic or suprasystemic. (2) Patients with nonobstructed TAPVC with or without mild pulmonary hypertension will in general do well with vertical vein ligation. (3) The high mortality in the ligated group indicates revision of our selection criteria to select more appropriate candidates for a patent vertical vein. Thus patients with obstructed TAPVC with moderate post-CPB pulmonary hypertension should have an unligated vertical vein, if there is a true benefit. (4) The requirement of second-stage operation for closure of the vertical vein in a percentage of patients with persistent left-to-right shunt and right heart failure does not warrant modification of our selection criteria for unligated vertical vein. The routine use of percutaneously adjustable vertical vein ligature in patients with obstructive supracardiac TAPVC with a discernible vertical vein and pulmonary hypertension allows gradual tightening or loosening of the ligature under optimal physiologic conditions without reoperation until the pulmonary vasoreactivity disappears. (5) A small ASD should be left open for all patients with TAPVC with moderate pulmonary hypertension for right ventricular decompression in the event of perioperative pulmonary hypertensive crisis. (6) Regardless of the patent vertical vein, a subset of patients with obstructed TAPVC and very small individual pulmonary veins are at prohibitively increased risk for death after surgery. The findings of increased medial thickness of the intrapulmonary vasculature on postmortem examination suggest alternative management strategies for this subgroup of patients.

Study Limitations

First, because this is a prospective study, follow-up is necessarily shorter than follow-up in previous, retrospective studies. Second, this study was not randomized. The occurrence of elevated PA pressure after coming off CPB on snaring the vertical vein was the determining factor for leaving the vertical vein open. Thus a prospective, randomized, controlled trial was not performed. Finally, the small numbers of patients and events in each subgroup are additional limitations.

Conclusions

We conclude that unligated vertical vein during repair of obstructed TAPVC is associated with decreased episodes of pulmonary hypertensive crisis and postoperative low output syndrome, lessened durations of ventilation and inotropic support, provided early normalization of hemodynamics, and decreased in-hospital mortality. Despite improved hemodynamics associated with selective vertical vein patency, the postoperative course of a subset of patients with ob-

structed TAPVC and very small individual pulmonary veins is complex, and the prognosis is poor. For an unligated vertical vein to undergo spontaneous closure, the left heart chambers must achieve normal size and function.

We propose routine use of an adjustable ligature around the vertical vein in all patients with supracardiac TAPVC with more than moderate post-CPB pulmonary hypertension. Such a band will allow easy tightening in increments, with gradual increase of ventricular afterload without the need for multiple reoperations.

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TABLE E1. Univariate predictors of mortality at 0 to 104 months after rechanneling of total anomalous pulmonary venous connection with and without vertical vein ligation

	No.	HD	Risk ratio	95% Confidence interval	P value
Age					
<1 mo	14	6	3.20	1.40-7.35	.026
>1 mo	44	5			
Body weight					
<50th percentile	31	9	1.75	1.16-2.64	.036
>50th percentile	27	2			
Anatomic type					
Supracardiac	53	11	1.12	1.01-1.24	.57
Others (infracardiac and mixed)	5	0			
Obstructive TAPVC					
Yes	30	9	1.83	1.20-2.79	.026
No	28	2			
Diffusely hypoplastic pulmonary veins and small pulmonary venous confluence					
Yes	6	4	8.56	1.79-40.9	.009
No	52	7			
Preoperative severe pulmonary arterial hypertension (>50 mm Hg)					
Yes	30	9	1.83	1.20-2.79	.026
No	28	2			
Preoperative RVSP/LVSP					
1.2 ± 0.2	30	9	1.83	1.20-2.79	.026
0.7 ± 0.2	28	2			
Preoperative ventilation					
Yes	9	1	0.53	0.07-3.84	.86
No	49	10			
Preoperative inotropes					
Yes	13	2	0.78	0.2-3.02	>.999
No	45	9			
Timing of surgery					
Emergency	28	9	2.02	1.30-3.16	.013
Elective	30	2			
Vertical vein					
Ligated	31	9	1.75	1.16-2.64	.036
Unligated	27	2			
Obstructive TAPVC					
Ligated	13	7	2.72	1.27-5.83	.02
Unligated	17	2			
Pulmonary hypertensive crises					
Yes	23	8	2.28	1.31-3.96	.002
No	35	3			
Postoperative low cardiac output					
Yes	25	9	2.40	1.48-3.90	.007
No	33	2			

HD, Hospital death; TAPVC, total anomalous pulmonary venous connection; RVSP/LVSP, right-to-left ventricular systolic pressure ratio.

TABLE E2. Predictors of mortality at 0 to 104 months by stepwise logistic regression analysis applied to all 58 patients

Step 6 variables (covariates adjusted)	Exp (B)	95% Confidence interval	P value
Age (<1 mo)	2.70	1.12-6.53	.027
Obstructive TAPVC	2.77	1.17-6.58	.02
Hypoplastic pulmonary venous confluence, diffusely hypoplastic pulmonary veins	4.67	1.73-12.61	.002
Pulmonary arterial hypertension	2.29	1.00-5.24	.05
Pulmonary hypertensive crisis	2.90	1.25-6.75	.013
Low cardiac output	2.93	1.28-6.73	.011
Vertical vein (ligated/unligated, 1/0)	3.28	1.08-9.99	.032

TAPVC, Total anomalous pulmonary venous connection.

TABLE E3. Postbypass hemodynamic profile of patients with supracardiac total anomalous pulmonary venous connection and unligated vertical vein (group I) with and without snaring of the same (n = 25)

Variable	Snared vertical vein	Unsnared vertical vein	P value
Pulmonary arterial pressure (mm Hg)			<.001
Mean $\pm$ SD	86.07 $\pm$ 10.12	54.78 $\pm$ 7.98	
Range	65-110	38-74	
Median	86	55	
Systemic arterial pressure (mm Hg)			<.001
Mean $\pm$ SD	69.78 $\pm$ 6.94	94.52 $\pm$ 6.92	
Range	50-75	80-110	
Median	72	94	
Left atrial pressure (mm Hg)			<.001
Mean $\pm$ SD	18.74 $\pm$ 1.56	12.89 $\pm$ 1.45	
Range	16-21	11-16	
Median	19	12	
RVSP/LVSP			<.001
Mean $\pm$ SD	1.21 $\pm$ 0.12	0.59 $\pm$ 0.14	
Range	1.0-1.4	0.4-1.1	
Median	1.2	0.6	

RVSP/LVSP, Right-to-left ventricular systolic pressure ratio.

Figure E1. Bar graph showing number of each type of operation during study period. *Black bar*, Group I; *gray bar*, group II.

Figure E2. Bar graph showing age distribution of study group of patients. *GRP*, Group.

Figure E3. Actuarial survival (Kaplan–Meier) curve of two groups of patients undergoing rechanneling of total anomalous pulmonary venous connection with or without vertical vein ligation.