LONG-TERM OUTCOME OF INFANTS WITH SINGLE VENTRICLE AND TOTAL ANOMALOUS PULMONARY VENOUS CONNECTION

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Background and methods: **Between January 1, 1984, and December 1, 1997, 73 infants with functional single ventricle and total anomalous pulmonary venous connection were admitted to our institution. A retrospective review was undertaken to determine factors influencing survival.** ***Results:*** **Heterotaxy syndrome was present in 52 patients and hypoplastic left heart syndrome in 14. Obstructed total anomalous pulmonary venous connection was present in 21 patients. The pulmonary venous connection was supracardiac in 32 patients, cardiac in 21 patients, infracardiac in 13, and mixed in 7. Twelve patients died before the operation. The remaining 61 patients underwent surgery at a median age of 5 days (range 1 day–2.5 years). Overall survival was 45% at 6 months of age, 37% at 1 year, and 19% at 5 years. Survival for patients undergoing surgery was 54% at 6 months of age, 44% at 1 year, and 23% at 5 years. By univariate analysis with the Cox proportional hazards model, younger age at the time of the initial operation and repair of total anomalous pulmonary venous connection were predictors of mortality. Lung tissue from 14 patients was available for histologic examination. The pulmonary veins were dilated and wall thickness was increased. Increased muscularization of the arteries was seen in 11 patients.** ***Conclusions:*** **The long-term prognosis for children undergoing staged reconstructive operations for single ventricle and total anomalous pulmonary venous connection is poor. Early mortality is high and late death is a continuing risk. Development of the pulmonary vasculature, especially the pulmonary veins, is abnormal, even in children without clinical evidence of pulmonary venous obstruction. (J Thorac Cardiovasc Surg 1999;117:506-14)**

The term functional single ventricle encompasses a heterogeneous group of anomalies including hypoplastic left heart syndrome (HLHS), tricuspid atresia, heterotaxy syndrome, and other complex cardiac defects. Many children with these anomalies are referred for treatment in the neonatal period and undergo a series of staged reconstructive procedures leading to an eventual Fontan operation. The short- and long-term outcomes for these children have improved significantly in recent years. Improvements in surgical techniques and perioperative management have contributed to significant decreases in mortality and morbidity after the Fontan procedure. Certain anatomic factors, however, including HLHS, heterotaxy syndrome, and total anomalous pulmonary venous connection (TAPVC), have been associated with increased early and late mortality after the Fontan procedure. The current study was undertaken to assess the impact of TAPVC on early mortality and long-term outcome in children with functional single ventricle.

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Read at the Seventy-eighth Annual Meeting of The American Association for Thoracic Surgery, Boston, Mass, May 3-6, 1998.

Received for publication May 8, 1998; revisions requested June 10, 1998; revisions received Oct 27, 1998; accepted for publication Nov 3, 1998.

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0022-5223/99 $8.00 + 0 **12/6/95597**

Methods

All patients with functional single ventricle and TAPVC treated at The Children's Hospital of Philadelphia between July l, 1984, and December l, 1997, were eligible for entry

Table I

	No. of patients
Group I: Heterotaxy (n = 52)	
Asplenia (n = 41)	
Unbalanced CAVC	41
DORV	29
Outflow tract obstruction	
Pulmonary	34
	(pulmonary atresia, n = 19)
Systemic	5
None	2
Biventricular	0
Pulmonary venous connection	
Supracardiac	17
Cardiac	9
Infracardiac	11
Mixed	4
Polysplenia (n = 9)	
Unbalanced CAVC	8
DORV	3
Outflow tract obstruction	
Pulmonary	4
	(pulmonary atresia, n = 1)
Systemic	4
None	0
Biventricular	1
Pulmonary venous connection	
Supracardiac	1
Cardiac	8
Infracardiac	0
Mixed	0
Normal spleen (n = 2)	
Both DORV/unbalanced CAVC	2
Pulmonary stenosis	1
Pulmonary atresia	1
Pulmonary venous connection	
Supracardiac	0
Cardiac	1
Infracardiac	0
Mixed	1
Group II: HLHS (n = 14)	
Aortic atresia or stenosis/mitral atresia	11
DORV/aortic atresia or stenosis/mitral atresia	3
Pulmonary venous connection	
Supracardiac	11
Cardiac	2
Infracardiac	1
Mixed	0
Group III: Other (n = 7)	
DORV/mitral atresia/no outflow tract obstruction	2
DORV/mitral atresia/pulmonary atresia or stenosis	2
Tricuspid atresia/pulmonary atresia or stenosis	2
DORV/hypoplastic LV/pulmonary atresia	1
Pulmonary venous connection	
Supracardiac	3
Cardiac	1
Infracardiac	1
Mixed	2

CAVC, Common atrioventricular canal; *DORV,* double-outlet right ventricle; *LV,* left ventricle.

Table II. *Initial palliation*

Procedure	*Early mortality*
Aortopulmonary shunt	11% (2/18)
Aortopulmonary shunt with TAPVC repair	83% (10/12)
Norwood procedure	67% (4/6)
Norwood procedure with TAPVC repair	46% (6/13)
Other procedures	42% (5/12)
Superior cavopulmonary connection (n = 4)	
Superior cavopulmonary connection with TAPVC repair (n = 1)	
Pulmonary artery band with TAPVC repair (n = 2)	
Pulmonary valvotomy with TAPVC repair (n = 1)	
TAPVC repair (n = 2)	
Modified Fontan procedure (n = 1)	
Atrioventricular valve annuloplasty (n = 1)	

TAPVC, Total anomalous pulmonary venous connection.

into the study. Patients were retrospectively identified by review of the cardiac surgical and echocardiography databases, as well as autopsy records. The medical records were reviewed and follow-up information was obtained from medical records and contact with referring physicians.

Data are presented as mean ± standard deviation or median as appropriate. Variables were compared by means of the Student unpaired *t* test. Confidence levels (95%) are presented as appropriate. For survival analysis, date of birth was taken as zero time. The patients were censored at the time of death or were withdrawn alive at the time of last follow-up contact. The Kaplan-Meier survival estimates with 95% confidence limits are provided. Survival distributions between groups were compared by means of the log rank test. The Cox proportional hazards model was used to examine the effects of anatomic and procedural variables on survival time both in the entire population (n = 73) and in the subgroup who underwent surgery (n = 61) (see Table III). A univariable analysis was performed and variables with $P < .1$ were included in the multivariable analysis. Data analysis was performed by means of SPSS version 7.5.1 (SPSS, Inc, Chicago, Ill) and SAS version 6.12 (SAS Institute, Inc, Cary, NC).

Results

Between July 1, 1984, and December 31, 1997, 73 children (40 boys and 33 girls) with functional single ventricle and TAPVC were admitted to The Children's Hospital of Philadelphia. Seven of these children were born before 1984. The patients were classified into 3 groups according to diagnosis (Table I). Heterotaxy syndrome was present in 52 children (group I); 41 patients had asplenia, 9 had polysplenia, and 2 had normal spleens. Splenic anatomy was confirmed by autopsy or other tests in 23 patients. HLHS was present in 14 patients (group II). Seven patients with other forms of

Table III. *Variables for Cox proportional hazards model*

Entire population (n = 73)	*Patients undergoing surgery (n = 61)*
Surgery	Age at initial operation
Obstructed TAPVC	TAPVC repair
Type of TAPVC	Ductus dependent
Ductus dependent	Obstructed TAPVC
Type of outflow obstruction	Type TAPVC
HLHS	HLHS
Heterotaxy syndrome	Heterotaxy syndrome
	Norwood procedure
	Recurrent pulmonary venous obstruction

TAPVC, Total anomalous pulmonary venous connection; *HLHS,* hypoplastic left heart syndrome.

single ventricle were classified as group III. The pulmonary venous connection was supracardiac in 32 patients, cardiac in 21 patients, infracardiac in 13, and mixed in the remaining 7. Obstructed pulmonary venous drainage was diagnosed clinically in 21 patients. Obstructed TAPVC was present in 14 group I patients (27%), 4 group II patients (29%), and 3 group III patients (43%). Obstruction to pulmonary blood flow was present in 45 patients and obstruction to systemic blood flow in 23 patients. Biventricular outflow tract obstruction was present in 1 patient, and 4 had no outflow tract obstruction. Pulmonary atresia was present in 23 patients. Either systemic or pulmonary blood flow was dependent on ductal patency in 49 patients.

Twelve patients died before palliative surgery. Reconstructive surgery was performed in 61 patients (Table II). Seven patients underwent surgery at other institutions. Six patients underwent initial placement of systemic-pulmonary shunts at other institutions. One patient underwent a bidirectional Glenn shunt at another institution after an initial shunt at The Children's Hospital of Philadelphia. These patients are included in the analysis. The median age at the time of initial palliation was 5 days (range 1 day–2.5 years). Forty patients underwent surgical intervention in the first week of life and 44 underwent surgical intervention in the first 30 days of life. Overall early mortality (death within 30 days of the initial operation or before hospital discharge) was 53% (39/73). For patients undergoing surgery, the early mortality was 44% (27/61). Initial palliation included aortopulmonary shunt in 18 patients, aortopulmonary shunt with TAPVC repair in 12, Norwood procedure in 6, Norwood procedure with TAPVC repair in 13, and other procedures in 12 (Table II). Early mortality for group I was 44% (18/41), group II 50% (7/14), and group III 33% (2/6). Repair of TAPVC, either alone or in association with other procedures, was performed during the initial operation in 31 patients. The early mortality for these patients was higher than that for the patients not undergoing TAPVC repair: 58% (18/31) versus 30% (9/30); $P = .03$. TAPVC was repaired in 17 of 41 patients in group I, 11 of 14 patients in group II, and 3 of 6 patients in group III. Three patients underwent repair of supracardiac TAPVC at a later operation and only 1 is a long-term survivor. The highest early mortality was in patients undergoing aortopulmonary shunt in combination with TAPVC repair (83%).

Thirty-two patients underwent a superior cavopulmonary connection (hemi-Fontan or bidirectional Glenn shunt) or a modified Fontan procedure, or both. Before the superior cavopulmonary connection, the mean pulmonary artery pressure was 15 ± 4 mm Hg with a transpulmonary gradient of 10 ± 4 mm Hg (n = 12). The arterial oxygen saturation was 77% ± 5%. Pulmonary artery pressure was not measured in all patients and 2 patients were excluded. One patient had undergone a Waterston shunt and had nearly discontinuous pulmonary arteries. The other patient had pulmonary venous obstruction as a result of anastomotic narrowing. Before the modified Fontan procedure, the pulmonary artery pressure was 14 ± 5 mm Hg with a transpulmonary gradient of 7 ± 6 mm Hg (n = 16). The arterial oxygen saturation was 79% ± 7%. Twenty-one patients underwent superior cavopulmonary connection with an early mortality of 38% (8/21). In 5 of these patients, superior cavopulmonary connection was performed as the initial procedure, with 2 early deaths. Nineteen patients underwent a modified Fontan procedure, 8 of whom had previously undergone a superior cavopulmonary shunt. One patient underwent the modified Fontan procedure as initial palliation. The early mortality was 42% (8/19). In 1 patient, the modified Fontan shunt was reduced to a superior cavopulmonary connection in the operating room and this patient died. There have been 2 late deaths after the Fontan procedure.

Recurrent pulmonary venous obstruction necessitating reoperation developed in 7 of the 13 survivors (54%) of initial TAPVC repair. Only 1 of these patients is a long-term survivor. Infracardiac TAPVC was present in 5 of these patients and supracardiac TAPVC in 2. Pulmonary venous obstruction had been present in 3 of the patients before the initial TAPVC repair.

Follow-up is complete (death or December 1, 1997) in 71 of the 73 patients (97%). In the 2 remaining patients, partial follow-up was available until their families moved abroad (11 months and 15 years after the

Table IV. *Cox proportional hazards model*

Variable	*Regression coefficient* β	*SE*	P	*Risk ratio*	*95% CL*
		Univariable analysis			
Entire group (n = 73)					
Palliative surgery	–1.588	0.372	.0001	0.204	(0.098, 0.424)
Obstructed TAPVC	.623	0.277	.02	1.864	(1.083, 3.210)
Patients undergoing surgery (n = 61)					
Repair of TAPVC	.698	0.296	.02	2.009	(1.125, 3.587)
Age at initial operation	–.004	0.002	.02	0.996	(0.993, 0.999)
		Multivariable analysis			
Entire group (n = 73)					
Palliative operation	–1.506	0.373	.0001	0.222	(0.107, 0.460)
Patients undergoing surgery (n = 61)					
Age at initial operation	–.003	0.002	.04	0.997	(0.994, 1.000)

SE, Standard error; *CL,* confidence limits; *TAPVC,* total anomalous pulmonary venous connection.

operation). As of December 1, 1997, 12 of the 73 patients were alive and 9 of these patients had successfully undergone the modified Fontan procedure. The median duration of follow-up for the entire group (n = 73) is 4 months (range 1 day–17 years). The median follow-up for patients who survived the initial hospitalization (n = 34) is 26 months (range 0.1 month–17 years). Fifty-one patients were followed up for at least 6 months, 25 for 1 year, 18 for 2 years, and 11 patients for more than 5 years. For the entire group (n = 73), survival was 45% (95% CL, 34%, 57%) at 6 months, 37% (95% CL 25%, 48%) at 1 year, and 19% (95% CL 10%, 29%) at 5 years. Survival was better for the patients who underwent surgery: 54% (95% CL 42%, 67%) at 6 months, 44% (95% CL 31%, 56%) at 1 year, and 23% (95% CL 12%, 34%) at 5 years, $P < .0001$ by log rank test (Fig 1). For the entire group, survival was worse for patients with obstructed TAPVC than for those with unobstructed TAPVC ($P = .02$). Repair of TAPVC at the initial operation was associated with worse survival ($P = .02$) (Fig 2).

The Cox proportional hazards model was used to assess the effect of anatomic and procedural variables on survival time (Table IV). For the entire group (n = 73), palliative surgery was associated with improved survival with a risk ratio of 0.204 ($P = .0001$). Obstructed pulmonary venous drainage was associated with a poorer survival, with a risk ratio of 1.864 ($P = .02$). For the subgroup of patients who underwent surgery (n = 61), repair of TAPVC and younger age at the time of the initial operation were associated with decreased survival time in the univariable analysis. For the entire group (n = 73), multivariable analysis showed only palliative surgery to be associated with improved survival. Obstructed drainage was present in 5 of 12 children (42%) who died before having an operation, compared with 16 of the 61 patients (26%) who did have an operation. In the multivariable analysis, only younger age remained significant.

Pulmonary tissue for histologic examination of the vasculature was available from autopsy for 14 patients (median age at death 23 days, range 2 days–8.8 months). Heterotaxy syndrome was present in 7 patients. The pulmonary venous connection was supracardiac in 8, infracardiac in 4, and mixed in 2. Clinical evidence of obstruction of pulmonary venous drainage was present in only 5 patients. Obstruction to pulmonary blood flow was present in 8 patients (4 with pulmonary atresia) and obstruction to systemic blood flow in 5. The remaining patient had no outflow tract obstruction. Palliative operations were performed in 12 of these patients and TAPVC repair in 10. In all 14 patients, the pulmonary veins were markedly dilated with increased wall thickness for age (Fig 3). Elastic tissue staining demonstrates multiple elastic laminae in the vein wall consistent with "arterialization" of the pulmonary veins, which is not seen in patients with normal pulmonary venous connection (Fig 4). Increased muscularization of the pulmonary arteries was present in 11 patients.

Discussion

The short- and long-term outcomes for children with functional single ventricle including HLHS have improved markedly in recent years.[1,2] Since the introduction of the Fontan procedure in the early 1970s, modifications of surgical techniques, improved patient selection, and improved perioperative management have resulted in significant decreases in both early and late mortality. The use of staged reconstruction in

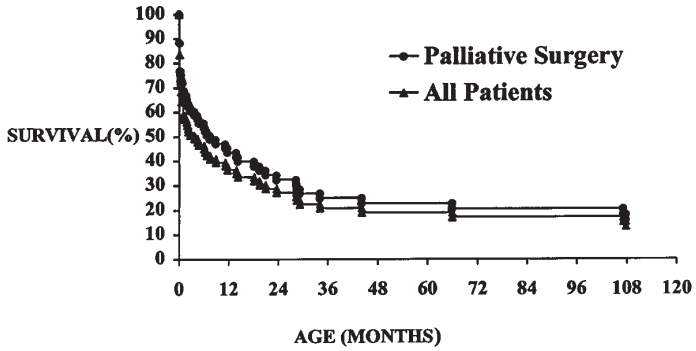

Fig 1. Actuarial survival (Kaplan-Meier) comparing outcome for all patients with outcome of those undergoing staged reconstructive operations.

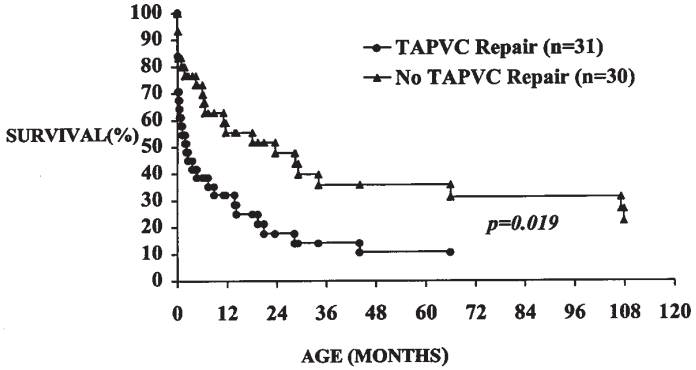

Fig 2. Actuarial survival (Kaplan-Meier) comparing outcome for patients who underwent TAPVC repair with outcome for those in whom TAPVC repair was not performed.

which a superior cavopulmonary connection is constructed before the completion of the Fontan procedure has further reduced early mortality and morbidity.[1] The early and long-term outcomes after surgical repair of isolated TAPVC are excellent.[3] Previous reports, however, have suggested that the association of TAPVC with single ventricle, particularly in patients with heterotaxy syndrome, is a risk factor for poor outcome.[4-8]

The current study was undertaken to assess the impact of TAPVC on early mortality and long-term outcome in infants with single ventricle. Heterotaxy syndrome was present in the majority of these children. This study demonstrates that the long-term prognosis for these children is poor. Palliative surgery resulted in improved survival; however, the mortality for the initial palliative procedure is high, and late death is a continuing risk. Mortality rates at the time of superior cavopulmonary connection and the Fontan operation were much greater than for children without TAPVC.[1] The cause of death often could not be determined from the medical record; however, in the majority of cases significant hypoxemia and inadequate cardiac output were evident. Obstruction to pulmonary venous drainage was a risk factor for mortality for the entire group. Younger age at the time of the initial operation and repair of TAPVC were associated with increased mortality. Early and late mortality were significantly greater in patients who underwent repair of TAPVC. Recurrent pulmonary venous obstruction was prevalent after TAPVC repair (>50%). Only 1 patient with recurrent pulmonary venous obstruction is a long-term survivor. The reasons for the increased incidence of recurrent pulmonary venous obstruction are unclear. Histologic examination of lung tissue from patients in this series demonstrates that development of the pulmonary vasculature, particularly the pulmonary veins, is abnormal in infants with single ventricle and TAPVC. The veins were abnormal even in the absence of clinical evidence of pulmonary venous obstruction, suggesting that current diagnostic techniques may underestimate the severity of obstruction.

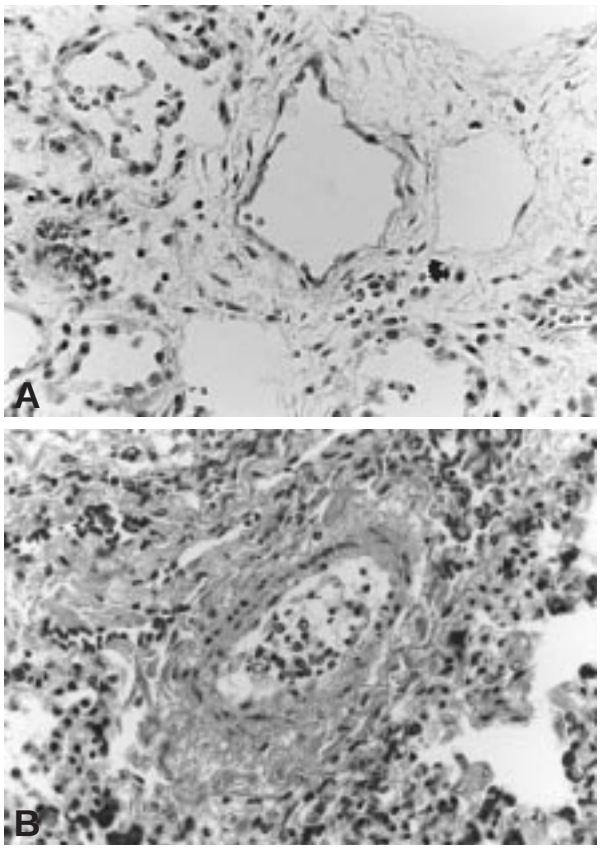

Fig 3. A, A pulmonary vein from a patient with HLHS and normal venous return appears in the center of the photograph as a dilated vessel without markedly thickened media; a dilated lymphatic vessel is at the right of the vein in the interlobular septum. **B,** A very abnormal pulmonary vein from a study patient is seen in the interlobular septum, surrounded by alveolar spaces. The vein wall is very thick and nuclei are seen in the mural fibers. (**A** and **B,** Hematoxylin and eosin stain; original magnifications ×400.)

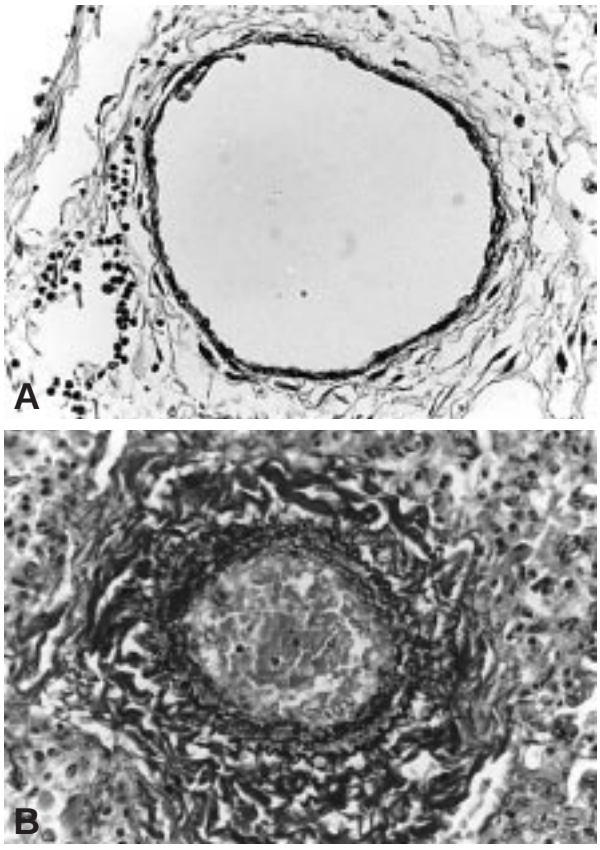

Fig 4. A, An elastic tissue stain of a pulmonary vein of the same patient as in **Fig 3, A,** shows a thin wall, without distinct inner and outer elastic tissue laminae. **B,** In contrast, an elastic tissue stain from a vein of the same patient as in **Fig 3, B,** shows multiple elastic tissue laminae, so-called arterialization of the venous wall. (**A** and **B,** Elastic van Gieson stain; original magnifications ×400.)

DeLeon and colleagues[4] reported early results after palliative surgery in 8 infants with obstruction to pulmonary blood flow and TAPVC. Heterotaxy syndrome was present in all patients and 7 patients had functional single ventricle. Four of these 7 patients died. Di Donato and colleagues[5] reported outcome after palliation in 14 children with right atrial isomerism (asplenia) and TAPVC. Thirteen patients underwent palliative operations consisting of aortopulmonary shunts in 10 patients and shunts with TAPVC repair in 3 patients. There were 7 hospital deaths (54%) and 2 late deaths. No patients had undergone cavopulmonary connection or a Fontan procedure at the time of these reports.

Heinemann and associates[6] reported their experience with initial palliation in 21 patients with heterotaxy syndrome and TAPVC. Pulmonary venous drainage was obstructed in 12 patients and unobstructed in 9. None of these patients had obstruction to systemic blood flow. The overall early mortality was 28.6% (6/21). The mortality for aortopulmonary shunt alone was 25% (2/8) and for shunt in combination with TAPVC repair, 33.3% (2/6). Mortality for TAPVC repair alone was 50% (2/4). Long-term follow-up was not reported.

Sadiq and coworkers[7] recently reported outcomes after surgical palliation of 20 children with right atrial isomerism. TAPVC was present in 16 patients. The overall mortality was 55% (11/20) and was 82% (9/11) in patients who underwent surgery during the first month after birth. Seven patients have undergone the

Fontan procedure, with 2 deaths. No patient who was referred to us during the first week of life with obstructed TAPVC and pulmonary atresia survived.

Hashmi and associates[8] reported outcomes for 91 patients with right atrial isomerism treated at The Hospital for Sick Children in Toronto between 1970 and 1996. Surgery was undertaken in 69 patients, and 64 of these underwent staged reconstructive surgery with the plan of an eventual Fontan procedure. TAPVC repair alone or in association with other procedures was performed in 20 children with an early mortality of 95%. At last follow-up, 40 of the 64 patients had died, 10 had successfully undergone the Fontan procedure, 13 were alive and awaiting the Fontan procedure, and 1 patient had undergone cardiac transplantation. Overall actuarial survival was 49% at 1 year and 35% at 5 years. Risk factors for mortality were absence of pulmonary outflow obstruction, presence of major atrioventricular valve anomaly, and obstructed TAPVC.

Alejos and colleagues[9] evaluated risk factors for mortality in 129 patients undergoing bidirectional Glenn shunts. Anomalous pulmonary venous connection, either partial or total, and heterotaxy syndrome were risk factors for death. McElhinney and colleagues[10] reported outcome after bidirectional Glenn shunts in patients with anomalies of systemic and pulmonary venous drainage. In this series, 11 patients had single ventricle and TAPVC. Heterotaxy syndrome was present in 10 of the 11 patients. Repair of TAPVC was necessary in only 3 patients. One early death and 1 late death occurred among the 11 patients.

Razzouk and associates[11] reported outcomes after cardiac transplantation in 12 children with complex cardiac defects and TAPVC. Heterotaxy syndrome was present in 9 patients and HLHS in 2. TAPVC was supracardiac in 10, infracardiac in 1, and mixed in 1. Six children had undergone a previous operation, but only 1 had undergone TAPVC repair. Transplantation was performed during the first 6 months after birth in 8 of the 12 patients. Overall survival was excellent, with only 1 early and 1 late death. Recurrent pulmonary venous obstruction developed in 2 patients. A more recent report of transplantation in 20 patients with heterotaxy syndrome (13 with TAPVC) demonstrated a 1-year survival of 93% and a 5-year survival of 65%.[12]

The findings of the current study are consistent with those of previously published results and demonstrate a significant early mortality and poor long-term outcome for children with functional single ventricle and TAPVC. Risk factors for mortality include younger age at the time of the initial operation, obstructed TAPVC, and need for TAPVC repair at the initial operation. Children with more severe obstruction to pulmonary venous drainage are likely to have more severe changes in the pulmonary vasculature and to be referred for treatment at an earlier age. The greatest risk for early death was in patients undergoing simultaneous creation of an aortopulmonary shunt and TAPVC repair. Interestingly, the presence of heterotaxy syndrome or HLHS was not associated with worse outcomes. Examination of the pulmonary vasculature from patients with single ventricle and TAPVC reveals very abnormal development, especially of the pulmonary veins. It is likely that increased pulmonary vascular resistance is a major cause of mortality for these children. The cause of the increased mortality for superior cavopulmonary connection and the Fontan procedure is less clear. The preoperative hemodynamic data do not suggest that the patients are at increased risk. However, the pulmonary vascular abnormalities may contribute to the increased mortality. Interestingly, despite the abnormal pulmonary vasculature, the early results after cardiac transplantation in these patients appear to be satisfactory.[11,12] Perhaps the pulmonary vascular abnormalities are better tolerated when a ventricle provides pulmonary blood flow rather than an arterial or venous shunt.

This study has several limitations. It is retrospective, and the data are limited by review of the medical records. To ensure inclusion of all patients, even those who did not undergo surgery, we reviewed multiple sources including the echocardiography database, surgical database, and autopsy records. The criteria for diagnosis of pulmonary venous obstruction were not standardized. A patient was classified as having obstructed TAPVC if the echocardiogram was considered to show obstruction of the draining vein or if the physician caring for the patient diagnosed obstructed venous drainage on the basis of the clinical course. There is obviously some bias in the selection of patients for histologic examination of the pulmonary vasculature. Because only autopsy specimens were available, the findings likely represent the more severely affected patients.

In conclusion, this study demonstrates that children with functional single ventricle and TAPVC have a very poor prognosis. The outcome of staged reconstructive surgery is poor. Alternative therapy such as cardiac transplantation may be indicated for these patients.

We appreciate the contributions of the many physicians and other personnel who cared for these patients, including Larry W. Stephenson, MD, John D. Pigott, MD, William I. Norwood, MD, and Marshall L. Jacobs, MD.

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Discussion

Dr William G. Williams *(Toronto, Ontario, Canada).* Dr Gaynor's review of infants with single ventricle and TAPVC demonstrates the dismal outlook for these children despite the authors' best efforts. I congratulate them for their candor, honesty, and courage in presenting this information.

Although better techniques in pediatric cardiac care have produced substantially improved results for newborn infants with either univentricular heart or TAPVC in isolation, the combination of the two lesions appears to be almost universally fatal.

First of all, I applaud their decision to include the babies identified with the diagnosis but not surviving long enough to undergo operation. The 16% who died before surgical intervention are an index of the severity of these lesions. As surgeons, we do have an obligation to these patients who do not survive long enough for our care. Our management protocols must evolve to salvage these children.

The most telling statistic is the failure to manage these babies at the time of cavopulmonary shunt. The 38% mortality at cavopulmonary shunt, an operation which for other lesions is a very low-risk procedure, is an index of the severity of the underlying disease that we do not clearly understand.

The cavopulmonary shunt is used as a staging procedure in patients with single ventricle to lessen the risk of a subsequent Fontan operation. In the authors' series, only 26% of the patients actually had a Fontan operation. This outcome is very similar to our experience in patients with heterotaxy, among whom only 22% eventually had the Fontan operation. Cavopulmonary shunt was not apparently protective, as illustrated by the 42% operative risk at the time of the Fontan operation and the subsequent 20% late mortality.

In an analysis of cavopulmonary shunts in our center, it is clear that there are some patients in whom conversion from a cavopulmonary shunt to a Fontan circulation offers no survival advantage and is probably contraindicated. Patients with heterotaxy, single ventricle, and TAPVC are good examples of this problem. Dr Gaynor's experience is similar to the series from Toronto reported by Hashmi and the series from Boston reported by Jenkins. In our experience, patients treated more recently have an even worse prognosis than those treated in the earlier era.

Dr Gaynor's group identified the following as risk factors: abnormal pulmonary veins, thickening of the muscular walls, increased elastin, and dilated lumen. Jenkins previously reported that small pulmonary artery diameter and a small pulmonary artery confluence are predictors of poor outcome.

Is there hope for these children? Razzouk and associates, from Loma Linda, reported on 30 children with heterotaxy who had a 65% survival 5 years after heart transplantation. Heterotaxy was not a risk factor among their transplant series.

I have two questions for Dr Gaynor. First, is the histology of dilated pulmonary veins that you report compatible with the observations of Jenkins that small pulmonary veins are detrimental to survival?

Second, what is the current or future protocol at The Children's Hospital of Philadelphia for managing infants with single ventricle and TAPVC in combination? If transplantation is recommended, what priority do these children warrant to procure a very scarce resource?

Dr Gaynor. Dr Williams, thank you very much for your comments. The pathology that we examined is of children who have undergone repair of TAPVC, and they may have had high atrial pressures. We examined small veins within the lung parenchyma. Because this is a retrospective study, we were unable to assess the size of the pulmonary veins at the site of entrance into the heart to know how small or how large those veins were. If there is obstruction at that level, the upstream veins may be dilated.

In terms of the current management of the children at our institution, certain children can be managed initially with only an aortopulmonary shunt. The major group includes children who have unobstructed pulmonary venous drainage, particularly drainage to the cardiac veins or to the cavoatrial junction. The mortality for shunt alone as the initial palliative procedure was acceptable. We would probably use a shunt in those children and then try to determine the optimal method of treatment at a later date, either cavopulmonary anastomosis leading to a Fontan operation or cardiac transplantation.

For children who are brought for treatment in the neonatal period and have pulmonary veins that must be repaired, particularly those with obstructed veins, cardiac transplantation is the best option. I think the presence of either a systemic shunt or a venous shunt in children who have these abnormal pulmonary vessels and a high degree of reactivity is the reason for the high mortality.

Many of the infant hearts available for transplantation are currently used for children with HLHS who do have another option, the Norwood procedure. In these children with TAPVC and single ventricle, there really is no other option.

Under the current organ allocation system, infants are not stratified as possible recipients for cardiac transplantation according to the availability of other possible procedures. As a group, we should amend that system to give priority to infants for whom cardiac transplantation is the only option.