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Repair of “Simple” Total Anomalous Pulmonary Venous Connection: A Review from the Pediatric Cardiac Care Consortium

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Abstract

Background—Outcomes for repair of Total Anomalous Pulmonary Venous Connection (TAPVC) from individual institutions suggest a significant improvement in mortality over the last several decades. The purpose of this study is to review the outcomes following repair of TAPVC from a large multi-institutional registry.

Methods—A retrospective review of the multi-institutional database, the Pediatric Cardiac Care Consortium (PCCC) was used to identify patients with the diagnosis of TAPVC who underwent complete correction between the years of 1982 to 2007. Data reviewed included age, decade of primary operation, anatomic type, presentation, and in-hospital mortality.

Results—Of the 118,084 surgical procedures submitted to the PCCC, 2191 (1.9%) were primary surgical correction of TAPVC. Sixty one percent of the cohort was male with 6.8% reported as premature. Overall in-hospital surgical mortality for simple TAPVC was 13%. Mortality was 20% from 1982 to 1989, 16% from 1990 to 1999, and 8% from 2000 to 2007. Obstruction to the anomalous pulmonary venous connection occurred in 29% with a mortality of 26%.

Conclusions—Surgical outcomes from repair of congenital cardiac anomalies have significantly improved over the last several decades. Multi-institutional large databases are needed to confirm results published from single institutional experiences. Although improvements in surgical repair of TAPVC have occurred over the last three decades, specific subtypes still experience significant mortality.

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Keywords

Cardiac anatomy/pathologic anatomy; Pediatric; Pulmonary arteries/veins

Introduction

Outcomes following operative correction of congenital cardiac defects have generally improved over the last several decades. Total Anomalous Pulmonary Venous Connection (TAPVC) is a relatively rare congenital defect with reported outcomes paralleling less technically challenging procedures. Mortality is high when primary repair is not undertaken within the first year of life [1]. Preoperative patient characteristics have been considered to have a significant impact on overall surgical results [2]. These risk factors include patient age at the time of repair, morphologic connection, presence of pulmonary venous obstruction, and associated cardiac defects. Recent reviews have reported the neutralization of these risk factors over the last several decades [3, 4]. The majority of this data has been produced by single center retrospective experiences [4, 5]. We sought to determine, utilizing this multi-institutional dataset, changes in mortality over the last several decades, as well as confirm which risk factors continue to have a significant impact on mortality following surgical correction.

Patients and Methods

Data utilized in this analysis was covered by the Data Use Agreement of the Pediatric Cardiac Care Consortium (PCCC) provided from individual member institutions. The study was approved by the Institutional Review Board at the University of Minnesota with an exception to obtain individual patient consent.

Data Collection

A retrospective review involving the PCCC was utilized to identify patients admitted with the diagnosis of TAPVC who underwent primary repair. All patients assigned the diagnosis code for TAPVC and the procedure code for correction of TAPVC between the years of 1982 to 2007 was reviewed. Data points were extracted from a dataset submitted by the member institution. Assignments of diagnosis and procedure codes were accomplished in a centralized fashion by the registry. The procedure and diagnosis codes were inclusive of additional anatomic and physiologic characteristics of the patients. Accuracy of the submitted data was confirmed by annual reviews of the individual institution's medical records confirming discharge and death information. Patients were defined as "simple" TAPVC if there were no associated cardiac anomalies (excluding PDA and ASD). The overall analysis was conducted on all patients that underwent repair at less than 18 years of life. Patients were excluded from analysis if data points were missing (surgical weight, n=12; anatomic connection, n=39) or they had a prior surgical procedure (n=322).

Mortality was defined as all in-hospital deaths following the primary repair of TAPVC. The time periods studied for statistical analysis were 1982–1989, 1990–1999, and 2000–2007.

Obstruction of pulmonary venous connection was determined by review of clinical and diagnostic information provided by the submitting institution.

Frequencies and proportions were computed for the overall group and by decade, age group, reported obstruction, and anatomic type. Categorical variables were defined by the investigators prior to the analysis. Age groups were defined as neonates (<30 days), infants (30–365 days), and children (>365 days). Timing of surgery was defined as emergent (day 0 or 1), urgent (day 2), and elective (greater than day 2). Low surgical weight was defined as less than 2.5 kilograms (kg). Pearson chi-square tests and Fisher exact tests were used to compare categorical variables. Multivariable logistic regression with generalized estimating equations (GEE) was used to compute marginal effects while accounting for potential correlation within hospital. The binary outcome was defined as within hospital mortality. An exchangeable correlation structure was specified.

No adjustments were made for multiple comparisons. All statistical analyses were completed using R version 2.14.1 [6].

Results

A total of 2191 patients underwent primary surgical repair of TAPVC between the years of 1982 and 2007. When evaluating patients with simple TAPVC (77%, n=1693), 91% (n=1543) were less than 18 years, while 86% (n=1454) were less than one year of life at the time of surgery. The analysis will focus on those less than 18 years of age at primary repair. Patient characteristics stratified by decade of primary repair are presented in Table 1. Sixty-two percent of this population was male. Approximately 5% of patients underwent repair with a weight less than 2.5 kg, with 7% (n=101) considered premature (gestational age of less than 37 weeks). Fifty-nine percent of patients (n=801) underwent primary repair during the neonatal period with the frequency significantly increasing between each decade.

The overall unadjusted in-hospital mortality for patients with simple TAPVC was 13%. There was a significant decrease in mortality within each decade studied (Table 2). When comparing all patients that underwent repair as neonates and infants, we found a significantly lower mortality in the latter group (19.1% vs. 4.9%, $p<0.001$). There was a significant decrease in mortality when comparing 1990–99 to 2000–07 for the infant group (6.3% vs. 1.7%, respectively, $p=0.021$) and the neonatal group (23% vs. 11.7%, respectively, $p<0.001$).

The frequencies of anatomic connections for patients with simple TAPVC are presented in Table 1, with supracardiac connection occurring most often. A total of 401 patients (29%) presented with obstruction of the pulmonary venous connection. Mortality varied significantly when stratified to the type of pulmonary venous connection (Table 2). The overall mortality for the supracardiac group was 10.5%. Of this group, 27% presented with obstruction prior to the primary repair. The mortality associated with obstruction to supracardiac connection was 22%, decreasing to 6% when obstruction was not present. Of the 273 patients with cardiac connection, mortality was 3.7%. When obstruction was not present mortality was 3%, but it increased to 14% with obstruction. One hundred and eighty

patients with infracardiac connection presented with obstruction (57.6%) with a mortality of 28%. Mortality of patients that did not present with obstruction was 16%. The risk of obstruction at presentation was statistically greater in the infracardiac group compared to the other anatomic types ($p=0.0001$). The mixed type ($n=155$) had an overall mortality of 19%. The majority of these patients presented without signs of obstruction and had a mortality of 15%. The patients that presented with obstruction had a mortality of 32%. Mortality for each anatomic group, with the exception of the cardiac connection, improved over the time periods studied.

For the cohort of patients that presented with simple TAPVC, 15% of patients underwent emergent repair, 7% urgent repair, and 78% elective repair. The frequency of emergent repairs increased from 10% of all cases during the first time period (1982–1989) to 17% during the last period (2000–2007) (Table 1). Mortality also changed over the period of data collection based on the timing to operative repair, significantly decreasing from the earliest to most recent decade for both the emergent (65% vs. 16%, $p<0.001$) and elective period (13.9% vs. 5.3%, $p<0.001$) (Table 2).

The time to operative repair for the entire TAPVC cohort varied significantly ($p<0.0001$) based on the anatomic connection of the anomalous pulmonary venous connection (infracardiac median=4 days, mixed median=30 days, supracardiac median=32 days, and cardiac median=46 days). Infracardiac type had the highest percentage of emergent and urgent repairs when compared to the other anatomic types ($p<0.0001$). The infracardiac group was stratified into obstruction vs. non-obstruction for the entire collection period. For this cohort, 21% of patients without obstruction and 37% with obstruction underwent emergent repair. During the last time period (2000–2007), when the percent of the emergent primary repairs increased significantly compared to the earlier two periods, the percentage of patients with obstructed infracardiac connection that underwent emergent repair was 45% ($n=45$), compared to 25% ($n=24$) without obstruction. The mortality associated with emergent repair of non-obstructed infracardiac anatomy was 42%, but decreased to 21% when the operation was undertaken on an elective basis ($p=0.0631$).

To identify predictors of mortality, a multivariable regression analysis was performed using variables listed in Table 1. Weight at operative intervention, decade which the procedure was performed, neonates, reported obstruction, and the need for emergent repair were all considered a positive predictor for mortality in patients with TAPVC. (Table # 3)

For the entire cohort ($n=2248$), one hundred and forty eight patients (7%) had a diagnosis of a major “two ventricle” cardiac anomaly. The most commonly reported anomaly was a Ventricular Septal Defect, with Double Outlet Right Ventricle, Tetralogy of Fallot, or Coarctation of the Aorta occurring less commonly (Table 4). Eighty-four percent of these two ventricle patients underwent correction of the associated defect at the same operation as the primary repair of TAPVC. Four hundred and seventy patients presented with an associated cardiac anomaly that would have precluded the creation of two ventricle physiology. Of these patients, 295 (63%) were classified as having Heterotaxy syndrome.

Comment

Utilizing a large multi-institutional surgical registry, we analyzed changes in mortality and predictors of mortality in patients that underwent primary repair of TAPVC over an extended period of time. Several single center retrospective studies have shown that survival for repair of TAPVC has generally improved over the last several decades [12, 13, 14]. Our goal was to confirm these findings utilizing a large cohort of patients.

The overall mortality for patients with simple TAPVC undergoing primary repair was 13%. These results improved over time, with a significant decrease (8%) during the most recent period studied. This observation corroborates several small, single center experiences showing a period dependent improvement in survival [2, 5, 7, 15].

Our study identified the weight at operative intervention, operative intervention within the first 30 days on life, and reported obstruction to the anomalous pulmonary venous return as risk factors for mortality. Operative correction during the neonatal period has been shown to improve survival for several congenital cardiac anomalies. In a recent study by Yong et al [5], 112 patients that underwent primary correction of TAPVC during the neonatal period were reviewed and showed an overall in-hospital mortality of 10.4%, although there wasn't a change in mortality over the duration of the review. Our study revealed a somewhat different pattern, with a significant improvement in survival between for each decade studied. This may reflect the individual institutional bias not to operate on neonates during the prior decades, with a transition to offering operative repair to complex lesions in the current era. Survival from repair of the non-neonatal population was significantly greater than seen in the neonates, even within the most recent time period. This difference is certainly multifactorial and may represent ongoing limitations in the ability to operate on the sickest neonates. Although our data analysis did not allow for identification of specific factors which accounted for these differences, recent publications have delineated several patient-specific factors that were associated with lower survival in this group [2, 8].

This study presents a larger number of patients that defined the frequency of the anatomic presentation and the outcomes associated with this anatomy. The presence of obstruction at the time of presentation had been considered a significant risk factor for increased mortality [2]. Our data agrees with this, as mortality was higher for both the overall group and within each of the anatomic connection. Several other recent studies have disagreed with these findings, concluding that the anatomic type and the presence of obstruction have been neutralized as a risk factor. Bando et al [9] concluded that these anatomic characteristics have been neutralized in recent years. Others have also concluded that connection type was not related to outcomes [10]. The discrepancies between our study and the others may be due to the patient size, in which they evaluated approximately 100 patients per study.

The impact of the timing of operative intervention on survival was investigated. The time of operative intervention from birth was categorized into emergent, urgent, and elective, based on previously published literature. Several authors have reported that the need for emergent/urgent operative intervention was no longer a risk factor for increased in-hospital mortality [4, 11]. This is in contrast to a recent study by Karamlou et al [2], which found that a

younger age at the time of repair was a significant risk factor for mortality. Our study revealed a similar finding in these patients undergoing emergent repair had a significantly increased mortality compared to procedures that occurred 48 hours within the most recent era. The reason for this is certainly multifactorial and likely reflects the general overall physiological status of the patient prior to operative repair, although our dataset did not allow us to investigate specific physiological risk factors. Karamlou et al [2] suggested that mortality was higher in patients requiring emergent intervention because the presence and severity of obstruction to the pulmonary venous return was worse than patients not requiring emergent repair. Our overall findings are in agreement with this statement.

Limitations

Several limitations exist within this dataset. The most important that this is a historic registry with information recorded for various sources over an extended period of time. Mortality was only record until discharge, therefore information on 30 day and longer term outcomes were not available. The determination of obstruction to the anomalous pulmonary venous return was made at the time of submission to the registry. Objective criteria may have not always been available and this determination may have been made based on subjective statements within the narratives provided by the submitting institutions.

Conclusions

Overall, mortality for primary repair of TAPVC has decreased for the last several decades. The most significant improvement in outcomes following repair of TAPVC occurred in the neonatal population. Certain risk factors for increased mortality have persisted over time, including operative intervention on small infants, presence of obstruction at the time of repair, and repair during the neonatal period.

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Table 1

Patient Characteristics

	Total	1982-89	1990-99	2000-07	P-value
<u>Sex</u>	1366	186 (13.6%)	605 (44.3%)	575 (42.1%)	
Females	521 (38.1%)	78 (41.9%)	228 (37.7%)	215 (37.4%)	0.516
Males	845 (61.9%)	108 (58.1%)	377 (62.3%)	360 (62.6%)	
<u>Age Group</u>					
Neonates (<30 days)	801 (58.6%)	89 (47.8%)	343 (56.7%)	369 (64.2%)	
Infants (30-365 days)	493 (36.1%)	88 (47.3%)	224 (37.0%)	181 (31.5%)	<0.001 ^a
Children (>365 days)	72 (5.3%)	9 (4.8%)	38 (6.3%)	25 (4.3%)	
<u>Low Surgical Weight</u>					
No (< 2.5 kg)	1299 (95.1%)	178 (95.7%)	573 (94.7%)	548 (95.3%)	0.822
Yes (<2.5 kg)	67 (4.9%)	8 (4.3%)	32 (5.3%)	27 (4.7%)	
<u>Anatomic Subtype</u>					
Supracardiac	626 (45.8%)	73 (39.2%)	283 (46.8%)	270 (47.0%)	
Cardiac	273 (20.0%)	35 (18.8%)	125 (20.7%)	113 (19.7%)	0.043
Infracardiac	312 (22.8%)	43 (23.1%)	136 (22.5%)	133 (23.1%)	
Mixed	155 (11.3%)	35 (18.8%)	61 (10.1%)	59 (10.3%)	
<u>Reported Obstruction</u>					
Yes	401 (29.4%)	57 (30.6%)	181 (29.9%)	163 (28.3%)	0.770
No	965 (70.6%)	129 (69.4%)	424 (70.1%)	412 (71.7%)	
<u>Timing of Surgery</u>					
Emergent (<2 days)	206 (15.1%)	20 (10.8%)	86 (14.2%)	100 (17.4%)	
Urgent (2 days)	93 (6.8%)	8 (4.3%)	46 (7.6%)	39 (6.8%)	0.077
Elective (>2 days)	1067 (78.1%)	158 (84.9%)	473 (78.2%)	436 (75.8%)	

Table 2

Mortality

	Total	1982-89	1990-99	2000-07	P-value
Sex					
Females	178/1366 (13.0%)	38/186 (20.4%)	94/605 (15.5%)	46/575 (8.0%)	<0.001 ^a
Males	58/521 (11.1%)	14/78 (17.9%)	28/228 (12.3%)	16/215 (7.4%)	0.032
	120/845 (14.2%)	24/108 (22.2%)	66/377 (17.5%)	30/360 (8.3%)	<0.001 ^b
Age Group					
Neonates (<30 days)	153/801 (19.1%)	31/89 (34.8%)	79/343 (23.0%)	43/369 (11.7%)	<0.001 ^c
Infants (30-365 days)	24/493 (4.9%)	7/88 (8.0%)	14/224 (6.3%)	3/181 (1.7%)	0.021
Children (>365 days)	1/72 (1.4%)	0/9 (0.0%)	1/38 (2.6%)	0/25 (0.0%)	
Low Surgical Weight					
No (< 2.5 kg)	156/1299 (12.0%)	33/178 (18.5%)	82/573 (14.3%)	41/548 (7.5%)	<0.001 ^d
Yes (<2.5 kg)	22/67 (32.8%)	5/8 (62.5%)	12/32 (37.5%)	5/27 (18.5%)	0.046
Anatomic Subtype					
Supracardiac	66/626 (10.5%)	14/73 (19.2%)	35/283 (12.4%)	17/270 (6.3%)	0.003
Cardiac	10/273 (3.7%)	0/35 (0.0%)	8/125 (6.4%)	2/113 (1.8%)	0.110
Infracardiac	72/312 (23.1%)	12/43 (27.9%)	40/136 (29.4%)	20/133 (15.0%)	0.013
Mixed	30/155 (19.4%)	12/35 (34.3%)	11/61 (18.0%)	7/59 (11.9%)	0.032
Reported Obstruction					
Yes	103/401 (25.7%)	18/57 (31.6%)	54/181 (29.8%)	31/163 (19.0%)	0.038
No	75/965 (7.8%)	20/129 (15.5%)	40/424 (9.4%)	15/412 (3.6%)	<0.001 ^e
Timing of Surgery					
Emergent (<2 days)	60/206 (29.1%)	13/20 (65.0%)	31/86 (36.0%)	16/100 (16.0%)	<0.001 ^f
Urgent (2 days)	19/93 (20.4%)	3/8 (37.5%)	9/46 (19.6%)	7/39 (17.9%)	0.470
Elective (>2 days)	99/1067 (9.3%)	22/158 (13.9%)	54/473 (11.4%)	23/436 (5.3%)	<0.001 ^g

Table 3

Association of Characteristics with Mortality

	Odds Ratio	95% Confidence Interval	P-value
<u>Sex</u>			
Females vs. Males	0.87	0.63 – 1.20	0.400
<u>Surgical Weight</u>			
<2.5 kg vs. 2.5 kg	2.88	1.60 – 5.20	<0.001
<u>Decade</u>			
1982–89 vs. 2000–07	3.71	1.88 – 7.32	<0.001
1990–99 vs. 2000–07	2.19	1.48 – 3.24	<0.001
1982–89 vs. 1990–99	1.51	0.83 – 2.74	0.175
<u>Age Groups</u>			
Infants vs. Neonates	0.33	0.19 – 0.56	<0.001
Children vs. Neonates	0.11	0.01 – 0.86	0.036
Children vs. Infants	0.34	0.03 – 3.29	0.351
<u>Reported Obstruction</u>			
Yes vs. No	2.51	1.81 – 3.49	<0.001
<u>Anatomic Subtype</u>			
Cardiac vs. Supracardiac	0.62	0.31 – 1.22	0.165
Infracardiac vs. Supracardiac	1.41	0.99 – 2.02	0.059
Mixed vs. Supracardiac	2.45	1.54 – 3.92	0.000
<u>Timing of Surgery</u>			
Emergent vs. Elective	1.76	1.22 – 2.55	0.003
Urgent vs. Elective	1.41	0.75 – 2.65	0.282

Table 4

Major Cardiac Two Ventricle Anomalies (n=146)

Anomaly	n (% of all patients)
VSD	61 (2.71%)
DORV	14 (0.62%)
TOF	13 (0.58%)
Coarctation of aorta	12 (0.53%)
Pulmonary stenosis	8 (0.36%)
Partial AVC	5 (0.22%)
Truncus arteriosus	4 (0.18%)
Complete AVC	3 (0.13%)
D-TGA	2 (0.09%)
D-TGA + VSD	2 (0.09%)
Mitral ring	2 (0.09%)
Vascular ring	2 (0.09%)
Bicuspid aortic valve	1 (0.04%)
Miscellaneous	17 (0.76%)

Legend:

AVC – Atrioventricular Canal

DORV – Double Outlet Right Ventricle

D-TGA – Transposition of Great Arteries

TOF – Tetralogy of Fallot

VSD – Ventricular Septal Defect