A single center, retrospective analysis of total anomalous pulmonary venous connection repair early outcome at a tertiary care center in India

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ABSTRACT

Context: In recent years, increasing awareness and early detection has made total anomalous pulmonary venous connection (TAPVC) a relatively common congenital heart condition presenting to children’s heart centers in India. The condition was associated with significant morbidity and mortality in the past due to various reasons. Improvement in perioperative management has markedly changed the outcomes of TAPVC even in a developing country.

Material and Methods: All patients with TAPVC operated between June 2013 and February 2018 at our center were included in the study. Post repair 30-days mortality and morbidity were analyzed.

Results: A total of 166 patients were divided into supracardiac (91), infracardiac (45), cardiac (18), and mixed type (12). It also divided our cohort into obstructed and unobstructed types. The duration of inotrope usage in the obstructed group was significantly higher compared to the unobstructed group. Statistically, significant difference was noticed for the duration of ventilation 85.17 ± 80.94 h in obstructed type versus 49.23 ± 60.7 h in the unobstructed group, and in ICU stay (days) in obstructed (9.64 ± 5.96) and unobstructed group (6.29 ± 5.12). The morbidity parameters such as duration of an inotrope, ventilation, and length of ICU stay had a negative correlation between body surface area (BSA) of the patient but no correlation in respect to duration of CPB and ACC time. Mortality was found to be higher in lower BSA, infracardiac type (7/9), and obstructed variants of TAPVC (9/9) patients.

Conclusions: Longer duration of inotrope usage, mechanical ventilation, and ICU stay were seen in obstructed TAPVC in comparison to unobstructed TAPVC patients. Duration of CPB or aortic cross-clamp had no effects on morbidity parameters. In our cohort of TAPVC patients, lower BSA was strongly associated with the longer requirement of inotropes, prolong ventilation time, and ICU stay. The risk factors for mortality in our study include lower BSA, infracardiac, and obstructed type of TAPVC.

Keywords: BSA, ICU stay, mechanical ventilation, total anomalous pulmonary venous connection

INTRODUCTION

Total anomalous pulmonary venous connection (TAPVC) as reported in the literature is a rare congenital malformation accounting for 1–3% of all congenital heart disease.[1-2]

The first description of this malformation was by Wilson in 1798.[2,3] The current outcomes of TAPVC repair are the result of the general enhancements in preoperative...
analytic strategies, intraoperative procedures, postoperative management techniques, and better teamwork that has happened in the course of the most recent decade in many specialized centers in developing countries including India. The surgical mortality after TAPVC repair is now in general below 10%. Patients were obtained from hospital medical records.

Children, especially newborns, presenting with TAPVC are an extremely sick subset of congenital heart disease. It may not be possible in all cases to achieve optimal preoperative stabilization before the child undergoes surgical repair. The underlying cardiac and hemodynamic status dictates the time of surgery in most cases. This could be a reason why the morbidity and mortality associated with TAPVC is still high as compared to other routinely seen congenital heart conditions. We, therefore, analyzed the outcome of TAPVC patients and tried to identify the important risk factors which affect the 30-day mortality.

MATERIAL AND METHODS

A retrospective study of all patients who underwent surgical repair of TAPVC at our center between June 2013 and February 2018 was conducted after obtaining hospital ethical committee approval. We have excluded patients who was having preoperative proven sepsis. All requisite data were obtained from hospital medical records.

Patients had standard preoperative work up which includes total blood counts, liver function test, renal function test, coagulation profile, electrolytes and blood group, and crossmatch (to arrange blood products). A detailed echocardiography was performed to confirm the diagnosis, access preoperative ventricular function, level of obstruction, and individual pulmonary vein anatomy. Preoperative echocardiography, chest X-ray, and ultrasonography of abdomen were performed in all patients as a protocol. Preoperative cardiac computed tomography (CT) scan was performed only in a few selected patients depending on the request of either cardiologist or cardiac surgeon. Preoperative optimization was achieved whenever needed with the use of diuretics, digoxin, invasive or noninvasive ventilatory support, and appropriate antibiotics.

All patients were classified depending on anatomic subtypes of TAPV: supracardiac, cardiac, infracardiac, and mixed which was originally described by Darling. Patients were further categorized as obstructed or non-obstructed based on evidence of pulmonary venous obstruction at presentation. Pulmonary venous drainage was described as obstructed when there was a mean pulsed Doppler gradient of >4 mmHg by two-dimensional ECG anywhere in the circulation of blood from the pulmonary veins to the right atrium with or without a restrictive interatrial communication. We have also considered all patients with infracardiac TAPVC to be obstructed.

Demographic data were analyzed using univariate and multivariate analysis for specific correlations between type of TAPVC, body surface area (BSA) of the patient with duration of mechanical ventilation, intensive care unit (ICU) stay, and mortality. As a unit protocol for TAPVC correction cases, we have used intravenous (IV) infusion of adrenaline with the dose range of 0.05–0.1 mics/kg/min and IV infusion of milrinone with dose range of 0.5–0.75 mics/kg/min as a “inotropic support.” Further, we have analyzed the duration of inotropic support for various type of TAPVC and have compared it with BSA.

Standard postoperative monitoring techniques included ECG, invasive arterial blood pressure, invasive central venous pressure by a triple lumen catheter placed in the femoral vein, etCO2, and arterial blood gas sampling at multiple stages during and after surgery. In all patients, pulmonary artery (PA) pressure monitoring was done with an 2.5 F soft catheter placed directly in the main PA at the time of surgery. This allows continuous real-time monitoring of the PA pressure postoperatively in the ICU and to intervene with appropriate measures if found to be high in the early postoperative period. Another noteworthy factor is that throughout the study period, the senior members of team including surgeons, anesthesiologists, and intensivists remained unchanged, which gave adequate uniformity and experience in managing such a sick cohort of patients.

We adopted aggressive management strategies to deal with high PA pressure (systolic PA pressure higher than 2/3 of systolic blood pressure) and our unit policies are as follows:

1. Optimize ventilation by lung recruitment, check for collapse, consolidation, pneumothorax, endotracheal (ET) tube position, and plural effusion. Target SpO2 >95% by adjusting FiO2, Target PaCO2 30–35 mmHg with ventilation setting adjustments.

2. Check for ventricular function by echocardiography and optimize by adding or modifying inotropes. We have used milrinone infusion (dose range- 0.5 to 0.75 mics/kg/min) as an inodilator and adrenaline infusion (dose range- 0.04 to 0.1 mics/kg/min) as an inotrope in all cases.

3. After optimizing above parameters and still high PA pressure, we have started inhaled nitric oxide.
(dose range-20–60 ppm) followed by Sildenafil infusion (dose: 1–1.6 mg/kg/day) during the weaning of nitric oxide. Adding tablet Bosentan with Sildenafil was based on PA pressure response and liver function test.

4. We adopted early extubation as one of the strategies to deal with postoperative PAH management, as tracheal tube in position is one of the strong stimuli for high PA pressure. Before extubation, as a unit policy, we document the normalization of ventricular function and diaphragm movement by echocardiography. Early use of noninvasive ventilation was adopted, if child remained tachypneic with high PaCO2 or low PaO2 within first 4 h of extubation.

RESULTS

Study design: Single center, retrospective study

Statistical method

Difference in parameters when classified according to anatomic type in continuous parameters were accessed with one-way ANOVA with post hoc Tukey’s test.

Clinical characteristics were summarized in terms of frequencies count and percentages for categorical variables and as minimum, maximum, range, and mean ± SD for continuous variables. Difference in parameters between obstructive and unobstructive patients was analyzed using independent sample t-test. Correlation was checked by using Pearson's correlation test. A P value less than 0.05 was considered statistically significant. For statistical analysis SPSS software v2.0 was used. A multiple regression was run to predict ICU stay, duration of inotropes, duration of ventilation from BSA, age, aortic cross clamp (ACC), cardiopulmonary bypass (CPB), anatomical type, and obstructive/unobstructive type. Though the regression model was significant, only BSA and obstructive/unobstructive type contributed to prediction equation and hence equation was rerun using only these two parameters. The prediction equation predicted ICU stay, dosage of inotrope, and duration of ventilation significantly \( P < 0.0001 \). Both BSA and obstructive/unobstructive type were significant contributors to the equation.

Statistical analysis results

There was a significant male preponderance (106/166) in this study. The mean age at time of surgery was 2.75 ± 2.14 days. Mean weight (kg) of patients was 4.03 ± 1.10 and mean height (cm) was 54.66 ± 11.53 [Table 1]. TAPVC was classified as supracardiac in 91 patients (54.8%), cardiac in 18 patients (10.8%), infracardiac in 45 patients (27.1%), and mixed in 12 patients (7.2%) [Figure 1]. The mean duration of ACC was 68.65 ± 25.97 min and the mean CPB time was 148.87 ± 31.68 min. There was a significant difference in BSA levels of the four groups. Supracardiac group had significantly higher BSA as compared to infracardiac group \( (P = 0.022) \). No other significant correlation was observed \( (P > 0.05) \). Delayed sternal closure was performed in a total of 44 patients out of which 29 (65.90%) cases were obstructed TAPVC.

The mean duration of inotrope usage (days) in obstructed group was 4.55 ± 2.15 with 95% CI (4.07–5.034) and 3.42 ± 1.84 with 95% CI (3.03–3.81) in unobstructed group \( (P < 0.001) \). The mean duration of ventilation (h) was 66.11 ± 72.97 in obstructed group 85.17 ± 80.94 (66.92–103.42) and 49.23 ± 60.70 (36.67–62.09) in unobstructed group which comes statistically significant [Table 2]. The mean duration of ICU stay (days) was 7.86 ± 5.96, in obstructed group TAPVC (9.64 ± 5.96) with CI of (8.30–10.98) and 6.29 ± 5.12 (5.21–7.38) in unobstructed group \( (P < 0.001) \).

Mean BSA of full cohort calculated was 0.24 ± 0.07. Statistically significant correlation was found when we studied full cohort BSA and morbidity parameters like duration of inotropes, duration of ventilation, and ICU stay using Pearson's correlation coefficient. Table 3 shows that there was a negative correlation of BSA with duration of inotrope requirement, longer duration of ventilation, and longer ICU stay indicating that inotrope requirement, longer duration of ventilation, and longer ICU stay increased as BSA decrease \( (P < 0.001) \). Our analysis could not find any statistically significant correlation between morbidity parameters and duration of CPB, ACC, time [Table 3].

DISCUSSION

TAPVC is a subset of complex congenital cardiac defects where all pulmonary veins have no direct connection with left atrium and they drain into one of the systemic veins or directly to the right atrium or coronary sinus.

Craig and Darling et al. has classified TAPVC as: a) Anomalous connection at supracardiac level- Supracardiac TAPVC, b) Anomalous connection at cardiac level- Cardiac TAPVC, c) Anomalous connection at infracardiac level- Infracardiac TAPVC and d) Anomalous connection at two or more of the above level – Mixed TAPVC.\({}^{[6]}\)

In literature, supracardiac TAPVC is the most common type reported, accounting for about 40% to 45% of the total TAPVC and second most is cardiac type TAPVC.\({}^{[7‑9]}\)
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Table 1: Presentation characteristics of patient with anatomical sub-type

| Variables                | Overall (N = 166) | Supra cardiac (n = 91) | Cardiac (n = 18) | Mixed (12) | Infra cardiac (n = 45) | P-value |
|--------------------------|-------------------|------------------------|------------------|------------|-----------------------|---------|
| Demography Data          |                   |                        |                  |            |                       |         |
| Age (month) *            | 2.75 ± 7.14       | 2.93 ± 6.62            | 2.13 ± 1.91      | 6.52 ± 16.88 | 1.43 ± .82            | 0.199   |
| Sex (male: Female)       | 106: 60           | 60:31                  | 11: 7            | 7: 5       | 28: 17                |         |
| Weight (kg)*             | 4.03 ± 4.10       | 4.59 ± 5.30            | 3.73 ± 1.07      | 3.69 ± 1.37 | 3.09 ± 7.75           | 0.240   |
| Height (cm)*             | 54.66 ± 11.53     | 55.29 ± 11.38          | 56.67 ± 6.37     | 53.08 ± 4.21 | 53.02 ± 14.41        | 0.588   |
| BSA                      | 0.24 ± 0.07       | 0.25 ± 0.08            | 0.24 ± 0.04      | 0.23 ± 0.05 | 0.18 ± 0.07           | 0.040   |
| Types                    |                    |                        |                  |            |                       |         |
| Obstructed (n)           | 78                 | 30                     | 1                | 2          | 45                    |         |
| Unobstructed (n)         | 88                 | 61                     | 17               | 10         | -                     |         |
| Operative Data           |                    |                        |                  |            |                       |         |
| ACC Time (Hour)          | 68.65 ± 25.97      | 70.38 ± 25.68          | 61.06 ± 30.06    | 79.17 ± 32.41 | 65.38 ± 22.31         | 0.202   |
| CPB Time (Hour)          | 148.87 ± 119.68    | 139.57 ± 46.06         | 167 ± 52.45      | 186.08 ± 7.86 | 136.00 ± 32.67        | 0.133   |

*: Mean ± SD, BSA = Body surface area, ACC = Aortic cross clamp, CPB = Cardiopulmonary bypass Time

Table 2: Comparisons of Obstructed and Unobstructed type of TAPVC vis a vis duration of inotrope use, duration of mechanical ventilation and duration of ICU stay

| Variable’s                | Overall | Obstructed (95% CI) | Unobstructed (95% CI) | P-value |
|---------------------------|---------|---------------------|-----------------------|--------|
| Duration of Inotrope use (days)* | 3.95 ± 2.07 | 4.55 ± 2.15 (4.07-5.034) | 3.42 ± 1.84 (3.03-3.81) | <0.001* |
| Duration of Ventilation (hrs)* | 66.11 ± 72.97 | 85.17 ± 80.94 (66.92-103.42) | 49.23 ± 60.70 (36.67 - 62.09) | 0.001* |
| Duration of ICU stay (days)* | 7.86 ± 5.76 | 9.64 ± 5.96 (8.30-10.98) | 6.29 ± 5.12 (5.21-7.38) | <0.001* |

*: P-value <0.05 was found statistically significant at 5% level of significance using t-test. CI: Confidence interval

Table 3: Correlation between BSA, CPB time and ACC time with duration of inotrope (day), duration of ventilation (hours), and ICU stay (day) are calculated using Pearson’s coefficient correlation

| Variable’s                | Overall | Obstructed (95% CI) | Unobstructed (95% CI) | P-value |
|---------------------------|---------|---------------------|-----------------------|--------|
| Duration of Inotropes (Day) | -0.310  | <0.001              | -0.92                 | 0.24   | 0.77 | 0.326 |
| Duration of Ventilation (Hours) | -0.313  | <0.001              | 0.013                  | 0.864  | 0.43 | 0.585 |
| ICU stay (Day)             | -0.303  | <0.001              | 0.02                   | 0.978  | 0.02 | 0.807 |

*: P-value <0.05 was found statistically significant at 5% level of significance using t-test. CI: Confidence interval

Figure 1: Flow chart of all TAPVC cases describes anatomic type and subdivided into obstructed and unobstructed variant of TAPVC. This flow chart also shows duration of inotrope use, duration of ventilation, duration of intensive care unit (ICU) stay, and number of mortalities in each obstructed and unobstructed subtype of TAPVC. (Obst = Obstructed, Unobst = Unobstructed)

Our study partially mirrored these observations with supracardiac (54.8%) being most common but infracardiac type was the second most common, accounting for about 27% cases.
The presence of an obstructive lesion in anomalous pulmonary venous channel significantly influences the preoperative, intraoperative, and postoperative course of the patients. Obstruction in TAPVC can be at various levels along the drainage pathway of the pulmonary veins. It could be a restrictive atrial septal defect (ASD), anatomical narrowing at vertical vein insertion or at level of individual pulmonary veins. In infracardiac TAPVC when anomalous connection is to the portal vein or to one of its tributaries, the hepatic sinusoids lead to increased resistance for pulmonary venous drainage and, therefore, we have considered all infracardiac TAPVCs as obstructed type in our study. The incidence of obstructed TAPVC in literature was in the range of 25–50% at initial diagnosis.\textsuperscript{[10‑12]} We found slightly higher incidence of obstructed TAPVC (53%). This may probably be due to our center being one of the tertiary referral centers for complex congenital cases.

Lucas \textit{et al.} in their study noted that there is male preponderance (3.6:1) in infracardiac TAPVC but not in other variants. In our study, all TAPVC variants have higher incidences in males.

Age at presentation of TAPVC patients depends on the severity of pulmonary venous obstruction and type of TAPVC. As we have noticed in our cohort, the earliest presentation is seen in infracardiac TAPVC (1.43 ± 0.82 months) where the degree of obstruction for pulmonary venous drainage is usually high. This also correlates with the finding that the BSA was least in infracardiac TAPVC (0.18 ± 0.07 m\textsuperscript{2}).

We have studied the correlation of BSA on morbidity parameters by using Pearson’s correlation and scatter plot draw diagram. We found a statistically significant negative correlation between BSA and ventilation time, ICU stay as well as duration of inotrope use [Figure 2]. This infers that lower body weight and early age presentation due to variable degree of obstruction have higher morbidity in this subset of disease also.

The mean cross clamp time (79.17 ± 32.41 min) and the mean CPB time (186.08 ± 39.68 min) was highest in the mixed type of TAPVC probably due to the fact that their complex anatomy takes more time for repair (multiple pulmonary vein – left atrial anastomoses), but the overall CPB and ACC times in various groups did not have any significant impact on morbidity or mortality outcomes in our study.

Various authors\textsuperscript{[11,13]} have described that low body weight, young age, prematurity, and longer CPB/ACC times were associated with an increased mortality in cardiac surgery. However, in our study CPB and ACC times were not significant risk factors as far as outcomes were concerned, and such an observation has also been described in other published reports.\textsuperscript{[1,7,5,10]}

Our study has shown statistically significant increase in duration of inotrope, ventilation time, and ICU stay in obstructed type of TAPVC group. But there are some studies which did not find any statistically significant correlation.\textsuperscript{[17‑10]} Surgical correction for obstructed TAPVC is usually done as an emergent or semi-emergent procedure. There may be inadequate time for preoperative stabilization. There is also an increased incidence of delayed sternal closure, ventricular dysfunction, and significant ventilation/perfusion mismatch perioperatively. These factors may have contributed to the altered morbidity parameters in obstructed TAPVC group. We have also found a higher ventilation and ICU stay duration in infracardiac and mixed variants.

The surgical mortality in early TAPVC series is in the range of 10% to 80%,\textsuperscript{[1,7,12]} but most recent reports revealed a surgical mortality of <10%.\textsuperscript{[8,10]} In our cohort, 30-days mortality was 5.4% and was down to 3% in the recent years. This figure is quite comparable to recent reports. One of the factors that has improved changed TAPVC outcomes in our center is the availability of a dedicated children’s heart team consisting of cardiology, surgery, anesthesia, intensive care, nursing, perfusion, and other

![Figure 2: Scatter plot of body surface area (BSA) with duration of ventilation (hours) and ICU stay (day). Scatter plot shows the patient with lower BSA had required longer duration ventilation and also longer duration of ICU stay.](image-url)
paramedical services who work in a coordinated manner to deliver outcomes. Another factor is the appropriate usage of pulmonary vasodilators like inhaled nitric oxide (iNO), sildenafil and bosentan,[18] protocol for managing high PA pressure, early extubation strategies, and early use of noninvasive ventilation which have brought down our morbidity parameters including early discharge from the ICU and reduced incidence of respiratory and blood infections[18] and mortality rates.

In our series out of total nine deaths, seven children had postoperative infection (five developed ventilator associated pneumonia, two had blood stream infections, renal failure, and eventually multiorgan failure) and two had succumbed to low cardiac output out of which one child was put on veno-arterial extracorporeal support postoperatively but could not be salvaged. In our analysis, we found lower BSA and obstructed type of TAPVC as a major risk factor for mortality. Similar observation was made by Hankock et al. where infracardiac and mixed TAPVC had the highest mortality. Morales et al. mentions preoperative pulmonary venous obstruction to be not a risk factor for surgical mortality, even in heterotaxy group of patients.[10]

CONCLUSIONS

Longer duration of inotrope usage, mechanical ventilation, and ICU stay were seen in obstructed TAPVC in comparison to unobstructed TAPVC patients. Duration of CPB or ACC has no effects on morbidity parameters. In our cohort of TAPVC patients, lower BSA was strongly associated with longer requirement of inotropes, prolong ventilation time, and ICU stay. The risk factors for mortality in our study include lower BSA, infracardiac, and obstructed type of TAPVC.

Limitation of study

This is a retrospective study and hence PA pressure fluctuations and its impact on outcome could not be studied due to inadequate data. Surgical techniques, size of common chamber, and pulmonary vein status were not included in this study and will also remain as one of the limitations of our analysis. We have analyzed outcome only up to 30 days and further follow-up data has not been included and analyzed.

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Conflicts of interest

There are no conflicts of interest.

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