ORIGINAL ARTICLE

Predictors of mortality and morbidity in total anomalous pulmonary venous connection with biventricular physiology: A 10-year Indian single centre experience of 492 patients

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ABSTRACT

Background : **Surgical correction of total anomalous pulmonary venous connection (TAPVC) remains associated with significant mortality despite advances in intra-operative and postoperative management. We retrospectively analyzed 492 consecutive TAPVC patients with biventricular physiology, who were operated at our centre, with regard to predictors of mortality, morbidity, and intermediate-term outcomes.**

Materials and Methods : **A total of 492 TAPVC patients with biventricular physiology were operated at our centre from August 2009 to November 2019. Their medical records were reviewed and were followed up during March-April 2020 for any symptoms of cardiac disease.**

Results : **Of 492, 302 (61.38%) were healthy at follow-up, 29 (5.89%) had postoperative mortality, 23 (4.67%) had mortality during the follow-up period, and 138 (28.05%) were lost to follow up. Age <1 month and weight <2.5 kg were associated with higher mortality with odds ratios (OR) of 6.37 and 5.56, respectively. There was no difference in mortality in different types of TAPVC. Obstructed TAPVC was associated with higher mortality with OR of 3.05. Acute kidney injury requiring peritoneal dialysis and sepsis were associated with higher mortality with ORs of 10.17 and 3.29, respectively. All follow-up mortality occurred in <1 year from the index operation. Anastomotic gradients were significantly higher in patients who died.**

Conclusions : **Although peri-operative TAPVC mortality has reduced, mortality on follow-up continues to occur and is partly due to the obstruction of pulmonary venous pathway. Meticulous follow-up holds the key in further reducing the mortality. Larger studies are needed for the identification of risk factors for pulmonary venous obstruction and its preventive strategies.**

Keywords : Intermediate outcomes, mortality predictors, regression analysis, total anomalous pulmonary venous connection surgery

INTRODUCTION

Total anomalous pulmonary venous connection (TAPVC) is congenital heart malformation involving nonunion

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of pulmonary veins and left atrium with persistent systemic – pulmonary venous communication[1] arising from the developmental anomalies of secondary heart field.[2] Depending on the positioning of communicating pathway, TAPVC can be supracardiac, infracardiac, intracardiac, or mixed types.[3] They have obligatory atrial septal defect (ASD) with right to left shunting. Obstruction of either communicating pathway or ASD complicates the condition with earlier presentation and severe symptoms. Obstruction and right ventricular volume overload contributes to pulmonary arterial hypertension (PAH) in them.[4] TAPVC occurs in both biventricular and univentricular physiologies with common associated conditions being ventricular septal defects (VSD), patent ductus arteriosus (PDA), transposition of great arteries, and Heterotaxy syndromes.

Surgical redirection of pulmonary veins into left atrium is the primary mode of correction and multiple techniques are described. Postoperative management of these patients has also improved over time. The current literature reports a mortality of 5%–10% in patients with biventricular physiology. Various risk factors have been shown to contribute to mortality and morbidity in them. We reviewed those who were treated at our centre and analyzed the factors that correlated with mortality, morbidity, and intermediate-term survival.

MATERIALS AND METHODS

A total of 492 patients were treated for TAPVC with biventricular physiology at Star Hospitals, Hyderabad, from August 2009 to November 2019. Diagnosis was based on echocardiography with computed tomography (CT) performed only to delineate complex anatomies. Obstruction was defined as evidence of turbulence with maximal Doppler flow velocity of >1.5 m/s at any point in the pulmonary venous pathway.[5] Individual pulmonary vein obstructions were defined based on isolated turbulence in suspected vein with maximal Doppler flow velocity of >1.1 m/s.[6] The study was approved by hospital ethics committee and individual consent was waived off. Hospital charts, operative notes, preoperative and postoperative echocardiography, and CT reports of these were reviewed. Patients were interviewed during the months of March and April 2020 for the symptoms of cardiorespiratory diseases. Follow-up echocardiograms were also reviewed. Patients lacking recent follow-up echocardiogram (<3 months from interview date) underwent repeat echocardiography.

Objectives

The objective of the study was to determine the predictors of early postoperative mortality and intermediate term mortality. Early mortality was defined as in hospital mortality or mortality occurring within 30 days from the index operation. Follow-up mortality was defined as mortality occuring beyond 30 days from the index operation.

Surgical technique

All procedures were done through median sternotomy under cardiopulmonary bypass (CPB). Heart was arrested with St Thomas or Del Nido cardioplegia. Deep hypothermic circulatory arrest was not used. Transient low flows were occasionally established to facilitate suture placement on pulmonary veins. Most underwent repair through William's approach.[7] Intracardiac TAPVC was repaired with pericardial baffle. Other techniques used were Shumacker – King technique[8] and Tucker's approach.[9] Sutureless technique was not used in any patient. Our usual practice was to close the ASD. Vertical vein was ligated after separation from CPB. Open sternum status was decided based on dysfunction, inotropic support, or extent of bleeding.

Statistical analysis

Data were presented as mean ± standard deviation or median with range as appropriate. Difference in means was presented with mean difference ± standard error. Continuous and nominal variables were evaluated with ANOVA and binomial and multinomial logistic regression analysis. ORs were determined for variables that emerged as significant predictors. Nominal proportions were compared by Fisher's exact test or Chi-square test. All reported *P* values were two-tailed. Survival analysis was done with Kaplan–Meier method and pairwise analysis was done with Gehan test. For analysis related to early mortality (postoperative mortality), entire group of 492 patients were included. For analysis related to total mortality (postoperative + late follow-up mortality), lost to follow-up patients (n = 138) were excluded. Statistical analysis was performed with SPSS software package (Version 23, SPSS Inc, Chicago, IL).

RESULTS

A total of 492 patients underwent TAPVC repair and the year-wise distribution is shown in Figure 1. Baseline demographics of these patients are shown in Table 1. There was an increase in the average number of cases operated year-wise from 40 cases (2010–2014) to 57 cases (2015–2019) with no difference in age distributions among different operating years (P = 0.198, Pearson Chi-square). Of the 492 patients, 29 (5.89%) had early mortality, 302 (61.38%) were healthy at follow-up, with 296 patients among them in NYHA I and 6 patients in NYHA II. Twenty-three patients (4.67%) had mortality during the follow-up period and in total 52 patients (10.57%, early + follow up) expired during the entire period. One hundred and thirty-eight patients (28.05%) could not be contacted and were noted as lost to follow up. Mean follow-up duration

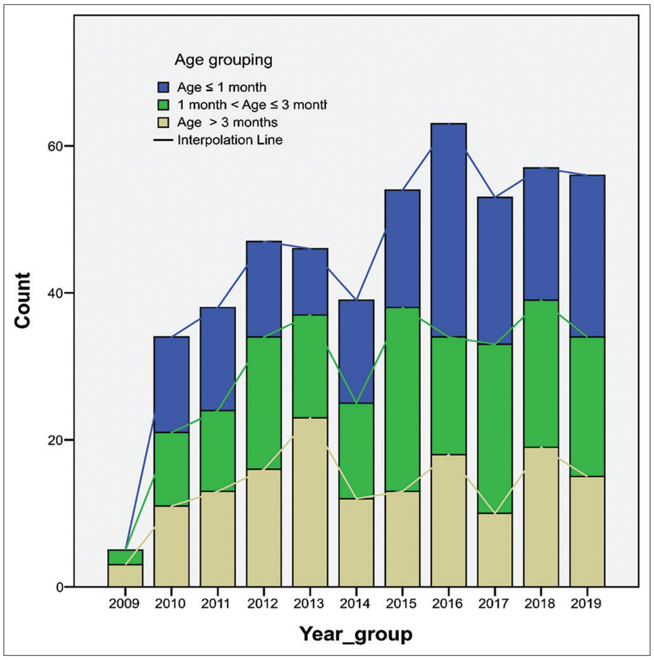

Figure 1: Year wise distribution from 2009 to 2019 differentiated based on age at initial surgery

was 51.3 ± 31.0 months. For comparison, patients were organized into six groups, viz: total patient group (n = 492), healthy patient group (n = 302), total mortality group (n = 52), early postoperative mortality group (n = 29), late follow up mortality group (n = 23) and lost to follow up group (n = 138).

Baseline characteristics of all the patients

Mean age, mean weight, mean BSA, and percent males of the total patient group at time of surgery were 0.31 ± 0.61 years, 3.74 ± 1.52 kg, 0.239 ± 0.063 m^2, and 69.3% respectively. Mean age, mean weight, mean BSA, and percent males for other groups are shown in Table 1 and plotted in Figures 2 and 3. Supracardiac, infracardiac, intracardiac, and mixed TAPVC constituted 48.4%, 14.8%, 27.6%, and 8.1%, respectively. Nearly 30% patients (149 patients) had obstructive TAPVC. Vast majority [475 patients (96.5%)] had isolated TAPVC with ASD or PFO with or without PDA. Seven (1.4%) and 3 (0.6%) patients had single and multiple VSD, respectively, and 3 patients (0.6%) had pulmonary stenosis. There were one each case of common atrium (1), D-transposition of great arteries (1), VSD with hypoplastic arch with coarctation (1) as associated anomalies. Preoperative sepsis and preoperative intubated state was noted in 3 and 13 patients, respectively. Mean CPB and aortic cross clamp (ACC) times in total patient group were 86.63 ± 36.04 and 49.30 ± 22.11 min, respectively. Mean CPB and ACC times in other groups are shown in Table 1. Open sternum was noted in 122 patients (24.8%).

Ventilation hours data were missing in 83 patients. After excluding them, mean ventilation hours of total group (n = 409) was 45.76 ± 79.81 h. Overall 79 patients (16.1%) had lung complications such as pneumonia/consolidation, segmental or lobar or whole lung collapse in the postoperative period. Forty-five patients (9.1%) required reintubation in the postoperative period, and of these, 9 patients had postoperative mortality. Pulmonary artery hypertension (PAH) crisis was noted in 15 patients (3.0%), of whom 5 patients had postoperative mortality. Endotracheal bleed was noted in 34 patients (6.9%), of whom 5 patients had postoperative mortality. Mean ventilation hours and other lung complication rates in other groups are displayed in Table 1. Continuous positive airway pressure (CPAP) support was required in 86 patients (17.5%). High frequency oscillatory ventilation (HFOV) was required in 18 patients (3.7%) with 1 requiring both HFOV and nitric oxide (NO).

Of total group, 461 patients (93.7%) had no acute kidney injury (AKI), 8 patients (1.62%) had AKI with no PD requirement, and 23 patients (4.67%) had AKI requiring PD. Among no AKI, AKI without PD and AKI with PD groups, 19 (4.1%), 3 (37.5%) and 7 (30.4%) patients had postoperative mortality. Postoperative sepsis was documented in 40 patients (8.1% of total group) with 6 patients (15%) having early mortality. LCOS (low cardiac output syndrome) was noted in 61 patients (12.4%), of whom 17 patients (27.9%) had postoperative mortality. The incidence of renal and other complications in the various groups are shown in Table 1. Re-exploration was done in 11 patients (2.2%), of whom only 1 had mortality. Re-bypass was instituted in 21 patients (4.3%) with anastomotic revision in 14 patients (2.8%). Diaphragm plication for left diaphragm palsy was done for 4 patients (0.8%). Mean intensive care unit (ICU) and hospital stay for total group were 6.69 ± 34.82 and 10.14 ± 6.59 days, respectively. Mean ICU and hospital stay for other groups are shown in Table 1 and Figure 4. Postoperative anastomotic gradients were available in 473 patients [Figure 5]. Mean gradient across anastomosis in TP group was 0.34 ± 0.08 mm of Hg. Mean gradients in other groups are shown in Table 1.

Comparison of total group with mortality groups

Preoperative variables

Mean ages were lower among patients who died as compared to the total group (P < 0.005, ANOVA) indicating that younger age at surgery was associated with higher mortality. Among 52 patients who expired, 35 patients (67.3%) were ≤1 month at time of surgery. Age ≤1 month was associated with higher risk of early and overall mortality with ORs of 6.38 and 5.49 respectively when compared to age >3 months (P = 0.0003, Logistic regression). Mean weight of total group was higher when compared to mortality groups (P < 0.005,

Table 1: Baseline characteristics of all groups of patients

	Total group (TP)	Healthy group (HP)	TM group
n (%)	492 (100)	302 (61.38)	52 (10.57)
Age (years)	0.31±0.61	0.32±0.67	0.12±0.14
Weight (kg)	3.73±1.52	3.79±1.47	2.88±0.64
Height (cm)	55.95±8.24	56.26±8.12	51.23±4.35
BSA (m^2)	0.24±0.06	0.24±0.06	0.20±0.03
Percent males (*n*)	341 (69.3)	201 (66.6)	44 (84.6)
Supracardiac TAPVC, *n* (%)	238 (48.4)	145 (48)	21 (40.4)
Infracardiac TAPVC, *n* (%)	73 (14.8)	45 (14.9)	13 (25)
Intracardiac TAPVC, *n* (%)	136 (27.6)	81 (26.8)	12 (23.1)
Mixed TAPVC, *n* (%)	40 (8.1)	30 (9.9)	4 (7.7)
Anastomotic obstruction TAPVC, *n* (%)	5 (1)	1 (0.3)	2 (3.8)
ACC time (min)	49±22	47±19	67±28
CPB time (min)	87±36	83±32	119±47
Ventilation (h)	45.76±79.81	38.31±67.94	99.23±123.77
Hospital stay (days)	10.14±6.59	9.83±6.49	12.17±8.36
LCOS, *n* (%)	61 (12.4)	30 (9.9)	22 (42.3)
AKI requiring PD, *n* (%)	23 (4.7)	8 (2.6)	10 (19.2)
Sepsis, *n* (%)	40 (8.1)	22 (7.3)	10 (19.2)
Lung complication, *n* (%)	79 (16.1)	52 (17.2)	15 (28.8)
PAH crisis, *n* (%)	15 (3)	8 (2.6)	5 (9.6)
Reintubation, *n* (%)	45 (9.1)	27 (8.9)	13 (25)
ET bleed, *n* (%)	34 (6.9)	19 (6.3)	6 (11.5)
Re-exploration, *n* (%)	11 (2.2)	5 (1.7)	1 (1.9)
Re-bypass, *n* (%)	21 (4.3)	8 (2.6)	11 (21.2)
CPAP, *n* (%)	86 (17.5)	53 (17.5)	16 (30.8)
Only HFOV, *n* (%)	17 (3.5)	3 (1)	9 (17.3)
HFOV and NO, *n* (%)	1 (0.2)	0	1 (1.9)
Open sternum, *n* (%)	122 (24.8)	73 (24.2)	26 (50)
	PM group	**FM group**	**LFU group**
n (%)	29 (5.89%)	23 (4.67%)	138 (28.05%)
Age (years)	0.11±0.14	0.13±0.14	0.38±0.60
Weight (kg)	2.89±0.69	2.86±0.60	3.92±1.76
Height (cm)	49.90±4.23	52.91±3.99	57.02±9.04
BSA (m^2)	0.20±0.03	0.20±0.03	0.20±0.03
Percent males, *n* (%)	25 (86.2)	19 (82.6)	96 (69.6)
Supracardiac TAPVC, *n* (%)	13 (44.8)	8 (34.8)	72 (52.2)
Infracardiac TAPVC, *n* (%)	9 (31)	4 (17.4)	15 (10.9)
Intracardiac TAPVC, *n* (%)	4 (13.8)	8 (34.8)	43 (31.2)
Mixed TAPVC, *n* (%)	2 (6.9)	2 (8.7)	6 (4.3)
Anastomotic obstruction TAPVC, *n* (%)	1 (3.4)	1 (4.3)	2 (1.4)
ACC time (min)	63±23	72±34	48±22
CPB time (min)	114±46	124±29	82±35
Ventilation (h)	132.65±155.99	57.86±39.63	39.92±72.97
Hospital stay (days)	11.17±9.79	13.43±6.07	10.05±5.93
LCOS, *n* (%)	17 (58.6)	5 (21.7)	9 (6.5)
AKI requiring PD, *n* (%)	7 (24.1)	3 (13)	5 (3.6)
Sepsis, *n* (%)	6 (20.7)	4 (17.4)	8 (5.8)
Lung complication, *n* (%)	11 (37.9)	4 (17.4)	12 (8.7)
PAH crisis, *n* (%)	5 (17.2)	0	2 (1.4)
Reintubation, *n* (%)	9 (31)	4 (17.4)	5 (3.6)
ET bleed, *n* (%)	5 (17.2)	1 (4.3)	9 (6.5)
Re-exploration, *n* (%)	1 (3.4)	0	5 (3.6)
Re-bypass, *n* (%)	8 (27.6)	3 (13)	2 (1.4)
CPAP, *n* (%)	7 (24.1)	9 (39.1)	17 (12.3)
Only HFOV, *n* (%)	9 (31)	0	5 (3.6)
HFOV and NO, *n* (%)	1 (3.4)	0	0
Open sternum, *n* (%)	14 (48.3)	12 (52.2)	23 (16.7)

BSA: Body surface area, TAPVC: Total anomalous pulmonary venous connection, ACC: Aortic cross clamp, CPB: Cardiopulmonary bypass, LCOS: Low cardiac output syndrome, AKI: Acute kidney injury, PD: Patent ductus, PAH: Pulmonary arterial hypertension, CPAP: Continuous positive airway pressure, HFOV: High frequency oscillatory ventilation, NO: Nitric oxide, PM: Postoperative mortality, FM: Follow up mortality, LFU: Lost to follow up, TM: Total mortality, ET: Endotracheal

Brown – Forsythe). When compared to patients with weight >3 Kg, patients with weight ≤2.5 kg had higher early and overall mortality with OR of 5.56 and 5.24 respectively ($P < 0.001$, Logistic regression). Patients with weight >2.5 kg and ≤3 kg had higher early and total mortality with OR of 3.35 and 3.58 respectively ($P = 0.013$, $P < 0.001$, Logistic regression) when compared to patients with weight >3 Kg. Mean BSA in total group was higher than mean BSA of Mortality groups ($P < 0.005$, Brown – Forsythe). Percentage of

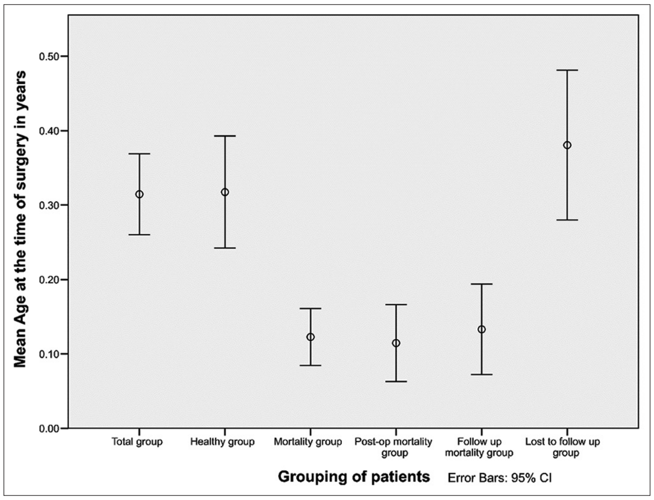

Figure 2: Mean age at time of surgery in different groups with 95% confidence intervals

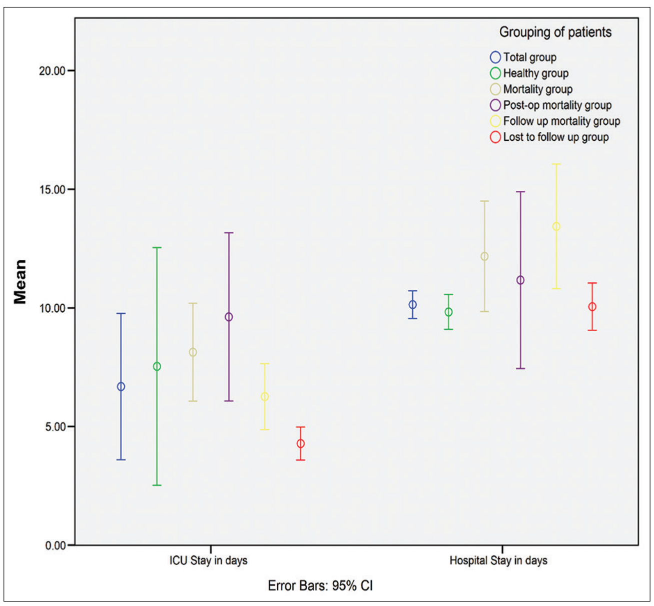

Figure 4: Mean ICU Stay and Hospital Stay among various patient groups. ICU: Intensive care unit

males in total mortality group (84.6%) was higher than total group (69.3%) with male sex having OR of 2.44 for mortality (P = 0.025, Logistic regression).

No significant difference with type of TAPVC was noted in Mortality groups when compared to total group (P = 0.114–0.918, Logistic regression). No specific type of TAPVC contributed to significantly increased mortality in our series. 149 patients (30.3%) had obstruction of whom 16 patients (10.7%) had early mortality. Of remaining 343 patients, 13 patients (3.8%) had early mortality. Early mortality in obstructed group was higher (P = 0.006, Fisher) with OR of 3.054 (P = 0.004, Logistic regression). One patient among 3 with preoperative sepsis had early mortality. This difference was not significant (P = 0.077). Three of

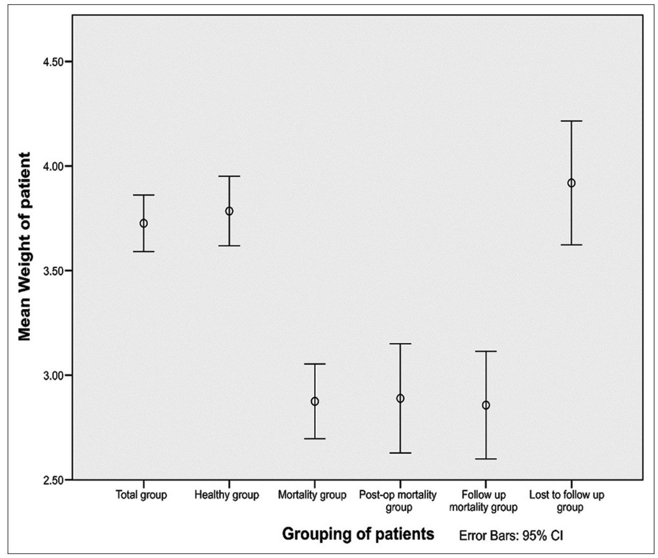

Figure 3: Mean weight at time of surgery in different groups with 95% confidence intervals

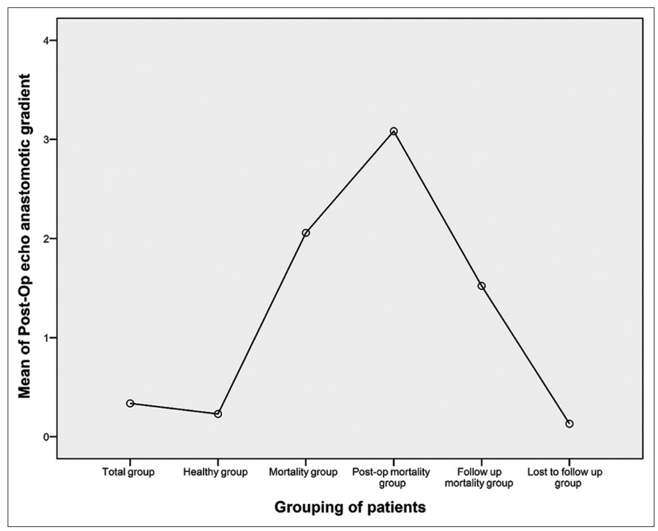

Figure 5: Mean postoperative anastomotic gradients for various patient groups

13 patients with preoperative intubated state had early mortality. This was significant with OR of 5.41 (P = 0.014, Logistic regression).

Operative variables

Mean CPB and ACC times in the total group were lower than the times in mortality groups (P < 0.005, Welch, Brown – Forsythe). Out of 52 patients who had mortality, 26 patients (50%) had open sternum. Of 302 healthy patients, 73 patients (24.2%) had open sternum. The incidence of open sternum was higher in mortality groups compared to healthy group (P < 0.01, Fisher) with OR of 3.58 (P < 0.001, logistic regression).

Ventilation and Lung complications

Mean ventilation hours in total group were lower than postoperative mortality group (P = 0.022, Games – Howell). 50 patients (12.2%) had prolonged ventilation of >72 h with 12 of them having mortality. Percent mortality was higher in prolonged ventilation group ($P < 0.01$, Fisher) with OR of 6.80 ($P = 0.039$, Logistic regression). LCOS was significantly associated with prolonged ventilation with OR of 2.90 ($P = 0.032$, Logistic regression).

Overall 52 patients (17.2%) of healthy group ($n = 302$) and 15 patients (28.8%) of total mortality group ($n = 52$) had lung complications. Lung complication incidence was higher in total mortality group when compared to those survived ($P = 0.048$, Chi-square). Lung complication was noted in 38 (16.0%) out of 238 Supracardiac TAPVC patients. Similarly, it was noted in 12 (16.4%, $n = 73$), 20 (14.7%, $n = 136$), 7 (17.5%, $n = 40$) and 2 (40%, $n = 5$) patients of Infracardiac, Intracardiac, Mixed TAPVC and anastomotic obstruction. There was no difference in incidence of lung complication in various types of TAPVC ($P = 0.152$–0.657, Logistic regression). Weight ≤3 kg was associated with higher incidence of Lung complication with OR of 3.43 ($P = 0.009$, Logistic regression). Lung complication was associated with higher incidence of LCOS with OR of 3.28 ($P = 0.001$, Logistic regression).

Age ≤1 month was associated with higher risk of reintubation with OR of 10.519 ($P = 0.047$, Logistic regression). Reintubation has led to prolongation of hospital stay ($P = 0.001$, Logistic regression). PAH crisis had higher risk of postoperative mortality ($P = 0.001$, Fisher) with OR of 19.32 ($P = 0.033$, Logistic regression). Endotracheal bleed had higher incidence in mortality group ($P = 0.041$, Fisher) with OR of 3.16 ($P = 0.031$, Logistic regression).

Renal and other complications

AKI without or with PD was associated with higher postoperative mortality ($P < 0.01$, Fisher) with AKI with PD group having OR of 10.18 ($P < 0.01$, Logistic regression). Sepsis was associated with higher mortality ($P = 0.023$, Fisher) with OR of 3.29 ($P = 0.015$, Logistic regression). Incidence of LCOS was significantly higher in mortality groups ($P < 0.01$, Fisher) with OR for mortality of 27.08 ($P < 0.01$, Logistic regression) when compared to patients with no LCOS. There was no difference in ICU or hospital stay in between groups ($P = 0.946$, 0.106, ANOVA, Brown – Forsythe).

Comparison of total group, healthy group and lost-to-follow up group

We had 28% of patients who were lost to follow up at time of our study. We believe that multiple factors including but not limited to socioeconomic status, migratory nature and level of education had contributed to this follow up attrition. All variables of the Lost to follow up group are also listed in Table 1. After thorough statistical analysis, we have noted no significant differences in between lost to follow up and total or healthy groups. Based on this analysis, it can be presumed that the mortality, if any, among the lost to follow up group is not significant enough to affect our results.

Survival analysis

In Kaplan–Meier survival analysis, it was noted that all events (Mortality) occurred in initial part of follow up. Furthest event from intervention (Surgery) was at 10 months [Figure 6]. Survival analysis was repeated with grouping by type of TAPVC [Figure 7] and there was no difference in survival in different types of TAPVC ($P = 0.260$, Mantel– Cox). Age ≤1 month is associated with lower survival when compared to Age >3 months ($P < 0.01$, Gehan). Weight ≤2.5 Kg was

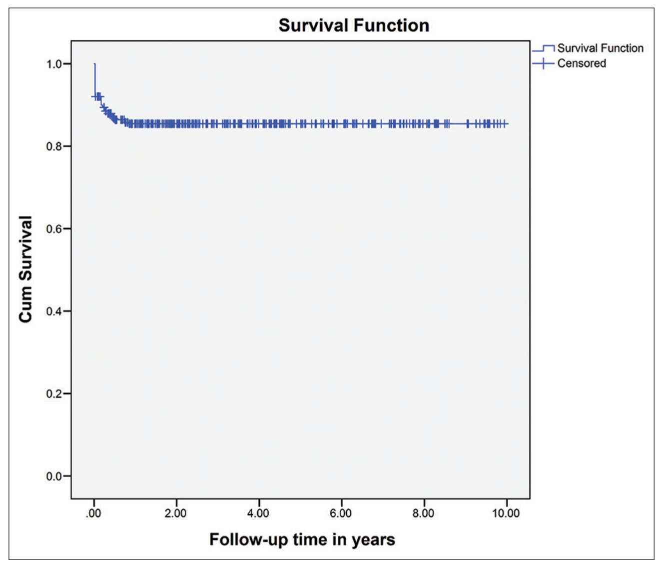

Figure 6: Survival curve for entire group

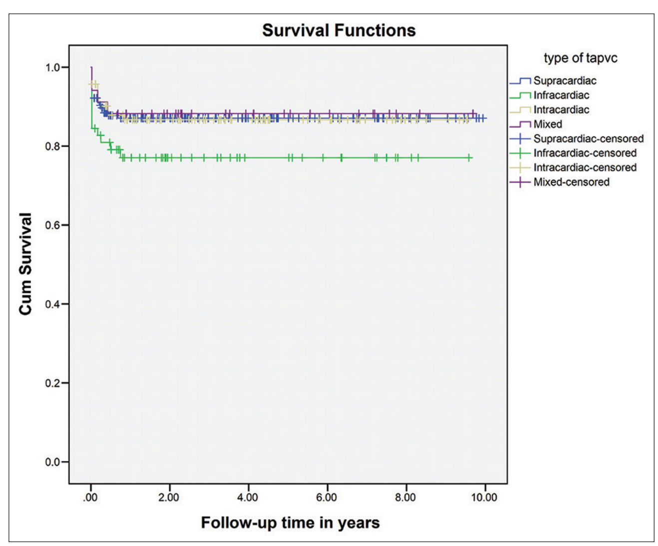

Figure 7: Survival curve for different types of TAPVC. TAPVC: Total anomalous pulmonary venous connection

associated with lower survival [Figure 8] when compared to Weight >3 Kg ($P < 0.01$, Gehan).

Postoperative mortality analysis

Of 29 early postoperative mortalities, 14 expired during 2009–2014 and 15 during 2015–2019 with no difference in year-wise mortality. Nineteen patients were ≤1 month, 7 patients were between 1 and 3 months and 3 patients were ≥3 months. Eleven of these patients were ≤2.5 kg, 9 patients were between 2.5 and 3 kg and 9 patients were ≥3 kg. 25 of these were males and 4 were females with 16 of them having obstructed TAPVC. 13 had Supracardiac, 9 had infracardiac, 4 had intracardiac, 2 had mixed types of TAPVC with 1 patient having anastomotic obstruction and underwent redosurgery. Five patients expired on POD 0–1, 12 patients expired between POD 2 and 7, 6 patients expired between POD 8–14, 5 patients expired between POD 15–28 and 1 patient expired on POD 36.

LCOS was noted in 17 of 29 patients with 12 of them ≤1 month age and 8 of them had AKI. Eleven of 29 patients had lung complications and 10 of them required HFOV. 6 of these 29 patients had sepsis. Eight of these 29 patients required re-bypass with 6 requiring anastomotic revision. Three of 29 patients were intubated in the preoperative period with another 1 patient having had preoperative sepsis. All five patients who expired on day 0–1 had severe LCOS. AKI, sepsis, lung complications, and LCOS were the principal causes in remaining.

Anastomotic gradients

Total patients, healthy patients and lost to follow up groups have lesser postoperative mean gradients compared to mortality groups ($P < 0.001$, ANOVA). analysis of follow up anastomotic gradients was difficult due to missing data in the follow up mortality group which we felt was critical in this analysis. Multiple patients expired before follow-up echo and their anastomotic gradients could not be noted. In the healthy group, follow up anastomotic gradient was 0.41 ± 0.06 (SE) mm of Hg with no difference in between this and postoperative anastomotic gradient ($P = 0.2$, Paired sample T test). Of 23 patients who expired during follow up, only 6 patients had echocardiogram done before expiry. Mean follow up gradient in these patients was 6.17 ± 1.77 (SE) mm of Hg and was higher than their post op mean anastomotic gradient of 1.52 ± 0.54 mm of Hg. Although this difference is significant, this data, we believe, is insufficient to identify a definite cut off gradient beyond the level of which mortality increases.

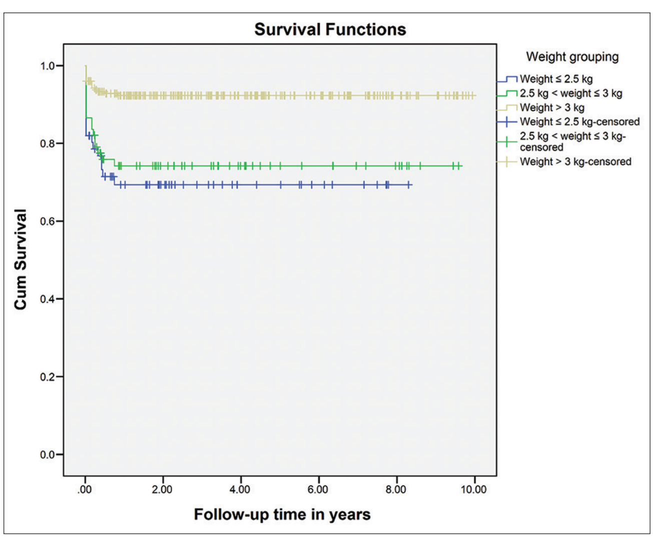

Figure 8: Survival curve for different weight groups demonstrating lesser survival in lower weight groups

DISCUSSION

We reviewed 492 surgical corrections of TAPVC with biventricular physiology at our institution over 10-year period. Multiple similar retrospective studies[10-16] had overall operative mortality ranging from 8% to 12%. Postoperative mortality in our series was 5.89%. Additional 4.67% patients expired during follow up period with overall mortality of 10.67% at mean follow up of 51.3 ± 31.0 months. Similar to a previous study[17] from Indian population, age ≤1 month was associated with higher risk of mortality with OR of 5.489 ($P = 0.003$). Effect of age on mortality is predictable with neonatal presentation correlating with sicker patients, obstructed status, operative difficulties with narrow calibre veins, deranged coagulation pathways, higher predilection for sepsis and difficulties with postoperative ventilatory managements. Similarly, weight ≤2.5 kg was associated with higher risk of overall mortality with ORs of 5.24 ($P < 0.001$) respectively.

Of important deviation from previous studies which had either Infracardiac[13] or mixed[10] TAPVC as risk factor, no type of TAPVC was a significant risk factor in our series. Reasons for this deviation are unclear. Obstructed TAPVC status and preoperative intubated state were associated with higher risk of mortality. Open sternum status was also significantly associated with increased incidence of mortality.

LCOS and prolonged ventilation were also associated with higher odds of mortality with significantly higher incidence of lung complications in these patients. Regression analysis of both LCOS and prolonged ventilation revealed that sepsis was strongly associated with both these factors. AKI requiring peritoneal dialysis was also strongly associated with mortality. PAH crisis occurred in 3% of patients and lead to increased incidence of reintubation and endotracheal bleed in our patients. Other notable complications in our patients were arrhythmias (4.3%), HFOV (3.7%) and diaphragm palsy (0.8%). Various risk factors for mortality and their odds ratios are tabularized in Table 2.

Table 2: Various risk factors for mortality with odds ratio and *P* value

Risk of overall mortality	OR	*P*
Age ≤1 month versus age >3 months	5.49	0.003
Weight <2.5 kg versus weight >3 kg	5.24	<0.001
2.5 kg <weight ≤3 kg versus weight >3 kg	3.58	<0.001
Males versus females	2.44	0.025
Obstructed versus nonobstructed	2.54	0.002
Preoperative intubated versus others	5.41	0.014
Prolonged ventilation of >72 h	6.80	0.039
Open sternum versus closed sternum	3.58	<0.001
LCOS versus no LCOS	8.19	0.001
AKI with PD versus others	9.26	0.00001
PAH crisis versus no PAH crisis	19.32	0.033

LCOS: Low cardiac output syndrome, AKI: Acute kidney injury, PD: Patent ductus, PAH: Pulmonary artery hypertension, OR: Odds ratio

Intraoperative high anastomotic gradient was the most common reason in 2/3rd of patients requiring re-bypass. Early anastomotic gradient was another factor that was higher in mortality groups, although exact cutoff value could not be determined. Follow-up anastomotic gradients were higher in follow-up mortality group leading to assumption that anastomotic gradients contribute to mortality in follow-up period, but this requires validation in larger studies. In our series, multiple patients in follow-up mortality group, who had initial non turbulent trans-anastomotic flow, developed anastomotic gradient and had eventual mortality. As we had less patients who had documented anastomotic obstruction and underwent redo corrective surgery, analysis of factors that lead to anastomotic obstruction could not be done. Our clinical experience suggests that pulmonary venous or anastomotic obstruction is either new onset or worsening of residual obstruction and develops rapidly in first 6 months after index surgery in those susceptible for obstruction. Hence, we recommend that all patients who underwent TAPVC repair should undergo monthly echocardiographic follow-up during the initial 6 months. Follow-up needs to be intensive in patients who have mildly elevated anastomotic gradients as these patients may progress to severe obstructive disease and eventual mortality.

CONCLUSIONS

TAPVC repair continues to have higher mortality despite advances in the management, especially in developing countries. Although peri-operative mortality has reduced, follow-up mortality continues to occur and is partly due to the obstruction of pulmonary venous pathway. Earlier diagnosis and reintervention in these patients are still a challenge. Aggressive follow-up may be important in further reducing mortality. Larger studies are needed for the identification of risk factors for pulmonary venous obstruction and its preventive strategies.

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Conflicts of interest

There are no conflicts of interest.

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