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Acute kidney injury and short-term renal support in the post-operative management of neonates following repair of transposition of the great arteries

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ABSTRACT

Neonates requiring congenital cardiac surgery are at risk of acute kidney injury, associated with significant morbidity, mortality, and increased hospital length of stay; treatment may require renal replacement therapy. Data for single cardiac defect cohorts is important to stratify risk, but is lacking for transposition of the great arteries. Our study aimed at collecting data for this single lesion.

A single-centre, retrospective analysis of 71 cases of arterial switch operation in neonates with isolated transposition of the great arteries, or transposition of the great arteries with ventricular septal defect, including length of stay, renal function and need for renal replacement therapy was performed.

Acute kidney injury developed in 50.7%, and was associated with longer paediatric intensive care and hospital stays ($p < 0.05$). Paediatric intensive care unit length of stay correlated with higher peak creatinine and urea ($p < 0.05$) and also with higher lactate levels at paediatric intensive care unit admission and 1 and 6 h post-admission ($p < 0.05$). Renal replacement therapy via peritoneal dialysis was delivered to 11.1%, but this was not found to prolong paediatric intensive care unit length of stay. Initiation of renal replacement therapy was associated with a positive fluid balance at 1 and 6 h ($p < 0.05$).

This study analyses renal outcomes in a cohort of neonates with transposition of the great arteries undergoing an arterial switch operation. Acute kidney injury is a significant complication, with accompanying need for renal replacement therapy. Development of acute kidney injury and a positive fluid balance were associated with increased length of stay. Initiation of renal replacement therapy was not associated with increased length of stay, and with some evidence from the literature that early or prophylactic peritoneal dialysis catheter insertion improves outcomes, these data report minimal complication rates which may be important when deciding to utilise peritoneal dialysis.

1. Introduction

Children undergoing congenital cardiac surgery, especially that involving cardiopulmonary bypass, are at risk of developing acute kidney injury [1–3], which can require renal replacement therapy [1].

Acute kidney injury is a serious complication that can be associated with significant morbidity and mortality [1–4]. Studies show that the incidence of acute kidney injury post-cardiac surgery ranges between 15%–64% [3] with the need for renal support requirement of approximately 1% [1]. Peri-operative events which place neonates at increased risk of developing acute kidney injury include the risk of hypovolaemia and consequential ischaemic-reperfusion injuries to the kidneys, the risk of infection associated with surgery and vascular access, and the acute inflammatory response which occurs after cardiopulmonary bypass [5].

Acute kidney injury leads to an increased length of stay in both intensive care and hospital [3], thereby increasing the potential need of prolonged mechanical ventilation post-operatively as well as increasing the risk of infection [1,4]. Risk factors identified for development of acute kidney injury include reduced pre-operative haemoglobin, reduced age and/or prematurity [4] and long cardiopulmonary bypass times [3,4]. This is thought to be a result of intrinsic immaturity of the renal tubule in a neonate, which has a reduced ability to manage cardiopulmonary bypass inflammation or an ischaemia-reperfusion insult [4]. Identifying modifiable risk factors for acute kidney injury may therefore contribute to the development of management strategies to reduce its incidence [4] and improve outcomes, such as reducing mortality and length of stay.

There are limited data examining acute kidney injury and renal replacement therapy use in children following arterial switch operation for transposition of the great arteries [6].

In this study, a cohort of neonates with transposition of the great

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arteries undergoing the arterial switch operation is presented, with emphasis on post-operative acute kidney injury and renal support.

This study's aim is to identify factors that are associated with the development of acute kidney injury and use or peritoneal dialysis in infants with transposition of the great arteries ± ventricular septal defect undergoing arterial switch operation ± ventricular septal defect repair, and evaluate whether intervention in the form of renal replacement therapy is associated with better outcomes.

2. Materials and Methods

This was a retrospective review of consecutive neonates presenting between 2005 and 2015 with transposition of the great arteries ± ventricular septal defect, who were undergoing arterial switch operation ± ventricular septal defect repair.

2.1. Ethical Approval

As the research was limited to anonymised secondary use of information previously collected in the course of normal care, formal ethical approval was waived.

2.2. Selection Criteria

All cases coded under “transposition of the great arteries” were identified using the PICANET database (Paediatric Intensive Care Audit Network: Universities of Leeds and Leicester. www.picanet.org.uk). Only those children with either isolated transposition of the great arteries or transposition of the great arteries-ventricular septal defect were included in the analysis; the presence of patent foramen ovale/atrial septal defect and patent ductus arteriosus were considered normal associations of transposition of the great arteries anatomy.

2.3. Data Collection

113 patients with transposition of the great arteries, presenting between 2005 and 2015, were identified from the PICANET database. Of these, 18 were excluded due to additional anatomical variations, and notes were unavailable for 24 (Fig. 1).

Seventy-one sets of notes and corresponding electronic laboratory results were reviewed and preoperative data, including anthropometry, comorbid states, and renal function; intraoperative data, including cardiopulmonary bypass times and aortic cross-clamp times; and post-operative data, including length of stay, need for renal replacement therapy, peak renal dysfunction, time to return to baseline serum creatinine, and PIM2r scores were collected. PIM2r estimates mortality risk from data readily available at the time of intensive care admission [7]. Due to the retrospective nature of the study and the provider-dependent decision of the initiation of renal replacement therapy, there were no pre-defined criteria for use of peritoneal dialysis.

Table 1
Modified KDIGO Neonatal Acute Kidney Injury criteria.

AKI stage	Serum creatinine (SCr)	Urine output
0	No change in SCr or rise < 0.3 mg/dL	≥ 0.5 mL/kg/h
1	SCr rise ≥ 0.3 mg/dL within 48 h or SCr rise ≥ 1.5–$1.9 \times$ reference SCr within 7 days	< 0.5 mL/kg/h for 6 to 12 h
2	SCr rise ≥ 2.0–$2.9 \times$ reference SCr	< 0.5 mL/kg/h for ≥ 12 h
3	SCr rise $\geq 3 \times$ reference SCr or SCr ≥ 2.5 mg/dL[a] or receipt of dialysis.	< 0.3 mL/kg/h for ≥ 24 h or anuria for ≥ 12 h

SCr - serum creatinine.
[a] 2.5 mg/dL = 221 μmol/L, represents GFR = 10 mL/min/1.73 m^2; 0.3 mg/dL = 26.52 μmol/L.

2.4. Data Analysis

Data were analysed using SPSS version 20 for Windows (SPSS Inc., Chicago, Illinois, United States of America). For all tests, a value of $p < 0.05$ was considered statistically significant. Acute kidney injury was categorised as per the modified Kidney Disease Improving Global Outcomes criteria (Table 1) [8]. Descriptive statistics were used for simple frequencies and percentages; difference in means was assessed by independent *t*-tests or Mann-Whitney U as appropriate; correlation was tested by Pearson's correlation.

3. Results

3.1. Patient Demographics

Demographic details are outlined in Table 2. Of this cohort, one patient (1.4% of cohort) died within 30 days of their surgery; the cause of death was biventricular failure, secondary to myocardial infarction with coronary arterial thrombosis.

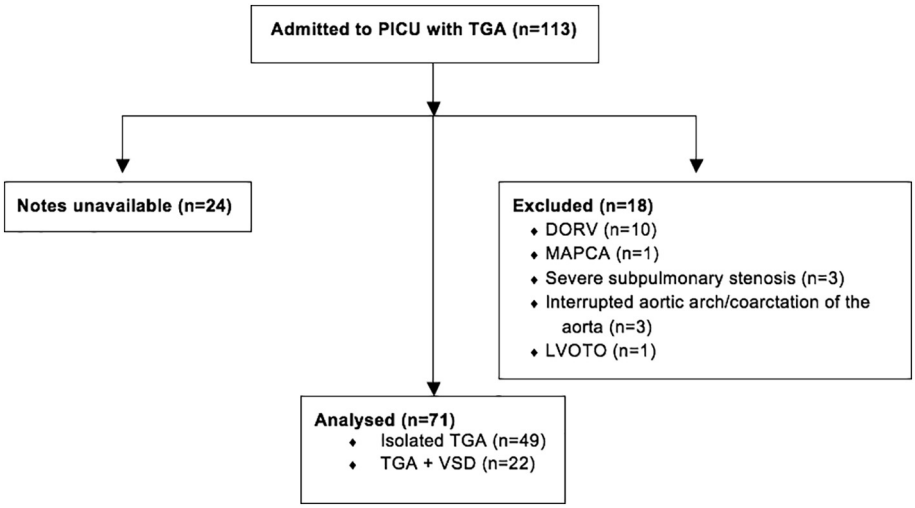

Fig. 1. Consort diagram describing patient selection. PICU – paediatric intensive care unit; DORV – double-outlet right ventricle; MAPCA – major aorto-pulmonary collateral arteries; LVOTO – left-ventricular outflow tract obstruction.

Table 2
Demographic details of the cohort.

Female/male	20 (28.2%)/51 (71.8%)
Age at operation, median	9.5 IQR 18 days
ASO/ASO + VSD repair	49 (69.0%)/22 (31.0%)
Weight, mean	3.59 (± 0.58) kg
Length, mean	50.57 (± 3.88) cm

Standard deviation in parentheses. ASO – arterial switch operation; VSD – ventricular septal defect.

3.2. Operative Details

Prior to definitive surgery, 70% of the cohort (50 neonates) required balloon atrial septostomy. UK protocol for this procedure does not include use of contrast and was not used in any cases. For all seventy-one cases, the mean cardiopulmonary bypass time was 162 min (± 45, range 112–393), and arterial cross clamp time was 99 min (± 26, range 55–188). All infants were successfully weaned from cardiopulmonary bypass, with no patient requiring mechanical support.

In addition to the arterial switch operation, twenty-two (30.6%) underwent concurrent repair of a ventricular septal defect, with only a single patient undergoing right ventriculotomy. Patients were classified into two groups based on risk adjustment for congenital heart surgery (RACHS) score: (A) category 3 (arterial switch operation alone) and (B) category 4 (arterial switch operation with ventricular septal defect closure) (see Table 3). Mean times were longer in the category 4 group compared to category 3, with a median cross clamp time of 91 ± 43 versus 101 ± 23 min ($F = 767$; $p < 0.01$). Cardiopulmonary bypass time was also longer in the category 4 group compared with category 3: 155 ± 40 vs 160 ± 28 min ($F = 734.5$ $p < 0.05$). The two groups' anthropometry, length of stay, fluid and blood requirement, C-reactive protein, renal function, fluid balance, urine output, and inotrope scores were not statistically different from one another.

3.3. Length of Stay

Following surgical repair, the mean length of stay on the paediatric intensive care unit was 4 days (± 2; median = 4) with mean hospital length of stay 13 days (± 10; median = 11). Higher peak creatinine and urea were correlated with a longer paediatric intensive care unit length of stay (Pearson's correlation 2-tailed significance of $r = 0.349$, $p < 0.05$ and $r = 0.501$, $p < 0.05$ for peak creatinine and urea, respectively) (Fig. 2). Increased fluid balance at 48 h was also positively correlated with paediatric intensive care unit length of stay ($r = 0.338$, $p < 0.05$), but not at 1, 6, 12 or 24 h (Fig. 3). Those with higher blood gas lactate levels at post-operative paediatric intensive care unit admission, and 1-h and 6-h post-admission had longer paediatric intensive care unit stays ($r = 0.343$, $p < 0.05$; $r = 0.315$, $p < 0.05$; and $r = 0.387$, $p < 0.05$, respectively).

3.4. Development of Acute Kidney Injury

Thirty six neonates (50.7%) developed acute kidney injury. Classified by acute kidney injury stage, this represented: 15 (21.1%), 12 (16.9%), and 9 (12.7%) for stage 1, 2, and 3, respectively.

Development of any stage of acute kidney injury was associated with significantly longer length of stay in both paediatric intensive care unit (4 ± 2.25 versus 5 ± 1 days, $F = 894$; $p < 0.05$) and hospital (9 ± 5.25 versus 12 ± 9.5 days, $F = 825$; $p < 0.05$). Blood lactate levels at all three time-points (paediatric intensive care unit admission, 1 h and 6 h post-paediatric intensive care unit admission) were significantly higher in those that developed acute kidney injury (Table 4).

In the renal replacement therapy group, 100% had acute kidney injury stage 3 by KDIGO definition of requiring renal replacement therapy. In those that did not require renal replacement therapy, 50.1% developed acute kidney injury; this was formed of 18 (28.6%), 7 (11.1%) and 7 (11.1%) for acute kidney injury stage 1, 2 and 3 respectively.

Table 3
Mean (standard deviation) of those in RACHS category 3 and those in RACHS category 4.

Variable	RACHS category 3 (n = 22)	RACHS category 4 (n = 49)	p value
Weight (kg)	3.51 ± 0.50	3.75 ± 0.72	0.172
Length (cm)	50.6 ± 4.20	50.4 ± 3.0	0.796
ACCT (min)[a]	91 ± 43	101 ± 23	***0.005***[*]
CPB (min)[a]	155 ± 40	160 ± 28	***0.015***[*]
Intraoperative fluid (mL/kg)	38.1 ± 23.6	32.1 ± 17.9	0.253
LOS PICU (days)	4.2 ± 21.8	4.4 ± 21.8	0.629
LOS hospital (days)[a]	10.5 ± 13.3	10.5 ± 8.3	0.295
Pre-op urea[a]	4.1 ± 4.45	3.9 ± 3.85	0.142
Urea on admission	3.51 ± 1.89	4.07 ± 1.91	0.258
Peak urea	7 ± 4	9 ± 3	0.119
Pre-op creatinine	49 ± 20	44 ± 19	0.280
Creatinine on PICU admission	43 ± 14	45 ± 14	0.501
Peak creatinine	61 ± 22	67 ± 21	0.312
Fluid balance at 1 h (mL)	−222 ± 32.3	−43.7 ± 53.6	0.212
Fluid balance at 2 h (mL)	−26.8 ± 32.6	−37.9 ± 63.7	0.534
Fluid balance at 6 h (mL)	−10.6 ± 63.1	4.7 ± 63.9	0.387
Fluid balance at 12 h (mL)[a]	27.3 ± 121.5	40.1 ± 135.2	0.112
Fluid balance at 24 h (mL)	31.2 ± 114.3	81.1 ± 89.6	***0.056***
Fluid balance at 48 h (mL)	−72.8 ± 147.3	−47.6 ± 158.1	0.566
UOP at 1 h (mL/kg)	9.3 ± 6.8	11.4 ± 10.2	0.480
UOP at 6 h (mL/kg)[a]	2.9 ± 1.7	1.3 ± 3.7	0.294
Lactate 0 h[a]	2.8 ± 2.1	2 ± 2.4	0.219
Lactate 1 h[a]	2.8 ± 1.9	2.1 ± 2.8	0.217
Lactate 6 h[a]	2.3 ± 1.3	1.6 ± 0.8	0.143

Mean values of those in RACHS category 3 and RACHS category 4. Standard deviation (SD) in parentheses.
Abbreviations: TGA - transposition of the great arteries; VSD - ventricular septal defect; ACCT - aortic cross clamp time; CPB - coronary bypass time; LOS - length of stay; PICU - paediatric intensive care; CRP - C-reactive protein; VIS - Vasopressor Inotrope Score; UOP - urine output; MV - mixed venous.
[a] In Variable column indicates non-parametric data - values stated are the median (interquartile range).
[*] Statistically significant. Results approaching significance or significant are in bold, italics and under-lined.

There was no significant difference in pre-operative haemoglobin concentration between those who developed acute kidney injury of any stage and those who did not develop acute kidney injury (151 ± 22 g/L versus 158 ± 25 g/L, $p = 0.170$).

3.5. Renal Replacement Therapy

91.7% of patients received intravenous furosemide within the first 48 h, either as a bolus (36.6%), continuous intravenous infusion at a maximum of 0.5 mg/kg/h (38.0%), or a combination of both (16.9%).

8 (11.1%) received renal replacement therapy, all of which was provided as peritoneal dialysis; no patients received haemofiltration. All the peritoneal dialysis catheters were inserted on the paediatric intensive care unit by intensivists using the Seldinger technique. Mean peritoneal dialysis catheter insertion time was 19 (± 22, median = 12) hours following admission to paediatric intensive care unit. Mean duration of peritoneal dialysis was 42.8 (± 35.3, median 31.5) hours. One patient had blockage of the peritoneal dialysis catheter necessitating removal. No other complications related to peritoneal dialysis, insertion or removal, e.g., omental herniation, were identified.

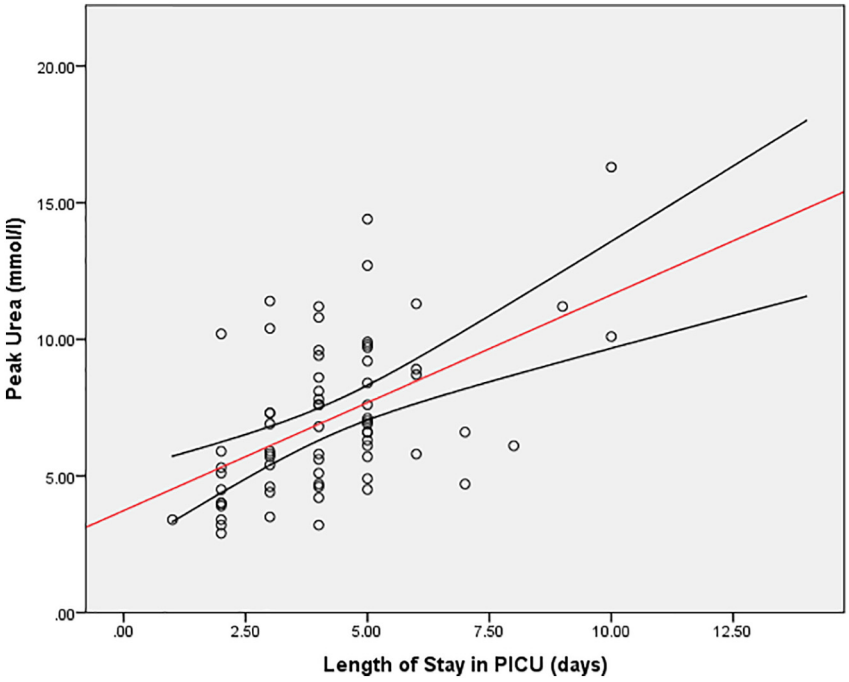

Fig. 2. Graph demonstrating correlation of peak urea (mmol/L) following admission and length of stay in paediatric intensive care (days). The red line represents the line of best-fit, with 95% confidence intervals in black. Pearson's correlation co-efficient was r = 0.501, with 2-tailed significance $p < 0.05$.

Initiation of peritoneal dialysis in this cohort did not prolong length of stay in the paediatric intensive care unit (4.0 ± 2.8 days versus 4.0 ± 2.0 days, p = 0.717) or hospital (14.5 ± 13.8 days versus 10.0 ± 5.5 days, p = 0.477).

The trend of fluid balance differences between those that received renal replacement therapy and those that did not suggests that an early positive fluid balance, and a lower urine output in the first hour, was associated with initiating renal replacement therapy, although this was not significant for fluid balance as a percentage of estimated dry weight. Table 5 outlines the differences in variables between those who did and those who did not receive renal replacement therapy. Of note, although there is a significant difference in PIM2r scores between those who did and those who did not receive renal replacement therapy, the mean scores were higher in the no renal replacement therapy group.

The proportion of infants requiring balloon atrial septostomy prior to surgery was similar in both the renal replacement therapy group and the no-renal replacement therapy group: 6 out of 8 (75%) versus (68%), respectively. Due to the unbalanced group sizes, further statistical analysis would not have been representative, and is therefore not presented here.

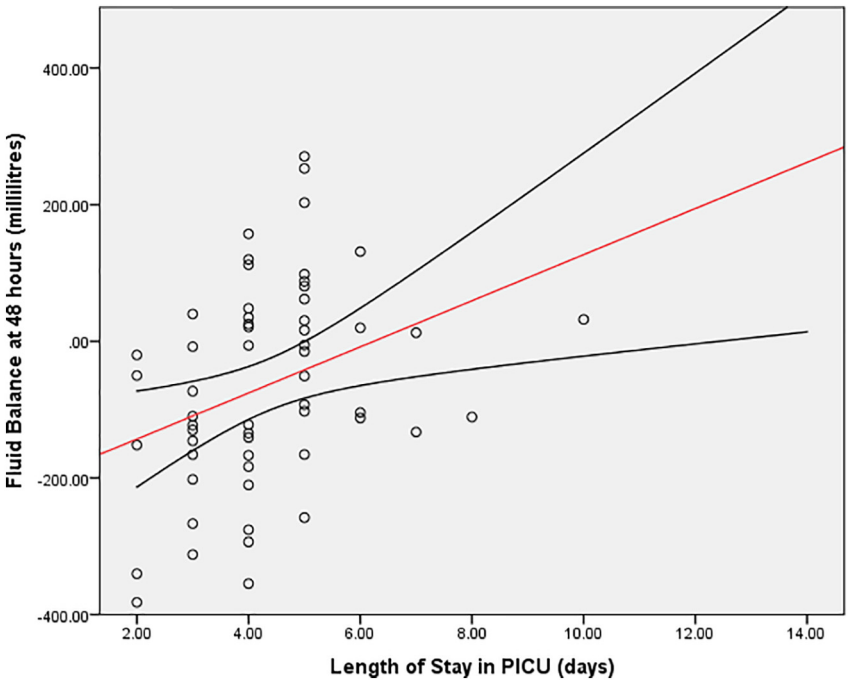

Fig. 3. Graph demonstrating correlation of fluid balance (mL) at 48 h and length of stay in paediatric intensive care (LOS PICU). The red line represents the line of best-fit, with 95% confidence intervals in black. Pearson's correlation co-efficient was r = 0.338, with 2-tailed significance $p < 0.05$.

Table 4
Mean values of those who did and did not develop acute kidney injury.

Variable	No AKI (± SD) (n = 36)	AKI of any stage (± SD) (n = 35)	p-Value
Age at time of operation (days)[a]	7 ± 6	9 ± 5	0.126
Weight (kg)[a]	3.6 ± 0.65	3.3 ± 0.7	0.06
Pre-op haemoglobin (g/L)	158 ± 25	151 ± 22	0.170
ACCT time (min)[a]	98 ± 30	96 ± 27	0.427
CPB time (min)[a]	154 ± 40	157 ± 41	0.796
Intraoperative fluid (mL/kg)[a]	30.9 ± 32.9	38.2 ± 40.6	0.565
Blood product requirement	9.9 ± 15.8	4.29 ± 21.9	0.835
LOS PICU (days)[a]	4 ± 2.3	5 ± 1	***0.002****
LOS hospital (days)[a]	9 ± 5.3	12 ± 9.5	***0.024****
Lactate at on PICU admission (mmol/L)[a]	2 ± 0.9	3.7 ± 1.9	***0.003****
Lactate at 1 h (mmol/L)[a]	1.8 ± 0.8	3 ± 1.9	***0.007****
Lactate at 6 h (mmol/L)[a]	1.4 ± 0.6	2.6 ± 2.8	***0.004****
MV sat on admission (%)	47 ± 12	41 ± 6	0.399
MV sat at 6 h (%)	50 ± 13	52 ± 10	0.568
PIM2r score on admission[a]	0.825 ± 1.67	0.94 ± 1.15	0.703

Standard deviation (SD) in parentheses. Abbreviations: AKI – acute kidney injury; LOS – length of stay; MV – mixed venous; PICU – paediatric intensive care unit; PIM2r – Revised Paediatric Index of Mortality; Sat - oxygen saturations.

* Statistically significant results are in bold, italics and under-lined.

[a] In Variable column indicates non-parametric data - values stated are the median (interquartile range).

Pre-operative haemoglobin was not significantly different between the no-renal replacement therapy group and the renal replacement therapy group (154 ± 23 g/L versus 158 ± 27 g/L, p = 0.663).

Comparing those with acute kidney injury who received renal replacement therapy and those with acute kidney injury who did not receive renal replacement therapy, there was a trend for lower urine output at 1 and 48 h, greater peak urea, lactate at 1 and 6 h, and fluid balance at 6 h. There was no difference in acute kidney injury score based on creatinine-criteria alone.

4. Discussion

This is the second study analysing a cohort comprised solely of infants with transposition of the great arteries rather than mixed diagnoses cohorts. Dittrich et al. [9] reported early initiation of peritoneal dialysis to be beneficial in reducing mortality in a cohort of infants who had undergone cardiopulmonary bypass for mixed lesions. In infants undergoing cardiopulmonary bypass and at high-risk of developing acute kidney injury, Kwiatkowski et al. [10] inserted peritoneal dialysis catheters as a prophylactic measure in theatre post-operatively, and found this group, compared to those that had no catheter inserted, had a reduced time to negative fluid balance, reduced time to extubation, and reduced inotrope scores.

The implications of such intervention in specific cardiac lesions are unclear due to the heterogenous nature of each lesion and its individual haemodynamics. Griksaitis et al. [11] found peritoneal dialysis renal support beneficial in managing fluid balance in a cohort of children undergoing tetralogy of Fallot repair. Studies of other cardiac lesion-specific cohorts are lacking, but would be of benefit for risk stratification and to evaluate benefits of interventions. This study therefore adds valuable data, not only because surgical correction of this cardiac lesion typically occurs in the neonatal period when the kidneys are particularly vulnerable, but also that it is likely that risk of renal injury varies depending upon the cardiac defect and resulting corrective procedure.

Cardiac surgery, especially that involving cardiopulmonary bypass, is a well-known risk factor for the development of acute kidney injury [1,12], and is associated with increased morbidity, financial costs, and mortality, not just confined to the immediate post-operative period [2]. These data show that half of infants undergoing arterial switch operation for transposition of the great arteries suffer from acute kidney injury, and a significant number receive renal replacement therapy. This

Table 5
Mean values of variables in those who received renal replacement therapy and those that did not.

Variable	RRT (± SD) (n = 8)	No RRT (± SD) (n = 63)	p-Value
Weight (kg)[a]	3.25 ± 0.60	3.5 ± 0.64	0.096
Length (cm)	48.5 ± 7.2	0.5 ± 0.3	0.414
Pre-op haemoglobin (g/L)	158 ± 27	154 ± 23	0.663
ACCT (min)[a]	101 ± 21	97 ± 30	0.241
CPB (min)[a]	163 ± 35	154 ± 39	0.203
Intraoperative fluid (mL/kg)[a]	38.2 ± 40.6	30.9 ± 32.9	0.910
LOS PICU (days)[a]	4.00 ± 2.8	4.0 ± 2.0	0.717
LOS hospital (days)[a]	14.5 ± 13.8	10.0 ± 5.5	0.477
Blood product requirement in first 24 h (mL/kg)[a]	4.3 ± 21.9	9.9 ± 15.8	0.783
Peak CRP (mg/L)	134 ± 58	152 ± 71	0.435
Pre-op urea (mmol/L)[a]	3 ± 4	3 ± 2	0.904
Peak urea (mmol/L)[a]	10 ± 8	6 ± 4	***0.005****
Pre-op creatinine (μmol/L)[a]	45 ± 26	43 ± 31	0.837
Peak creatinine (μmol/L)	75 ± 37	61 ± 18	0.334
Fluid balance at 1 h (mL)[a]	7.9 ± 29.9	−26.2 ± 47.4	***0.011****
Fluid balance at 6 h (mL)	44.1 ± 44.9	−12.3 ± 62.7	***0.015****
Fluid balance as % of estimated dry weight at 1 h (%)	0.26 ± 1.54	−3.22 ± 4.12	*0.215*
Fluid balance as % of estimated dry weight at 6 h (%)	4.41 ± 4.49	−1.23 ± 6.27	*0.356*
Fluid balance at 12 h (mL)	95.3 ± 100.8	29.6 ± 78.3	0.176
Fluid balance at 24 h (mL)	78.3 ± 140.3	43.8 ± 105.5	0.548
Fluid balance at 48 h (mL)	8.9 ± 166.1	−73 ± 147.4	0.293
Volume requirement in first 12 h (mL/kg)[a]	57.4 ± 54.2	26.8 ± 22.2	0.127
Volume requirement in first 24 h (mL/kg)[a]	48.6 ± 67.4	40.0 ± 30.6	0.913
VIS at 1 h	9.91 ± 6.04	25.19 ± 103.61	0.252
VIS at 6 h	18.36 ± 18.12	14.38 ± 26.01	0.591
VIS at 12 h	399.46 ± 1059.31	15.23 ± 20.28	0.339
VIS at 24 h	82.48 ± 173.65	20.76 ± 60.21	0.351
VIS at 48 h	163.43 ± 417.44	14.63 ± 66.38	0.382
UOP at 1 h (mL/kg)[a]	3.2 ± 4.2	8.3 ± 11.1	***0.010****
UOP at 6 h (mL/kg)	2.2 ± 1.1	3.0 ± 2.2	0.091
UOP at 12 h (mL/kg)[a]	1.9 ± 2.1	2.6 ± 3.2	0.406
UOP at 24 h (mL/kg)	2.3 ± 0.9	2.9 ± 1.4	0.135
UOP at 48 h (mL/kg)[a]	2.1 ± 1.5	3.7 ± 1.2	***0.002****
Lactate on PICU admission (mmol/L)[a]	3.7 ± 1.9	2.0 ± 0.9	***0.012****
Lactate at 1 h (mmol/L)[a]	3.0 ± 1.9	1.8 ± 0.8	***0.002****
Lactate at 6 h (mmol/L)[a]	2.6 ± 2.8	1.4 ± 0.6	***0.005****
Central venous saturations on PICU admission (%)	41 ± 6	48 ± 12	***0.032****
Central venous saturations at 6 h (%)	52 ± 10	50 ± 12	0.574
PIM2r score on admission	1.09 (± 0.41)	2.50 (± 3.20)	***0.002****
Balloon atrial septostomy - number and percentage of group requiring	6 (75%)	43 (68%)	*N/A*

Standard deviation (SD) in parentheses. Abbreviations: ACCT – aortic cross-clamp time; CPB – cardio-pulmonary bypass; CRP – C-reactive protein; LOS – length of stay; PICU – paediatric intensive care unit; PIM2r – Revised Paediatric Index of Mortality; Pre-op – pre-operative; UOP – urine output; VIS – vasoactive-ionotropic score.

* Statistically significant results are in bold, italics and under-lined.

[a] In Variable column indicates non-parametric data - values stated are the median (interquartile range).

is in keeping with previous literature [3,4,6]. The study did not find variables which predict initiation of renal replacement therapy; however the association of an early positive fluid balance and lower urine output in the first hour with initiation of renal replacement therapy may reflect the need for fluid volume for low cardiac output state/systemic inflammatory response and a poor urine output. These data would suggest initiation of earlier peritoneal dialysis may be beneficial in management of fluid balance when there is an early suggestion of poor urine output, positive fluid balance, high lactate and low SvO2 on admission to paediatric intensive care unit and within the first hour.

Prompt recognition and treatment of acute kidney injury is important to prevent significant morbidity or indeed mortality. Uraemia may be a feature, consequence of diminished excretion of endogenous and exogenous waste products, with potential adverse effects including nausea, vomiting, cardiac dysrhythmias and neurological manifestations including seizures [13]. Cardiac dysfunction may occur as consequence of AKI alone, however the presence of uraemia may impair this further by causing reduced cardiac contractility and/or pericarditis. Pulmonary oedema may be a consequence of fluid overload in acute kidney injury and another mechanism in associated cardiac dysfunction, or indeed result of cardiac dysfunction in its own right; neonates who have undergone an arterial switch operation are therefore highly vulnerable to such consequences [14].

In concordance with other cohorts encompassing older children and adults [3,4], these data demonstrate that increased length of stay in both paediatric intensive care unit and hospital is associated with the development of acute kidney injury irrespective of renal replacement therapy use. This adds to the already formidable evidence of the large financial cost of acute kidney injury to healthcare systems.

Basu et al. [6] found an association of acute kidney injury with length of stay, fluid balance and inotrope score. In the data presented here, an association between acute kidney injury and length of stay was identified, but not for fluid balance and inotrope score. The reason for this discordance may be due to the different thresholds used to define acute kidney injury between the studies.PIM2r scores were significantly lower in the group requiring renal replacement than in the group not requiring renal replacement therapy. In this study, children requiring renal replacement therapy were sicker than those who did not require renal replacement therapy, it may therefore be expected that their mortality risk would be the higher of the two groups. This result cannot be fully explained; it may reflect the smaller sample size of the renal replacement therapy group, or may also reflect the lack of specificity for this condition within the PIM2r scoring matrix [7].

In this study, positive fluid balance was correlated with length of stay. There is evidence that fluid overload has a negative impact on outcomes, especially in paediatric patients, being associated with impaired oxygenation and morbidity [15]. Current evidence reviewed by Selewski and Goldstein suggests that a cut-off of 10–20% fluid overload be a threshold to use when considering intervention with renal replacement therapy, although there is no definitive trial to date that demonstrates this [16]. The exact relationship in cohorts similar to the one presented here is not clear and requires further investigation before potential implementation of guidelines regarding fluid balance cut-offs, for example. In this cohort, furosemide use was almost universal (91.7%). In adults, it has been shown that use of furosemide may well have a detrimental effect on renal function when being used post-operatively to gain negative fluid balance [17], and has recently been reported to fare worse compared to peritoneal dialysis in a randomised-control trial when assessing fluid overload, time receiving ionotropic support and time receiving ventilatory support [18]. The use therefore, of peritoneal dialysis for this may well be worth considering, especially in those children who may be more vulnerable to the nephrotoxicity of loop diuretics.

Those with acute kidney injury but who did not receive peritoneal dialysis were drier than those who received peritoneal dialysis. This may reflect that the decision to initiate peritoneal dialysis was based on fluid overload, and/or that better fluid control is achieved through the use of peritoneal dialysis.

Initiation of peritoneal dialysis was not associated with increased paediatric intensive care unit or hospital stay per se, nor were any additional complications of peritoneal dialysis insertion demonstrated. This is note-worthy, as this may be part of the decision matrix of introducing a peritoneal dialysis catheter on balancing potential benefits and risks. The lack of an increase in paediatric intensive care unit and hospital stay despite the initiation of renal replacement therapy may be explained by the hypothesis that although these children were sicker, the intervention improved their trajectory. Additionally, although not assessed here, early peritoneal dialysis has been associated with decreased mortality following cardiac surgery [19].

Current local practice requires insertion of a peritoneal catheter on the paediatric intensive care unit if the child is felt to have acute kidney injury necessitating renal replacement therapy, however for this cohort this was a provider-dependent decision. The facility to predict this requirement, pre- or immediately post-operatively would enable placement of the peritoneal dialysis catheter in a more controlled manner in the theatre environment, and also facilitate earlier commencement of renal replacement therapy, with the potential to improve outcomes. In addition, the placement of peritoneal dialysis catheter eliminates the potential of developing intra-abdominal compartment syndrome, and its cause of acute kidney injury and significant risk of mortality. There is some evidence suggesting that early insertion of peritoneal dialysis catheter may confer benefit, including better fluid balance and electrolyte control and reduced mortality [9,10,20,21]. Prospective trials are required to prove benefit of early or prophylactic peritoneal dialysis catheter insertion.

Episodes of acute kidney injury can hold significant risks of long-term renal problems of hypertension, proteinuria and decreases in glomerular filtration rate [22,23], and those with congenital heart disease may well be more susceptible to development of chronic kidney disease following acute kidney injury due to factors over and above that of cardiac surgery [24]. Mitigation of this risk through prevention of renal insults in early life may therefore be important, but prospective studies are needed to examine the risk of developing chronic kidney disease in specific, higher-risk populations.

4.1. Limitations

The retrospective natures of our study, spanning a decade of data was a limitation, particularly with regard to lack of specific criteria for the initiation of renal replacement therapy; there is not a standardized protocol locally or nationally for this. Whilst this study provides an initial exploration of this area in a specific cohort, a prospective randomised trial using such standardized criteria is needed. Additionally, there was variation in the timings of blood samples being taken and follow-up, and some notes of patients who met inclusion criteria for our study were not available. Positive fluid balance and the need for renal replacement therapy were associated, however additional outcomes related to fluid overload, such as mechanical ventilation requirements and need for chest or peritoneal drains were not included and would warrant exploration in future prospective studies. Finally, this was a single-centre study, which may have some implications on the techniques and management used, which may vary from other centres.

5. Conclusions

In conclusion, acute kidney injury is a significant complication for neonates undergoing arterial switch operation for transposition of the great arteries, and there is a substantial requirement for renal replacement therapy. Prediction of acute kidney injury and/or renal replacement therapy remains difficult. The role of early or prophylactic peritoneal dialysis catheter insertion is yet to be fully evaluated in this population, but may have benefits of better fluid balance with no

increase in time within paediatric intensive care unit. Ongoing, prospective analyses of cardiac-lesion specific cohorts are needed to stratify risk and tailor care.

Conflicts of Interest and Source of Funding

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