Pediatr Cardiol 22:321–326, 2001
DOI: 10.1007/s002460010238

Pediatric
Cardiology

Acute Renal Insufficiency and Renal Replacement Therapy After Pediatric Cardiopulmonary Bypass Surgery

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Abstract. The aim of the study was to investigate renal function and renal replacement therapy after cardiopulmonary bypass surgery in children. Patient characteristics (sex, age, diagnosis), operation type, and death were listed. The study was performed retrospectively using serum creatinine level before, and peak values after, cardiopulmonary bypass surgery for assessment of renal function. Of the children on renal replacement therapy, indication, efficacy, and complications were recorded. In a 5-year period, 1075 children had cardiopulmonary bypass surgery at the Department of Cardiothoracic Surgery at Leiden University Medical Center and Academic Medical Center of Amsterdam. One-hundred eighty (17%) patients developed acute renal insufficiency. Twenty-five (2.3%) patients required renal replacement therapy. Peritoneal dialysis is a safe and effective treatment for children after cardiopulmonary bypass surgery. However, 15 (60%) of 25 children on renal replacement therapy died of nonrenal causes. In 9 out of 10 surviving children, renal function was normal at time of discharge from hospital. Acute renal insufficiency is a frequent complication after open-heart surgery, although renal replacement therapy was infrequently necessary. Peritoneal dialysis is a safe and effective therapeutic measure for children after cardiac bypass surgery.

Key words: Cardiopulmonary bypass surgery — Acute renal insufficiency — Acute renal failure — Child — Peritoneal dialysis — Pediatric cardiac surgery

Acute renal insufficiency is a frequent complication of cardiopulmonary bypass surgery. This complication sometimes leads to acute renal failure, necessitating renal replacement therapy, which is associated with high mortality (20% to 75%) [1, 2, 4–6, 10–12]. We studied the incidence of acute renal insufficiency in children after cardiopulmonary bypass surgery, which has not been described before, in a 5-year period at our institution. Furthermore, we investigated the indication, efficacy, and complications of all children who received peritoneal dialysis after cardiopulmonary bypass surgery in the same period.

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Methods

From January 1994 to January 1999, cardiopulmonary bypass surgery was performed on 1075 children (<17 years) at Leiden University Medical Center and Academic Medical Center of Amsterdam. Postoperative renal function and indication, efficacy, and complications of renal replacement therapy at the Pediatric Intensive Care are studied retrospectively from medical records.

Acute Renal Insufficiency

Age, sex, type of cardiac surgery performed, preoperative serum creatinine level, peak postoperative serum creatinine level, the day peak postoperative serum creatinine level occurred, and death within 30 postoperative days are recorded. Although serum creatinine may not be the most sensitive marker of renal function, since it cannot detect minor changes in glomerular filtration rate, it meets the requirements of this study. Acute renal insufficiency is defined as at least doubling of preoperative serum creatinine level in children older than 8 weeks. For children younger than 8 weeks, a postoperative serum creatinine level >75 μmol/L is considered acute renal insufficiency. Serum creatinine level is measured using a photometric method on an automatic analyzer (Hitachi 747-100; Roche, Almere, The Netherlands).

Renal Replacement Therapy

In a second part of the study, all children who received renal replacement therapy were analyzed retrospectively from medical records. Peritoneal dialysis (PD) was chosen as renal replacement therapy because of its relatively easy employment and infrequent complications. The indications for PD are anuria (>24 hours), hyperkalemia (>5.5 mmol/L), hyperphosphatemia (>4 mmol/L), or severe edema. In our study, patients who received renal replacement therapy had acute renal failure. The causes of acute renal failure were divided in low cardiac output and/or acute tubular necrosis. A patient was considered to have acute tubular necrosis if, after prolonged resuscitation, acute renal failure occurred with exclusion of persisting low cardiac output. A standard Dacron-cuffed pediatric silicone catheter (Tenckhoff, Sherwood Medical Company, St. Louis, MO 63103, USA) was surgically inserted through a paraumbilical tunneled approach. Standard PD solutions (initially glucose 2.27%, and later, if necessary, either glucose 3.86% or 1.36%) were used. Peritoneal dialysis was started with a dialysate volume of 10 ml/kg, a dwell time of 30 minutes, and a drainage time of 20 minutes. After 24 hours, dialysate volume was doubled and, if necessary, dwell time was adjusted. Age, sex, weight, diagnosis, type of cardiac surgery performed, cardiopulmonary bypass time, and aortic cross-clamp time of the patients were recorded. Postoperative artificial ventilation, continuous intravenous inotropic agents, cause of acute renal failure, indication for renal replacement therapy, prerenal replacement therapy values for central venous pressure, serum sodium, -potassium, -calcium, -phosphate, -bicarbonate, -urea, and -creatinine, were noted. Elapsed time after open heart surgery to institution of PD, duration of PD, dialysis efficacy measured by fluid removal rate (ml/kg/day) and time to correction of hyperkalemia, and complications were investigated. Nephrotoxic medication (e.g., aminoglycosides) was avoided, or the dose was adapted to renal function, and, if possible, was checked by serum levels. Death and cause of death were noted. Of surviving children, serum urea and creatinine level before discharge from hospital were studied.

Statistics

Logistic regression analysis was used to estimate the probability of renal insufficiency using age and preoperative serum creatinine level as independent risk factors (covariates); likewise, the probability of death was estimated as a function of age and renal insufficiency. The risk factors were entered both as main effect and as their interaction. Interaction terms were retained if the *p*-value was below 0.10, and main effects were considered significant if the *p*-value was below 0.05.

Results

Acute Renal Insufficiency

Of 1075 children <17 years who had cardiopulmonary bypass surgery, 637 (59%) were boys. One hundred eighty (17%) patients had renal insufficiency. Seventy (6.5%) children died <30 days after cardiopulmonary bypass surgery. Table 1a denotes the type of cardiac surgery performed, age, preoperative- and peak postoperative serum creatinine level, and the day the peak serum creatinine level occurred. Table 1b depicts the type of cardiac surgery performed, the number of patients with postoperative acute renal insufficiency, patients requiring renal replacement therapy, and death of patients.

The age of the patients is inversely related to both renal insufficiency ($p < 0.001$) and death ($p = 0.001$). Furthermore, children with renal insufficiency have a significantly higher chance of dying (odds ratio 5.4 95% CI 3.3–8.8) as compared with children without renal insufficiency. Likewise, the interaction between age and renal insufficiency was significantly related to death of patients. Preoperative serum creatinine level, corrected for the age of the patient, is significantly correlated to renal insufficiency ($p < 0.001$). The difference between the group with renal insufficiency (mean serum creatinine level 53 [sd 27] μmol/L) and group without renal insufficiency (mean serum creatinine level 44 [sd 15] μmol/L), however, is minor.

Renal Replacement Therapy

Of all children after open heart surgery, 25 (2.3%) patients required renal replacement therapy. Patient characteristics are recorded in Table 2. In Table 3, diagnosis and type of cardiac surgery performed are listed. All but one child requiring renal replacement therapy were on artificial ventilation, and all received continuous intravenous inotropic agents at the initiation of renal replacement therapy. The predominant cause of acute renal failure, requiring renal replacement therapy, was low cardiac output ($n = 15$; 60%). Sometimes low cardiac output was combined with acute tubular necrosis after prolonged resuscitation ($n = 4$; 16%). For some patients, acute tubular necrosis after prolonged resuscitation ($n = 6$; 24%) was the single reason for acute renal failure requiring renal replacement therapy. The indications for, and time from, operation to institution of renal replacement therapy are given in Table 2. Peritoneal dialysis was chosen as renal replacement treatment because of its relatively easy employment and infrequent complications. Mean central venous pressure before initiation of PD was 16 (SD 4) cmH_2O. Mean (SD) predialysis serum levels were: creatinine 204 (96) μmol/L, urea 20.1 (9.2) mmol/L, sodium 140 (8) mmol/L, potassium 5.0 (1.0) mmol/L, calcium 1.81 (0.3) mmol/L, phosphate 2.47 (0.86) mmol/L, and bicarbonate 18 (4) mmol/L. Peritoneal dialysis was continued for a median time of 67 hours (range 9 hours–26 days) until recovery of renal function or death occurred. Effective fluid withdrawal could be achieved in nearly all patients (Table 2). Hyperkalemia (potassium >5.5 mmol/L) normalized after a median time of 7 (range 3–14) hours. Complications of PD were minor (Table 2). No patient developed peritonitis. However, 15 (60%) of 25 children on renal replacement therapy died. The predominant cause of death was cardiac failure ($n = 11$), 2 patients were brain dead after resuscitation, and 2 children died of miscellaneous causes. None of the patients died of renal causes. Of the children who died, two children experienced peritoneal dialysis catheter malfunction or leakage, whereas, among the surviving patients, only one had leakage. The peri-

Table 1a. Age and serum creatinine of patients before and after cardiopulmonary bypass surgery

Cardiopulmonary bypass surgery	Age median (range)	Screat preop μmol/L	Screat postop μmol/L	Peak level on day × postop
Atrial septum defect closure	3 y 11 m (4 m–16 y 7 m)	40 (16)	45 (41)	1 (1–21)
Ventricular septum defect closure	1 y 1 m (1 m–15 y 3 m)	38 (11)	47 (23)	2 (1–9)
Atrioventricular septum defect correction	5 m (3 w–15 y)	43 (9)	70 (46)	2 (1–14)
Tetralogy of Fallot (re)operation	1 y 5 m (2 w–16 y 9 m)	42 (12)	60 (45)	2 (1–10)
Arterial switch	7 d (1 d–2 y 5 m)	67 (30)	91 (36)	3 (1–8)
Common arterial truncus correction	2 m 2 w (11 d–9 y 1 m)	42 (9)	105 (62)	3 (2–4)
Double outlet right ventricle correction	10 m (2 m–6 y 11 m)	41 (6)	53 (13)	2 (1–14)
Pulmonary valve surgery	2 y 1 m (1 d–16 y 11 m)	41 (18)	44 (19)	1 (1–4)
Conduit replacement	10 y 5 m (5 y 2 m–15 y)	57 (11)	57 (11)	2 (1–8)
Mitral valve surgery/replacement	7 y 11 m (5 w–16 y 8 m)	47 (14)	65 (73)	2 (1–9)
Aortic valve surgery/replacement	4 y 6 m (3 d–15 y 2 m)	59 (27)	97 (120)	2 (1–8)
Resection subvalvular aortic stenosis	5 y 10 m (1 m–16 y 7 m)	42 (15)	45 (23)	1 (1–3)
Ross operation	10 y 2 m (5 w–16 y 9 m)	57 (13)	64 (20)	2 (1–8)
TAPVD/Scimitar correction	2 m (7 d–10 y 4 m)	44 (15)	65 (28)	2 (1–7)
Fontan/Total Cavo-Pulmonary connection	4 y 11 m (1 y 9 m–13 y 5 m)	44 (10)	123 (116)	2 (1–13)
Glenn/Bidirectional Cavo-Pulmonary shunt	2 y 1 m (5 w–5 y 7 m)	42 (8)	63 (62)	1 (1–19)
Rastelli operation	3 y 7 m (1 y 11 m–12 y 9 m)	46 (9)	123 (84)	2 (1–6)
Miscellaneous	1 y 5 m (1 d–16 y 7 m)	49 (23)	97 (99)	2 (1–18)
Total	1 y 11 m (1 d–16 y 11 m)	45 (18)	67 (61)	2 (1–21)

Screat, Serum creatinine mean (SD) μmol/L preoperative and peak postoperative levels; Peak level on day x postop, peak serum creatinine level on day x postoperative given as median (range); Pulmonary valve surgery consists of commissurotomy/reconstruction pulmonary valve and correction supravalvular pulmonary artery stenosis. Aortic valve surgery/replacement includes neonatal critical aortic stenosis, endocarditis, and ascending aorta aneurysms. Arterial switch includes transposition with VSD and Taussig-Bing anomalies. TAPVD total anomalous pulmonary vein drainage (re)operation. Miscellaneous operations consist of 1-stage repairs (e.g., VSD and coarctatio aortae, VSD and interrupted arch); correction of pulmonary atresia, VSD, and Major Aorto-Pulmonary Collateral Arteries; aorto-pulmonary window; ascending aorta and aortic arch repairs or replacements; correction Ebstein's disease; correction Aberrant Left Coronary Artery from Pulmonary Artery; hemitruncus; operations for monoventricular heart other than Glenn or Fontan, Norwood stage 1, and others. y, year; m, month; w, week; d, day.

toneal catheters were revised or replaced. In 9 out of 10 surviving children, renal function was normal at time of discharge from hospital. Mean (SD) serum urea and creatinine levels of the surviving patients were 5.7 (2.7) mmol/L and 45 (10) μmol/L, respectively.

Discussion

Acute Renal Insufficiency

The incidence of acute renal insufficiency (17%) complicating open-heart surgery in children remains high, and the incidence is often related to the complexity of the operation. On one hand, better and more sophisticated surgical and cardiopulmonary bypass techniques are available. On the other hand, however, children with more complicated cardiac lesions requiring longer cardiopulmonary bypass time are operated on [8]. As is expected after relatively short and simple operations such as atrial septum defect closure, few children develop acute renal insufficiency (0.7%). After more complicated operations with long cardiopulmonary bypass times, such as arterial switch operation and common arterial truncus correction, there is a high incidence of acute renal insufficiency (59% and 53%, respectively) (Tables 1a, b).

Cardiopulmonary bypass is deleterious because it triggers an important inflammatory reaction, including the release of kinins, coagulation factor XII, and complement factors by endothelial cells and leucocytes [7]. This reaction is largely related to the ratio of the circuit area to the patient's body surface area and is therefore maximal in children. Clinically, this is associated with a capillary leak syndrome, resulting in hypovolemia and renal hypoperfusion.

Furthermore, we found a high incidence of acute renal insufficiency in children with postoperative low flow state, for example, after a Fontan procedure (38%). The low-flow state similarly can cause renal hypoperfusion and can lead to renal insufficiency. Of the patients after Fontan procedure, a high percentage (21%) required renal replacement therapy.

Although preoperative serum creatinine level, corrected for the age of the patient, is significantly corre-

Table 1b. Type of cardiopulmonary bypass surgery, acute renal insufficiency, renal replacement therapy, and mortality <30 days after open-heart surgery

Cardiopulmonary bypass surgery	Number of patients *n*	Acute renal insufficiency *n* (%)	PD *n*	death <30 days *n* (%)
Atrial septum defect closure	139	1 (0.7)	—	—
Ventricular septum defect closure	165	8 (4.8)	1 (0.6)	6 (3.6)
Atrioventricular septum defect correction	100	24 (24)	2 (2.0)	7 (7.0)
Tetralogy of Fallot (re)operation	158	17 (11)	2 (1.3)	10 (6.3)
Arterial switch	71	42 (59)	2 (2.8)	5 (7.0)
Common arterial truncus correction	15	8 (53)	1 (6.7)	4 (27)
Double outlet right ventricle correction	10	—	—	2 (20)
Pulmonary valve surgery	19	1 (5.3)	—	1 (5.3)
Conduit replacement	18	—	—	—
Mitral valve surgery/replacement	48	4 (8.3)	2 (4.2)	2 (4.2)
Aortic valve surgery/replacement	20	6 (30)	—	4 (20)
Resection subvalvular aortic stenosis	36	1 (2.8)	—	—
Ross operation	40	1 (2.5)	—	2 (5.0)
TAPVD/Scimitar correction	27	6 (22)	—	4 (15)
Fontan/Total Cavo-Pulmonary connection	29	11 (38)	6 (21)	3 (10)
Glenn/Bidirectional Cavo-Pulmonary shunt	37	6 (16)	—	2 (5.3)
Rastelli operation	7	3 (43)	1 (14)	1 (14)
Miscellaneous	136	41 (30)	8 (5.9)	17 (12)
Total	1075	180 (17)	25 (2.3)	70 (6.5)

PD, Peritoneal dialysis. Pulmonary valve surgery consists of commissurotomy/reconstruction pulmonary valve and correction supravalvular pulmonary artery stenosis. Aortic valve surgery/replacement includes neonatal critical aortic stenosis, endocarditis, and ascending aorta aneurysms. Arterial switch includes transposition with VSD and Taussig–Bing anomalies. TAPVD total anomalous pulmonary vein drainage (re)operation. Age is given as median (range). Miscellaneous operations consist of 1-stage repairs (e.g., VSD and coarctatio aortae, VSD and interrupted arch); correction of pulmonary atresia, VSD, and Major Aorto-Pulmonary Collateral Arteries; aorto-pulmonary window; ascending aorta and aortic arch repairs or replacements; correction Ebstein's disease; correction Aberrant Left Coronary Artery from Pulmonary Artery; hemitruncus; operations for monoventricular heart other than Glenn or Fontan, and others.

Table 2. Data of patients on peritoneal dialysis after cardiopulmonary bypass surgery

Patient characteristics		Indications for PD	*n* (%)
Age	1 y 10 m (6 days–8 y 9 m)	Anuria (>24 hours)	21 (84)
Weight	11.5 (2.5–25.8) kg	Hyperkalemia (>5.5 mmol/L)	11 (44)
Males	17 (68%)	Hyperphosphatemia (>4 mmol/L)	1 (4)
Cardiopulmonary bypass time	183 (SD 69) minutes	Severe edema	3 (12)
Aortic cross clamp time	88 (SD 43) minutes		
PD characteristics		*Complications of PD*	
Time to initiation of PD	54 hours (21 hours–86 days)	Hyperglycemia	16 (64)
Duration of PD	67 hours (9 hr–26 days)	Insulin therapy	2 (8)
Fluid withdrawal day 1	44 (−3–140) ml/kg/day	Leakage PD catheter	2 (8)
Fluid withdrawal day 2	46 (−3–101) ml/kg/day	Revision PD catheter	1 (4)
Fluid withdrawal day 3	48 (7–84) ml/kg/day	PD catheter replacement	2 (8)

PD, peritoneal dialysis; y, year; m, month. Data are given as median (range), mean (SD), or percentage (%)

lated to renal insufficiency, the difference between the renal insufficiency group and the group without renal insufficiency is minor. This difference cannot be used clinically to predict renal insufficiency postcardiopulmonary bypass surgery. For the patients without renal insufficiency, there was a sharp decrease in the risk of dying with age. However, for patients with renal insufficiency, the risk of dying was significantly higher and moreover was hardly decreasing with age.

Renal Replacement Therapy

2.3% of patients required renal replacement therapy; this is in concert with other studies (1.6% to 7.7%) on chil-

Table 3. Diagnosis, operation, and survival of 25 patients on renal replacement therapy after open-heart surgery

No.	Diagnosis	Open-heart surgery	Alive
1	TOF, hypoplastic LPA	Correction of TOF	No
2	TOF	Correction of TOF	No
3	TGA	Switch	Yes
4	CAVSD, coarctatio aortae	Correction CAVSD, coarctectomy	Yes
5	Tricuspid atresia	Fontan	No
6	TGA	Switch	Yes
7	MI after Fontan	MVR	No
8	Monoventricle	Fontan	No
9	VSD, PDA	Occl. Aortic arch after closure VSD and PDA	Yes
10	TOF, hypoplastic LPA	Fontan	No
11	Ebstein	Correction Ebstein	No
12	Multiple VSD	Closure multiple VSD, debanding PA	No
13	Endocarditis mitral valve prothesis	MVR	No
14	cTGA, PS, VSD, ag RPA, TI, bad RV funct	TVR	Yes
15	Heterotaxia	Biventricular correction (Rastelli)	No
16	CAVSD, TOF	Total correction	Yes
17	Monoventricle	Fontan	No
18	CAVSD	Correction CAVSD	Yes
19	PA, VSD, MAPCAs	Part. corr with homograft, fenestr VSD patch	No
20	PA, VSD, MAPCAs	Total correction	No
21	CAVSD, TOF	Total correction	No
22	DORV, TGA, PS	Fontan	Yes
23	Heterotaxia, monoventricle, coarctatio aortae	Banding AP, coarctectomy, closure PDA	No
24	Monoventricle	Fontan	Yes
25	Common arterial truncus	Corr arterial truncus with aortic valve repl	Yes

TOF, tetralogy of Fallot; LPA, left pulmonal artery; TGA, transposition of great arteries; CAVSD, complete atrioventricular septum defect; MI, mitral insufficiency; MVR, mitral valve replacement; VSD, ventricular septum defect; PDA, patent ductus arteriosis, cTGA, corrected TGA; TGA, transposition of great arteries; PS, pulmonal valve stenosis; ag RPA, agenesia right pulmonal artery; TI, tricuspid insufficiency; bad RV funct, bad right ventricle function; TVR, tricuspid valve replacement; MAPCAs, major aortic-pulmonal collateral arteries; part corr, partial correction; fenestr VSD patch, fenestrated VSD patch; corr arterial truncus with aortic valve repl, correction arterial truncus with aortic valve replacement

dren after open-heart surgery [1, 2, 5, 6, 10–12]. Only Dittrich treated a much higher percentage (33%) of infants after cardiopulmonary bypass surgery, but PD was started profylactically at the end of the operation. Thus, Dittrich was treating relatively healthy children [3]. The patients in our study on renal replacement therapy had complex cardiac surgery (Table 3), and most children had low postoperative cardiac output resulting in renal hypoperfusion. Peritoneal dialysis was chosen as renal replacement therapy because of its relatively easy employment, efficacy, and infrequent complications. In our patient group, fluid withdrawal (median 46 [range −3–140] ml/kg/day) was effective in most patients, and hyperkalemia was corrected within hours, (median 7 [range 3–14] hours after initiating PD). These results are comparable to those of Werner, who reported mean fluid removal of 48 (SD 28) ml/kg/day with PD in a similar patient group [13]. Sorof achieved a higher mean ultrafiltration of 93 (range 43–233) ml/kg/day in less critically ill patients with extracellular volume overload and relatively normal renal function after cardiopulmonary bypass surgery [12]. Nevertheless, there is an ongoing controversy on the choice of renal replacement therapy after open-heart surgery [4, 9, 14]. Fluid withdrawal may be more effective when using continuous veno-venous hemofiltration. Fleming found an average fluid deficit of 9.2 ml/hr (range 3.5–26 ml/hr) in children on PD after open-heart surgery, as compared with 23 ml/hr (range 3.9–34 ml/hr) in patients on continuous veno-venous hemofiltration [4]. On the other hand, continuous arterovenous and veno-venous hemofiltration require anticoagulation. Anticoagulation might be hazardous soon after cardiopulmonary surgery. Furthermore, vascular access for hemofiltration may pose a problem, especially in neonates.

Complications from PD in our study were minor. No patient developed peritonitis. However, in concert with previous studies (58% to 75%), mortality of patients requiring renal replacement therapy remains high (60%) [1, 4–6, 10, 11]. Nonetheless, three studies documented lower mortality in children (20% to 30%) [2, 3, 12]. In two studies, PD was performed for a selection of “healthier” patients, which may account for the lower mortality [3, 12]. In one study, PD was often already started prophylactically at the end of the operation [3]. In another study, PD was undertaken after a mean period of

22 hours postoperatively, whereas mean urine output of the patients still was 2.2 ml/kg/hr. No patients were anuric [12]. Death in our patients was not related to renal failure, but was generally the result of cardiac failure. Renal function normalized in 9 of 10 (90%) surviving children. This is in agreement with other studies, where 93% to 100% of survivors of renal replacement therapy after cardiopulmonary bypass surgery had normal renal function at discharge from hospital [1, 2, 5, 7, 10, 11].

Conclusion

Acute renal insufficiency is a frequent (17%) complication after cardiopulmonary bypass surgery in children, although renal replacement therapy was infrequently (2.3%) necessary. Peritoneal dialysis is a safe and effective treatment for children after cardiopulmonary bypass surgery. However, 15 (60%) of 25 children on renal replacement therapy died of nonrenal causes. In 9 of 10 surviving children, renal function was normal at discharge from hospital.

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