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ORIGINAL ARTICLE

Pediatric RIFLE for Acute Kidney Injury Diagnosis and Prognosis for Children Undergoing Cardiac Surgery: A Single-Center Prospective Observational Study

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Abstract This study evaluated the performance of the pediatric RIFLE (pRIFLE) score for acute kidney injury (AKI) diagnosis and prognosis after pediatric cardiac surgery. It was a single-center prospective observational study developed in a pediatric cardiac intensive care unit (pCICU) of a tertiary children's hospital. The study enrolled 160 consecutive children younger than 1 year with congenital heart diseases and undergoing cardiac surgery with cardiopulmonary bypass. Of the 160 children, 50 (31 %) were neonates, and 20 (12 %) had a univentricular heart. Palliative surgery was performed for 53 patients (33 %). A diagnosis of AKI was determined for 90 patients (56 %), and 68 (42 %) of these patients achieved an "R" level of AKI severity, 17 patients (10 %) an "I" level, and 5 patients (3 %) an "F" level. Longer cross-clamp times ($p = 0.045$), a higher inotropic score ($p = 0.02$), and a higher Risk-Adjusted Classification for Congenital Heart Surgery score ($p = 0.048$) but not age ($p = 0.27$) correlated significantly with pRIFLE class severity. Patients classified with a higher pRIFLE score required a greater number of mechanical ventilation days ($p = 0.03$) and a longer pCICU stay ($p = 0.045$). Renal replacement therapy (RRT) was needed for 13 patients (8.1 %), with two patients receiving continuous hemofiltration, and 11 patients receiving peritoneal dialysis. At the start of dialysis, the distribution of RRT patients differed significantly within pRIFLE classes ($p = 0.015$). All deceased patients were classified as pRIFLE "I" or "F" ($p = 0.0001$). The findings showed that pRIFLE is easily and feasibly applied for pediatric patients with congenital heart disease. The pRIFLE classification showed that AKI incidence in pediatric cardiac surgery infants is high and associated with poorer outcomes.

Keywords Acute kidney injury · Cardiopulmonary bypass · Pediatric cardiac surgery · pRIFLE

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Introduction

Children undergoing cardiac surgery for congenital heart disease are more likely to experience the development acute kidney injury (AKI) in the immediate postoperative period [3, 8, 9, 13] due to hypotension, inflammation, and nephrotoxic medication use [13]. Recently, a pediatric modification of the RIFLE (Risk for renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function, and End-stage renal disease) score [2, 11] has been proposed for AKI diagnosis and classification of children based on glomerular filtration rate (GFR) and urine output criteria [1].

The main objective of this study was to assess the diagnostic performance of the pediatric pRIFLE score in a large cohort of young infants with congenital heart diseases. The secondary objective was to evaluate whether progressively higher pRIFLE classes are associated with recognized risk factors of postcardiosurgical AKI (age, diagnosis, surgery complexity) and with hard outcome variables (length of mechanical ventilation, need for dialysis, hospital length of stay, death).

Methods

A retrospective analysis of data derived from a single-center prospective observational study [12] was performed. All infants younger than 1 year who needed elective cardiac surgery with cardiopulmonary bypass (CPB) were enrolled in the study from June 2010 to June 2011. The exclusion criteria ruled out preoperative cardiac failure, preoperative extracorporeal membrane oxygenation (ECMO), preoperative need for mechanical ventilation or inotropes/vasopressors, and preexisting renal disease. Pediatric AKI was defined according to pRIFLE score [1] (Table 1).

After enrolment, we collected demographic, baseline, preoperative, and postoperative data. Urinary output, plasmatic levels of creatinine, diuretic dosage, pRIFLE level, and need for extracorporeal renal replacement therapy (RRT) or peritoneal dialysis (PD) were collected from the day before surgery to 7 days afterward. The indication for RRT, determined by the attending physician, commonly was triggered by positive fluid balance and oliguria. The Risk-Adjusted Classification for Congenital Heart Surgery (RACHS) score, cross-clamp time, type of anatomy (uni- or biventricular), and inotropic score also were collected in the database [12]. The inotropic score (IS) indicates different inotropic and vasopressor drug regimens, reflecting the dosage of vasoconstrictors/inotropic drugs. The value of IS can be calculated as follows:

$$\begin{aligned} \text{IS} = {} & \text{dopamine } \mu\text{g/kg/min} \times 1 \\ & + \text{ dobutamine } \mu\text{g/kg/min} \times 1 \\ & + \text{ milrinone } \mu\text{g/kg/min} \times 15 \\ & + \text{ epinephrine } \mu\text{g/kg/min} \times 100. \end{aligned}$$

The length of mechanical ventilation and the pediatric cardiac intensive care unit (pCICU) stay also were recorded.

Statistical Analysis

All data were recorded in an Excel database specifically prepared for this study. Continuous variables were reported as median (interquartile range). One-way analysis of variance (Kruskal–Wallis test with a Dunns posttest) was used to evaluate the distribution of examined continuous variables within pRIFLE classes. The chi-square test was used to evaluate categorical variables. A p value lower than 0.05 was considered significant. Statistical analysis was performed by the GraphPad Prism 5.0 software package (GraphPad Software, San Diego, CA, USA).

The institutional review board approved the study and waived the need for informed consent due to its observational nature.

Results

Data from 160 patients were analyzed. Their baseline and physiologic characteristics are summarized in Tables 2 and 3.

The pRIFLE criteria for an AKI diagnosis was met by 90 patients (56 %), with 68 patients (42 %) showing an "R" level of AKI severity, 17 patients (10 %) showing an "I" level, and 5 patients (3 %) showing an "F" level (Fig. 1). The pRIFLE class was established by GFR criteria for 144 patients (90 %) and by urine output criteria for the remaining 16 patients (10 %). Urine criteria were more frequently applied to "I" and "F" patients than to "R" patients (odds ratio [OR], 2.75; 95 % confidence interval [CI], 1.53–5.3; $p = 0.01$).

The patients with AKI were slightly younger (106 days; range, 18–199 days vs 134 days; range, 21–430 days; $p = 0.1$) and had significantly longer procedures (6 h; range, 3–7 h vs 5 h; range, 4–8 h; $p = 0.048$), longer cross-clamp times (104 min; range, 69–139 min vs 88 min; range 43–142 min; $p = 0.045$), higher IS values (11; range, 6–18.5 vs 8.5; range, 5.25–16; $p = 0.01$), and higher RACHS scores (2; range, 2–6 vs 2; range, 1–4; $p = 0.049$). A diagnosis of AKI was determined by pRIFLE for 10 (50 %) of 20 children with a univentricular heart (UVH) and 80 (57 %) of 140 children with a biventricular heart (OR, 0.75; 95 % CI, 0.53–1.3; $p = 0.54$). Furthermore, an increase in cross-clamp times ($p = 0.045$), inotropic score ($p = 0.02$) and RACHS scores ($p = 0.048$) were significantly associated with pRIFLE class progression but not with a reduction in age ($p = 0.27$) (Table 4).

Table 1 Pediatric RIFLE criteria (modified from [1])

	Estimated CCl	Urine output
Risk	eCCl decrease by 25 %	<0.5 ml/kg/h for 8 h
Injury	eCCl decrease by 50 %	<0.5 ml/kg/h for 16 h
Failure	eCCl decrease by 75 % or eCCl < 35 ml/min/1.73 m^2	<0.3 ml/kg/h for 24 h or anuric for 12 h
Loss	Persistent failure > 4 weeks	
End stage	Persistent failure > 3 months	

CCl creatinine clearance, *eCCl* estimated creatinine clearance according to the Schwartz formula

Table 2 Diagnoses of examined patients

Diagnoses	*n*
Ao Coarct with Hypopl arch	6
PA + VSD	9
PA + IVS	5
TOF	23
AVCc	18
TGA	16
TGA-VSD	7
TA	6
VSD	15
HLHS	7
UVH with PA	10
Other	38
Total	160

Ao-coarct aortic coarctation, *Hypopl* hypoplastic, *PA* pulmonary atresia, *VSD* ventricular septal defect, *IVS* intact ventricular septum, *TOF* tetralogy of Fallot, *AVCc* complete atrioventricular canal, *TGA* transposition of the great arteries, *TA* truncus arteriosus, *HLHS* hypoplastic left heart syndrome, *UVH* univentricular heart

Table 3 Demographic data of enrolled patients

	n (%)
Total	160 (100)
Male	88 (55)
Age (days)	134 ± 117
Weight (kg)	5 ± 2
BSA (m^2)	0.28 ± 0.07
Neonates	50 (31)
UVH	20 (12)
Palliative surgery	53 (33)
CPB/cross-clamp duration (min)	199 ± 88/102 ± 57
MV duration (days)	3.2 ± 4
pCICU LOS (days)	6.0 ± 6.5
Dead	4 (2.5)

BSA body surface area, *UVH* univentricular anatomy, *CPB* cardiopulmonary bypass, *MV* mechanical ventilation, *pCICU* pediatric cardiac intensive care unit, *LOS* length of stay

Patients with AKI (as defined by any pRIFLE score) turned out to have a longer mechanical ventilation time (2 days; range, 1–4 days vs 1 day; range, 1–4 days; $p = 0.04$) and a longer pCICU stay (4 days, range, 2.75–7 days vs 3 days; range, 2–6 days; $p = 0.045$). The higher the pRIFLE score, the longer was the duration of mechanical ventilation ($p = 0.03$) and the pCICU stay ($p = 0.045$) (Table 4).

Renal replacement therapy (RRT) was needed for 13 patients (8.1 %), with 2 patients receiving continuous hemofiltration and 11 patients receiving peritoneal dialysis. Interestingly, nine "no AKI" or "R" class patients received RRT,

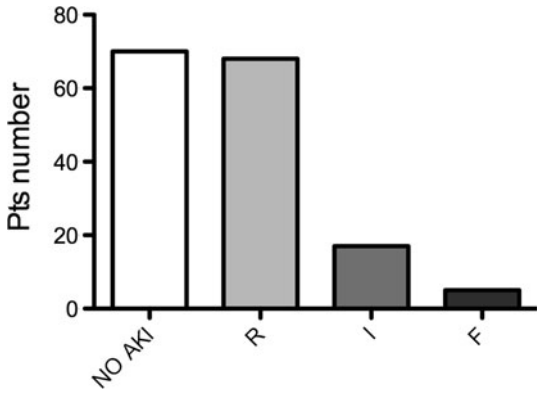

Fig. 1 Acute kidney injury (AKI) incidence and distribution within pediatric RIFLE classes

whereas only four patients were treated by RRT within the "I" and "F" classes (OR, 2.7; 95 % CI, 0.74–10.6; $p = 0.12$). At the start of dialysis, however, the proportional distribution of RRT patients differed significantly within the pRIFLE classes ($p = 0.0015$) (Fig. 2). All deceased patients were classified as pRIFLE "I" or "F" ($p = 0.0001$) (Table 4).

Discussion

Acute kidney injury is one of the most common and severe complications after cardiac surgery due to intraoperative alteration of the renal blood flow, postoperative low output syndrome, and diminished autoregulation [8, 13]. Furthermore, cardiac surgery for patients with congenital heart disease, cyanosis, younger age, and large volume of blood component shifts during CPB also contributes to diminished kidney function [4].

In our study, AKI diagnosis according to pRIFLE criteria had an incidence of 56 %. This result is higher than in other pediatric studies using the same diagnostic criteria [15, 17] probably because children younger than 1 year are more prone to the development of AKI. Furthermore, two thirds of our patients were classified as pRIFLE-R. It is conceivable that pRIFLE sensitivity to lower severity of AKI is high, with a low specificity and a tendency to overestimate actual "clinical AKI." This finding may be a consequence of creatinine clearance estimation, which may frequently be decreased by more than 25 % on postoperative day 1, followed by a quick restoration of renal function [12].

On the other hand, the infrequent use of urine output criteria for infants with lower AKI severity may be due to excessively restrictive urine criteria for the pediatric population. However, in our opinion, pRIFLE still is useful for increasing awareness of milder AKI forms as well as subclinical AKI [6, 16]. In addition, the proportional distribution of patients within pRIFLE classes was similar to that reported by Zappitelli et al. [17].

Table 4 Pediatric RIFLE severity and correlated variables

	No AKI	Risk	Injury	Failure	*p* value
Cross-clamp duration (min)	92 ± 57	104 ± 55	115 ± 45	166 ± 95	0.045
IS	10 ± 7	12 ± 7	15 ± 9	20 ± 6	0.02
RACHS score	1.5 ± 1	2.5 ± 1.5	3 ± 2	4.5 ± 3	0.048
Age (days)	145 ± 124	147 ± 94	125 ± 116	38 ± 33	0.27
Mechanical ventilation (days)	2.6 ± 3.6	3.2 ± 3.9	4.5 ± 6	5.7 ± 6	0.03
pCICU LOS (days)	5.4 ± 6.5	5.2 ± 5	8.3 ± 9	9.3 ± 8	0.045
RRT (%)	4.2	8.7	11	75	0.015
Deceased (*n*)	0	0	1	3	0.0001

IS inotrope score during postoperative day 1, *RACHS* risk assessment for congenital heart surgery, *pCICU* pediatric cardiac intensive care unit, *LOS* length of stay, *RRT* renal replacement therapy

Data are expressed as mean ± SD

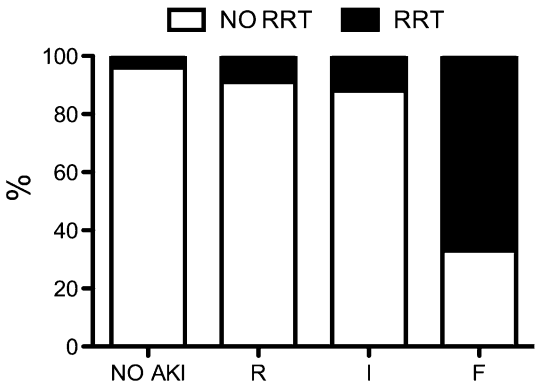

Fig. 2 Renal replacement therapy (RRT), proportional incidence, and distribution within different pediatric RIFLE classes

Our findings confirmed that cross-clamp times, inotropic score, and RACHS scores are a clear predictor of AKI incidence [5, 10, 15, 17] and that they present progressively higher values within pRIFLE classes, showing good clinical reliability of this AKI classification type. Even if age in our young cohort was not a significant predictor of AKI diagnosis, all pRIFLE "F" patients were younger than 2 months. Furthermore, limiting age enrolment criteria to less than 1 year (already considered as indicating higher AKI risk [17]) probably blunted the impact of age as a specific AKI risk factor.

Surprisingly, UVH physiology seemed not to affect the development of AKI compared with biventricular anatomy, probably due to the relatively small number of enrolled patients with a single-ventricle anatomy. Furthermore, it is possible that neonatal palliation of UVH patients poses a higher risk for postoperative AKI, whereas older patients undergo a risk similar to that of biventricular/acyanotic children.

In our UVH population, only four major neonatal surgical procedures were performed (Norwood operation), and in three cases, a hybrid approach (bilateral pulmonary artery banding and ductal stenting) was adopted. The remaining 13 UVH patients were not neonates. A specific evaluation of AKI risk for this challenging population should be performed.

Concerning pRIFLE prognostic value, patients in any pRIFLE class required a longer pediatric intensive care unit (PICU) stay and a greater number of mechanical ventilation days. Again, the greater the number of PICU and mechanical ventilation days, the higher was the AKI severity class. These results are in line with those reported by Toth et al. [15] and highlight the delicate interaction between kidneys and cardiopulmonary function, recently described as the "pediatric cardiorenal syndrome" [7].

In our population, the patients undergoing RRT were proportionately distributed in higher pRIFLE classes. However, it must be acknowledged that, probably because of the institutional approach to an early RRT start, many patients were treated by RRT but had a diagnosis of "no AKI" or "R" class. This also may be due to the fact that these patients commonly are fluid overloaded (with consequent dilution of the creatinine levels) and receive high-dose diuretics (with a low tendency to oliguria, as defined by pRIFLE). This aspect should support the use of novel biomarkers of AKI (in association with the pRIFLE score) to help clinicians toward RRT indication [12].

This study was limited by the fact that it was a single-center study with a relatively low number of patients and heterogeneous congenital heart defects. However, little information is available on the incidence, risk factors, and prognosis of AKI in infants with congenital heart disease [15, 17]. Finally, although the use of pRIFLE and its clinical reliability have been argued recently [14], our study is one of the first clearly to highlight the correlation of pRIFLE scores with clinical risk factors and outcome parameters after cardiac surgery. We speculate that pediatric cardiac surgery is an optimal setting for this AKI classification.

Conclusion

The pRIFLE criteria used for AKI diagnosis and prognosis after pediatric surgery show that the incidence of renal dysfunction is very high, especially when prolonged cross-clamp times are present, and that early postoperative creatinine or urine changes are associated with a complicated PICU recovery and a higher risk of RRT requirement.

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