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Outcomes

Indications and outcomes in children receiving renal replacement therapy in pediatric intensive care☆

Erin D. Boschee, BSc [a], Dominic A. Cave, MBBS, FRCPC [b], Daniel Garros, MD [c], Laurance Lequier, MD, FRCPCP [c], Donald A. Granoski, RRT [c], Gonzalo Garcia Guerra, MD [c], Lindsay M. Ryerson, MD, FRCPC [c,*]

[a] Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada
[b] Department of Anesthesiology, University of Alberta, Edmonton, Alberta, Canada
[c] Department of Pediatrics, University of Alberta, Edmonton, Alberta, Canada

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ABSTRACT

Purpose: We aimed to describe patient characteristics, indications for renal replacement therapy (RRT), and outcomes in children requiring RRT. We hypothesized that fluid overload, not classic blood chemistry indications, would be the most frequent reason for RRT initiation.
Materials and Methods: A retrospective cohort study of all patients receiving RRT at a single-center quaternary pediatric intensive care unit between January 2004 and December 2008 was conducted.
Results: Ninety children received RRT. The median age was 7 months (interquartile range, 1-83). Forty-six percent of patients received peritoneal dialysis, and 54% received continuous renal replacement therapy. The median (interquartile range) PRISM-III score was 14 (8-19). Fifty-seven percent had congenital heart disease, and 32% were on extracorporeal life support. The most common clinical condition associated with acute kidney injury was hemodynamic instability (57%; 95% confidence interval [CI], 46-67), followed by multiorgan dysfunction syndrome (17%; 95% CI, 10-26). The most common indication for RRT initiation was fluid overload (77%; 95% CI, 66-86). Seventy-three percent (95% CI, 62-82) of patients survived to hospital discharge.
Conclusions: Hemodynamic instability and multiorgan dysfunction syndrome are the most common clinical conditions associated with acute kidney injury in our population. In the population studied, the mortality was lower than previously reported in children and much lower than in the adult population.

1. Introduction

The role of renal replacement therapy (RRT) in critically ill pediatric patients is expanding. Classic indications for RRT in the pediatric population include metabolic/electrolyte imbalance, uremia with bleeding and/or encephalopathy, fluid overload (FO) with pulmonary edema/respiratory failure, intoxications, inborn errors of metabolism (IEM), and nutritional support [1]. Renal replacement therapy encompasses intermittent hemodialysis, peritoneal dialysis (PD), and continuous RRT (CRRT). Since the late 1990s, the latter has become the modality of choice in many pediatric intensive care units (PICUs) [1]. Continuous RRT is a mainstay of treatment in PICU for acute kidney injury (AKI) due to well-maintained hemodynamic stability with slow predictable fluid and solute removal [2]. The decision to initiate RRT is influenced by patient characteristics, physician beliefs, and institution-specific factors [3].

Despite the rapid expansion of RRT in the PICU, there are no set guidelines that describe when RRT should be initiated and in whom. The inability to generalize findings from adult RRT studies to critically ill children due to differences in age, size, disease, and comorbidities necessitates further research into the current indications and outcomes of pediatric RRT [4]. We aimed to describe the population of critically ill children requiring RRT at our institution in terms of patient characteristics, degree of AKI, indications for RRT, and outcomes. A secondary objective was to identify risk factors for mortality in those patients who needed RRT.

2. Materials and methods

2.1. Patients

The Health Research Ethics Board at the University of Alberta approved this study. The requirement for individual informed patient consent was waived. Data on all patients who received RRT at Stollery Children's Hospital between January 2004 and December 2008 were reviewed. *Renal replacement therapy* was defined as any form of acute blood purification in the PICU including PD and CRRT.

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* Corresponding author. WMC 3A3.19, Edmonton, AB, Canada T6G 2B7.
E-mail address: ryerson@ualberta.ca (L.M. Ryerson).

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Subjects who were RRT dependent before PICU admission were excluded. Patients were identified by the prospectively collected Pediatric ICU Evaluations (PICUES) database and cross-referenced with our PICU RRT patient database. Data were retrospectively gathered from the PICUES and RRT databases as well as from individual patients' medical records.

Patient characteristics included age, sex, height, weight, and PRISM-III score at the time of PICU admission. The primary diagnosis at PICU admission was classified into 7 categories: post–cardiac surgery, systemic inflammatory response syndrome/sepsis/shock, respiratory failure, cardiac arrest, primary renal disease, liver disease/transplant, and drug overdose. Any diagnosis that did not fit one of these categories was labeled "other" and was detailed on the case report form. Chronic diagnoses including cancer, history of previous transplant, congenital heart disease, diabetes, chronic renal failure (not RRT dependent), and chromosomal abnormalities were also recorded. Any other major chronic diagnoses deemed as potentially contributing to the patient's PRISM-III score at the time of PICU admission were noted in a separate category termed *other*. Use of mechanical ventilation, inotropes and/or vasopressors, or extracorporeal life support (ECLS) was recorded.

Associations with AKI were classified as hemodynamic instability, multiple-organ dysfunction syndrome (MODS), tumor lysis syndrome (TLS), hemolytic uremic syndrome/thrombotic thrombocytopenic purpura, IEM, or other. *Hemodynamic instability* was defined as a systolic blood pressure less than the fifth percentile for age, despite fluid resuscitation, with concurrent use of intravenous inotropes and/or vasopressors. *Multiple-organ dysfunction syndrome* was defined as the presence of at least 3 failed organ systems concomitantly during the PICU admission [2].

The degree of AKI was determined by the pediatric-modified RIFLE (pRIFLE) score, which stratifies AKI into levels as Risk, Injury, Failure, Loss or End-stage, based on criteria described by Akcan-Arikan et al [5]. This was achieved by calculation of eGFR or prior 24-hour urine output [5].

Indications for RRT were deduced from the medical records and classified into the following: FO (>10%), metabolic acidosis (pH < 7.1), hyperkalemia (>5.5 mmol/L), symptoms of uremia, TLS, IEM, intoxication, or other. Patients may have had more than 1 indication for RRT. The percent FO (% FO) was calculated by determining fluid input and output from the time of PICU admission until RRT initiation using the following formula by Goldstein et al [6].

$$\%\,\mathrm{FO} = ([\text{total fluid intake} - \text{total fluid output (L)}]/\text{admission body weight in kg})^{*}100$$

Fluid overload greater than 10% was chosen as a cutoff value based on the published literature demonstrating a significant increased mortality with FO greater than 10% [7–9]. Duration of RRT, length of time in the PICU before RRT initiation, and the need for multiple runs of RRT were recorded. In addition, RRT complications were recorded including bleeding, thrombosis, infection, central nervous system events, shock requiring fluid resuscitation, and catheter malfunction.

2.2. Renal replacement therapy

PRISMA and PRISMAFLEX (Cobe-Gambro Healthcare, Lakewood, Col) hemofiltration machines were used. Blood flow rates ranged from 50 to 200 mL/min. Data on mode of CRRT initially ordered: (continuous venovenous hemodialysis, continuous venovenous hemofiltration, or continuous venovenous hemodiafiltration) was collected. Anticoagulation was either heparin for patients on ECLS or citrate for all others, unless contraindicated.

Peritoneal dialysis was initiated by the placement of a Tenckhoff catheter in the peritoneal cavity and subsequent dialysis. Some neonates returned to PICU after palliative cardiac surgery with a Tenckhoff catheter in place; these patients were not included in the analysis, unless PD cycles were started in the PICU. Small volume (10 mL/kg) and continuous cycles (30-60 minutes) were used. Dialysate fluid (1.5%-4.25% glucose) was used with 25 mmol/L sodium bicarbonate and a variable potassium prescription.

2.3. Statistics

The primary outcomes were 28-day mortality and survival to hospital discharge. Secondary outcomes were PICU length of stay (LOS), hospital LOS, ventilator days, and RRT dependence at hospital discharge. We explored the data for possible risk factors to identify mortality in those patients who needed RRT.

Descriptive statistics were used to summarize both continuous and categorical variables. Survivors and nonsurvivors were compared for their baseline characteristics and parameters of renal function. Continuous data are presented as means with SD or median with interquartile range (IQR), where appropriate. Nonnormally distributed data were analyzed using the Mann-Whitney *U* test. Categorical data are presented as counts with percentages and analyzed using the Fisher exact test or the χ^2 test. Statistical analysis was performed using Stata version 10.0 software (Stata Corporation, College Station, Tex). A *P* value less than .05 was considered statistically significant.

3. Results

Between 2004 and 2008, 98 patients were identified as having received RRT. Seven patients were excluded because of a primary diagnosis of chronic renal failure and preexisting RRT before their PICU admission. One patient was excluded because there was no available PRISM-III score at PICU admission. This left 90 patients who received RRT over the 5-year period for the analysis.

The median (IQR) age was 7 (1-83) months, and the median (IQR) weight was 6.2 (3.5-20) kg. Sixty-three percent were male. Details of patient baseline demographics and clinical characteristics are presented in Table 1. The most common primary diagnosis was post–congenital cardiac surgery. These patients are presented separately (Table 2). Two patients had a primary diagnosis of acute renal disease; these patients were not RRT dependent before their PICU admission and were included in our analysis. The median (IQR) length of time in PICU before RRT initiation in all subjects was 2 days (1-4). Most patients were intubated and mechanically ventilated (94%) and received inotropes and/or vasopressors (82%). Twenty-nine patients (32%) were on ECLS. Hemodynamic instability was the most common association with AKI in 51 patients (57%). Fifteen patients (17%) had MODS.

Survivors and nonsurvivors were compared. Multiple-organ dysfunction syndrome was 3 times more common in nonsurvivors ($P = .021$). Nonsurvivors had a median 7 days in PICU before RRT initiation compared with 2 days in survivors ($P = .089$; Table 1). Serum urea and eGFR were similar in both groups at the initiation of RRT. The most common indication for initiation of RRT was FO (77%). Other classic indications included uremia (22%), hyperkalemia (26%), and metabolic acidosis (22%). Intoxication, TLS, and IEM as indications for RRT were found in only a few patients. Median % FO was clinically different but not statistically different between the survivors and the nonsurvivors ($P = .27$). Survivors and nonsurvivors had similar numbers of patients with pRIFLE class I or F. No patients had a pRIFLE diagnosis of loss or end-stage AKI.

Postoperative cardiac patients were significantly younger ($P < .0001$) and smaller ($P < .0001$) compared with the non–postoperative group (Table 2). There was no difference in the incidence of AKI diagnosed by pRIFLE between the 2 groups. The median creatinines, both at PICU admission ($P = .007$) and RRT initiation ($P = .006$), were significantly different, but this is merely reflective of the differences in