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ORIGINAL ARTICLE

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Pediatric acute renal failure: outcome by modality and disease

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Abstract Two hundred and twenty-six children who underwent renal replacement therapy (RRT) from 1992 to 1998 were retrospectively reviewed. The mean age, at the onset of RRT, was 74±11.7 months and weight was 25.3±9.7 kg. RRT therapies included hemofiltration (HF; *n*=106 children for an average of 8.7±2.3 days), hemodialysis (HD; *n*=61 children for an average of 9.5±1.7 days), and peritoneal dialysis (PD; *n*=59 children for an average of 9.6±2.1 days). Factors influencing patient survival included: (1) low blood pressure (BP) at onset of RRT (33% survival with low BP, vs 61% with normal BP, vs 100% with high BP; $P<0.05$), (2) use of pressors anytime during RRT (35% survival in those on pressors vs 89% survival in those not requiring pressors; $P<0.01$), (3) diagnosis (primary renal failure with a high likelihood of survival vs secondary renal failure; $P<0.05$), (4) RRT modality (40% survival with HF, vs 49% survival with PD, vs 81% survival with HD; $P<0.01$ HD vs PD or HF), and (5) pressor use was significantly higher in children on HF (74%) vs HD (33%) or PD (81%; $P<0.05$ HD vs HF or PD). In conclusion, pressor use has the greatest prediction of survival, rather than RRT modality. Patient survival in children with the need for RRT for ARF is similar to in adults and, as in adults, is best predicted by the underlying diagnosis and hemodynamic stability.

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Introduction

The care of a child with multiorgan system failure (MOSF) and the need for renal replacement therapy (RRT) has changed dramatically over the last 15 years [1]. In the 1970s and 1980s, the RRT of choice was (primarily) acute peritoneal dialysis (PD) with some acute hemodialysis (HD) [2]. In the area of intoxications or inborn errors of metabolism, HD, if available, was considered a first-line RRT [3, 4]. Over the last decade improvement in vascular access, pediatric specific equipment, and improved techniques, as well as understanding in the area of critical care nephrology, have allowed for improved care of children with MOSF who need RRT [5–9].

In 1992 the Division of Pediatric Nephrology at the University of Michigan developed a database to identify patients requiring RRT at the C.S. Mott Children's Hospital. Indications for RRT included: (1) primary or secondary renal failure; (2) inborn errors of metabolism; and (3) intoxications.

The database allowed compilation of information such as age, sex, and indication for RRT, type of modality, access, and patient survival (Table 1). This large series of children requiring RRT permitted us to delineate patient survival variables based on the RRT modality as well as their disease process.

This database is approved by the Institutional Review Board (IRB) at the University of Michigan.

Table 1 Demographics of the database

– Age	– BP at onset
– Weight	– Use of vasopressors
– Diagnosis	– Complications
– Indication	– Renal recovery
– RRT modality	– Function
– Duration	– Survival
– Access	– Change in modality

Materials and methods

The indications for starting RRT and the type of RRT were based on the decision of the nephrologist on service at that time. Over time the general trend has changed from PD to HD and hemofiltration (HF). The indications to begin RRT include oliguria, rising blood urea nitrogen (BUN), hyperkalemia (K >5.5 mEq/dl), pulmonary edema, and insufficient urine output to allow for medication infusion and/or nutrition. Previous work by Fleming et al. has demonstrated that RRT such as HF may allow for greater nutritional delivery when compared with PD [10].

The majority of children were located in one area in the Pediatric Intensive Care Unit (PICU) that housed both medical and surgical patients. A smaller group of children were either in the Cardiac Intensive Care Unit or the Neonatal Intensive Care Unit.

From 1992 to 1998, a total of 379 children underwent RRT. Indications included end stage renal disease (ESRD, *N*=96), acute renal failure (ARF, *N*=226), ARF while on extracorporeal membrane oxygenation (ECMO, *N*=35), inborn errors of metabolism (*N*=11), and intoxications (*N*=11). This report will focus on the 226 children who underwent RRT for ARF. Of these 226 children, 106 children underwent hemofiltration (HF), 61 underwent hemodialysis (HD), and 59 underwent peritoneal dialysis (PD).

The usual PD prescription included the use of either commercially available or pharmacy made (bicarbonate) PD solution. This choice was based upon the metabolic acidosis and hepatic function of the child at the onset of RRT. In children weighing less than 20 kg a manual PD system (Gesco Pedialyate, San Antonio, TX) was used, while in larger children the use of the Pac-Xtra (Baxter, Deerfield, IL) was utilized. Volumes per pass were 10–15 ml/kg with glucose concentration, heparin and antibiotics based upon clinical needs [11].

The usual HD prescription used Baxter 1550 (Deerfield, IL) machine with appropriate neonatal, pediatric, or adult bloodlines. The dialysate bath was adjusted only for potassium and the net ultrafiltration. The duration and frequency of each treatment was determined based upon the needs of the child. Dialyzer was based upon the size of the child but included the use of the HG-100 (COBE, Lakewood, CO), CA-50–170 series (Baxter Deerfield, IL) and the CT-110–190 series (Baxter, Deerfield, IL). Blood flow rate was targeted to 4–5 ml/kg/min [11].

The usual HF prescription utilized either an adapted HF machine (Gambro AK-10, Lakewood, CO) or the PRISMA (Gambro, Lakewood, CO). Hemofiltration membrane choice in children with the adapted system included the Miniplus (Minnetech, Minneapolis, MN), HF-400 (Renal Systems, Minneapolis, MN) or the M-60 (COBE, Lakewood, CO). Blood flow rate was targeted to 4–5 ml/kg/min and replacement fluid in those undergoing CVVH or dialysate fluid in those undergoing CVVHD was prescribed at 2000 ml/h/1.73 m^2. This prescription has been previously addressed in work by Maxvold et al. looking at urea clearance in CVVH vs CVVHD [12]. The attending nephrologist made the choice of CVVH or CVVHD on service at onset of RRT. Replacement fluid, or dialysate fluid, was always a pharmacy-made solution containing bicarbonate. In those children receiving a phosphorus-based solution, a calcium infusion was used and the rate of infusion was adjusted based upon hourly to every hour analysis of the ionized calcium [11].

Daily communication occurred between the nephrology and critical care staff in order to optimize the amount of nutrition and to avoid excessive potassium or phosphorus delivery by the nutrition. Initially protein delivery was targeted to 1.5 g/kg/day but adjusted upwards based upon measurement of energy expenditure and nitrogen balance [12].

Statistics

Data are presented as means ± SEM. Statistical analysis was performed with the Fisher exact test and statistical significance set at $P<0.05$.

Table 2 Diagnosis (*n*) and (%) survival by diagnosis in children on RRT (*BMT* bone marrow transplant, *TLS/Mal* tumor lysis syndrome/malignancy, *CHD* congenital heart disease, *Ht Tx* heart transplant, *HUS* hemolytic uremic syndrome, *ATN* acute tubular necrosis, *Liv Tx* liver transplantation)

Diagnosis	*N*	Survival	Diagnosis	*N*	Survival
BMT	26	42%	HUS	16	94%
TLS/Mal	17	58%	ATN	46	67%
CHD	47	39%	Liv Tx	22	17%
Ht Tx	13	67%	Sepsis	39	33%

Results

The mean age at the time of starting RRT was 74±11.7 months (range: newborn to 216 months), and mean weight was 25.3±9.7 kg (range: 3.5–83 kg). Fifty-one percent of these children were male and 32% of the children were hypotensive as defined as <5% of normal blood pressure for age of RRT [13]. Of the 226 children who underwent therapy for ARF, the primary diagnoses included bone marrow transplant (BMT; *N*=26), tumor lysis syndrome/malignancy (*N*=17), congenital heart disease (*N*=47), cardiac transplant (*N*=13), hemolytic uremic syndrome (HUS) (*N*=16), ARF with acute tubular necrosis (*N*=46), status postliver transplant (*N*=22), and sepsis (*N*=39; Table 2).

Duration of RRT

Time on RRT therapy for the total 226 children was 8.7±2.3 days on HF, 9.5±1.7 days on HD, and 9.6±2.1 days on PD. No significant difference between time of therapy among the three modalities was found.

Anticoagulation requirement

The decision to use heparin was based upon the coagulation status of the child at the onset of RRT. Many children were coagulopathic due to their underlying cause of illness. In those children with a pre RRT activated clotting time (ACT) of >150 s, an attempt to treat them without heparin during RRT was made. In total, 51% on HF underwent heparin-free therapy while 28% on HD underwent heparin-free therapy ($P<0.01$).

Hemofiltration filter life was similar in those who were run with heparin (68.5±7.3 h) versus those who were run heparin "free" (65.9±8.9 h; NS).

Access

One hundred percent of the children on HF had acute (non-cuffed) access, 59% on HD had acute access, and 53% of PD patients required acute access ($P<0.01$ for HF vs HD or PD). The PICU physician placed the acute

vascular access while the acute PD catheters were placed by the pediatric nephrologist [14].

Vascular access for HF or HD was preferable in the right internal jugular but the critical care physician on service at the time decided placement. The choice of acute access for HF or HD was either a 7-French dual lumen [(Bunchman coaxial or minipuncture) Cook Critical Care, Bloomington, IN, or Medcomp, Harleysville, PA], 8-French dual lumen (Quinton, Bothell, WA or Arrow International Inc., Reading, PA) or a 12-French triple lumen (Arrow International Inc., Reading, PA).

Cuffed (chronic) access was placed by the surgical staff in 41% of HD patients and 47% of the PD patients. The HD access was either an 8-French or 10-French dual lumen access (Medcomp, Harleysville, PA) while the PD access was either a single or double cuffed catheter (Quinton, Bothell, WA).

Vasopressor requirements

Vasopressor use in the PICU was based on the clinical requirements of the child. Of those children undergoing RRT, 74% were on pressors at some point while on HF, 33% were on pressors at some point of HD, and 81% were on pressors at some point of PD (P<0.05 HD vs HF or PD).

Evaluation by blood pressure at onset of RRT: correlation with survival

A review of BP at commencement of RRT revealed 33% of the children with hypotension at onset of RRT survived, 61% with normal blood pressure at onset survived and 100% of the children with high blood pressure survived (P<0.01 of high blood pressure vs normal or low). Blood pressure parameters were defined by the percentiles of <5% (hypotension), >5% – <95% (normal) and >95% (high) as defined by the Task Force on Blood Pressure for Children [13].

Survival by vasopressor use

In this ARF population, children who required vasopressor agents at any time had a 35% survival rate while children who required no use of pressors had a 89% survival rate (P<0.01; Fig. 1).

Weight at onset of RRT: correlation with survival

The mean weight of survivors was 27.9±3.7 kg vs non-survivors with 23.7±4.9 kg (NS). When one looked at survival by *RRT* and *weight* there were no differences in the weight of survivors vs non-survivors in those children undergoing HF or HD. However, there was a significant difference in children undergoing PD, with those of greater weight having a more favorable outcome (Fig. 2). Looking at the PD population, in the smaller children, there was an increase in infants with congenital heart disease. A trend toward PD occurred in the congenital heart patients due to surgical bias that at times placed PD catheters in the operating room prior to notification of nephrology.

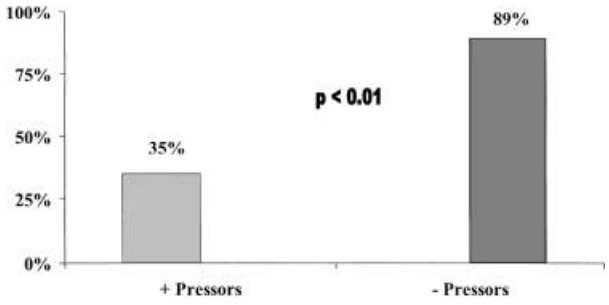

Fig. 1 Survival by analysis of vasopressor use during RRT. There was a greater survival rate in those children not requiring vasopressors any time during RRT as compared to those requiring vasopressors during RRT (P<0.01)

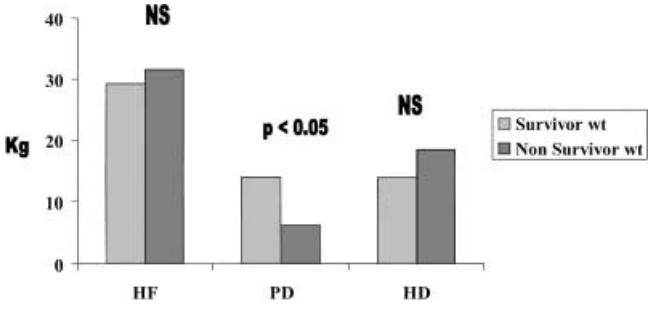

Fig. 2 Survival by weight and RRT choice. There was no difference in survival in analysis by weight of those children on HF or HD. In those children on PD, there was a significant difference in weight between survivors and non-survivors (P<0.05)

Evaluation by gender

Comparison by sex revealed that 63% of females survived while 45% of males survived (P<0.01).

Survival

The overall survival rate of children with ARF was 54%. More specifically, the survival rate of children treated with HF was 40%, with PD 49%, and with HD 81% (P<0.01 HD vs HF or PD).

Overall survival by diagnosis is noted in Table 2. A subanalysis of the 226 children with ARF revealed that children receiving HD had a higher survival rate than those receiving HF (an example of this can be seen in the BMT and sepsis population as outlined in Fig. 3). To explain this difference one needs to look at the vasopressor used by diagnosis and RRT modality. Upon review of RRT modality and disease state, patients undergoing HD

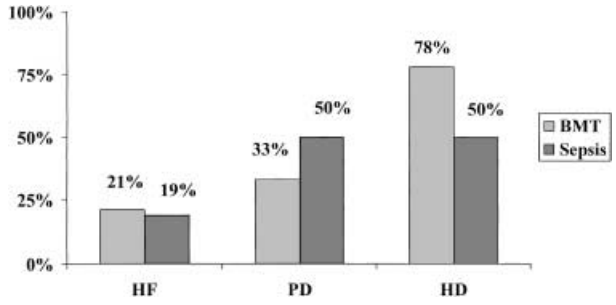

Fig. 3 Survival by diagnosis and RRT: In the bone marrow transplant (BMT) population, there was a greater survival rate in those children who required only HD as compared to PD or HF ($P<0.05$ HD vs PD or HF), while in the sepsis patients, there was poorer survival rate in those on HF as compared to PD or HD ($P<0.05$ HF vs HD or PD). This finding was consistent in all causes of ARF

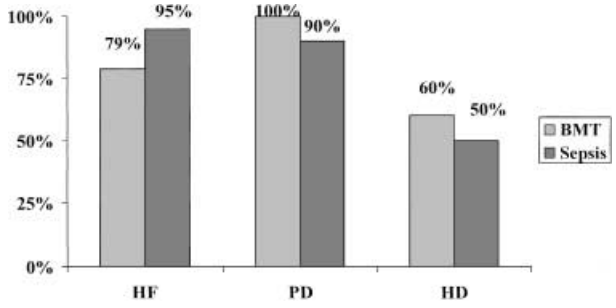

Fig. 4 Pressor use by diagnosis and RRT modality: In the BMT and sepsis population less vasopressor use occurred in those receiving intermittent HD vs those on continuous HF or PD ($P<0.01$ HD vs PD or HF in both BMT and sepsis). This finding was consistent in all causes of ARF

had much less vasopressor use than those on HF or PD (an example of this can be seen in the BMT and sepsis population as outlined in Fig. 4). The reason for less vasopressor use was not due to the HD modality but the rationale of choosing the HD modality. HD was used in patients who were deemed to have clinical hemodynamic instability that would subsequently tolerate rapid fluid shifts that occur with HD. Multivariant analysis identified the use of vasopressor agent as the greatest indicator of survival in this population.

Complications

Complication rates during RRT (e.g., hypotension, bleeding, infections) were minimal. Complications related to access for placement for HD and HF (done by the Critical Care Staff) were few. There was no evidence of pneumothorax and only one had a hemothorax. Seven cases out of the 140 (5%) requiring acute access had some bleeding around the site and 8 out of 140 (6%) had clotted accesses.

Thirty-one acute, non-cuffed, peritoneal dialysis catheters were placed by the pediatric nephrology faculty. No evidence of perforated viscus or bleeding was noted, and less than a 5% complication rate of inflow or outflow problems occurred. These were remedied by the replacement of the catheter in a different position.

No peritonitis occurred in the PD population or "line infection" in the HF or HD population although all of these children were on antibiotics at the onset of RRT, possibly affecting the relative risk of infection.

Discussion

Outcome for children requiring RRT varies throughout the world [14–18]. Reports to date have compared PD vs HF or PD vs HD and there was also a recent report by this group that looked at a retrospective outcome in HD vs HF [10, 18–20]. The outcome of children requiring RRT is usually not directly related to the RRT modality, but rather to the seriousness of the underlying illness of the patient as defined by vasopressor requirement [21]. This is similar to ARF outcome data in adults, which identify underlying diagnosis requiring RRT and evidence of MOSF (as measured by APACHE scores) as the best predictors of survival [22].

The data herein suggest that the requirement for pressors is most predictive of outcome in children. This suggests that those children with MOSF requiring pressors have a greater risk of not surviving. Rather than suggest that these patients should not be taken care of, the onus is on the clinician to learn from this experience and look for better ways to take care of these children, potentially prior to the onset of the need for pressors. Data suggest that early intervention of RRT might affect outcome, and perhaps RRT as an intervention prior to the need for pressors may make a difference in this population [23, 24]. Further, mixing and matching RRT modalities may also improve outcome. This may explain in part what appears to be an improving survival in the BMT population compared to historical reports [25].

Other factors influencing outcome are appropriate dosing of antibiotics, as well as nutritional adequacy. Nutrition has been shown to affect ARF outcome [26]. Modalities such as HF have been shown to remove nutritional components especially amino acids during ongoing therapy [12, 27]. Therefore, attention to nutrition requirements and assurance that "adequate" nutrition is given to patients undergoing RRT is important to optimize the nutritional competency for recovery.

The outcome of children requiring RRT requires a cooperative effort between the PICU and nephrology. Past and present RRT modalities such as PD or HF are often seen as the domains of either the PICU or nephrology. Other programs have developed a cooperative way to comanage patients adequately in order to ensure optimal care. Although no data are available, logically, a cooperative effort between the nephrologist and intensivist would seem most likely to result in optimal patient care.

In order to provide support for modalities, such as HF, a highly educated nursing staff is required. HF may be done only occasionally due to the relative infrequency of pediatric ARF requiring HF at many programs. If done intermit-

tently or seldomly, in some units, the expertise of nursing staff may not be as well developed, therefore potentially negatively impacting the outcome of patients. It is often in the best interest of children to be transferred to a unit (either within the hospital or perhaps to another hospital) that has nursing expertise. Alternately, a mobile well-trained nursing staff could travel to the child for HF [28].

Finally, through mutual cooperation between industry and physicians, new equipment including access and pediatric-specific HD and HF equipment has been developed and found to have had a positive impact on RRT. There may still be specific difficulties for applications in the smaller children; experience over time has proven this newer equipment to be effective [29, 30].

Summary

The outcome of children requiring RRT appears to be directly related to their underlying diagnosis as well as their requirements for pressor use. It is suggested that in some children the choice of RRT may influence outcome, yet no prospective randomized studies have been conducted for children to date to look at this question. Furthermore, attention to drug dosing, fluid management, nutritional delivery and losses during RRT, as well as overall medical care, is important in the care of children requiring RRT. We believe this can best be done cooperatively between skilled pediatric nephrologists and critical care physicians in the care of these children.

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