Pediatric Nephrology (2023) 38:3811–3821
https://doi.org/10.1007/s00467-023-06013-w

ORIGINAL ARTICLE

Long-term kidney follow-up after pediatric acute kidney support therapy for children less than 15 kg

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Received: 6 February 2023 / Revised: 24 April 2023 / Accepted: 25 April 2023 / Published online: 17 May 2023

Abstract

Background In small children, acute dialysis (pediatric acute kidney support therapy (paKST)) is increasingly used; however, it is challenging for many reasons. We compared clinical characteristics and predictors of long-term outcomes of patients < 15 kg on peritoneal dialysis (PD), hemodialysis (HD), and continuous kidney replacement therapy (CKRT).

Methods Patients with history of paKST (CKRT, HD, PD) weighing < 15 kg and ≥ 6 months of follow-up at Hacettepe University were included. Surviving patients were evaluated at last visit.

Results 109 patients (57 females) were included. Median age at paKST was 10.1 months (IQR: 2–27 months). In total, 43 (39.4%) patients received HD, 37 (34%) PD, and 29 (26.6%) CKRT. 64 (58.7%) patients died a median 3 days (IQR: 2–9.5 days) after paKST. Percentages of patients using vasopressor agents, with sepsis, and undergoing mechanical ventilation were lower in those who survived. After mean follow-up of 2.9 ± 2.1 years, 34 patients were evaluated at mean age 4.7 ± 2.4 years. Median spot urine protein/creatinine was 0.19 (IQR: 0.13–0.37) and 12 patients (35.3%) had non-nephrotic proteinuria. Three patients had estimated glomerular filtration rate (eGFR) < 90 mL/min/1.73m^2 and 2 (6%) had hyperfiltration. In total 22 patients (64.7%) had ≥ 1 kidney risk factor (elevated blood pressure/hypertension, hyperfiltration, eGFR < 90 ml/min/1.73m^2, and/or proteinuria) at last visit. Among 28 patients on paKST < 32 months, 21 had ≥ 1 risk factor (75%), whereas among 6 patients who had paKST ≥ 32 months, one patient had ≥ 1 risk factor (16.7%), (p = 0.014).

Conclusions Patients on paKST who undergo mechanical ventilation and vasopressor treatment should be followed-up more closely. After surviving the acute period, patients on paKST need to be followed-up closely during the chronic stage.

Keywords Acute dialysis · Small children · Long-term follow-up · Mechanical ventilation · Vasopressor treatment

Introduction

Pediatric acute kidney support therapy (paKST) in pediatric patients is most commonly performed for the management of acute kidney injury (AKI), in which kidney function decreases within hours or days. In addition to AKI, paKST

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can also be implemented for the elimination of toxic metabolites or an overdosed drug [1–3].

Dialysis treatment in neonates and infants is more multifaceted than in adolescents and adults. In neonates and infants, vascular access is problematic, as the size of the central venous line required for adequate blood flow is often disproportionately larger than their vascular structures [4]. When choosing the appropriate kidney replacement therapy (KRT) method for patients with low body weight and height, patient characteristics, dialysis targets, treatment team experience, and availability of equipment should be taken into consideration. Despite the increasing use of continuous KRT (CKRT) in developed countries, peritoneal dialysis (PD) and hemodialysis (HD) remain important for various scenarios [1].

In neonates and infants PD is the modality of first choice for KRT because of its inherent advantages over HD and CKRT [1]. The use of HD and CKRT in infants is limited by such technical problems as vascular access difficulty, low blood plasma volume relative to the extracorporeal circuit volume of the KRT machine, and inability to control ultrafiltration. These problems have been overcome with the development of small double-lumen vascular catheters, low extracorporeal volume dialyzers, and ultrafiltration (UF)-controlled dialysis machines [1, 5, 6]. After paKST, children are at risk for life-long kidney morbidity like chronic kidney disease (CKD) and hypertension. Therefore, data regarding long-term follow-up of patients who have had paKST is needed, as stated in a consensus statement. This issue is important as these patients continue to be followed up in pediatric nephrology centers and recently research has focused on medium and long-term sequelae of AKI, including loss of kidney function and hypertension [2, 3].

In our study, we aimed to compare the clinical characteristics of patients who had PD, HD or CKRT when weighing less than 15 kg and investigate their long-term outcomes and their predictors based on dialysis modality.

Materials and methods

Patient characteristics

Patients with a history of paKST (CKRT, HD, or PD) when weighing < 15 kg, and ≥ 6 months of follow-up at Hacettepe University, School of Medicine, İhsan Doğramacı Children's Hospital, Ankara, Turkey, between May 2013 and October 2021 were included in this retrospective cohort study. Surviving patients transferred to the pediatric wards and discharged were regularly followed up and evaluated at the last visit. Patients who had preexisting kidney problems (CKD, hypertension (HT) and/or proteinuria), who had a previous AKI and/or paKST history, and patients who had recurrent AKI and/or paKST history after discharge were not included (Fig. 1). Patient demographic and clinical data were collected from the patients' medical records. The standard mortality rate (SMR) was calculated using the Pediatric Risk of Mortality (PRISM) III score. The study protocol was approved by the Hacettepe University Clinical Research Ethics Committee (GO-20/477) and written informed consent was obtained from the parents of each patient.

CKRT, IHD, and PD procedures

All patients were treated using HD machines (B. Braun®, Dialog +, Germany). Intermittent HD (IHD) was performed in patients undergoing HD at times determined according to their clinical status. Each HD session lasted for 4 h. The numbers of HD sessions were calculated. CKRT was applied in the pediatric intensive care unit (PICU) patients in whom it was indicated, in the form of continuous venovenous hemodiafiltration (CVVHDF) with (Baxter®, Prisma Flex, USA). Central venous catheters were inserted by intensivists in the PICU under ultrasound guidance. In contrast, patients who underwent PD were treated as continuous PD. PD catheters were typically placed at bedside in the PICU patients by pediatric surgeons, versus by cardiovascular surgeons in patients following cardiac surgery. Standard PD fluids with glucose concentrations of 1.36%, 2.27%, and 3.86%, were used. The initial fill volume was 20 ml/kg and gradually increased to 30 ml/kg, if needed. The initial exchange duration, including inflow, dwell and drain times was every 60–90 min.

Data collection

Patient age, gender, height, body weight, paKST modality used, primary disease, indications for paKST, dialysis start date, dialysis duration, number of dialysis sessions performed, dialysis end date, reason for dialysis termination, dialysis complications, access route for dialysis, dialysis catheter size, and the type of dialysis solution were obtained from the patients' files. Physical examination at the last follow-up visit was performed in all surviving patients. Blood urea nitrogen (BUN), the serum creatinine and albumin levels, complete urinalysis, 24-h urine protein, and venous blood gas parameters at the last follow-up visit were evaluated.

Office blood pressure (BP) measurement was performed for each patient via the auscultation method using an appropriate cuff size on the right arm after ≥ 20 min of rest. BP was measured three times with an interval of 3 min between measurements and the average of last two was used. HT was defined as BP > 95th percentile for age, gender, and height. American Academy of Pediatrics (AAP) 2017 guidelines were used for office BP staging [7]. The SunTech AccWin Pro v3® holter device and the oscillometric

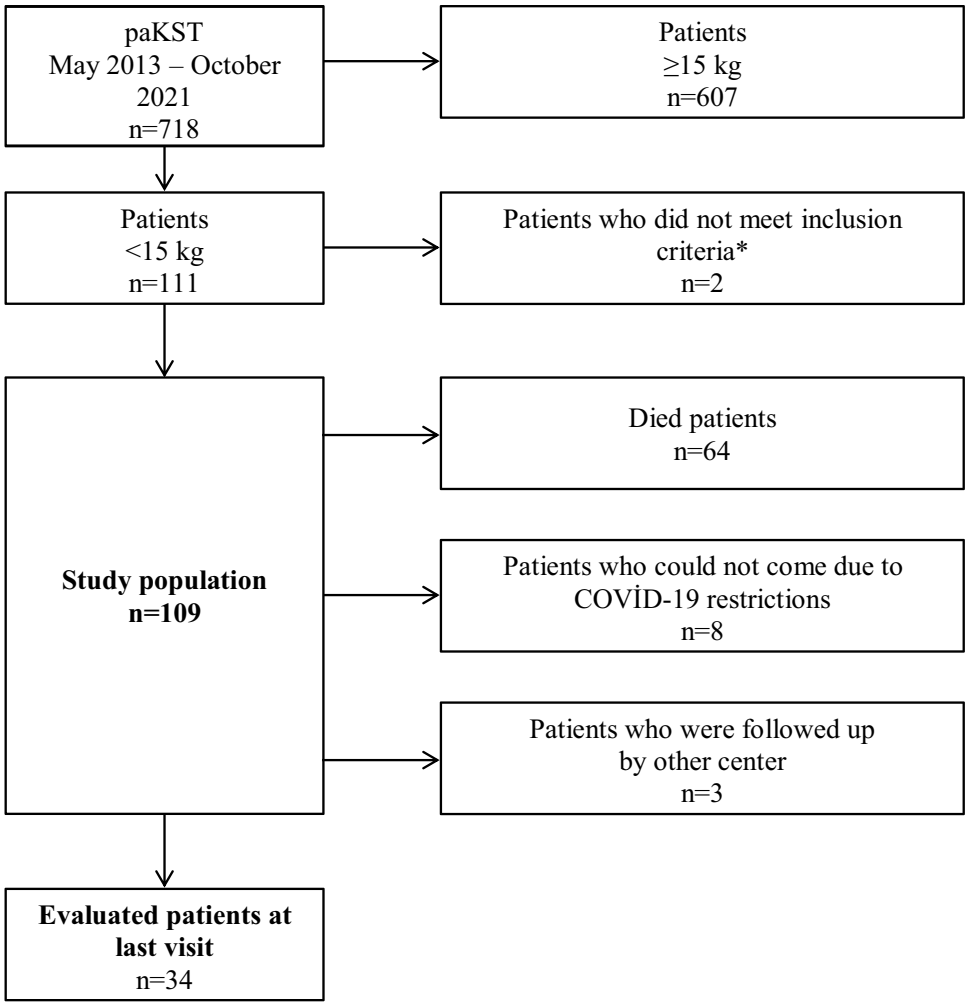

Fig. 1 The distribution of the patients in the study. (*Two patients had < 6 months follow-up duration after discharge)

method were used for 24-h BP measurement. An ambulatory BP monitoring (ABPM) device was fitted only in children aged > 5 years, using a cuff suitable for the child's non-dominant arm, so as to prevent artifacts. Children were asked to continue their usual daily activities during ABPM. BP measurements were programmed to record every 20 min during daytime and every 30 min during nighttime. A valid ABPM profile was defined as follows: 24 h recording with at least 70% of expected measurements, at least 40 to 50 readings for a 24-h period; and at least two valid daytime and one nighttime measurement per hour [8, 9]. All patients' parents were asked about their daily activities, and sleep and wake times. BP percentiles according to ABPM results were evaluated based on the values suggested by Wühl et al. [10]. Ambulatory HT was defined as a mean ambulatory systolic or diastolic BP ≥ 95th percentile (or adolescent cut points) (at last visit all patients were less than 13 years of age) [8].

The 2012 KDIGO guidelines were used to evaluate the CKD status of the patients who came for the last follow-up visit. Stage 5 CKD was defined as a glomerular filtration rate (GFR) < 15 ml/min/1.73 m^2 or the need for kidney replacement therapy (KRT) [11]. The modified Schwartz formula was used to calculate estimated GFR (eGFR). GFR values above 187 ml/min/1.73 m^2 was defined as hyperfiltration [11, 12].

Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows v.26.0 (IBM Corp. Armonk, NY). Descriptive statistics are presented as frequency (n) and percentage (%) for categorical variables, mean ± SD for normally distributed continuous variables, and median (range) and interquartile range (IQR) values for non-normally distributed variables. Pearson's chi-square test and Fisher's exact test were used to analyze the relationships between categorical variables. The Mann–Whitney U test was used to analyze the differences in non-normally distributed data between 2 independent groups, versus Student's t-test for normally distributed data. The Kruskal–Wallis test was used for non-parametric comparison of continuous variables between ≥ 3 groups, and when the difference was significant, post hoc analysis with Bonferroni correction was performed.

For parametric analysis of changes in the patients' follow-up parameters over time, the ANOVA test was performed in repeated measurements, and the differences between the measurements were determined; for significant differences pairwise comparison with Bonferroni correction was performed. When data regarding changes with respect to time were not normally distributed the Friedman test was used and for significant differences post-hoc testing with Bonferroni correction was performed. The level of statistical significance was set at $P < 0.05$.

Results

Patient characteristics

The study included 109 patients (57 females and 52 males). The median age at the time of paKST was 10.1 months (IQR: 2–27 months). In total, 43 (39.4%) patients received HD, 37 (34%) received PD, and 29 (26.6%) received CKRT. The most common underlying primary disease for which paKST was indicated was kidney and urinary system diseases (n = 32 (29.4%)). The most common kidney and urinary tract disease was hemolytic uremic syndrome (n = 16 (50%)). In this cohort, paKST was applied in 99 patients for the management of AKI and in 10 patients for the elimination of metabolites/drugs. Overall SMR was found to be 0.91 (AUC: 0.85; sensitivity: 82%; specificity: 79%) (Table 1).

Intermittent hemodialysis patients

IHD was performed in 43 patients (24 females and 19 males). The mean maximum blood flow was 117.7 ± 18 mL/min and UF was performed in 32 (74.4%) patients. Mean UF volume was 506.7 ± 216.5 mL. Priming was performed in 32 (74.4%) patients and fresh-frozen plasma (FFP) was the most common blood product used for priming (n = 23 (71.9%)), followed by packed red blood cells (PRBc) (n = 8 (25%)) and albumin (n = 1 (3.1%)). The internal jugular vein was the most common vascular access route (n = 28 (65.1%)), followed by the femoral vein (n = 10 (23.3%)) and subclavian vein (n = 5 (11.6%)). The median number of HD sessions was 3 (IQR: 2–6) (Table 2).

Table 1 General characteristics of patients according to their body weight

	< 5 kg (n = 35)	5–10 kg (n = 31)	10.1–15 kg (n = 43)	*p* value
Age (month), median (IQR)	0.2 (0.1–1.8)	10.2 (6.1–14.8)	31.4 (20.4–41.4)	**< 0.001**
Distribution according to the age, n (%)				
< 1 month	24	0	0	**< 0.001**
1–12 months	11	20	3	
12.1–24 months	0	9	12	
24.1–36 months	0	2	15	
36.1–48 months	0	0	5	
48.1–60 months	0	0	5	
60.1–72 months	0	0	2	
72.1–84 months	0	0	1	
Gender, n (%)				
Boy	21 (60)	12 (38.7)	19 (44.2)	0.19
Girl	14 (40)	19 (61.3)	24 (55.8)	
Underlying primary diseases, n (%)				
Kidney and urinary system diseases	6 (17.1)	7 (22.6)	19 (44.2)	**0.02**
Inherited metabolic diseases	3 (8.6)	4 (12.9)	4 (9.3)	0.82
Cardiac surgery	8 (22.9)	9 (29)	7 (16.3)	0.42
Oncological diseases	0 (0)	5 (16.1)	10 (23.3)	**0.01**
Prematurity	7 (28)	0 (0)	0 (0)	**< 0.001**
Sepsis	9 (25.7)	5 (16.1)	3 (7)	0.08
Other	2 (5.7)	1 (3.2)	0 (0)	0.51
Dialysis Modality, n (%)				
IHD	1 (2.9)	11 (35.5)	31 (72.1)	**< 0.001**
PD	24 (68.6)	9 (29)	4 (9.3)	
CVVHDF	10 (28.5)	11 (35.5)	8 (18.6)	

CVVHDF; continuous venovenous hemodiafiltration, *IHD*; intermittent hemodialysis, *IQR*; interquartile range, *PD*; peritoneal dialysis

Statistically significant parameters were shown in bold

Peritoneal dialysis patients

PD was performed in 37 patients (18 females and 19 males). In all, 17 (45.9%) patients were neonates at the time PD was performed. The median duration of hospitalization was 11 days (IQR: 3–31 days). Mean dwell volume was 20.1 ± 5.0 mL/kg and the median number of the sessions was 47 (IQR: 33.5–132). The most common glucose concentration of PD fluids was 1.36% (n = 27 (74%)), followed by 2.27% (n = 8 (21.6%)) and 3.86% (n = 2 (5.4%)). In total, 18 (48.6%) patients had potassium added to the PD solution. The median number of PD sessions was 47 (IQR: 34–132) (Table 2).

Continuous kidney replacement therapy patients

CKRT was performed in 29 patients (14 males and 15 females). The median age of the CKRT patients was 6.1 months (IQR: 1.9–26.2 months) and 5 (17.2%) patients were neonates at the time CKRT was performed. Priming was performed in all patients. PRBc was the most common blood product used (n = 26 (89.7%)), followed by isotonic physiological serum (n = 3 (10.3%)). The median duration at CKRT was 4 days (IQR: 2–11 days). The most frequent vascular access was ECMO tubing in tandem (n = 15 (51.7%)) and, followed by the jugular vein (n = 11 (37.9%)) and femoral vein (n = 3 (10.3%)). Standard heparin was used in all patients (Table 2).

Table 2 General characteristics of patients according to dialysis modality

	HD (n = 43)	PD (n = 37)	CVVHDF (n = 29)	*p* value
At the start of dialysis				
Age (month), median (IQR)	25.1 (15.9–34.2)	1.7 (0.1–7.8)	6.1 (1.9–26.2)	**< 0.001**
Height (cm), mean ± SD	84.7 ± 13.5	52.3 ± 13.8	64 ± 16.7	**< 0.001**
Weight (kg), median (IQR)	11 (3.4–15)	3.4 (2.1–5.7)	6 (3.9–11)	**< 0.001**
Body surface area (m^2), mean ± SD	0.5 ± 0.1	0.2 ± 0.1	0.4 ± 0.1	**< 0.001**
Gender, n (%)				
Male	19 (44.2)	19 (51.4)	14 (48.3)	0.81
Female	24 (55.8)	18 (48.6)	15(51.7)	
Primary diagnosis group, n (%)				
Kidney and urinary system diseases	20 (46.5)	10 (27)	2 (6.9)	**0.001**
Inherited metabolic diseases	4 (9.3)	3 (8.1)	4 (13.8)	0.73
Cardiac surgery	2 (4.7)	11 (29.7)	11 (37.9)	**0.001**
Oncological diseases	14 (32.6)	0 (0)	1 (3.4)	**< 0.001**
Prematurity	0 (0)	7 (18.9)	0 (0)	**0.001**
Sepsis	3 (6.9)	3 (8.1)	11 (37.9)	**0.001**
Other	0	3 (8.1)	0	**< 0.001**
Reason for dialysis termination, n (%)				
Death	5 (11.6)	17 (45.9)	20 (69)	**< 0.001**
Recovery	34 (79.1)	14 (37.8)	8 (27.6)	**< 0.001**
Complication	4 (9.3)	5 (13.5)	1 (3.4)	0.37
Dialysis complications, n (%)				
None	32 (74.4)	30 (81.1)	19 (65.5)	0.35
Hypotension	10 (23.3)	0 (0)	6 (20.7)	**0.01**
Hypokalemia	1 (2.3)	0 (0)	0	0.46
Catheter infection	0 (0)	2 (5.4)	0	0.14
Peritonitis	0 (0)	1 (2.7)	0	0.38
Catheter dysfunction	0 (0)	3 (8.1)	4 (13.8)	0.06
Intestinal perforation	0 (0)	1 (2.7)	0	0.38
paKST duration (day), median (IQR)	3 (2–6)	4 (2–6)	4 (2–11)	0.37
Hospitalization (day), median (IQR)	22 (13–37)	11 (3–31)	8 (2–25)	0.10
Use of vasopressor, n (%)	13 (30.2)	32 (86.5)	29 (100)	**< 0.001**
Use of mechanical ventilation, n (%)	15 (34.9)	35 (94.6)	28 (95.6)	**< 0.001**

CVVHDF; continuous venovenous hemodiafiltration, *IHD*; intermittent hemodialysis, *IQR*; interquartile range, *paKST*; pediatric acute kidney support therapy, *PD*; peritoneal dialysis, *SD*; standard deviation

Statistically significant parameters were shown in bold

Kidney survival

In total, 64 (58.7%) patients died a median 3 days (IQR: 2–9.5 days) after paKST. Dialysis-related mortality was observed in 1 patient (bowel perforation after PD catheter placement); the remaining causes of mortality included multiple organ failure (n = 44), cardiac arrest (n = 9), respiratory arrest (n = 8), bowel perforation secondary to necrotizing enterocolitis (n = 1), and iodine intoxication (n = 1). The median age, median body weight and length were lower in patients who did not survive. Patients who had paKST under 5 kg had higher in-hospital mortality compared to the patients 5–10 kg and 10.1–15 kg ($p < 0.001$) (Fig. 2). Moreover, the percentage of patients who used vasopressor agents, had sepsis, and underwent mechanical ventilation, was lower in the patients who survived than in those who died (Table 3).

Evaluation of patients at the last follow-up visit

After a mean follow-up period of 2.9 ± 2.1 years, 34 patients (15 females, 19 males) were evaluated at last follow-up visit (8 patients did not come for the last follow-up due to the COVID-19 pandemic restrictions and 3 patients were followed-up at other centers). The mean age at last visit was 4.7 ± 2.4 years. All patients at last visit had paKST due to AKI. The median spot urine protein/creatinine was 0.19 (IQR: 0.13–0.37). Besides, 12 patients (35.3%) had non-nephrotic proteinuria. Mean eGFR was 132.2 ± 35.4 mL/min/1.73 m^2. Three patients (unilateral nephrectomy due to Wilms tumor (n = 2) and atypical hemolytic uremic syndrome (n = 1)) had eGFR < 90 mL/min/1.73 m^2 and they were at CKD stage 2. Besides, 2 patients (6%) had hyperfiltration. At the last follow-up visit, all patients had normal serum electrolyte levels and blood gas findings. On office measurements, elevated BP was observed in five patients (14.7%) and stage 1 HT was observed in six patients (17.6%). At the time of the last follow-up visit, 15 of the patients were aged > 5 years, of which 9 patients' parents consented to 24-h ABPM and 4 of them had optimum ABPM results, of which only 1 patient had HT who had normal office measurement.

In total, 22 patients (64.7%) had at least one kidney risk factor (elevated BP/HT, hyperfiltration, eGFR less than 90 ml/min/1.73 m^2, and/or proteinuria) at the last visit. In this cohort, 13 patients (59%) had 1 risk factor, and 9 patients had 2 risk factors (41%). None of the patients had three or more risk factors. Among patients at the last visit, 28 patients had paKST less than 32 months and 6 patients had paKST older than 32 months. Among patients who had paKST less than 32 months (n = 28), 21 of them had at least one risk factor (75%). On the other hand, among 6 patients who had paKST older

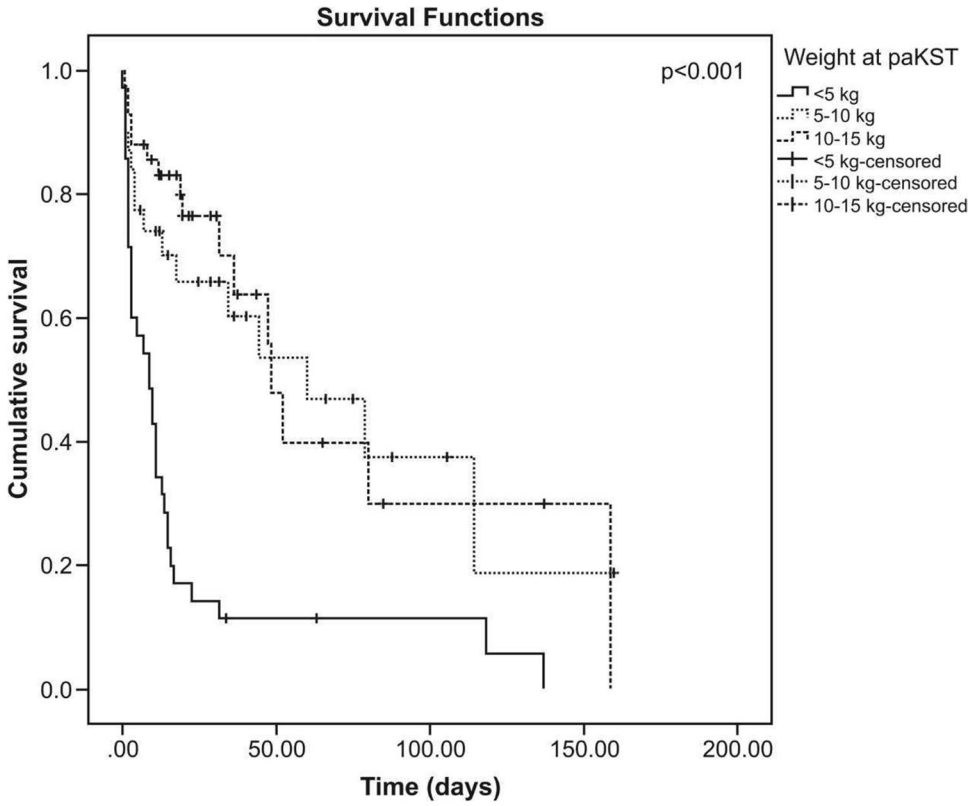

Fig. 2 Survival analysis according to the body weight groups

Table 3 General characteristics of patients according to survival

	Survivors (n = 45)	Nonsurvivors (n = 64)	*p* value
At the start of dialysis			
Age (month), median (min–max)	16.9 (0.8–55.9)	4.2 (0.1–73.9)	**< 0.001***
Height (cm), mean ± SD	79 ± 15	61.7 ± 20.2	**< 0.001***
Weight (kg), median (min–max)	10.8 (1–15)	4.8 (0.5–14.9)	**< 0.001***
Gender, n (%)			
Male	23(51.1)	29(45.3)	0.551
Female	22(48.9)	35(54.7)	
Dialysis modality, n (%)			
IHD	30(69.8)	13(30.2)	**< 0.001***
PD	11(29.7)	26(70.3)	**< 0.001**
CVVHDF	4(13.8)	25(86.2)	**< 0.001***
Primary diagnosis group, n (%)			
Kidney and urinary system diseases	20(44.4)	12(18.8)	**0.005***
Cardiac surgery	9(20)	15(23.4)	0.672
Oncological diseases	9(20)	6(9.4)	0.113
Inherited metabolic diseases	4(8.9)	7(10.9)	0.727
Prematurity and early neonatal sepsis	1(2.2)	6(9.4)	0.236
Sepsis	1(2.2)	16(25)	**0.001***
Other	1(2.2)	2(3.1)	0.689
Reason for dialysis termination, n (%)			
Recovery	42(93.4)	14(21.9)	**< 0.001***
Complication	2(4.4)	8(12.5)	0.191
Dialysis duration (day), median (min–max)	3(1–15)	4(1–136)	0.440
Presence of dialysis complications, n (%)	6(21.4)	22(78.6)	0.130
Use of vasopressor drugs, n (%)	15(20.3)	59(79.7)	**< 0.001***
Use of mechanical ventilation, n (%)	17(21.8)	61(78.2)	**< 0.001***

AKI; acute kidney injury, *CVVHDF*; continuous venovenous hemodiafiltration, *IHD*; intermittent hemodialysis, *PD*; peritoneal dialysis, *Significance holds after adjustment by age

Statistically significant parameters were shown in bold

than 32 months, one patient had at least one risk factor (16.7%). The difference is statistically significant (p = 0.014). The mean age, length, and weight of these 22 patients at paKST were 18.6 ± 6.5 months, 79 ± 10.8 cm, and 10.3 ± 2.8 kg, respectively, and these parameters were not different compared to the patients without any risk factors (p = 0.49, p = 0.96, p = 0.85, respectively). The most common paKST modality of these 22 patients was HD (n = 18, 81.8%) followed by PD (n = 4, 18.2%). None of the patients with CKRT (n = 3) had any risk factor at last visit. Among 22 patients, the most common underlying primary disease was kidney and urinary system diseases (n = 11, 50%). The underlying primary diseases, hospitalization, the dialysis durations, and mechanical ventilation/vasopressor usage were not different in patients with and without risk factor at last visit (p = 0.09, p = 0.16, p = 0.09, and p = 0.16, respectively). Other clinical characteristics of the patients are shown in Table 4.

Discussion

Although the quantity of data regarding the classification and management of AKI has increased in recent years, the optimum dialysis strategy differs from center to center worldwide. In addition, many uncertainties remain concerning dialysis in neonates and infants. The present study focused on dialysis in neonates and infants, and their long-term follow-up. Total SMR of the study group being < 1 (0.91) connotes diminished mortality for critically-ill-pediatric patients who underwent paKST.

In our cohort, small patients less than 5 kg generally had PD. In this group, primary diagnoses were sepsis and cardiac surgery which usually cause hemodynamic instability. And in our center, continuous KRT (CVVHDF) is not technically available for this group of infants. On the other hand, in our cohort, patients between 10.1–15 kg had intermittent hemodialysis (IHD). In this group, kidney and urinary system diseases and oncological diseases constitute

Table 4 Clinical characteristics of the patients at last visit

Parameters	Patients (n = 34)
Median age (months) (IQR)	51.3 (30.8–80.1)
Height (cm), (mean ± SD)	104 ± 14.9
Body weight (kg), (mean ± SD)	17.7 ± 6.5
Gender, n (%)	
Female	15 (44.1)
Male	19 (55.9)
Modality, n (%)	
IHD	24 (70.6)
PD	7 (20.6)
CKRT	3 (8.8)
Primary disease group, n (%)	
Kidney and urinary system diseases	15 (44.1)
Oncological diseases	12 (26.5)
Cardiac surgery	4 (11.8)
Prematurity	1 (2.9)
Sepsis	1 (2.9)
Others	1 (2.9)
Median spot urine/creatinine, (mg/mg) (IQR)	0.19 (0.13–0.37)
eGFR (ml/min/1.73 m^2) (mean ± SD)	132.2 ± 35.4
Patients with at least one risk factor, n (%)	22 (64.7)
HD	18 (52.9)
PD	4 (11.8)
CKRT	0
Elevated BP/Hypertension, n (%)	12 (35.3)

CKRT; continuous kidney replacement therapy, *IHD*; intermittent hemodialysis, *IQR*; interquartile range, *PD*; peritoneal dialysis, *SD*; standard deviation

approximately 70% of the whole group. These two types of diseases usually have minimal effects on hemodynamic stability, in contrast to sepsis or cardiac surgery. For patients 5–10 kg, the distribution of KRT preferences is approximately equivalent to each other. Besides, our study was based on a retrospective cohort, the choice of the attending physician and the feasibility of the technical equipment are other factors which affect the differences in KRT types.

The etiology and outcome of AKI in our country was evaluated by Duzova et al. [13]. In that study, 472 pediatric patients were evaluated and 32.6% of the patients were newborns. The most common medical conditions were prematurity and congenital heart disease [13]. In North America CKRT has become the preferred dialysis modality for critically ill pediatric patients [14, 15]. Guzzo et al. [16] conducted a survey of 35 European pediatric nephrology centers to investigate acute dialysis (AD) practices in pediatric patients with AKI. The centers collected 891 patients per year and AKI was the most common (70%) cause. Moreover, 20% of the patients underwent AD for systemic infection, SIRS, or ARDS, without AKI, versus 10% for the removal of toxic metabolites during metabolic crises secondary to inborn errors of metabolism. Cardiac surgery was the most common primary diagnosis. In the present study, AKI was a more frequent (90%) indication for paKST compared to that reported by Guzzo et al. [16]. Besides, kidney and urinary system diseases were the most common indications for AD (29.4%). In Guzzo et al.'s study PD and CKRT were the 2 most commonly used dialysis modalities, whereas in the present study HD was the most commonly used KRT [16]. Similar to the Guzzo et al. study, the internal jugular vein was the most common vascular access site for extracorporeal dialysis in the present study's HD patients. Furthermore, in the present study CVVHDF was the most common CKRT modality and heparin was the most commonly used anticoagulant (used in all CKRT patients), as reported by Guzzo et al. [16]. The prognosis of CKRT patients has also changed in recent years. Chen evaluated their experience in CKRT in 289 critically-ill children with a median age of 4 years. They reported that the survival rate of patients has improved over past 10 years [17].

In an earlier study, Sadowski et al. [5] reported their HD experience in 33 infants with a median weight of 3.5 kg at the time dialysis was initiated. Technical problems, such as inadequate blood flow and clotting, were observed in 45% of their patients. Additionally, their mortality rate was 48%. In contrast, in the present study median weight was much higher (11 kg) at the time dialysis was initiated and the mortality rate was much lower (30.2%). Both the size of the patients and technical improvements may have contributed to the difference in mortality. Raina et al. [2] performed a systemic review of studies on HD in infants aged < 12 months. The mean age of the infants was 4.2 months and their weight at the initiation of HD varied from 0.7 kg to 11.8 kg. They reported that the infant survival rate varied from 50 to 100%. In the present study the median age and weight of the HD patients were 25.1 months and 11 kg, respectively, and the overall survival rate was 69.8%. The fact that the present study's patients were older and weighed more than those in Raina et al.'s [2] study may explain the difference in mortality between the two studies.

In the present study, 68.6% of the patients weighing < 5 kg underwent PD and among the PD study cohort ~ 50% of the patients were neonates. Akbalık-Kara et al. investigated the indications and outcomes of PD in 67 full-term neonates and reported that the most common indication for PD was inborn errors of metabolism [18]. Among the present study's PD patients, cardiac surgery was the most common indication for PD. In Akbalık-Kara et al.'s study the mortality was 49.2%, versus 45.9% in the present study [18]. Although ~ 50% of the present study's PD patients were neonates, the mortality rate did not differ significantly between the two studies. Akbalık-Kara et al. [18] excluded premature

neonates from their study, and the weight and height of the patients were similar to those in the present study, which may account for the similarity of the mortality rate in both studies. In the present study, the mortality rate in the PD patients was higher than that in the HD patients, and the difference might have been due to the comorbidities observed in the PD patients.

Garzotto et al. [19] studied 26 neonates and young infants who underwent 165 CKRT sessions. Patient median age and weight were 1 day and 2.9 kg, respectively, versus 6.1 months and 6 kg, respectively, in the present study. In addition, they reported that cardiac disease was the most common primary diagnosis, followed by sepsis. Similarly, in the present study cardiac surgery and sepsis were the two most common diagnoses. All of Garzotto et al.'s [19] patients were critically ill; 58% received ventilatory support and 27% were vasopressor dependent. In contrast, the mechanical ventilation rate (95.6%) and the vasopressor usage rate (100%) in the present study were much higher, which may be considered indicative of poor prognosis. In accordance, the mortality rate in the present CKRT patients (69%) was much higher than that reported by Garzotto et al. [19]. In our cohort, approximately 70% of PD patients and 90% of CKRT patients did not survive. Among the present study's patients who did not survive following paKST, the rates of sepsis, use of vasopressor drugs, and mechanical ventilation were higher than in those who did survive; therefore, patients undergoing paKST that weigh < 15 kg need to be followed up closely to prevent mortality. Infection and sepsis are well-known risk factors for AKI. However, a growing body of evidence suggests that AKI is also a risk factor for sepsis [20]. Therefore, patients who had sepsis, mechanical ventilation, and vasopressor treatment should be cared for more closely regarding the higher mortality. Selewski et al. [21] showed that the development of AKI (KDIGO stage 3) yielded 4.2 additional days under mechanical ventilation.

Animal models show there is a link between AKI and CKD, including triggers of chronic fibrosis and permanent nephron loss, which cause hyperfiltration-mediated damage [22]. Several studies report that children with AKI have a higher incidence of long-term CKD and HT than the general pediatric population [23–25]. A prospective study of 277 children showed that stage 2 or worse AKI during PICU admission is associated with a sixfold increased risk of CKD or pre-hypertension, based on a 6-year follow-up [26]. Unfortunately, data concerning the long-term effects of dialysis in patients weighing < 15 kg are scarce. Akkoc et al. evaluated long-term follow-up of patients after AKI in neonatal period. In this cohort, 9.7% of the patients had KRT. Approximately, one third (33.8%) of the patients had at least one of either microalbuminuria, office hypertension, or hyperfiltration [27].

In present study, after a mean follow-up period of ~ 3 years, 64.7% of the patients had at least one risk factor (elevated BP/HT, hyperfiltration, GFR less than 90 ml/min/1.73 m^2 and/or proteinuria). In the literature, there are scarce data about the long term effects of paKST in small children. Alao et al. [28] studied 29 children with an age range of 5 months–16 years who had acute PD. The 18-month-survival was 66% and 14 patients were evaluated at last visit. Among them, six (42.9%) had fully recovered kidney function, while 8 (57.1%) progressed to CKD. Our PD cohort had a smaller age group and 57.1% of patients had one kidney risk factor at last follow-up visit. Robinson et al. [29] evaluated long-term kidney outcomes following dialysis-treated childhood AKI. They included 1688 pediatric dialysis-treated AKI survivors (median age 5 years) and 6752 matched comparators. Similar to our study, in the patient cohort, 44.3% of patients had PD, 32.8% had HD and 23% had CKRT. The follow-up duration of dialysis-treated AKI-survivors was longer than our cohort (9.1 years). In this cohort, HT and CKD occured in 12.1% and 13.1% of the patients respectively. In our cohort, the rate of CKD was 8.8% (n = 3). The follow-up duration of our patients was shorter than this study and this may explain the lower rate of CKD in our cohort.

The most important limitation of the present study is its small sample who presented for the last follow-up visit, at which time only 33% of the patients could be evaluated. A total of 11 surviving patients could not be assessed at last visit due to various reasons and this may have affected the evaluation of kidney parameters. Beyond mortality in the acute period, the COVID-19 pandemic had an effect on this issue. In all, 9 of the present study's patients underwent 24-h ABPM, of which 4 had optimum ABPM results. The age of the patients precluded performing optimum 24 h-ABPM. Additionally, other parameters, including cognitive and mental functions, were not investigated.

In conclusion, the use of paKST modality depends on many factors and should be tailored according to each patient's needs. Patients on mechanical ventilation and vasopressor treatment should be followed-up more closely for in-hospital mortality. After surviving the acute period, paKST patients need to be followed-up closely during the chronic stage. In patients who survive the acute period, long-term follow-up can reveal such kidney sequelae as HT and proteinuria.

Supplementary information The online version contains supplementary material available at https://doi.org/10.1007/s00467-023-06013-w.

Acknowledgements This study was based on the thesis in pediatrics of the first author.

Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Ömer Nazım Gülçek, Bora Gulhan, Selman Kesici, Eda Didem Kurt Şükür, Mutlu Hayran, Fatih Ozaltin, Ali Duzova, Benan Bayrakçı, Rezan Topaloglu. The first draft of the manuscript was written by Ömer Nazım Gülçek, Bora Gulhan and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose. No funding was received for conducting this study. The study protocol was approved by the Hacettepe University Clinical Research Ethics Committee (GO-20/477 and 2020/12-30) and written informed consent was obtained from the parents of each patient.

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