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Survival and clinical outcomes of children starting renal replacement therapy in the neonatal period

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End-stage renal disease requiring renal replacement therapy (RRT) during the neonatal period is a very rare condition, and little information is available regarding long-term RRT and outcomes. To gain more information, we performed a collaborative study on patient characteristics and treatment outcomes in children who started RRT as neonates during their first month of life between 2000 and 2011 who were prospectively registered in the ESPN/ERA-EDTA, the IPPN (since 2007), the Japanese registry, or the Australian and New Zealand Dialysis and Transplant (ANZDATA) registry. During the first month of life, 264 patients from 32 countries started RRT and were followed for a median of 29 months (interquartile range 11–60 months). Most neonates (242) started on peritoneal dialysis, 21 started on hemodialysis, and 1 patient with a transplant. The most important causes of renal failure were congenital anomalies of the kidney and urinary tract in 141, cystic kidneys in 35, and cortical necrosis in 30. Within 2 years after the start of RRT, 69 children changed dialysis modality and 53 received a renal transplant. After a median of 7 months, 45 children had died, mainly because of infection, resulting in an estimated 2-year survival of 81%, and 5-year survival of 76%. Growth retardation (63%), anemia (55%), and hypertension (57%) were still major problems after 2 years. Thus, relatively good medium-term patient survival may be achieved with RRT started during the neonatal period, but specific therapeutic challenges continue to exist in this age group.

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Although the need for renal replacement therapy (RRT) for end-stage renal disease in children less than 2 years of age occurs at an incidence of 7.1–8.3 per million age-related population (pmarp) (Orr *et al.*[1] and ESPN/ERA-EDTA registry, personal communication), the number of neonates requiring RRT is extremely small. Issues with children who start RRT in the first month of life are different from those who start at a later stage. A comparison between neonates and children who start RRT between the age of 1 month and 2 years revealed similar race and gender distributions but different causes of renal failure, different treatment options, and a higher rate of hospitalization.[2] In another small study, no differences were found with respect to height or body weight s.d. scores.[3] A particular problem with assessing the demographics of end-stage renal disease in this age group is that RRT is not offered to all children in whom it might be required.[4]

Decisions concerning starting RRT in neonates are based on local resources and background, patient comorbidities, anticipated quality of life, and family acceptance.[5] Improvement of technology together with evolving social acceptance of disabilities has led to significant changes in medical and ethical decision-making during the past decades. In a recent international survey, 98% of pediatric nephrologists offered RRT at least in some infants younger than 1 month of age, and 30% offered treatment to all infants with end-stage renal disease.[6] In a previous survey from the same authors in 1998, 80% of pediatric nephrologists considered that parental rights to refuse RRT for their child were acceptable.[4] In another survey among French-speaking pediatric intensivists

and nephrologists in 2001, starting RRT in neonates was well accepted in only 9% of neonatal units and systematically rejected by 24%; 24% of the neonatal units were moderately in favor of starting RRT, whereas 35% preferred treatment withdrawal.[7] Quality of life, family circumstances, parental rights, and the child's prognosis are the main criteria applied in decision-making.[8]

To make an informed judgment, for both the attending physicians and the patient's family, information on the future prospects of these children is essential and requires up-to-date, unbiased outcome data from a large group of patients. To overcome the challenge of the low incidence of neonatal RRT, we performed a collaborative study on patient characteristics and treatment outcomes in children who started RRT at neonatal age. We undertook an unprecedented global effort to obtain a sufficiently sized, representative and recent patient sample for analysis, combining data from national and international pediatric RRT registries covering 40 countries.

RESULTS

A total of 264 patients (64.8% male) from 32 countries started RRT during the first month of life. Including data from those countries in which no neonates were started on RRT but which had complete population-wide coverage for a particular period, neonates represented 18.3% of the population of infants (<2 years) among Western European countries, 18.1% among Eastern European countries, whereas this was 6.8% in Australia and New Zealand and 8.6% of all <5-year-olds in Japan.

Half of the neonates started RRT in their first week of life (51%). The most common causes of renal failure were congenital anomalies of the kidney and urinary tract (CAKUT, 54.6%), followed by cystic kidneys (13.3%, of which 80% autosomal recessive polycystic kidney disease (ARPKD) and the remainder medullary cystic kidney disease) and cortical necrosis (11.4%) (Table 1). The first RRT modality was peritoneal dialysis (PD) in 91.7%, whereas 8.0% of neonates started on hemodialysis (HD), and a single patient (0.4%) started with a transplant. There were no marked differences with respect to gender, cause of renal failure, or week of start between the patients starting with PD versus HD.

Patients were followed up for a median of 28.6 (interquartile range 11–60) months. During 2 years of follow-up 45 patients died, resulting in a 2-year survival rate of 81.2% (Figure 1). All patients, besides four, died on dialysis. The 5-year survival rate was 76.4%. Among the patients who died during the first 2 years, the median time to death was 7.2 months (interquartile range 3–10 months), and all patients except 7 died in the first year of life. The main causes of death were infection ($n=16$, 35.6%) and cardiac arrest ($n=4$, 8.9%), but they were unknown in many cases (Table 2). There were no significant differences in the risk of death regarding week of RRT initiation, initial treatment modality, gender, underlying renal disease, birth weight, registries, and countries. Whereas the overall survival rate was independent of the presence or absence of comorbidities, concomitant neurological disorders increased the risk of death fivefold (hazard ratio 5.2, 95% confidence interval 1.7–15.4, $P=0.003$).

During the first 2 years of life, 39.4% of the patients switched the treatment modality (excluding death and recovery of renal function). The treatment distribution every 6 months between 0 and 5 years is shown in Figure 2a, whereas the first two changes in treatment modality are depicted in Figure 2b. Forty-five patients received a transplant within the first 2 years after birth (Figure 1),

Table 1 | Patient characteristics at the start of RRT

	Patients, $N=264$ (%)
Data source	
ESPN/ERA-EDTA registry	202[a]
IPPN	60[a]
Japan	18
ANZDATA	4
Age at start of RRT	
Days 1–7	141 (53.4%)
Days 8–14	57 (21.6%)
Days 15–21	32 (12.2%)
Days 22–31	34 (12.9%)
Gender	
Male	171 (64.8%)
Treatment modality at the start of RRT	
PD	242 (91.7%)
HD	21(8.0%)
Tx	1 (0.4%)
Primary disease	
Congenital anomalies of the kidney and urinary tract	144 (54.6%)
Cystic kidney disease	35 (13.3%)
Cortical necrosis	30 (11.4%)
Renal vascular disease	9 (3.4%)
Congenital nephrotic syndrome	15 (5.7%)
Hemolytic uremic syndrome	3 (1.1%)
Angiotensin-receptor blockade fetopathy	3 (1.1%)
Oxalosis	2 (0.8%)
Other not specified	23 (8.7%)

Abbreviations: HD, hemodialysis; PD, peritoneal dialysis; RRT, renal replacement therapy; Tx, transplantation.
[a]20 Patients are in both registries.

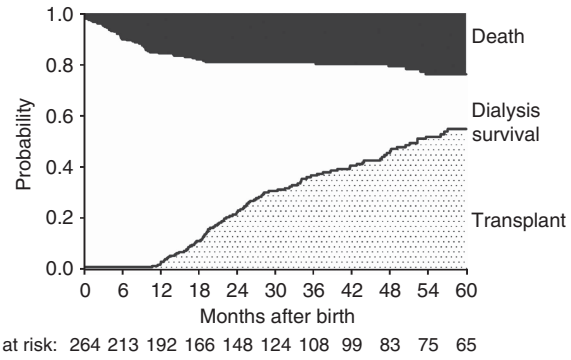

Figure 1 | Survival after the start of renal replacement therapy (RRT), and the probability of getting a transplant.