

Recovery of Kidney Function in Children Treated with Maintenance Dialysis

Marjolein Bonthuis,¹ Jérôme Harambat,² Etienne Bérard,³ Karlien Cransberg,⁴ Ali Duzova,⁵ Liliana Garneata,⁶ Maria Herthelius,⁷ Adrian C. Lungu,⁸ Timo Jahnukainen,⁹ Lukas Kaltenegger,¹⁰ Gema Ariceta,¹¹ Elisabeth Maurer,¹² Runolfur Palsson,¹³ Manish D. Sinha,¹⁴ Sara Testa ,¹⁵ Jaap W. Groothoff,¹⁶ Kitty J. Jager,¹ and on behalf of the ESPN/ERA-EDTA Registry

Abstract

Background and objectives Data on recovery of kidney function in pediatric patients with presumed ESKD are scarce. We examined the occurrence of recovery of kidney function and its determinants in a large cohort of pediatric patients on maintenance dialysis in Europe.

Design, setting, participants, & measurements Data for 6574 patients from 36 European countries commencing dialysis at an age below 15 years, between 1990 and 2014 were extracted from the European Society for Pediatric Nephrology/European Renal Association-European Dialysis and Transplant Association Registry. Recovery of kidney function was defined as discontinuation of dialysis for at least 30 days. Time to recovery was studied using a cumulative incidence competing risk approach and adjusted Cox proportional hazard models.

Results Two years after dialysis initiation, 130 patients (2%) experienced recovery of their kidney function after a median of 5.0 (interquartile range, 2.0–9.6) months on dialysis. Compared with patients with congenital anomalies of the kidney and urinary tract, recovery more often occurred in patients with vasculitis (11% at 2 years; adjusted hazard ratio [HR], 20.4; 95% confidence interval [95% CI], 9.7 to 42.8), ischemic kidney failure (12%; adjusted HR, 11.4; 95% CI, 5.6 to 23.1), and hemolytic uremic syndrome (13%; adjusted HR, 15.6; 95% CI, 8.9 to 27.3). Younger age and initiation on hemodialysis instead of peritoneal dialysis were also associated with recovery. For 42 patients (32%), recovery was transient as they returned to kidney replacement therapy after a median recovery period of 19.7 (interquartile range, 9.0–41.3) months.

Conclusions We demonstrate a recovery rate of 2% within 2 years after dialysis initiation in a large cohort of pediatric patients on maintenance dialysis. There is a clinically important chance of recovery in patients on dialysis with vasculitis, ischemic kidney failure, and hemolytic uremic syndrome, which should be considered when planning kidney transplantation in these children.

Clin J Am Soc Nephrol 13: 1510–1516, 2018. doi: <https://doi.org/10.2215/CJN.01500218>

Introduction

ESKD is defined as a state of very low GFR in combination with uremic symptoms or overhydration, necessitating chronic kidney replacement therapy. Although ESKD is presumed to describe an irreversible loss of kidney function, a small percentage of patients requiring maintenance dialysis experience enough recovery of their kidney function to come off dialysis. Most studies in this field have been performed in single centers or adult patients (1–8). Single-center studies have reported recovery rates of 3%–6% (9), whereas a few larger registry studies in adults in Australia and New Zealand showed that kidney function recovery occurred in 1%–2% of patients commencing maintenance dialysis (3,6). A recent large study in patients in the United States even showed a recovery rate of 7% (7). These different recovery rates are likely to be the result of variable definitions or different periods of follow-up.

Reasons for recovery of kidney function are not completely clear, but in adults the underlying kidney disease appeared to be the sole predictive factor (9). Studies in children are scarce and limited to case reports (2) or to studies in patients with AKI (10,11). Hence, kidney function recovery rates among children whose kidney failure was perceived as chronic are not known. As causes of kidney failure in children are entirely different from those in adults, it is unknown to what extent underlying kidney diseases in children with ESKD are associated with late recovery of kidney function resulting in a nondialysis-dependent level of kidney dysfunction. This is of clinical importance as, particularly in children, early kidney transplantation is regarded as the optimal mode of kidney replacement therapy. We hypothesized that if certain diseases tend to have a greater likelihood of delayed recovery of kidney function, there might be an indication to deviate from this early transplantation

Due to the number of contributing authors, the affiliations are listed at the end of this article.

Correspondence: Dr. Marjolein Bonthuis, ESPN/ERA-EDTA Registry, Department of Medical Informatics, Academic Medical Centre, University of Amsterdam, PO Box 22700, 1100 DE Amsterdam, The Netherlands. Email: m.bonthuis@amc.uva.nl

strategy. Therefore, we aimed to investigate if another strategy would be justified in certain cases by using a large population-based cohort of European children on maintenance dialysis included in the European Society for Pediatric Nephrology/European Renal Association-European Dialysis and Transplant Association (ESPN/ERA-EDTA) Registry. Moreover, we aimed to study the likelihood and determinants of kidney function recovery.

Materials and Methods

Data Source and Study Population

The ESPN/ERA-EDTA Registry was established in 2007 to consolidate data collected by European population-based national renal registries on children with ESKD treated with kidney replacement therapy. Data are collected annually in a standardized manner on various patient- and treatment-related characteristics, and are subject to regular data quality checks both on the national and on the Registry level (12). Included patients are presumed to have ESKD and to undergo maintenance dialysis only. Core data are mandatory for participation in the Registry and are collected for every patient, including date of birth, sex, primary kidney disease, date and treatment modality at onset of kidney replacement therapy, all subsequent changes in treatment modalities, and date and cause of death. We included all patients from 36 countries, starting dialysis between 1990 and 2014, at an age below 15 years, as older children may be treated in treatment centers for adult patients.

The periods of contribution to the Registry differed by country and are included in Supplemental Table 1, along with the number of patients who experienced a recovery of kidney function. Most countries provided data from 2007 to 2014. Patients from Germany were excluded because data on dialysis and transplanted patients are derived from different sources that could not be linked.

The national legislation with regards to ethics committee approval and patient informed consent was followed for all national registries providing data to the ESPN/ERA-EDTA Registry.

Study Outcome

Events were coded according to European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) event type codes, including hemodialysis, peritoneal dialysis, transplantation, graft failure, recovery of kidney function, death, transfer out of registry, lost to follow-up, and limited care/stopped treatment (without recovery of kidney function) (13).

Recovery of kidney function was defined as the registration of discontinuation of dialysis therapy in nontransplanted patients for a period of at least 30 days.

Definition of Variables

Causes of kidney failure were categorized into ten categories according to the ERA-EDTA primary kidney disease coding system adapted for children (13), including a missing/unknown category. Patients were divided into the following age categories: 0–1, 2–5, 6–11, and 12–14 years. There were no missing values for patient-related variables, as the variables used in this study are all part of the core data set. Being part of the voluntary data collection,

eGFR was only available for a limited number of subjects from 27 countries and was calculated with the bedside Schwartz equation (14).

Statistical Analyses

Data are presented as numbers and percentages for categorical variables or as median and interquartile range (IQR) for continuous variables. Baseline characteristics of patients recovering kidney function were compared with patients staying on kidney replacement therapy using chi-squared tests and Kruskal–Wallis tests for categorical and continuous variables, respectively.

We used a cumulative incidence competing risk approach, taking into account the competing risks of kidney transplantation or death, to study the unadjusted time to recovery (15). Cox proportional hazard models with country as a random effect were used to estimate the factors associated with recovery of kidney function, adjusting for potential confounders (16), including age, sex, and primary kidney disease. Follow-up time was censored at 2-years after commencement of dialysis, patient death, kidney transplantation, loss to follow-up, or end of study period (December 31, 2014), whichever came first. The proportional hazards assumption was investigated graphically for all variables and was not violated.

To test whether patients recorded in the Registry were on maintenance instead of acute dialysis, we performed a sensitivity analysis excluding patients on dialysis for <90 days.

Results

Patient Characteristics

Characteristics of the 6574 patients commencing dialysis between 1990 and 2014 are depicted in Table 1. The majority of patients were boys (56%), started on peritoneal dialysis (58%), and one third had congenital anomalies of the kidney and urinary tract (CAKUT) as the cause of kidney failure. Median age at dialysis initiation was 8.2 (IQR, 2.6–12.2) years.

Recovery of Kidney Function 2 Years after Dialysis Onset

Two years after dialysis onset, 130 (2%) patients had experienced recovery of their kidney function, allowing discontinuation of dialysis (Figure 1). Seven patients (0.2%) were lost to follow-up during the study period and 2-year mortality risk was 5%. A flow chart of patients is shown in Supplemental Figure 1. The 2-year crude recovery rate was 15.8 per 1000 patient-years at risk.

A substantial proportion of patients experiencing kidney function recovery was below 2 years of age ($n=43$; recovery rate of 3%), including 19 patients who commenced dialysis in the neonatal period (first month of life; 8% of all neonates commencing dialysis).

eGFR at start of dialysis was reported for a subset of patients only, and was comparable in patients with recovery of kidney function (median, 9.0 [IQR, 6.3–13.0] ml/min per 1.73 m², $n=33$) and those remaining on kidney replacement therapy (median, 7.9 [IQR, 6.0–10.5] ml/min per 1.73 m², $n=2635$) ($P=0.14$).

Among those who experienced recovery, median time to recovery was 5.0 (IQR, 2.0–9.6; range, 0.03–22.9) months. Most patients had a recovery soon after commencing

Table 1. Characteristics of European pediatric patients commencing maintenance dialysis between 1990 and 2014

Characteristic	All (n=6574), N (%)
Boys	3699 (56)
Dialysis modality at onset	
Hemodialysis	2662 (41)
Peritoneal dialysis	3828 (58)
Unknown dialysis	84 (1)
Age at dialysis onset, yr	
Median (IQR)	8.2 (2.6–12.2)
0–1	1429 (22)
2–5	1183 (18)
6–11	2235 (34)
12–14	1727 (26)
Primary kidney disease	
CAKUT	2308 (35)
GN	1161 (18)
Cystic kidney disease	730 (11)
Hereditary nephropathy	500 (8)
Ischemic kidney failure	121 (2)
Hemolytic Uremic Syndrome	330 (5)
Metabolic disorders	227 (4)
Vasculitis	136 (2)
Miscellaneous	614 (9)
Missing, unknown	447 (7)
Period of dialysis onset	
1990–1999	1761 (27)
2000–2009	2964 (45)
2010–2014	1849 (28)
eGFR at dialysis onset	n=2635
Median (IQR), ml/min per 1.73 m ²	7.9 (6.0–10.5)

IQR, interquartile range; CAKUT, congenital anomalies of the kidney and urinary tract.

dialysis, with a gradual decrease in the number of patients who experienced a recovery thereafter. Overall, 57% of the patients who recovered their kidney function did so within 6 months after commencing dialysis. Still, 16% (n=21) experienced a recovery of kidney function beyond 12 months of dialysis initiation (“late” recovery). Comparison of the characteristics of patients experiencing recovery of their kidney function within or beyond 12 months of dialysis initiation did not demonstrate statistically significant differences, except a significantly higher number of patients commencing dialysis on peritoneal dialysis in the late recovery group (71% versus 40%) (P=0.009).

Duration of Kidney Function Recovery

Of the patients experiencing a recovery of kidney function, 32% (n=42) had to resume kidney replacement therapy after a median recovery time of 19.7 (IQR, 9.0–41.3) months. Of these patients, ten (24%) returned to hemodialysis, ten (24%) to peritoneal dialysis, and 22 patients (52%) received a kidney transplant.

None of the patient characteristics were significantly associated with returning to kidney replacement therapy after recovery of kidney function (data not shown).

Determinants of Kidney Function Recovery

Patients commencing dialysis before the age of 2 years had a higher likelihood of recovery than older patients

(Table 2). Several primary kidney disease groups were associated with a higher likelihood of recovery. Compared with patients with CAKUT, those with ischemic kidney failure (12% recovery; adjusted hazard ratio [aHR], 11.4; 95% confidence interval [95% CI], 5.6 to 23.1), hemolytic uremic syndrome (HUS) (13% recovery; aHR, 15.6; 95% CI, 8.9 to 27.3), and vasculitis (11% recovery; aHR, 20.4; 95% CI, 9.7 to 42.8) were more likely to experience a recovery of kidney function, independent of age, sex, and country.

Compared with peritoneal dialysis, starting maintenance dialysis on hemodialysis was associated with a shorter time to kidney function recovery. Patients initiating dialysis after 2010 were more likely to achieve recovery of their kidney function than patients commencing dialysis between 2000 and 2009 (aHR, 1.6; 95% CI, 1.1 to 2.5). This association was even stronger when considering only countries participating throughout the follow-up period (aHR, 3.1; 95% CI, 1.4 to 6.9).

Primary Kidney Disease

When stratifying our analyses by primary kidney disease, patients with vasculitis who started dialysis after 2010 were more likely to demonstrate recovery than patients with vasculitis who started dialysis between 2000 and 2009 (aHR, 5.1; 95% CI, 1.3 to 20.5). No other clinically relevant associations were found between patient characteristics and likelihood of recovery in analyses stratified by primary kidney disease.

The cumulative incidence of kidney function recovery over time differed by cause of kidney failure (Figure 2). Patients with HUS showed the highest chance to recover in the first months after dialysis initiation, with a gradual decrease thereafter. Chance of recovery for patients with ischemic kidney failure was also highest in the first months on dialysis, whereas in the following months around 1%–3% of the patients experienced recovery. For patients with vasculitis, chance of recovery was stable around 3% in the first 9 months after dialysis onset and fewer patients experienced a recovery thereafter.

Sensitivity Analyses

Among the 130 patients who experienced recovery of their kidney function, 82 patients were on maintenance dialysis for at least 90 days. Analysis of these 82 patients yielded similar results. Two-year recovery rate was slightly lower (1.4%), but patients with ischemic kidney failure

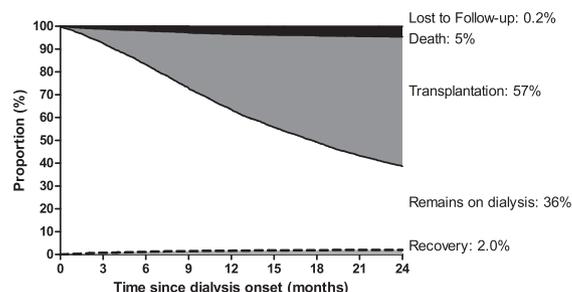


Figure 1. | Two-percent of recovery of kidney function after two years on maintenance dialysis, and the competing risks death, lost to follow-up, and kidney transplantation.

Table 2. Two-year recovery of kidney function among patients who started maintenance dialysis

Characteristic	Full Cohort			Excluding Patients Who Experienced Recovery before 90 d on Dialysis		
	N (%) ^a	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	N (%)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Recovery	130 (2)			82 (1.4)		
Sex^b						
Boys	67 (2)	1.0 (ref)	1.0 (ref)	37 (1)	1.0 (ref)	1.0 (ref)
Girls	63 (2)	1.2 (0.8 to 1.7)	1.3 (0.9 to 1.8)	45 (2)	1.6 (1.0 to 2.4)	1.3 (0.9 to 1.8)
Dialysis modality at onset^c						
Hemodialysis	71 (3)	1.7 (1.2 to 2.5)	2.1 (1.4 to 3.0)	42 (2)	1.6 (1.0 to 2.4)	1.7 (1.1 to 2.8)
Peritoneal dialysis	59 (2)	1.00 (ref)	1.0 (ref)	40 (1)	1.0 (ref)	1.0 (ref)
Age at dialysis onset, yr^d						
Median (IQR)	5.2 (1.0–11.0)	2.0 (1.2 to 3.4)	2.4 (1.4 to 4.3)	5.6 (1.5–10.5)	1.7 (0.9 to 3.4)	2.2 (1.1 to 4.7)
0–1	43 (3)	1.9 (1.1 to 3.3)	1.7 (0.9 to 3.1)	25 (2)	1.9 (0.9 to 3.8)	1.7 (0.8 to 3.7)
2–5	29 (3)	1.3 (0.8 to 2.2)	1.4 (0.8 to 2.5)	18 (2)	1.6 (0.8 to 3.0)	1.7 (0.9 to 3.4)
6–11	36 (2)	1.0 (ref)	1.0 (ref)	26 (1)	1.0 (ref)	1.0 (ref)
12–14	22 (1)			13 (1)		
Primary kidney disease^e						
CAKUT	19 (0.8)	1.0 (ref)	1.0 (ref)	14 (0.7)	1.0 (ref)	1.0 (ref)
GN	11 (1)	1.0 (0.5 to 2.1)	1.2 (0.6 to 2.5)	6 (0.6)	0.8 (0.3 to 2.0)	0.8 (0.3 to 2.1)
Cystic kidney disease	7 (1)	1.2 (0.5 to 2.8)	1.2 (0.5 to 3.0)	4 (0.6)	0.9 (0.3 to 2.7)	0.9 (0.3 to 2.6)
Hereditary nephropathy	0 (0)	—	—	0 (0)	—	—
Ischemic kidney failure	14 (12)	12.8 (6.3 to 25.7)	11.4 (5.6 to 23.1)	10 (9)	11.4 (5.0 to 25.9)	10.1 (4.4 to 23.4)
Hemolytic Uremic Syndrome	42 (13)	15.2 (8.8 to 26.3)	15.6 (8.9 to 27.3)	27 (10)	12.7 (6.6 to 24.3)	12.0 (6.1 to 23.4)
Metabolic disorders	1 (0.4)	0.5 (0.1 to 3.9)	0.5 (0.1 to 4.0)	1 (0.5)	0.7 (0.1 to 5.3)	0.7 (0.1 to 5.1)
Vasculitis	15 (11)	13.9 (7.0 to 27.6)	20.4 (9.7 to 42.8)	11 (10)	13.9 (6.2 to 30.8)	16.5 (6.9 to 39.5)
Miscellaneous	14 (2)	2.4 (1.2 to 4.8)	2.4 (1.2 to 4.8)	6 (1)	1.3 (0.5 to 3.6)	1.3 (0.5 to 3.4)
Missing, unknown	7 (2)	1.6 (0.7 to 3.9)	1.9 (0.8 to 4.5)	3 (0.8)	1.0 (0.3 to 3.6)	1.1 (0.3 to 3.9)
Period of dialysis onset^f						
1990–1999	30 (2)	0.9 (0.6 to 1.5)	1.0 (0.6 to 1.5)	18 (1)	0.9 (0.5 to 1.6)	0.9 (0.5 to 1.6)
2000–2009	58 (2)	1.00 (ref)	1.0 (ref)	38 (1)	1.00 (ref)	1.0 (ref)
2010–2014	42 (2)	1.4 (0.9 to 2.1)	1.6 (1.1 to 2.5)	26 (2)	1.4 (0.8 to 2.3)	1.7 (1.0 to 2.8)

HR, hazard ratio; 95% CI, 95% confidence interval; ref, reference group; IQR, interquartile range; CAKUT, congenital anomalies of the kidney and urinary tract; —, no patients in this category.

^aPercentages shown are calculated from the total patient cohort (n=6574).

^bHR adjusted for country and age.

^cHR adjusted for country, sex, age, and primary kidney disease.

^dHR adjusted for country, sex, and primary kidney disease.

^eHR adjusted for country, sex, and age.

^fHR adjusted for country, age, and primary kidney disease.

(aHR, 10.1; 95% CI, 4.4 to 23.4), HUS (aHR, 12.0; 95% CI, 6.1 to 23.4), and vasculitis (aHR, 16.5; 95% CI, 6.9 to 39.5) had an increased likelihood of recovery compared with patients with CAKUT (Table 2).

Additionally, a sensitivity analysis excluding children who initiated dialysis before the age of 1 year obtained similar results, showing a 2-year recovery rate of 1.8% and compared with patients with CAKUT, patients with ischemic kidney failure (aHR, 17.7; 95% CI, 6.9 to 45.9), HUS (aHR, 21.7; 95% CI, 10.6 to 44.4), and vasculitis (aHR, 20.3; 95% CI, 8.6 to 48.0) had an increased likelihood of recovery.

Discussion

In this large study on kidney function recovery in pediatric patients on maintenance dialysis, we found a recovery rate of 2% 2 years after dialysis initiation. Young

age, initiating dialysis on hemodialysis, and most importantly ischemic kidney failure, HUS, or vasculitis as primary disease were associated with significantly higher rates of kidney function recovery.

Our results, covering the period from 1990 to 2014, are in line with previously reported recovery rates, ranging from 1% in large adult registry reports from Australia and New Zealand (3,6) to as high as 7% in adult patients on hemodialysis in the United States (7). Reported recovery rates were usually substantially higher in smaller single-center studies (9). This variation may reflect different follow-up periods, as well as variable definitions of ESKD and kidney function recovery, which may also be reflected by the varying recovery rates between countries in our study (Supplemental Material). Single-center studies tended to include more patients starting dialysis because of AKI, resulting in higher recovery rates. The ESPN/ERA-EDTA

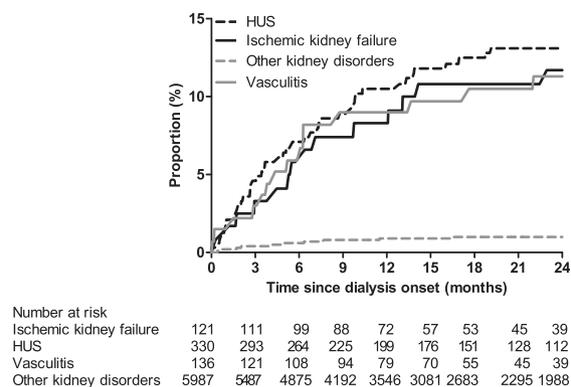


Figure 2. | Much higher cumulative incidence of patients experiencing recovery of kidney function in HUS, ischemic kidney failure, and vasculitis, compared with other primary kidney disorders. HUS, hemolytic uremic syndrome.

Registry includes only patients on maintenance kidney replacement therapy because of presumed ESKD and, therefore, we assumed that all patients who experienced recovery were correctly diagnosed with ESKD rather than AKI. However, given the short time between dialysis initiation and recovery in some patients, this did not seem to be true for all patients. Nevertheless, our sensitivity analysis among patients who were on dialysis for at least 90 days yielded similar results.

Similar to a study in adult patients on hemodialysis in the United States (7), we found a higher probability of kidney function recovery in the most recent period of dialysis initiation (>2010), which may either reflect better identification or registration of recovery of kidney function, or improved patient care, including more aggressive treatments. Because of the lack of information on reasons for kidney function recovery, we were not able to study this in more detail.

Carey *et al.* (17) reported a higher recovery rate among neonatal patients on dialysis compared with patients aged 1–24 months initiating dialysis. In our study, younger age at dialysis initiation was also associated with a higher likelihood of recovery, independent of sex, cause of kidney failure, or country. In fact, 15% of all recovery patients started dialysis as neonates. Similarly, in a study among 192 infants with ESKD from the United Kingdom, recovery occurred in 4% of patients ($n=8$), and the majority of them initiated dialysis as neonates ($n=5$) (18). GFR matures over the first 2 years of life (19). As many infants with CKD are born preterm, this further hampers the ascertainment of either AKI or ESKD, and the conclusion appears to be made on the basis of local standards of clinical care (10). Unfortunately, preterm birth history was not available from the ESPN/ERA-EDTA Registry.

Recovery of kidney function could theoretically occur in almost every type of kidney disease, but similar to others (3,7,8), patients with ischemic kidney failure, HUS, and vasculitis were most likely to experience kidney function recovery. However, in primary kidney disease stratified analyses, none of the patient characteristics were significantly associated with a higher likelihood of recovery, suggesting that cause of kidney failure is by far the most

important factor for recovery of kidney function. So, when a patient with HUS, ischemic kidney failure, or vasculitis requiring kidney replacement therapy presents to the pediatric nephrologist, it can be hard to predict whether recovery will occur. Yet, the likelihood of recovery is significantly higher than for other kidney diseases and timing of kidney transplantation might be scheduled accordingly as there is a reasonable chance of recovery. Surprisingly, we found that patients who initiated dialysis on hemodialysis were more likely to experience recovery compared with patients who started on peritoneal dialysis. After all, higher recovery rates have been observed among patients on peritoneal dialysis, probably through better preservation of residual kidney function (5). However, a study from the Australia and New Zealand Dialysis and Transplant Registry did not find any differences in the likelihood, timing, or durability of kidney function recovery between patients on peritoneal dialysis and patients on hemodialysis (6). These contradictory results might be due to selection bias and the difficulty to adequately control analyses for all confounding variables. Although we carefully adjusted for several confounding variables, we cannot rule out the possibility of residual confounding due to unmeasured covariates. Moreover, some patients starting on hemodialysis might have been wrongly classified as having ESKD rather than AKI. We found a significantly higher number of patients starting on hemodialysis among patients who experienced a recovery within the first year after dialysis commencement compared with those who had a recovery beyond the first year. However, in our sensitivity analysis, including patients treated with dialysis for at least 90 days, those starting on hemodialysis also showed a higher likelihood of recovery.

Of the patients who experienced recovery, restoration of dialysis-independent kidney function occurred within 6 months of initiating dialysis in 60% and within 1 year in 85% of patients. The majority of patients regained sufficient kidney function to discontinue dialysis treatment, but for one third of patients recovery was temporary, lasting for a median of 20 months. However, we cannot preclude that patients who demonstrated sustained recovery may need to resume kidney replacement therapy later in life (beyond our study period). This requires further investigation over a longer follow-up period. We did not find any differences between patients with sustained recovery and those who had to restart kidney replacement therapy. Kidney transplantation is widely accepted as the treatment of choice for children with ESKD and pediatric nephrologists usually aim to transplant these children as soon as possible (20). However, native kidney function recovery has been reported in children who already received a transplant (21). Given the high recovery rates, it might be sensible to perform a kidney biopsy, to intensively monitor urine output and residual kidney function in patients with presumed ESKD due to ischemic kidney failure, HUS, and vasculitis.

Although the strength of this study includes the large sample size, including virtually all children under 15 years of age in Europe who experienced kidney function recovery after a period of dialysis for presumed ESKD, some limitations need to be acknowledged. Although the Registry prospectively collects multiple variables, data collection for some important variables, including comorbidities, urine output, reasons for recovery, and distinction between typical and atypical HUS is limited. As a result we were not able to control

our analyses for these factors or to study them in more detail. Furthermore, we collect data on pediatric patients with ESKD until loss to follow-up, transfer to adult nephrology care, or death. As a consequence, we have no further follow-up information beyond the date of recovery for those not returning to kidney replacement therapy.

In conclusion, this study demonstrates that recovery of dialysis-independent kidney function in the first 2 years in pediatric patients on dialysis is possible, but rare (2%), and is mainly determined by the underlying kidney disease and age. As a result, for patients with ischemic kidney failure, HUS, and vasculitis, the possibility of recovery of kidney function should be considered and kidney transplantations scheduled accordingly.

Acknowledgments

We would like to thank the patients, their parents, and the staff of all of the dialysis and transplant units who have contributed data *via* their national registries and contact persons. We also would like to thank E. Levchenko, D. Haffner, Z. Massy, A. Bjerre, and C. Stefanidis for being members of the European Society for Pediatric Nephrology/European Renal Association-European Dialysis and Transplant Association (ESPN/ERA-EDTA) Registry Committee, D. Shtiza, R. Kramar, S. Baiko, A. Sukalo, K. van Hoeck, and the Centre contributors to the Belgian Registry Committee, D. Pokrajac, D. Roussinov, D. Batinić, M. Lemac, J. Slavicek, D. Milosevic, A. Elia, T. Seeman, K. Vondrak, J.G. Heaf, Ü. Toots, P. Finne, A. Pylsy, P.-H. Groop, C. Couchoud, M. Lassalle, E. Sahpazova, N. Abazi, T. Davitaia, K. Rascher, E. Nüsken, L. Weber, G. von Gersdorff, J. Dötsch, F. Schaefer, K. Krupka, B. Höcker, L. Pape, B. Tönshoff, N. Afentakis, A. Kapogiannis, N. Printza, G. Reusz, C.s. Berecki, A. Szabó, T. Szabó, A. Barczy, O. Lakatos, E. Kis, V. Edvardsson, B. Gianoglio, I. Guzzo, B. Minale, R. Roperto, E. Vidal, E. Verrina, H. Čerņevskis, V. Kuzema, S. Rudaitis, A. Jankauskiene, V. Said-Conti, S. Gatcan, O. Berbeca, N. Zaikova, N. Revenco, S. Pavićević, A. Åsberg, A.V. Reisæter, A. Zurowska, I. Zagozdzon, C. Mota, R. Stone, C. Afonso, G. Mircescu, E.A. Molchanova, N.A. Tomilina, M. Kostić, B. Spasojević, M. Cvetković, I. Gojković, D. Paripović, G. Miloševski-Lomić, L. Podracka, G. Kolvek, N. Battelino, G. Novljan, J. Buturovic-Ponikvar, A. Alonso Melgar, and the Spanish Pediatric Registry, K.G. Prütz, M. Stendahl, M. Evans, S. Schön, M. Segelmark, T. Lundgren, G.F. Laube, C.E. Kuehni, H. Chehade, C. Rudin, and the Swiss Paediatric Renal Registry, L. Heuveling and M.H. Hemmelder on behalf of the Nefrovisie foundation, all centers participating in the RichQ-study, and R. Topaloglu, D.D. Ivanov, S.P. Fomina, A. Hamilton, F. Braddon, A. Casula, and H. Maxwell, for contributing data to the ESPN/ERA-EDTA Registry.

This article was written on behalf of the ESPN/ERA-EDTA Registry and the ERA-EDTA Registry which is an official body of the ERA-EDTA.

This has been published previously in abstract form (22).

Disclosures

None.

References

1. Agraharkar M, Nair V, Patlovanly M: Recovery of renal function in dialysis patients. *BMC Nephrol* 4: 9, 2003
2. Brunner K, Bianchetti MG, Neuhaus TJ: Recovery of renal function after long-term dialysis in hemolytic uremic syndrome. *Pediatr Nephrol* 19: 229–231, 2004
3. Craven AM, Hawley CM, McDonald SP, Rosman JB, Brown FG, Johnson DW: Predictors of renal recovery in Australian and New

- Zealand end-stage renal failure patients treated with peritoneal dialysis. *Perit Dial Int* 27: 184–191, 2007
4. Fehrman-Ekholm I, Bergenhag AC, Heimburger O, Schön S: Recovery of renal function after one-year of dialysis treatment: Case report and registry data. *Int J Nephrol* 2010: 817836, 2010
5. Goldstein A, Kliger AS, Finkelstein FO: Recovery of renal function and the discontinuation of dialysis in patients treated with continuous peritoneal dialysis. *Perit Dial Int* 23: 151–156, 2003
6. Macdonald JA, McDonald SP, Hawley CM, Rosman J, Brown F, Wiggins KJ, Bannister K, Johnson DW: Recovery of renal function in end-stage renal failure—comparison between peritoneal dialysis and haemodialysis. *Nephrol Dial Transplant* 24: 2825–2831, 2009
7. Mohan S, Huff E, Wish J, Lilly M, Chen SC, McClellan WM; Fistula First Breakthrough Initiative Data Committee: Recovery of renal function among ESRD patients in the US Medicare program. *PLoS One* 8: e83447, 2013
8. Siddiqui S, Norbury M, Robertson S, Almond A, Isles C: Recovery of renal function after 90 d on dialysis: Implications for transplantation in patients with potentially reversible causes of renal failure. *Clin Transplant* 22: 136–140, 2008
9. Chu JK, Folkert VW: Renal function recovery in chronic dialysis patients. *Semin Dial* 23: 606–613, 2010
10. Goldstein SL: Renal recovery at different ages. *Nephron Clin Pract* 127: 21–24, 2014
11. Mammen C, Al Abbas A, Skippen P, Nadel H, Levine D, Collet JP, Matsell DG: Long-term risk of CKD in children surviving episodes of acute kidney injury in the intensive care unit: A prospective cohort study. *Am J Kidney Dis* 59: 523–530, 2012
12. ESPN/ERA-EDTA Registry: European Registry for Children on Renal Replacement Therapy. Available at: <http://www.espn-reg.org/>. Accessed March 1, 2018
13. ERA-EDTA Registry: ERA-EDTA Registry Annual Report 2015. Available at: <https://www.era-edta-reg.org/files/annualreports/pdf/AnnRep2015.pdf>. Accessed July 25, 2018
14. Schwartz GJ, Muñoz A, Schneider MF, Mak RH, Kaskel F, Warady BA, Furth SL: New equations to estimate GFR in children with CKD. *J Am Soc Nephrol* 20: 629–637, 2009
15. Noordzij M, Lefondré K, van Stralen KJ, Zoccali C, Dekker FW, Jager KJ: When do we need competing risks methods for survival analysis in nephrology? *Nephrol Dial Transplant* 28: 2670–2677, 2013
16. van Stralen KJ, Dekker FW, Zoccali C, Jager KJ: Confounding. *Nephron Clin Pract* 116: c143–c147, 2010
17. Carey WA, Talley LI, Sehring SA, Jaskula JM, Mathias RS: Outcomes of dialysis initiated during the neonatal period for treatment of end-stage renal disease: A North American Pediatric Renal Trials and Collaborative Studies special analysis. *Pediatrics* 119: e468–e473, 2007
18. Coulthard MG, Crosier J: Outcome of reaching end stage renal failure in children under 2 years of age. *Arch Dis Child* 87: 511–517, 2002
19. Schwartz GJ, Furth SL: Glomerular filtration rate measurement and estimation in chronic kidney disease. *Pediatr Nephrol* 22: 1839–1848, 2007
20. Gillen DL, Stehman-Breen CO, Smith JM, McDonald RA, Warady BA, Brandt JR, Wong CS: Survival advantage of pediatric recipients of a first kidney transplant among children awaiting kidney transplantation. *Am J Transplant* 8: 2600–2606, 2008
21. Nunan TO, Stevens EA, Croft DN, Hilton PJ, Jones NF, Wing AJ: Recovery of renal function after prolonged dialysis and transplantation. *Br Med J (Clin Res Ed)* 287: 248–249, 1983
22. Bonthuis M, Harambat J, Groothoff JW, Jager KJ: Recovery of renal function in children on chronic dialysis: a report from the ESPN/ERA-EDTA Registry. *Pediatr Nephrol* 32(9): 1674, 2017

Received: February 2, 2018 Accepted: July 17, 2018

Published online ahead of print. Publication date available at www.cjasn.org.

This article contains supplemental material online at <http://cjasn.asnjournals.org/lookup/suppl/doi:10.2215/CJN.01500218/-/DCSupplemental>.

AFFILIATIONS

¹European Society for Pediatric Nephrology/ European Renal Association-European Dialysis and Transplant Association Registry, Department of Medical Informatics, Academic Medical Center, University of Amsterdam, Amsterdam Public Health Research Institute, Amsterdam, The Netherlands; ²Pediatric Nephrology Unit, Bordeaux University Hospital, Bordeaux, France; ³Department of Pediatric Nephrology, Centre Hospitalier Universitaire de Nice-Hôpital Archet2, Nice, France; ⁴Department of Pediatric Nephrology, Erasmus Medical Center, Sophia Children's Hospital, Rotterdam, The Netherlands; ⁵Division of Pediatric Nephrology, Department of Pediatrics, Faculty of Medicine, Hacettepe University, Ankara, Turkey; ⁶Department of Internal Medicine and Nephrology, Carol Davila University of Medicine and Pharmacy, Dr. Carol Davila Teaching Hospital of Nephrology, Bucharest, Romania; ⁷Karolinska Institutet, Karolinska University Hospital Huddinge, Stockholm, Sweden; ⁸Department of Pediatric Nephrology, Fundeni Clinical Institute, Bucharest, Romania and Carol Davila University of Medicine, Pediatrics, Bucharest, Romania; ⁹Department of Pediatric Nephrology and Transplantation, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; ¹⁰Division of Pediatric Nephrology and Gastroenterology, Department of Pediatric and Adolescent Medicine, Medical University of Vienna, Vienna, Austria; ¹¹Pediatric Nephrology Department, Hospital Universitari Vall d'Hébron, Universitat Autònoma de Barcelona, Barcelona, Spain; ¹²Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland; ¹³Division of Nephrology, Landspítali—The National University Hospital of Iceland, Reykjavik, Iceland and Faculty of Medicine, School of Health Sciences, University of Iceland, Reykjavik, Iceland; ¹⁴Department of Pediatric Nephrology, Evelina London Children's Hospital, Guys and St Thomas' National Health Service Foundation Trust, London, United Kingdom; ¹⁵Pediatric Nephrology and Dialysis Unit, Fondazione Istituto di Ricovero e cura a Carattere Scientifico, Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; and ¹⁶Department of Pediatric Nephrology, Emma Children's Hospital, Academic Medical Center, Amsterdam, The Netherlands