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CASE REPORT

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Successful transplantation of four kidney grafts from two small pediatric donors with anuric acute renal failure into adult recipients

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Abstract

Background: Kidneys from infants with anuric acute kidney injury (AKI) only rarely get accepted for transplantation despite encouraging data that such kidneys can have very good long-term outcome.

Methods: We report the transplantation of four kidney grafts from two pediatric donors (3 and 4 years) with anuric acute kidney injury as single kidneys into four adult recipients.

Results: All grafts gained function within 14 days posttransplantation, only one recipient needed dialysis after transplantation. None of the recipients suffered from surgical complications. One month after transplantation, all recipients were free of dialysis. Estimated glomerular filtration rates (eGFR) 3 months after transplantation were 37, 40, 50, and 83 mL/min/1.73 m^2. eGFR increased further through month 6, reaching 45, 50, 58, and 89 mL/min/1.73 m^2.

Conclusion: These cases highlight the feasibility of successful transplantation of single pediatric kidney grafts into adult recipients despite anuric AKI of the donor.

KEYWORD
pediatric kidney transplant

1 | INTRODUCTION

Kidneys from small infants rarely get accepted for kidney transplantation (KTx). Out of 67 KTx centers in the Eurotransplant (ET) area, only 36 regularly accept donors under 5 years; 12 centers do so exceptionally (Data provided by Ineke Tieken, ET). Pediatric grafts with acute anuric kidney failure are less likely being accepted for transplantation and even excluded from the very few studies available on pediatric grafts with acute kidney injury.[1,2]

In the year 2022, only 29 kidneys of donors aged 2–5 years have been allocated in the whole ET area. Nineteen organs have been transplanted in children (four as dual-kidney grafts, 15 as single grafts). Ten organs were transplanted to adults via regular allocation ($n=6$, all as dual grafts) and four as rescue allocation (Data provided by Ineke Tieken, ET). Within ET, pediatric donor kidneys are first allocated to pediatric recipients; therefore, we can conclude that 10 of 29 kidneys between 2 and 5 years of age could not be transferred to pediatric patients. This might be due to the fact that most pediatric transplant

Abbreviations: AKI, acute kidney injury; CKD, EPI Chronic Kidney Disease Epidemiology Collaboration; DGF, delayed graft function; eGFR, estimated Glomerular Filtration Rate; ET, Eurotransplant; HLA, Human leucocyte antigen; KTx, kidney transplantation.

centers have entered a restrictive HLA profile into the ET database or, more likely as in the cases described here, due to the reluctance to accept kidneys with acute renal failure for pediatric recipients.[1]

Interestingly, only four of 19 kidneys allocated to children via regular allocation were transplanted as dual grafts. In conclusion, 17 pediatric patients profited from 19 grafts. In opposition, all six grafts allocated to adults via regular allocation were transplanted as dual kidneys, so that only three patients could benefit from these grafts. This might be caused by published data that *en-bloc* kidney grafts have superior results in adults compared to standard adult donors, but from the same publication it is evident that also single/solitary grafts from donors <5 years have very good long-term results with a higher glomerular filtration rate (GFR) compared to standard adult donors after 5 years.[3]

Since it is recommended by Eurotransplant to procure kidneys from donors ≥2 and ≤5 years *en-bloc*, and it is left to the accepting center to transplant the kidneys as single kidney or *en-bloc* as dual grafts (Eurotransplant Manual 2021); it seems reasonable to accept both kidneys for one recipient. On the other hand, donor organs are rare and results of single pediatric grafts are also promising.[3] Furthermore, the transplantation of *en-bloc* kidneys is surgically challenging[4]; therefore, it should also be considered that more recipients could be transplanted with single kidneys.

We report here on the 6- and 12-month results of the four small pediatric grafts from donors aged 3 and 4 years with anuric acute kidney failure allocated as rescue allocation in 2022.

Allocation had not been possible in the entire ET region and no other transplant center within ET was willing to accept the grafts for any recipient.

While it has been shown that pediatric grafts, in general, can be transplanted into adult recipients with good long-term results,[5] data on small pediatric grafts with acute kidney injury (AKI) are rare and unavailable for acute anuric renal failure. We assumed infant kidneys to be free of chronic structural changes and therefore have a high regenerative potential and we selected recipients without severe comorbidities, who were expected to be able to tolerate delayed graft function (DGF).

To our knowledge, this is the first report of small anuric pediatric grafts transplanted successfully as single kidneys into adult recipients.

2 | PATIENTS

2.1 | Donors

Donor 1 was a 4-year-old boy (19 kg) who had suffered traumatic injuries and was declared brain-dead after resuscitation (30 min). He was anuric 24 h before procurement. Baseline s-creatinine at admission was 0.5 mg/dL and 5 days later at procurement was 4.4 mg/dL.

Donor 2 was a 3-year-old boy (13 kg) who had died from arrhythmia and was declared brain-dead after resuscitation (120 min). He was anuric, on CVVH for 4 days, and had been on VA-ECMO placement.

Baseline s-creatinine at admission was 0.6 mg/dL.

2.2 | Recipients

All allocations were center offers: we were free to select recipients. When the first two kidneys were offered, we happened to have two young patients who were about to undergo ABO-incompatible living-donor transplantation. Since living donation is subsidiary in Germany, we decided to offer these kidneys to both young men. When the kidneys from the second donor were offered, we chose two patients with the highest ET point score for the grafts.

We excluded immunized patients, patients awaiting re-transplantation, ESP patients and patients with challenging anatomy due to previous operations or severe arteriosclerosis, and patients with critical cardiac conditions due to the expected primary poor function.

Recipient 1 was a 20-year-old male with a history of 2.5 years on dialysis. Human leukocyte antigen (HLA) mismatch was 2-1-1.

Recipient 2 was a 27-year-old male who was due for pre-emptive living-donor transplantation. His HLA mismatch was 2-1-1.

Recipient 3 was a 62-year-old female with a history of 6 years of hemodialysis. With an HLA mismatch of 1-1-2, she was ranked 408 on the ET match list.

Recipient 4 was a 38-year-old male with a history of 3 years of hemodialysis. With an HLA mismatch of 2-2-1, he was ranked 602 on the ET match list.

All recipients consented to possible increased risks for surgical complications and delayed graft function.

Recipient characteristics are summarized in Table 1.

Kidney function after transplantation is reported as eGFR calculated with the CKD-EPI formula.[6]

3 | RESULTS

3.1 | Procurement and organ quality

In opposition to the ET recommendations, kidneys were procured as single kidneys from both donors. All grafts were rated as "quality good" by the procurement surgeon. Preimplantation biopsies are not routinely available in Germany; therefore, no histological evaluation of the kidneys was done before transplantation. The macroscopic appearance of the grafts of donor 1 was unremarkable and a biopsy

TABLE 1 Recipient characteristics.

Recipient	Gender	Age (years)	Weight (kg)	Time on dialysis (years)	Donor
1	m	20	61	2.5	1
2	m	27	106	0	1
3	f	62	64	6	2
4	m	38	55	3	2

Abbreviations: m, male; f, female.

due to slow graft function was done in one recipient 10 days after transplantation. The result of this biopsy is shown in Figure 1A.

Both kidneys of donor 2 showed small perfusion deficiencies, e.g., infarctions. The macroscopic appearance of the left kidney of donor 2 is shown in Figure 1B.

3.2 | Transplantation and graft function

There were no surgical complications in the four recipients. No vascular reconstruction was necessary, vascular anastomoses took 20–26 min. Skin-to-skin times were 110–130 min.

Slow graft function was observed in all recipients, but only one recipient needed hemodialysis (six sessions due to hypervolemia and hyperkalemia). Within 14 days posttransplantation, all grafts gained function (Figure 2).

Recipient 1 had no residual urine production. On discharge after 26 days, diuresis was 2.8 L/d, creatinine was 3.5 mg/dL, and eGFR was 24 mL/min/1.73 m^2. After 3 and 6 months, creatinine levels and eGFRs were 2.4 and 2.1 mg/dL, and 37 and 45 mL/min/1.73 m^2, respectively. This patient suffered from acute antibody-mediated rejection 10 months posttransplantation and was treated with steroids, plasmapheresis, and Rituximab. Kidney function was stable at 12 months.

Recipient 2 had normal urine production before transplantation. On discharge after 15 days, creatinine was 3.4 mg/dL (eGFR, 24 mL/min/1.73 m^2). After 3 and 6 months, creatinine levels and eGFRs were 2.2 and 1.8 mg/dL and 40 and 50 mL/min/1.73 m^2, respectively.

Recipient 3 had been oliguric. She started to diurese immediately and was discharged with steadily decreasing creatinine on day 11. After 3 and 6 months, creatinine was 1.2 and 1.0 mg/dL.

Recipient 4 had been anuric and also started to diurese immediately after transplantation. He was discharged on day 10 with constantly decreasing creatinine. After 3 and 6 months, the creatinine was 1.1 and 1.1 mg/dL.

Results after transplantation are summarized in Table 2.

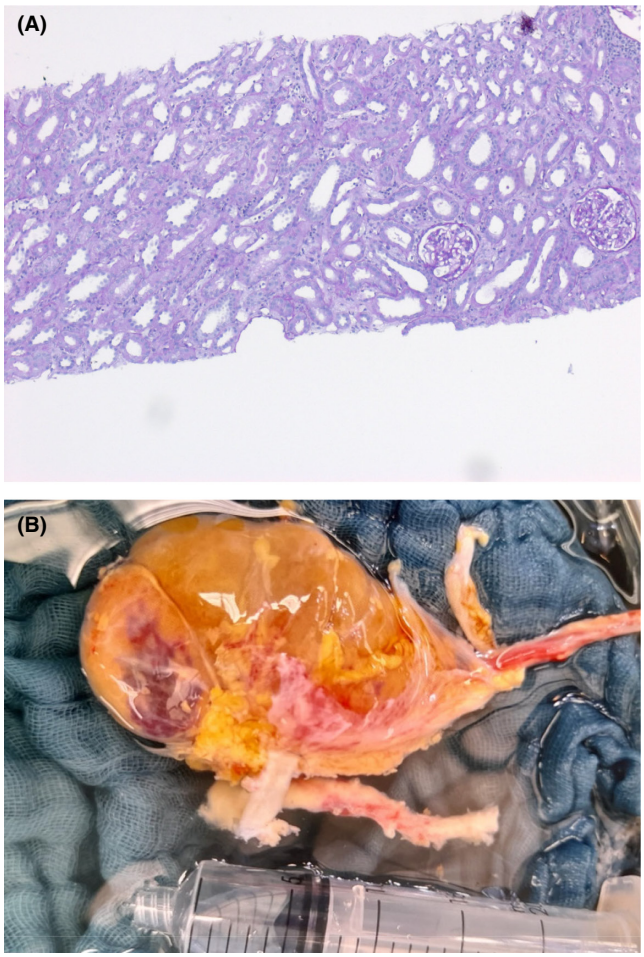

FIGURE 1 (A) Kidney biopsy of recipient 1, donor 1 10 days after transplantation. PAS staining ×10 without structural changes and without rejection. (Courtesy of K. Amman, Erlangen). (B) Macroscopic appearance of the left kidney from donor 2. A perfusion deficiency/infarction is evident on the upper pole.

4 | DISCUSSION

Within the ET area, every year, a high amount of small pediatric grafts between 2 and 5 years of age is allocated to adults (in 2020 six of 14, in 2021 five of 28, and in 2022 ten of 29 kidneys). In adults, a high percentage of these grafts is transplanted *en-bloc* (in 2020 all six kidneys, in 2021 four of five, and in 2022 six of 10), resulting in only 13 recipients transplanted with 21 kidneys within 3 years (data provided by Ineke Tieken, ET).

This rises two questions: why is it not possible to allocate these pediatric grafts to pediatric recipients and is it really necessary to transplant these grafts *en-bloc* leading to a lower number of recipients?

It is possible that these 21 organs out of 71 from donors aged 2–5 years offered in 2020–2022 could not be allocated to children because of immunological mismatch and three were allocated as combined grafts with pancreas usually not transplanted in children.

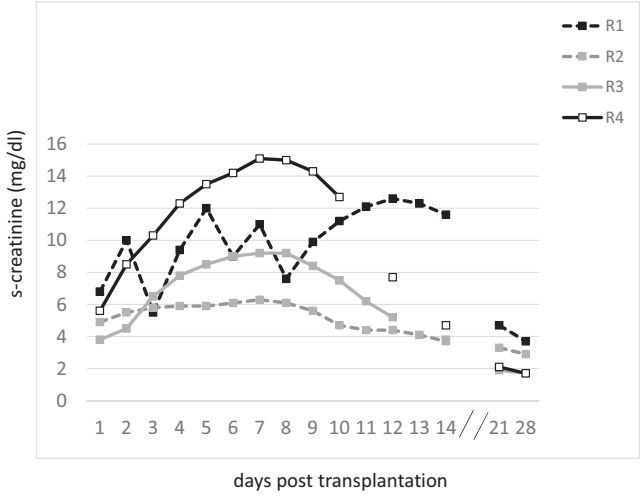

FIGURE 2 Course of s-creatinine in the first month of all four recipients.

TABLE 2 Transplant outcome.

Recipient	CIT (min)	Dialysis sessions post KTx	Surgical complications	s-creatinine (mg/dL)/eGFR (ml/min/1.73 m^2)			
				Month 1	Month 3	Month 6	Month 12
1	301	6	No	3.5/24	2.4/37	2.1/45	2,1/43
2	313	0	No	2.9/28	2.2/40	1.8/50	1.7/53
3	805	0	No	1.7/32	1.2/50	1.0/58	
4	1098	0	No	1.7/49	1.1/83	1.1/89	

However, we contend that another reason was the general reluctance to accept kidneys with AKI,[1] especially of grafts from anuric donors as in the cases described here: Four kidneys from two pediatric donors with anuric acute renal failure were transplanted into four adult recipients with good clinical outcomes.

Our transplant center has no pediatric transplant program. Due to the experience of one of the authors (MK) with pediatric KTx and the convincing data that pediatric kidney grafts can safely be transplanted into adults,[2,3,5] we decided to accept the organs despite the fact that no other center in the ET area had accepted them, most likely because of the established anuric AKI.

It has been shown by several authors that grafts from young adult donors with AKI have a higher rate of DGF, but comparable long-term outcomes to grafts from donors without AKI.[7–10] AKI in most publications is not defined as anuric or dialysis-dependent renal failure, but as an increase in s-creatinine. There is only one study by Anil Kumar et al.[11] defining acute kidney failure as persistent anuria/oliguria and increased s-creatinine levels by twofold or more without a trend for improvement. This seems to be most comparable to our donors. Anil Kumar et al compared 55 kidney grafts from donors younger than 50 years (pediatric donors were excluded) without history of kidney disease, hypertension, or diabetes with standard criteria and extended criteria donors. In this study, a baseline kidney biopsy with normal kidney structure was required. Patient and graft survival was not different between grafts with AKI and standard criteria donors after 3 years.

Although no baseline biopsies were available from our donors, we assumed that pediatric grafts from donors with acute incidences (trauma, arrhythmia) and normal kidney function at admission were devoid of chronic structural damage. Therefore, we expected a favorable outcome of these grafts.

Fortunately, all four organs gained function without complications. These results are encouraging, since in Germany, and apparently throughout ET, (pediatric) nephrologists seem to be very reluctant, especially with small pediatric grafts and even more with small grafts with AKI.

As described above, there is sufficient literature that the use of selected "healthy" donor kidneys with AKI is feasible. The second challenge in our cases was the fact the organs were procured separately, though we did not have the chance to decide to transplant them as single or dual grafts. Since single kidneys of this age group also show very good long-term results,[3,5,12] this was not a contraindication for our decision.

Very little is known about the outcome of transplanting grafts from infants with AKI. These are rare situations, but every single successful transplantation counts. In a retrospective case–control study that compared 27 small *en-bloc* grafts with AKI with 27 matched small grafts without AKI, the long-term outcomes of the adult recipients were comparable, and the risk of short-term complications was not affected by the presence or absence of AKI in the donor.[2] Of note, the pediatric kidneys in this study were all transplanted *en-bloc*, and anuric and/or dialysis-dependent donors were excluded. By comparison, our cases demonstrate that transplantations of single infant kidneys can be successful, even in the presence of anuric and/or dialysis-dependent AKI.

To our knowledge, this is the first report of successful transplantation of small pediatric grafts with anuric AKI into four adult recipients, and we hope to encourage transplant physicians and pediatric nephrologists to reconsider their stance on pediatric grafts with AKI and to rethink the efficient use of pediatric grafts as single or dual kidney grafts.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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