LETTER TO THE EDITORS

Transplantation of adult living donor kidneys in small children, a single-centre initial experience

Josianne C. H. B. M. Luijten^{1,2} (D), Marieke Voet³, Robert P. E. de Gier⁴, Anneliese Nusmeier⁵, Horst Scharbatke², Johannes Adam van der Vliet² & Elisabeth A. M. Cornelissen¹ (D)

 Department of Paediatric Nephrology, Radboud University Medical Center, Nijmegen, The Netherlands
Department of Vascular and Transplant Surgery, Radboud University Medical Center, Nijmegen, The Netherlands
Department of Pediatric Anesthesiology, Radboud University Medical Center, Nijmegen, The Netherlands
Department of Pediatric Urology, Radboud University Medical Center, Nijmegen, The Netherlands

5 Department of Pediatric Intensive Care, Radboud University Medical Center, Nijmegen, The Netherlands

E-mail: marlies.cornelissen@radboudumc.nl

Dear Editors,

Kidney transplantation (KTx) is the best treatment for children with ESRD [1]. Pre-emptive KTx results in better survival and graft function when compared to KTx after initiation of dialysis [2,3]. To prevent impaired neurologic development, KTx should not be delayed [4]. Early transplantation, however, is hampered due to shortness in paediatric donor kidneys. Fortunately, parents are often willing to donate, but the transplantation of an adult-sized kidney (ASK) in a small recipient is associated with some challenges. Firstly, there are technical challenges related to the difference between allograft size and recipient body cavity space and the mismatch of recipient and ASK vessel diameters [5]. Secondly, there are hemodynamic challenges to cope with. A transplanted ASK demands a renal blood flow of about 500-700 ml/min, requiring 50-70% of the recipient cardiac output (CO). Aggressive fluid management is necessary to ensure optimal renal perfusion and prevent postoperative acute tubular necrosis, graft thrombosis or even primary nonfunction [6,7]. Thirdly, young children are more prone to complications and infections after transplantation, so tight follow-up and immunosuppressive management are essential [8].

We evaluate our new programme for adult KTx in children under the age of 4 years. Donor and recipient

characteristics, data on surgical technique and ischaemia times (IT) were recorded and outcome measures, such as eGFR, growth, graft and patient survival, were analysed. We transplanted seven boys and three girls. The girls and one boy were on haemodialysis, and six boys were transplanted pre-emptively. The mean age of the 10 recipients was 2.7 years. The mean pretransplant height was 88 (range 72.5–97) cm, and the mean pretransplant weight was 13.5 (range 10.0–17.9) kg. All had congenital origin for ESRD: posterior urethral valves (n = 4), renal dysplasia (n = 2) and nephrotic syndrome (n = 2), nephronophthisis (n = 1) and reflux nephropathy (n = 1). The four recipients with posterior urethral valves underwent valve resection prior to KTx. No bladder augmentation was necessary.

All donors were parents (60% mothers) with a mean age of 36 years (range 24–45). All underwent an uncomplicated laparoscopic nephrectomy and were discharged from hospital on postoperative day 5 (range 4–7).

All recipients underwent a transverse laparotomy with a right intestinal medial rotation and vascular anastomoses on the abdominal aorta and inferior caval vein. The kidney was then placed intra-abdominally, without compression of the graft or adjacent structures and without graft vessel kinking. The ureter was implanted by an extravesical implantation technique and without an antireflux mechanism.

Heart rate, central venous pressure, cardiac output and arterial blood pressure were monitored. All children received a jugular central venous catheter, a radial arterial catheter and a thermistor-tipped femoral arterial catheter (PiCCO catheter) for intermittent CO estimation using the transpulmonary thermodilution (TPTD) technique, which is a gold standard for CO measurement in children [9,10].

The warm (combined 1st and 2nd) and cold IT were 35 min (range 16.9–51) and 3.5 h (range 2.5–3.9), respectively. Mean recipient operating time was 178 min (range 128–276), which is relatively short [5],



Figure 1 eGFR pre-KTx 24-month follow-up.

possibly due to the efforts of a dedicated team. Our mean total warm IT of 35 min compares favourably to other publications in which total warm IT ranged from 45 to 80 min. All grafts functioned immediately (starting diuresis in OR). The median recipient hospital stay was 22 (range 13–44) days, and the median ICU stay was 10 (range 3–25) days.

Early complications were drug-induced delirium (n = 2), septicaemia (n = 1) and early postoperative haemorrhage requiring reoperation in another. In the case of nephronophthisis with pre-existent liver fibrosis, excessive postoperative lymph ascites was encountered. This necessitated huge fluid administration (maximum 5 l/day) and prolonged ICU stay, but resolved spontaneously after parenteral feeding for some weeks. There were no urological complications.

All children started immunosuppression according to the 'transplantation without steroids' (TWIST) protocol (basiliximab, tacrolimus and mycophenolate), with allometric dosing, as well as CMV prophylaxis and antibiotic uroprophylaxis for 3 months. After 1 year, only 30% still received tacrolimus and mycophenolate, 30% was on Tacrolimus and Azathioprine, 20% Tacrolimus, Mycophenolate and Prednisone and 20% Tacrolimus and Prednisone. Reasons for switching immunosuppressive therapy were gastrointestinal side effects (n = 5), urosepsis postoperatively (n = 1) and Epstein–Barr virus (EBV) infection (n = 2).

Patient and graft survival are both 100%, with a median follow-up of 22 months. There were no cases of acute rejection, despite four biopsies due to declining renal function.

Mean GFR was 8 before KTx (n = 10) (range 3.6–12.2), 89 at 12 months (n = 10) and 77 ml/min/1.73 m² at 24 months after KTx (n = 7) (Fig. 1).

Nearly all recipients showed a catch-up growth; mean height increased from 88 to 98 cm at 1 year post-KTx (-4 SD to 1.5 SD).

Infections were a major challenge in this cohort, most of them being mild respiratory tract infections and gastrointestinal infections. Urinary tract infections (UTI) occurred quite frequently. A total of 11 UTI after 3 months (in four of 10 patients, all with urethral valves) and 10 extra after 1 year (in 6 patients) were recognized.

In the first 3 months, we did not encounter any EBV or cytomegalovirus (CMV) infection while monitoring by PCR was performed monthly. One BK virus nephropathy was treated successfully.

Many challenges in paediatric ASK transplantation are evident from the foregoing data. The impediments to success are different and of greater magnitude than those seen with adults, primarily because of different causes of ESRD and different surgical and medical considerations in these very small children. Nevertheless, excellent results can be obtained with strict adherence to surgical detail, careful pre- and postoperative hemodynamic monitoring, aggressive fluid management and tight immunosuppressive management during follow-up by a dedicated team.

This programme was started with a multidisciplinary and dedicated team consisting of a paediatric nephrologist, a vascular and transplantation surgeon, a paediatric surgeon, a paediatric urologist, a paediatric anaesthesiologist and a paediatric ICU specialist, as well as a paramedical team, resulting in a programme with promising outcomes. Presently, all transplanted children are alive and thriving with adequate graft function, proving that paediatric ASK transplantation is an excellent option for the very young recipient. Parents were relieved to be able to help their child to being transplanted as soon as possible, giving it the highest possible quality of life.

REFERENCES

- Walther AE, Coots AC, Goebel JW, et al. Laparoscopic donor nephrectomy for the pediatric recipient population: risk factors for adverse outcomes. *Pediatr Transplant* 2015; 19: 836.
- Meier-Kriesche H, Port FK, Ojo AO, et al. Deleterious effect of waiting time on renal transplant outcome. *Transplant Proc* 2001; 33: 1204.
- Asderakis A, Augustine T, Dyer P, et al. Pre-emptive kidney transplantation: the attractive alternative. Nephrol Dial Transplant 1998; 13: 1799.
- 4. Polinsky MS, Kaiser BA, Stover JB, Frankenfield M, Baluarte HJ. Neurologic

development of children with severe chronic renal failure from infancy. *Pediatr Nephrol (Berlin, Germany)* 1987; 1: 157.

- Giessing M, Muller D, Winkelmann B, Roigas J, Loening SA. Kidney transplantation in children and adolescents. *Transplant Proc* 2007; **39**: 2197.
- Salvatierra O Jr, Millan M, Concepcion W. Pediatric renal transplantation with considerations for successful outcomes. *Semin Pediatr Surg* 2006; 15: 208.
- Salvatierra O Jr, Singh T, Shifrin R, et al. Transplantation of adult-sized kidneys into infants induces major

blood flow changes. *Transplant Proc* 1999; **31**: 236.

- Dharnidharka VR, Fiorina P, Harmon WE. Kidney transplantation in children. N Engl J Med 2014; 371: 549.
- Tibby S. Transpulmonary thermodilution: finally, a gold standard for pediatric cardiac output measurement. *Pediatr Crit Care Med* 2008; 9: 341.
- Lemson J, de Boode WP, Hopman JC, Singh SK, van der Hoeven JG. Validation of transpulmonary thermodilution cardiac output measurement in a pediatric animal model. *Pediatr Crit Care Med* 2008; 9: 313.