A prospective study on size and function of paediatric kidneys (<10 years) transplanted to adults

Aksel Foss1, Pål-Dag Line1, Knut Brabrand2, Karsten Midtvedt3 and Anders Hartmann3

1Surgical Department, Section of Transplant Surgery, 2Department of Radiology and 3Medical Department, Section of Nephrology, Rikshospitalet-Radiumhospitalet University Hospital, Oslo, Norway.

Abstract

Background. There is increasing evidence that paediatric kidneys transplanted to adults have good graft function and satisfactory graft survival. The relationship between size increment and functional potential of paediatric kidneys following transplantation is not defined in detail. We therefore initiated a prospective single centre study, comprising detailed and repeated measurements of size and function of paediatric kidneys transplanted to adults.

Methods. Nineteen adults receiving a first kidney transplant from a paediatric donor (<10 years of age) were included in the study. All patients were followed for 12 months post-transplant. Increment in size and function of the transplanted kidneys were assessed by ultrasound, glomerular filtration rate (GFR) and effective renal plasma flow (ERPF). All tests were performed during the first week, post-transplant and subsequently repeated at 1, 3, 6 and 12 months.

Results. Kidney volume increased 2.6-fold at 12 months ($P < 0.001$). GFR and ERPF showed a slightly more moderate increase, 1.8-fold and 1.6-fold, respectively. Patient and graft survival at 1 year were 100% and serum creatinine was 91 μmol/l (66–169).

Conclusion. The study indicates that paediatric kidneys for transplantation may be considered as excellent rather than being referred to as suboptimal for adult recipients, at least the first year after transplantation.

Keywords: kidney size; kidney transplantation; paediatric donors; transplant function

Introduction

There is an increasing gap between supply and demand of kidneys for transplantation. More than 20000 patients are awaiting a kidney transplant in Europe [1]. Kidneys from children comprise a considerable part of the deceased donor pool representing up to 15% of assessable kidneys for transplantation [2]. However, registry data show that not all of these kidneys are used for transplantation [3]. It has been suggested that technical problems and inadequate kidney size of small kidneys could cause vascular thrombosis, promote proteinuria, hypertension and focal glomerulosclerosis, eventually leading to progressive renal failure [4–7]. Several authors have reported that paediatric kidneys are associated with less favourable graft survival compared with adult kidney donors [8–10]. However, recent data describe good graft function and satisfactory graft survival and advocate the use of kidneys from young donors to adult recipients [11–16]. Nevertheless, data from the Collaborative Transplant Study show inferior graft survival for donors aged between 1 and <10 years [17]. The ability of transplanted kidneys to increase in size and their function over time in the clinical setting is not thoroughly studied. In a prospective study, size and function of paediatric kidneys (donors <10 years of age) transplanted to adult recipients were investigated.

Subjects and methods

Nineteen adults (eleven men/eight women) receiving a paediatric kidney as a first renal transplant, were included in the study. The organs were allocated according to standard criteria, e.g. ABO compatibility, HLA A, B and DR mismatches and time on the waiting list. All patients were panel reactive antibody (PRA) negative. Mean age of the recipients was 49.9 years (range, 20.5–76.5). Their mean weight and body mass index (BMI) were 70.6 kg (44–119) and 24.0 (16.8–33.3), respectively. Mean age of the donors was 4.5 years (range, 1.25–9.5) and mean weight 17.5 kg (range, 9–37). Kidney grafts from donors aged aged less than 2 years, weighing 9 to 12 kgs, were transplanted en bloc ($n = 5$) to one recipient (Table 1). The operations were performed by experienced transplant surgeons, using 2.5 or 3.5 magnification loupes for the anastomoses. The patients
were followed carefully after the operation and small changes in serum creatinine or reduction of urine production implied immediate action, including blood tests, ultrasound of the kidney and eventually biopsy. Acute rejection was initially diagnosed clinically by a rise in serum creatinine of more than 20% in the absence of urinary tract obstruction, nephrotoxic medication (including inappropriate elevation of whole blood ciclosporin levels), dehydration and infection. Post-transplant hospitalization time was 1–2 weeks and patients were thereafter seen as out-patients. The follow-up time of the study was 12 months.

**Size of the transplanted kidney**

Size of the transplanted kidneys was estimated by ultrasound (Siemens Acuson Sequoia™, 4C1 transducer) at different time points. Maximal craniocaudal length, anteroposterior thickness and transversal width were measured on two scans vertical to each other, one longitudinal and one transversal scan, both through the renal hilum. On repeat studies the previous scans were re-studied in order to reduce measurement inaccuracies due to different placement of the electronic calipers. Kidney volume was calculated by the ellipsoid method described by Jones et al. [18]:

\[
\text{Volume} (V) \text{ ml} = L \times W \times T \times \pi / 6.
\]

Kidney volume was recorded <7 days (mean 4, range 1–6) following the transplantation and at 1, 3, 6 and 12 months post-operatively. In recipients with en bloc grafts, the sum of both kidneys was calculated as the graft volume.

**Function of the transplanted kidney (GFR and ERPF)**

Glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) were measured within 7 days (mean 4, range 1–6) following the transplantation for functioning grafts and then 1, 3, 6 and 12 months post-operatively. GFR was measured as inulin clearance at a steady plasma concentration of about 200 to 300 mg/l. Inulin was analysed by the resorcinol method [19]. ERPF was calculated from hippuran clearance (PAH) at a steady state plasma concentration of 20 to 40 mg/l. PAH was determined as described by Smith et al. [20]. After oral water loading and 1 h of equilibration, clearance periods of 45 min were obtained by spontaneous voiding. Corresponding blood samples were taken both at the start and end of each period, and the mean values of all periods were used for the clearance calculations. Filtration fraction (FF) was calculated as GFR divided by ERPF with no corrections.

The patients received standard immunosuppression, which consisted of steroids, ciclosporin and azathioprine for the first 13 recipients enrolled in the study. In six patients, basiliximab (n = 3) or mycophenolate mofetil (n = 3) were used instead of azathioprine.

**Statistical methods**

Sample size was calculated by a 30% increase in size and functional parameters with the power of 80% at a statistical level of significance of \( P < 0.05 \). Data in the figures are expressed as mean and 95% confidence interval (CI). Demographic data (Table 1) are expressed as mean and range. For comparisons of size (volume) and function (GFR, ERPF and serum creatinine) a two-tailed repeated measures analysis of variance was performed. A linear regression analysis was used to assess the association between size of the kidneys, BMI and baseline volume. The statistical software SPSS (SPSS 13, Inc., Chicago, IL, USA) was used to perform the calculations.

**Results**

The size of the transplanted kidneys showed a 65% increase in volume at 1 month post-transplant, from 83 ml (71–96) to 136 ml (114–158). At 1 year, the growth increased 2.6-fold from baseline, to 219 ml (100–380) \( (P < 0.001) \) (Figure 1). GFR and ERPF showed a similar but slightly more moderate improvement over time. GFR at the first week post-transplant was 32 ml/min increasing to 40 at 1 month \( (P < 0.01) \), with a further increase to 58 ml/min (1.8-fold) at 1 year after transplantation.

**Table 1. Demographics of recipients and donors**

<table>
<thead>
<tr>
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<th>Recipients (mean range)</th>
<th>Donors (mean range)</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.9 (20.5–76.5)</td>
<td>4.5 (1.3–9.5)</td>
</tr>
<tr>
<td>BMI</td>
<td>24.0 (16.8–33.3)</td>
<td></td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>70.6 (44–119)</td>
<td>17.5 (9–37)</td>
</tr>
<tr>
<td>HLA A, B mismatch</td>
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<td></td>
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<tr>
<td>HLA DR</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>Cold ischaemia (CIT.h)</td>
<td>13.8 (4–28.5)</td>
<td></td>
</tr>
<tr>
<td>Time on waiting list</td>
<td>11 (4–26)</td>
<td></td>
</tr>
<tr>
<td>Single kidney</td>
<td>14</td>
<td></td>
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<tr>
<td>&quot;En bloc&quot; transplant, n</td>
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**Fig. 1.** Kidney volume during the first year after transplantation. Mean and 95% CI is shown
ERPF at 1 week was 159 ml/min and 248 ml/min at 12 month, a 1.6-fold increase \( (P < 0.001) \) (Figure 2). The increment in size and function was of the same magnitude irrespective of whether one kidney or two 'en-bloc' kidneys were used. There was no correlation between recipients' BMI and the increment in size of the kidney(s), assessed by regression analysis. FF increased from 0.20 at 1 week to 0.24 at 6 and 12 months post-operatively (Figure 3). Average HLA-AB mismatches were 2.7 and HLA-DR mismatch was 0.6. Cold ischaemia time (CIT) was 13.8 h (range, 4–28.5) (Table 1).

Seventeen of the 19 patients had immediate graft function. Two patients had delayed graft function. One needed haemodialysis support four times, the other, only one session before the kidneys functioned properly. In these patients, GFR and ERPF were measured 1 week after the kidney started to function (day 9 and 12 post-operatively). Serum creatinine at 1 week after the transplant started to function and averaged 168 μmol/l (range, 111–280). Patient and graft survival at 1 year were 100%.

At that time mean serum creatinine for all patients was 91 μmol/l (range, 66–169). Three patients were re-operated the first week post-transplant due to technical problems, one due to post-operative haematoma and two because of ureter complications. Two other patients had surgery during the first year because of lymphocele.

Ten patients out of 19, experienced, one or more episodes of acute rejection, during the first year. Unfortunately, only half of them were biopsy verified. Standard treatment was 5 days of high-dose i.v. methylprednisolone (total dose of 1375 mg). Two rejections were considered steroid resistant and were treated with antithymocyte globuline (ATG) i.v. All were successfully treated. Hypertension did not worsen as estimated from the number of antihypertensive drugs given.

**Discussion**

This prospective single centre study shows that paediatric kidneys transplanted to adults have a substantial potential for growth and improvement of function during the first year. Interestingly, the kidney
size increased somewhat more than GFR and renal blood flow, as estimated by the increase in ERPF. This finding indicates a growth and increase of nephron size beyond the increment in function. This predominant increase in size is potentially beneficial since adequate renal mass is considered to be of paramount importance for sustained long-term function [21]. However, a 20% increase in filtration fraction was noted at 6 and 12 months post-operatively. A correlation of BMI and increment in size of the transplanted kidney could be suspected, but was not seen. BMI is a crude measure and does not necessarily reflect lean body mass or kidney size. None of the patients developed worsening of hypertension. There were no graft losses. The excellent function at 1 year and lack of signs of hyperfiltration damage give prospects for good long-term function of these paediatric kidneys.

Ngheim et al. [22] showed in 21 ‘en-bloc’ transplantations of paediatric kidneys to adults a 2- to 3-fold growth and perfect function of the kidneys during the first year. In that study, GFR measured scintigraphically, increased 4- to 5-times during the same time period. However, this measure is actually only an approximation of GFR and should at best be considered an estimate. None of the recipients exhibited proteinuria or other signs of hyperfiltration injury. They concluded that en bloc kidneys provided excellent function in adult recipients and that paediatric en bloc kidneys should be used more often to reduce organ shortage. Based on their own data and that from others, they advocated en bloc transplantation of kidneys from donors <20kg [23]. In a study from Borboroglu et al. [15], excellent function and no sign of hyperfiltration injury were found in 15 patients transplanted with a single kidney if the length of the donor kidney was 6 cm or more and if the donor weight was >14 kg. This is supported by our study where single kidneys from donors weighing ≥12 kg functioned perfectly well in recipients of 70 kg. On the other hand, Pelletier et al. [3] compared graft outcomes from small pediatric donors (<21 kg), transplanted en bloc (n=1301) and as single kidneys (n=1175) and found an adjusted 5-year graft survival of 72.7% and 54.8%, respectively. Further studies are necessary to define the optimal use of paediatric kidneys for transplantation.

Transplantation of paediatric kidneys has a higher incidence of technical complications than adult to adult transplantations and the technical problems increase inversely with the size of the kidney. Hobart et al. [24] reported up to 39% surgical complications in 33 patients transplanted with en bloc kidneys compared with 9% in the adult to adult group and Memel et al. [25] reported an arterial thrombosis rate of 10% in paediatric kidneys transplanted to adults. In our series, there were no graft losses due to technical complications. However, although no kidneys were lost in this study, we have experienced graft loss due to arterial and venous thrombosis, both prior to and after the study.

Paediatric donor kidneys seem to have an increased incidence of episodes of acute rejection compared with adult kidneys. Gourlay et al. [26] reviewed outcomes of 83 recipients receiving kidneys from very young donors (5 months to 10 years of age) and compared them with results in 100 adult allograft recipients. They found that paediatric vs adult donor allograft recipients had an increased number of total rejection episodes (71% vs 59%). In our study 10 patients out of 19 experienced one or more episodes of clinical rejection during the first year. This is slightly higher than in adult to adult transplantations in our centre at that time. Only one half of them were biopsy proven, due to the risk of bleeding complications. Therefore it would be inappropriate to draw any conclusions about the frequency of acute rejections in our material.

Some authors advocate careful selection of donors according to weight and medical and immunological risk factors, e.g. ABO compatibility, HLA A, B and DR mismatches and time on the waiting list [11,27]. We did not select recipients specifically for the study, the organs were allocated according to standard criteria. Coincidentally, all were first transplants and none PRA positive.

Although paediatric kidneys comprise an essential part of the deceased donor pool, they are still ignored for transplantation at some centres. It is important to utilize as many of these organs as possible to fill the gap between supply and demand. Extended use of these and other deceased donors with a surplus of a high rate of live kidney donation has contributed to a low and stable waiting list for kidney transplantation in Norway [available at http://www.nephro.no/registry.html. 2006].

To conclude, this study shows a rapid and significant increase in size and improvement of function of paediatric kidneys up to 1 year after transplantation when transplanted to adults. With the present refined surgical technique and immunosuppressive therapy to prevent early serious rejections, paediatric kidneys may be considered excellent for adult recipients.

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Conflict of interest statement. None declared.

References


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