Long-term clinical outcome of paediatric kidneys transplanted to adults

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Abstract

Background. We have earlier shown an increase in the size and excellent graft function of paediatric kidneys transplanted to adults up to 1 year following transplantation. This study was performed to assess the long-term outcome of these transplants.

Methods. From a primary cohort of 19 adults, receiving a first kidney transplant from a paediatric donor <10 years of age, 16 patients were available for a complete long-term follow-up, 5–9 years post-transplant. Of these, eight patients were transplanted with a donor of <5 years. All medical files and registry data of the cohort, from the time of transplantation to the follow-up time point, were recalled and events were registered. The patients' general condition, body weight, blood and urine tests, blood pressure (BP), use of antihypertensive agents and GFR were recorded. To explore the temporal increment in the size of paediatric donor kidneys transplanted to adults, the maximal cranio-caudal length of the kidneys from the time of transplantation to follow-up was established by ultrasound. Volumes (length × width × thickness × π/6) of en bloc kidneys versus single paediatric kidneys and adult-to-adult transplants were compared.

Results. Long-term (7 years, median) patient and graft survival was 95% and 89%, respectively. Mean serum creatinine was 85 µmol/l (range, 32–131). The mean estimated GFR was 84 ml/min/1.73 m². The mean BP was 134/79 mmHg (range, 120–185/70–90). The number of antihypertensive agents used was not statistically different from the number used at 1 year post-transplant. None of the patients had significant proteinuria as a sign of hyperfiltration injury of the graft. There were no statistically significant increases in the maximal cranio-caudal length of the transplanted kidney(s) from 1 year post-transplant to follow-up; however, the en bloc kidneys tended to be larger than single paediatric grafts (240 ml and 204 ml) and adult-to-adult grafts (170 ml).

Conclusion. Paediatric kidneys transplanted to adults should be considered as excellent for transplantation on a long-term basis.

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

Introduction

Although live donation in kidney transplantation is steadily increasing, the uraemic population awaiting a kidney transplant is expanding [1,2]. There is evidence that paediatric kidneys transplanted into adult recipients have good graft function and satisfactory graft survival [3–5]. Still, data show that a significant part of paediatric donor kidneys is not used for transplantation and that graft survival, when transplanted to adults, often is inferior compared to adult kidney grafts [6,7]. Due to the scarcity of donors and a high mortality rate of the dialysis population, it is of utmost importance to clarify and analyse all aspects for the optimal use of paediatric donor kidneys. In a recent prospective, single-centre study, we have shown that paediatric kidneys transplanted to adults have a substantial potential for growth, improvement of function and excellent graft function (100%) up to 1 year post-transplant [8]. When initial complications are avoided, several authors have suggested that paediatric kidneys may be considered as excellent, rather than marginal, for transplantation to adults [3–5,8]. Data regarding long-term function and single or en bloc transplantation of small paediatric kidneys are diverging. In the present study, a complete long-term follow-up of the patients from the mentioned primary study was performed with primary focus on continued growth and graft function.

Subjects and methods

In the primary study, 19 adults received a kidney from a donor of <10 years of age. The study was prospectively designed. Increment in the size post-transplant and
measurements of function were evaluated at 1, 3, 6 and 12 months post-transplant [8]. At 1 year post-transplant, patient and graft survival was 100%, indicating that paediatric kidneys are excellent for transplantation to adult recipients at least up to 1 year following transplantation. At transplantation the patients received standard immunosuppression, which consisted of steroids, cyclosporine and azathioprine for the first 13 recipients enrolled in the study. In the last six patients, basiliximab ($n = 3$) or mycophenolate mofetil ($n = 3$) was used instead of azathioprine.

After the first year post-transplant, the patients have been regularly examined by their local nephrologist. Each year, updated reports of all patients have been received and recorded in the Norwegian Nephrology Registry. In the present study, all patients from the primary study were summoned for a complete long-term check-up, 6–9 years post-transplant (median, 7 years). The general condition of the patients, body weight, blood and urine tests, blood pressure (BP), immunosuppression and use of antihypertensive agents were recorded. GFR was estimated based on the updated MDRD study equation, i.e. $\text{GFR} = 38.89 \times (\text{standardized } \frac{S_c}{\text{Cr}})^{−1.154} \times (\text{age})^{−0.203} \times 0.742 \times (0.742$ was replaced by 1.0 if the subject was male), and expressed as ml/min/1.73 m$^2$ [9].

To evaluate if paediatric renal transplants increase in size beyond the first year post-transplant, U/S measurement of the cranio-caudal length of the transplanted grafts was repeated and compared with measurement performed at 1 year post-transplant. The same U/S machine was used in the follow-up study as in the primary study (Siemens Acuson SequoiaTM, 4C1 ultrasound transducer). All examinations in the follow-up study were done by one radiologist (A.G.). The maximal cranio-caudal length was measured on a longitudinal scan through the renal hilum. In recipients with two en bloc grafts, the sum of both kidneys was calculated as the graft length. Scans were retrospectively compared to the scans from the primary study (1 year post-transplant) in order to reduce measurement inaccuracies due to different placement of the electronic callipers.

Kidney transplants from donors <5 years, and particularly en bloc transplants, are of special interest. The cohort is too small to give valid answers to what extent en bloc kidneys increase in size. However, to give a hint, volumes ($\text{length} \times \text{width} \times \text{thickness} \times \pi/6$) of en bloc kidneys and single transplanted kidneys at 7 years post-transplant were compared. To assess whether en bloc kidneys reach the size of an adult kidney volume, measures of en bloc kidneys were compared with nine functioning adult-to-adult kidney grafts 5–10 years after transplantation. All medical files and registry data of the cohort, from the time of transplantation to the follow-up time point, were recalled and events were registered.

Statistical methods

Statistical level of significance was set to $P < 0.05$. Data in the figure are expressed as mean and 95% confidence interval (CI) and in the table as mean and range. For comparisons of 1-year data and long-term data, two-tailed repeated measures analyses of variance were performed. To assess the association between the maximal cranio-caudal length of the kidneys and BMI, a linear regression analysis was performed. SPSS (version 13, SPSS Inc., Chicago, IL, USA) was used for the statistical calculations.

### Results

At 7-year (range 6–9 years) follow-up after transplantation, 18 out of 19 patients were still alive. Mean age was 56 years (range 28–75 years). One patient, transplanted with a donor of 66 months, developed a stricture of the ureter due to a chronic polyomavirus infection at 13 months after the transplantation. A cysto-pyelostoma was successfully performed. Two years post-transplant the patient lost the graft due to chronic allograft nephropathy (CAN) and later he died due to intracerebral haemorrhage. Another patient transplanted with a single kidney from a donor of 42 months also lost the graft due to diagnosed CAN. One patient with a functioning graft is living in a nursing home at the age of 75. Thus, of the 19 patients from the primary study, 16 patients were available for long-term evaluation. Long-term patient and graft survival of the cohort was 95% and 89%, respectively (Table 1). Mean serum creatinine was 85 µmol/l (range; 32–131). The mean calculated GFR was $84 + 43 \text{ml/min/1.73 m}^2$. For comparison, the 1-year post-transplant calculated GFR was $80 + 32 \text{ml/min/1.73 m}^2$. Two patients had estimated GFR <60 (38 and 54 ml/min/1.73 m$^2$) at follow-up; both of these transplants were from donors >5 years at the time of transplantation.

None of the patients had significant proteinuria as the sign of hyperfiltration injury of the transplant.

The maximal cranio-caudal length of the transplanted kidney(s) from the time of transplantation to follow-up is shown in Figure 1. As seen, there was a further growth of the kidney beyond the first year; however, the increment in the length from 1 year post-transplant to follow-up was not statistically significant. At follow-up, mean BMI of the cohort increased from 24.0 (16.8–33.3) to 25.9 (21.2–32.2), but there was no significant correlation between the kidney size (cranio-caudal length) and BMI evaluated by regression analysis.

Of the 16 patients eligible for long-term follow-up, 8 were transplanted with a donor of <5 years. Five donors were ≤2 years or had a body weight of <12 kg. These kidneys were transplanted as two en bloc kidneys. At long-term follow-up, the length of two en bloc kidneys together

### Table 1. Long-term clinical outcome versus 1-year data

<table>
<thead>
<tr>
<th></th>
<th>1 year</th>
<th>7 years</th>
<th>Statistical level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient survival (%)</td>
<td>100</td>
<td>95</td>
<td>ns</td>
</tr>
<tr>
<td>Graft survival (%)</td>
<td>100</td>
<td>89</td>
<td>$P &lt; 0.05$</td>
</tr>
<tr>
<td>Creatinine (mean) (µmol/l)</td>
<td>91</td>
<td>85</td>
<td>ns</td>
</tr>
<tr>
<td>GFR (estimated* ml/min/1.73 m$^2$)</td>
<td>80</td>
<td>84</td>
<td>ns</td>
</tr>
<tr>
<td>Kidney size (length, cm)</td>
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<td>13.7</td>
<td>ns</td>
</tr>
<tr>
<td>BMI</td>
<td>24.0</td>
<td>25.9</td>
<td>ns</td>
</tr>
<tr>
<td>BP (sys/dias., mmHg)</td>
<td>130/80</td>
<td>134/79</td>
<td>ns</td>
</tr>
<tr>
<td>BP medication (No.)</td>
<td>1.5</td>
<td>1.2</td>
<td>ns</td>
</tr>
</tbody>
</table>

*MDRD equation.

BMI: body mass index, BP: blood pressure.
tended to be longer than the length of one single kidney alone (16.5 cm versus 12.5 cm), but the difference was not statistically significant. The mean volume of two en bloc kidneys was 240.1 ml (range, 217.1–271.9) and for single kidneys it was 204.1 (range, 96.0–358.2), ns. Finally, the volumes of two en bloc kidneys were larger than the size of single adult-to-adult grafts (170.2 ml, range 116.6–236.1).

The mean number of antihypertensive drugs was 1.5 drugs/patient at 1 year and 1.2 drugs/patient at 7 years post-transplant. Immunosuppression consisted of prednisolone (n = 16), ciclosporine (n = 14) or tacrolimus (n = 2) and azathioprine (n = 11) or MMF (n = 3). Two patients developed skin cancer, one spincellular and one basal cell carcinoma. Both were successfully treated with surgical excision. Only one patient experienced acute rejection after the first year post-transplant. The rejection was successfully treated with steroids.

Discussion

The results from this study indicate that long-term graft function of paediatric kidneys transplants to adult recipients is excellent. At 6–9 years following transplantation, graft survival was excellent, approaching 90%. Kidney transplant function was excellent and all patients, but two, had normal kidney function with normal serum creatinine and GFR >60 ml/min/1.73 m². There was no evidence of worsening of hypertension or development of proteinuria as the sign of hyperfiltration injury.

In this series, there were no technical complications at the time of transplantation and no early acute rejections, which potentially could have had negative impact on graft survival. This is in accordance with Sureshkumar et al. who found that paediatric en bloc kidneys, once they survived the early postoperative course, have a better long-term function than living donor kidney transplants [3].

Lately, there has been increasing interest, especially for the very small paediatric donors, those <5 years of age [4–6]. Dharnidharka et al. showed that en bloc kidney transplantation had better long-term graft survival than comparable single kidney transplants, 71% and 63%, respectively [5]. Pelletier et al. compared graft outcomes of small paediatric 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 [6]. When we compared the size of paediatric en bloc kidneys with single paediatric grafts and adult-to-adult kidney grafts at long-term post-transplant, the sum of the two kidneys together was larger than the size of a single paediatric graft and adult-to-adult grafts. Possibly, larger renal mass explains a superiority of paediatric en bloc transplants compared to other kidney transplants [3–6].

Since donors <5 years comprise a considerable part of the deceased paediatric donor pool, it is important not to generalize and conclude that all such kidneys should be transplanted en bloc. In many cases, even smaller single kidneys can work perfectly long term. In a study from Borboroglu et al. 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 [10]. In our cohort 9 of 19 donors were <5 years. Of these, only one transplant was lost (due to CAN) at 5 years post-transplant and all single kidneys from donors >2 years or ≥12 kg have functioned perfectly long term.

The next step for maximal utilization of the paediatric donor pool for adults is to define strategies to lower the age and weight threshold for single kidney transplantation. Several factors for optimal allocation (single kidney or en bloc kidneys) of paediatric donor kidneys seem obvious, such as graft quality, cold ischaemia time (CIT), surgical expertise and recipient characteristics. However, also the desired level of graft survival must be taken into consideration. As waiting lists for kidney transplantation increase and mortality while waiting for a transplant is considerable, the desired optimum for graft survival must be discussed in this context [11,12].

This study has investigated transplantation of paediatric donor kidneys to adults. It has been shown that paediatric kidneys perform better in children than kidneys from adults [13,14]. Therefore, a paediatric donor kidney should primarily be allocated to a paediatric recipient. Only if no paediatric recipient is available should the kidney be allocated to an adult recipient.

To conclude, as demonstrated in this study, when initial complications post-transplant are avoided, paediatric kidneys transplanted to adults should be considered as excellent for transplantation on a long-term basis.

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Conflict of interest statement. None declared.

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