Kidney transplantation in small children with live related donors: 20 years of experience

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Received 18 October 2005; accepted 3 May 2006
Available online 10 July 2006

Abstract  Objectives: Kidney transplantation (Tx) with a live related donor is the best option available for the treatment of end-stage renal disease at any age. Modern dialysis has allowed many very young and small children to receive a renal transplant with good results in spite of the limitations of space and the size of the adult kidney. Here, we report our experience with renal Tx with live related donors in this complex group of pediatric patients.

Material and methods: From 1978 to 2004 a kidney transplantation was performed in 211 pediatric patients. Of this group, 23 patients between 1 and 10 years of age (16 males and seven females) of less than 17 kg (8.9–16.9 kg) received their first live related donor transplantation between 1985 and 2004. Renal insufficiency was secondary to nephropathy in 11 patients, infravesical obstruction in six and renal dysplasia or renal infarcts in six.

Results: Patient and graft survival was 100% and 95.6% with an average follow up of 89.6 months (6–231). There were no vascular or urological complications. Urinary infection in five (21.7%) and acute rejection in three (13%) were the most common complications. One patient has returned to dialysis 11 years after Tx.

Conclusions: Young pediatric patients with a low body weight did not suffer a higher percentage of postoperative surgical complications, and the follow-up results are similar to those in older patients. A complex urological malformation has not prevented a living related Tx. These results encourage us to perform this procedure more frequently in younger patients when a live donor is available.

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Introduction

Kidney transplantation is the best option available to treat end-stage renal disease (ESRD) at almost every age [1,2]. For the last 30 years kidney transplantation has been performed in children and teenagers, but is still used less frequently in small and very young children because it is technically more demanding. There are complex surgical, anesthetic and pediatric intensive care requirements. All living related donors in children's renal transplantation are adults for legal reasons (by law in our country they must be older than 21 years), and thus the relationship between kidney length and the available space in the retroperitoneum is out of proportion. The difficulty is even greater in very small children because younger patients present specific anesthetic problems related to vascular and hemodynamic changes after graft revascularization.

In the last 20 years the possibility of very young children with ESRD receiving a kidney transplantation has increased because of numerous technical advances in renal replacement. These include the ability to perform continuous ambulatory peritoneal dialysis or continuous cycling peritoneal dialysis in neonates and small children during the night at home. Other factors that have permitted transplantation in small children are the new methods of treating acute rejection and preventing and treating viral infections. These new therapies have improved patient and graft survival in the short and long term, reducing the frequency and seriousness of the complications of acute rejection and cytomegalovirus infection [3,4].

This group of small patients are probably most affected by surgical and perioperative aspects of treatment. The work of the pediatric urologist is very important and impossible to replace. Our purpose here is to present the results of the work of a group of pediatric surgeons, pediatric urologists and nephrologists during the last 20 years with kidney transplantation in a selected group of pediatric patients with ESRD and low body weight.

Material and methods

From 1978 to 2004, 213 children and adolescents received a kidney transplant in the Department of Pediatrics of the Hospital Italiano of Buenos Aires. Since 1985, 23 patients between 1 and 10 years of age (16 males, seven females) with ESRD and a body weight lower than 17 kg (8.9–16.9) received their first transplantation from a live related renal donor. Mother was the donor for 14 patients, father for eight and an aunt for one. Peritoneal dialysis was used preoperatively in 12 patients, hemodialysis in three, four patients received both types of dialysis and four patients had no dialysis before transplantation (pre-emptive).

If any patient had a history of catheters being used for hemodialysis in the femoral veins a Doppler investigation of both iliac veins and the inferior vena cava was performed preoperatively to identify potential anastomotic difficulties. Grafts were harvested when possible from the side with only one renal artery. We preferred to use the left side (20) rather than the right (3) because of the length of the renal vein. Implants were always placed in the right side of the receptor, it being technically easier to perform the venous anastomosis to the inferior vena cava. When the graft came from the right side it was turned upside down, freeing the renal pelvis from the lower renal pole to avoid ureteral kinking.

The etiologies of ESRD that led to kidney transplantation are reviewed in Table 1. Only seven patients (63.6%) of the 11 patients with a congenital pathology had a renal abnormality diagnosed on prenatal ultrasound. Previous or concomitant surgery was nephrectomy [5], undiversion [3], Mitrofanoff [2], and herniotomy, pyeloplasty, colostomy closure, Fowler–Stephens first stage, ureterocystoplasty and colonic resection each in one patient. This last patient had a serious complication from a hemolytic uremic syndrome (HUS) that obliged us to surgically repair a colonic stenosis to avoid performing a kidney transplantation in a patient with a colostomy. One patient received a transplant inspite of maintaining a vesicostomy due to the impossibility of maintaining a proper dialysis program.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
<th>%</th>
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<tr>
<td>Nephropathy</td>
<td>11</td>
<td>47.8</td>
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<tr>
<td>Hemolytic uremic syndrome</td>
<td>7</td>
<td></td>
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<tr>
<td>Congenital nephrotic syndrome</td>
<td>4</td>
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<tr>
<td>Dysplasia, polycystic renal disease and renal infarct</td>
<td>6</td>
<td>26.08</td>
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<tr>
<td>Renal dysplasia</td>
<td>3</td>
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<tr>
<td>Polycystic kidney disease</td>
<td>2</td>
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<tr>
<td>Renal infarct</td>
<td>1</td>
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<tr>
<td>Infravesical obstruction</td>
<td>6</td>
<td>26.08</td>
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<tr>
<td>Posterior urethral valves</td>
<td>3</td>
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<tr>
<td>Prune belly syndrome</td>
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The donor kidney was harvested in a second surgical room close to the recipient’s. Perfusion with a cold solution of Ringer’s lactate, lidocaine 1%, heparin and methylprednisone was carried out for complete clearing of blood and adequate cooling of the kidney. A wide hockey-stick incision was performed through an extraperitoneal approach with exposure from the diaphragm to the pelvis, improving the possibility of visualization and dissection of the iliac vessels, aorta and inferior vena cava. When needed, an ipsilateral nephrectomy was performed at the same time. Extensive lymphatic control was required with electrocoagulation and tie sutures in order to avoid a lymphocele. Vascular anastomosis with optical magnification (3.5 or 5×) was performed on big vessels in every case, maintaining the inferior mesenteric artery in all patients (Fig. 1). Three patients required two arterial anastomoses. Urinary anastomoses were performed with a Lich–Gregoire extravesical reimplantation in 21 (Fig. 2), a Politano–Leadbetter reimplantation in one and a pyeloureteral anastomosis in one. A double J catheter to protect the anastomosis was used in seven patients.

Transitory postoperative urinary diversion was carried out with a silicone urethral catheter in 18 patients, through a Mitrofanoff in two, cystostomy in two and maintaining the original vesicostomy in one patient. Immunosuppressive medical therapy was given to the first eight patients with a classical combination of cyclosporin (Sandimmun®), azathioprine (Imuran®) and corticosteroids such as prednisone (Deltisona®). From 1993, a more selective antimetabolite than azathioprine, such as mycophenolate mofetil (CellCept®), replaced azathioprine (six patients), and from 2001 a calcineurin inhibitor, such as tacrolimus (Prograf®), replaced cyclosporine (nine patients). Nowadays, and in the last 11 patients, a five-dose course of daclizumab (Zenapax®), a humanized monoclonal antibody, is included in the immunosuppressive protocol. In cases of acute rejection, pulses of methylprednisolone (Solumedrol®) and monoclonal antibodies such as OKT3 (Orthoclone®) or polyclonal antibodies such as thymoglobulin have been the most commonly used drugs.

Results

Patient and graft survival was 100% and 95.6%, respectively, with an average follow up of 89.6 months (range 6–231 months). There were no surgical complications such as lymphocele, or vascular or postoperative urologic complications such as leaks or stenoses. A mild form of acute tubular necrosis was present in four patients (17.3%) but none required postoperative dialysis. Urinary infection in five (21.7%) and acute rejection in three
(13%) were the more common complications. One of the patients who presented with urinary infection and prune belly syndrome as the original diagnosis developed VUR to the transplanted kidney that required treatment with an endoscopic subureteral injection of a bulking agent.

Two patients showed decreased glomerular filtration because of chronic allograft nephropathy (CAN) and one of them has returned to hemodialysis. One patient had a cytomegalovirus symptomatic infection and another calcineurin inhibitor toxicity because of tacrolimus; both needed to be treated as an inpatient. As expected, because of the original diagnosis, no recurrences of the original disease that led children to ESRD have been reported.

Glomerular filtration rate (GFR) in the 21 patients without CAN decreased from 140–73 ml/min/1.73 m² (mean 107.57) at 1 month after surgery to 95–36 (mean 74.4) after nearly 9 years of mean follow up. Twenty patients (86.7%) are attending normal school; one patient is deaf and receives special education. The other two patients presented with ESRD as part of a complex syndrome with mental retardation. All donors are doing well with normal renal function.

Discussion

Recent developments in prenatal diagnosis and subsequent treatment of patients with a urological abnormality have reduced perinatal mortality from renal insufficiency and pulmonary hypoplasia. There is therefore increased survival beyond the first months of life of a very special group of young patients with ESRD. These children have difficulties in growing and gaining adequate weight. Most of the time they require renal replacement therapy because of very low creatinine clearance and metabolic disturbances secondary to ESRD [5]. It is now possible to perform effective renal replacement therapy, especially with peritoneal dialysis and by improving nutritional status by parenteral nutrition or permanent enteral feeding, in order to achieve weight gain for a kidney transplantation. The frequent availability of a live related donor for a child (usually a parent) has enabled the avoidance of long waiting lists, improved the chance of graft survival and allowed the quality of life to improve at an early age.

In this retrospective review we report our results in kidney transplantation in pediatric patients using live related donors selected only by low body weight. These patients represent a very small sample (23 patients) over a very long period of time. During these years, many important changes have been developed to improve renal transplantation results. Although it is not possible to make any of these results statistically valid, this retrospective analysis has been very useful to us, as it confirms that good results can be maintained not only in the short term but after long-term follow up as well. Patient and graft survival has been excellent in small children in other reports in the pediatric urology literature [6–8]. The etiology of ESRD in our patients is quite similar to that in the NAPRTC reports [4,5], with 50% of structural congenital defects, being only different because of the high percentage of children with HUS, an extremely serious regional illness in Argentina. One of the most interesting points related to the etiology of ESRD is that none of the 23 patients had a theoretical possibility of recurrence of the original pathology in the transplanted kidney. This is obviously very important in terms of the long-term follow up.

Live related transplantation is synonymous with immediate urine production (practically always in the surgical room) in nearly 100% of patients. This simplifies postoperative management, avoiding the necessity of trying to dialyse a patient who has just undergone surgery. Obtaining an intraoperative normal urine output is clearly one of the best ways of avoiding the onset of acute rejection in the early postoperative days [5,9]. In a large series it was shown that until 1997 graft survival was statistically better in live related than cadaveric transplantation (P < 0.005) [4]. This fact is now less significant (comparing all pediatric age groups), as the last series with nearly 7545 pediatric kidney transplantations [10] showed that there had been a very important reduction, from 35% to 10%, in cadaveric transplantations in patients younger than 10 years old. We have used the same general criteria in the last 20 years, selecting a live related donor when one was available. There are two very interesting reviews of the same subject that reach the same conclusions [11,12]. As we have not performed cadaveric transplantation in young children since 1985, it is difficult to imagine what would have been our results with cadaveric kidneys due to all the improvements in harvesting, preservation and transportation of cadaveric organs in our country, and in the treatment of rejection. A study performed by the NAPRTCS comparing cyclosporine with tacrolimus showed improved graft function at 1 and 2 years of follow up, and in a European multicenter study there was a reduction in rejection episodes [13,14]. The reduction of GFR measured with creatinine clearance in the 21 patients without CAN (one on
dialysis and the other with very low GFR) is much better than expected by most of the reports [2,11,15], showing a graft survival rate of 86.7% after nearly 9 years of follow up.

In Fig. 3 we compare this group with the rest of the pediatric patients receiving a kidney transplant at our institution in the last 11 years. Positive differences in terms of organ survival can be seen in the long-term follow up, showing the importance of adequate management of all the previously mentioned factors in the small and young patients. Though results are obviously very good, we have not had extremely young children (less than 1 year) or old donors, with whom final results are poorer. We have also not carried out transplants in black people or adolescents, both groups with poorer final results as clearly stated in NPRACTS and other reports [1,3,16], adding another positive factor and helping us to achieve better results than with older patients, as has been recently published [17]. For long-term follow up, we are lucky that none of our 23 patients has the possibility of recurrence of the original illness in the new kidney, because of the nature of the original pathology that led to ESRD. Only school attendance was evaluated in our report because it was simple to review, but other important factors need to be measured in the future, such as growth, obesity, psychological problems and quality of life.

Surgical technique was not different from that used in older children, with the exception of a wider incision in order to expose the abdominal vessels without opening or tearing the peritoneum, and allow us to perform an adequate vascular anastomosis to avoid vascular kinking after closure of the wound. We did not find that surgical time is longer or surgery more difficult than in older children leading to delayed graft function as has been published [11]. Even in very small patients (less than 12 kg) it was not necessary to use an intraperitoneal approach as previously described in other reports, with the advantages of rapid tolerance of oral feeding, absence of postoperative intestinal adhesions, and the possibility to maintain peritoneal dialysis in the immediate postoperative period and fix the kidney in the right position avoiding torsion of the renal vessels of the transplanted kidney [18]. Though nephrectomy of the native kidney is not always necessary, it can be performed to create enough space for the transplanted kidney, especially in polycystic renal disease, or to use the native complete pelvis and ureter for a ureterocystoplasty, as was performed simultaneously using both ureters in one boy with a very small bladder secondary to urethral valves and high bilateral ureterostomy since the first days of life. In the last 2 months we have performed another successful kidney transplantation in a very small patient (13 kg) not included in this report, with simultaneous ureterocystoplasty and a Mitrofanoff urinary diversion. This seems to be a new surgical approach for selected patients with megaureter and small bladders. The absence of lymphocele in spite of the large retroperitoneal dissection in these patients must be stressed, and is the result of meticulous lymphatic control during the vessels’ surgical exposure.

Many reports in recent years have stressed that graft survival is not adversely affected when the transplanted ureter drains into an abnormal reconstructed bladder if the capacity is adequate, compliance is high, and complete emptying is obtained by spontaneous voiding or intermittent catheterization through the urethra or a continent

![Figure 3](image-url)  
**Figure 3**  Comparison of graft survival between pediatric patients (less than 17 kg) with live related donor and the rest of the pediatric patients receiving a kidney transplantation (live and cadaveric) in the last 11 years.
urinary diversion [19–22]. Urinary infection must be controlled after transplantation; prophylactic antibiotics and permanent nocturnal urinary drainage in augmented bladders could be effective ways to reduce symptomatic urinary infections [11,23]. If a patient has prune belly syndrome and one or both intra-abdominal testes have not been treated before kidney transplantation, during the extraperitoneal approach the first stage of Fowler–Stephens orchidopexy can be performed. Some months later testicular descent can be completed using a laparoscopic approach (these patients did not need any more continuous ambulatory peritoneal dialysis) using deferential vessels as the main source of testicular vascularization. As in most of the published series and books on pediatric kidney transplantation, we have performed an extravesical Lich–Gregoire ureteral reimplantation on the native bladder as first choice without double J catheters, because of the lack of urinary complications when the donor ureter is healthy, well vascularized and with a normal, small diameter [17,24]. We only used double J catheters when a pyelo (donor) ureteral (receptor) anastomosis was performed, or in very small bladders where ureteral reimplantation was technically difficult and the bladder wall was extremely thin. Intuitively, it seems important to perform an efficient transitory urinary diversion to obtain a good seal of the ureteral anastomosis, especially in a previously anuric patient, until the bladder has recovered its normal capacity and compliance.

This last comment is very important in patients with urethral valves or prune belly syndrome whose bladder has not functioned for a very long time, i.e. since the first days of life (ureterostomy, vesicostomy). A urethral catheter may be good enough in most of the patients but a cystostomy tube can be useful in these situations; with periodic clamping of the cystostomy tube normal bladder capacity may be obtained. The Mitrofanoff procedure previously located in the umbilicus is not only very comfortable and prevents problems with ureteral reimplantation but permits an extremely good urinary diversion through a bladder catheter. Only four patients were transplanted without previous dialysis (pre-emptive) [25,26], which we perform more frequently in older children and adolescents. This difference can be explained because of the need, in most of our young patients, to begin or maintain peritoneal dialysis or hemodialysis while they gain weight, or while a urinary tract reconstruction or undiversion is carried out, or infrequently to wait for delayed renal function improvement in patients with HUS.

Conclusions

We pediatric urologists have in the past been very worried about the future of the very small patients with ESRD, most of whom were under our personal follow up or treatment since they were fetuses. The possibility of offering a kidney transplantation to small and very young children without a higher percentage of postoperative surgical complications and with good or even better results than in older patients is a very promising concept. A surgically corrected serious urological abnormality has not been in our experience a limitation for a living related kidney transplantation. Many previous or simultaneous reconstructive operations will be an obligatory part of the treatment. These results should encourage pediatric urologists and nephrologists to perform these type of procedures in young patients more frequently when a live related donor is available.

References

Kidney transplantation in small children


