Pediatric Kidney Transplant With Laparoscopic Donor Nephrectomy

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Abstract

Objectives: To evaluate outcomes and complications with pediatric living-donor kidney transplant, mostly performed with laparoscopic donor nephrectomy.
Materials and Methods: In the 25 years between February 1987 and December 2012, there were 493 children aged ≤ 17 years who received a kidney transplant. Demographic characteristics, graft and patient survival, rejection episodes, and complications were recorded. Analysis was performed for 3 sequential periods (1987-1994, 1995-2002, and 2003-2012).
Results: The mean patient age was 13 ± 4 years (age range, 2.5-17 y). There were 290 males (59%). Glomerulonephritis was the most common cause of end-stage renal disease. Preemptive kidney transplant was performed in 412 patients (84%). Donor nephrectomy was performed laparoscopically in 445 patients (90%). The 5-year graft and patient survival were improved from 1987-1994 to 2003-2012. The overall death-censored graft survival was 96% at 1 year, 78% at 5 years, and 66% at 10 years after transplant. The overall patient survival was 96% at 1 year, 83% at 5 years, and 75% at 10 years after transplant.
Conclusions: Kidney transplant is available for most pediatric patients and has acceptable graft and patient survivals. Laparoscopic donor nephrectomy improves donor satisfaction and morbidity, and may provide excellent graft outcomes in children.

Introduction

End-stage renal disease (ESRD) contributes to multiple problems in children, including growth retardation, cognitive and psychosocial delay, impaired exercise capacity, changes in body habitus, disturbance of cardiovascular health, and decreased quality of life. Substantial improvements in pediatric renal replacement therapy (dialysis and transplant) have occurred during the past 40 years.[1] However, dialysis and related therapies confer major restrictions on the child and family. Kidney transplant is the treatment of choice for children who have ESRD.[2] Life expectancy after transplant is almost 2-fold greater than that for patients who remain on dialysis.[3]

The first pediatric kidney transplants were performed in the 1970s. The number of transplants increased slowly during the 1980s and has been stable since 2000. Most transplant centers report that approximately two-thirds of children and adolescents in ESRD programs have a transplant.[4,5] Follow-up studies of survival for 20 years have been published.[6,7] We previously presented a randomized controlled study that compared open and laparoscopic donor nephrectomy in children and adults.[8,9] The purpose of the present historical cohort study was to evaluate and document our results of pediatric kidney transplant with more patients and longer follow-up (from 1987 to 2012).

Materials and Methods

In this historical cohort study, the medical records of all children aged ≤ 17 years (n = 493 patients) who underwent kidney transplant between February 1987

and December 2012 were reviewed. Demographic characteristics, graft and patient survival, rejection episodes, and surgical and other complications were recorded. Graft and patient survival data were obtained from the Collaborative Transplant Study registry in Heidelberg, Germany, in which all patients had been registered. Analysis was performed for 3 sequential periods (1987-1994, 1995-2002, and 2003-2012). Statistical methods included simple descriptive analysis and Kaplan-Meier method. Statistical significance was defined by $P \leq .05$.

The study was approved by the Ethical Review Committee of the institute. All protocols conformed with the ethical guidelines of the 1975 Helsinki Declaration. Informed consent was obtained from all subjects.

Results

The mean patient age was 13 ± 4 years (age range, 2.5-17 y). There were 290 males (59%). There were 45 patients (9%) aged 3 to 7 years, 177 patients (36%) aged 8 to 12 years, and 271 patients (55%) aged 13 to 17 years. There were 77 patients (16%) from 1987 to 1994; 179 patients (36%) from 1995 to 2002; and 237 patients (48%) from 2003 to 2012. Glomerulonephritis was the most common cause of end-stage renal disease. The most common urologic causes of chronic kidney disease were neurogenic bladder in 16 patients (3.2%), reflux nephropathy in 12 patients

(2.4%), urolithiasis in 7 patients (1.4%), and posterior urethral valve in 6 patients (1.2%).

Donor nephrectomy was performed laparoscopically for 445 patients (90%). Vascular anastomosis was performed to the aorta and inferior vena cava in 13 patients (2.6%), and the other patients had anastomosis to the iliac vessels. A Modified Lich-Gregoir technique with ureteral stent insertion for 3 to 4 weeks was performed for ureteral reimplant. Preemptive kidney transplant was performed in 412 patients (84%). Revision transplant was performed in 8 patients. The main immuno-suppressive agents were azathioprine, prednisone, cyclosporine, and mycophenolate mofetil. The most frequent complications were delayed graft function and acute graft rejection (Table 1). Rejection episodes

Table 1. Surgical and Nonoperative Complications in Pediatric Kidney Transplant Recipients*

Complication	Total	Year Range		
		1987-1994	1995-2002	2003-2012
No. of transplants	493	77 (16%)	179 (36%)	237 (48%)
Delayed graft function	91 (18%)	38 (49%)	34 (19%)	19 (8%)
Acute graft rejection	58 (12%)	22 (29%)	25 (14%)	11 (5%)
Transplant nephrectomy	13 (3%)	3 (4%)	6 (3%)	4 (2%)
Urolithiasis	11 (2%)	3 (4%)	6 (3%)	2 (1%)
Ureteral fistula	9 (2%)	4 (5%)	3 (2%)	2 (1%)
Major lymphocele	9 (2%)	4 (5%)	3 (2%)	2 (1%)
Ureteral stenosis	8 (2%)	3 (4%)	3 (2%)	2 (1%)
Wound infection	8 (2%)	2 (3%)	3 (2%)	2 (1%)
Urologic malignancy	7 (1%)	2 (3%)	3 (2%)	2 (1%)
Renal vein thrombosis	7 (1%)	2 (3%)	2 (2.5%)	3 (1%)
Renal artery stenosis	5 (1%)	1 (1%)	3 (2%)	1 (0.4%)
Total No. of complications	226	84	91	51

*N = 493 patients. Data reported as number (%).

Figure 1. Survival in Pediatric Kidney Transplant Recipients (February 1987 to December 2012)
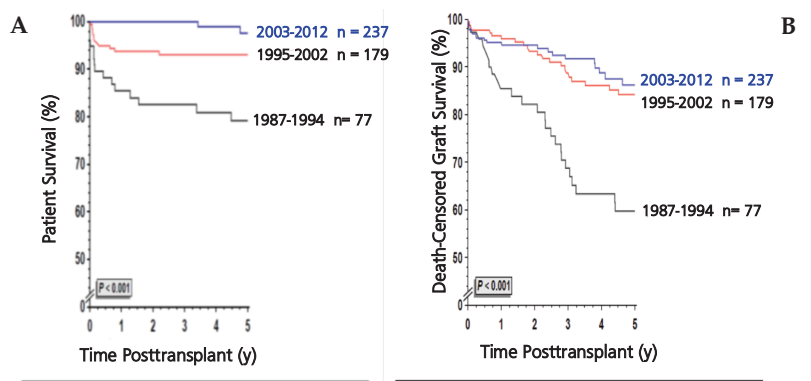
Years	1	2	3	4	5
1987-1994	95.4	92.2	68.8	63.3	59.7
1995-2002	95.9	93.3	88.7	86.1	84.2
2003-2012	95.2	94.6	91.8	88.8	86.2

Years	1	2	3	4	5
1987-1994	85.4	82.5	82.5	80.9	79.1
1995-2002	93.8	93.8	93	93	93
2003-2012	100	100	100	99	97.6

(A) Graft survival. **(B)** Patient survival.

Figure 2. Graft Survival in Pediatric Kidney Transplant Recipients

Recipient Age (y)	1	2	3	4	5
3-7	98	98	98	94.6	94.6
8-12	93.9	91.6	98	85.6	82.8
13-17	92.4	90.4	82.5	78.7	75.6

Recipient Age (y)	1	2	3	4	5
3-7	93.1	90.7	88.9	87.1	85.2
8-12	93.5	90.1	87.2	83.9	80.4
13-17	93.3	89.5	84.9	81.1	76.8
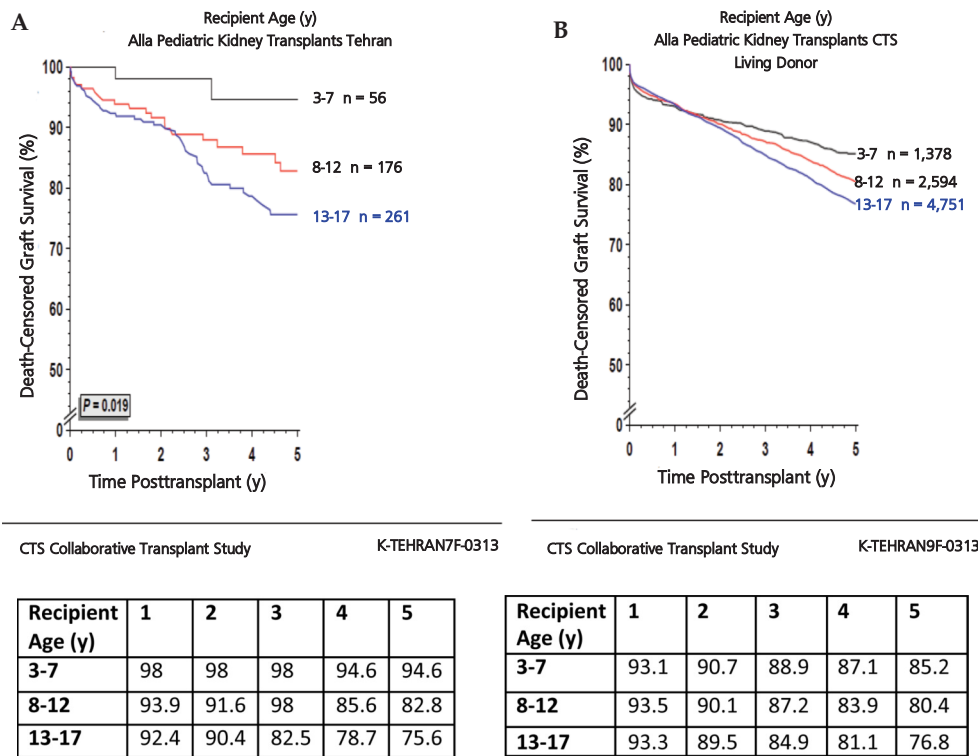
(A) Comparison of graft survival in present study and all Collaborative Transplant Study registry outcomes. **(B)** Comparison based on recipient age subgroups (February 1987 to December 2012).

were treated with methylprednisolone, antithymocyte globulin, tacrolimus, and basiliximab.

The 5-year graft and patient survival were improved from 1987-1994 to 2003-2012 (Figure 1). The overall death-censored graft survival was 96% at 1 year, 78% at 5 years, and 66% at 10 years after transplant. The overall patient survival was 96% at 1 year, 83% at 5 years, and 75% at 10 years after transplant. Death after transplant occurred in 44 patients (9%), most commonly because of sepsis (52%), cardiovascular disease (38%), and malignancy (10%). The 1- and 5-year graft survival was better in patients aged 3 to 7 years than in patients aged 8 to 12 years or in patients aged 13 to 17 years (Figure 2).

Discussion

The incidence of ESRD is 6.9 per million people aged 0 to 4 years and 21.8 per million people aged 15 to 19 years.[10] Most of these patients need renal replacement therapy. Most studies show a survival advantage for patients who receive transplant than dialysis, and mortality is 7-fold lower in transplant than dialysis patients.[11] The present study included data about death-censored graft and patient survival in pediatric kidney transplant recipients (Figure 1).

Limited data are available for comparison with Middle East Society for Organ Transplantation countries. A Jordanian retrospective study with 71 pediatric living-related kidney transplant patients aged < 14 years (January 2004 to July 2011) showed that graft survival at 1 year was 95.5%; 3 years was 90.4%; and 5 years was 80.2%. A Saudi Arabian retrospective study of 50 pediatric kidney transplant recipients (1986-2007) showed that 15-year survival was 92% for grafts from living donors. A retrospective study from Egypt in 216 living-related kidney transplants in patients aged < 18 years showed that survival at 1 year was 93%; 5 years was 73%; and 10 years was 48%.[12,13] The present study is among the largest single-center series of pediatric kidney transplants reported from a member country of the Middle East Society for Organ Transplantation.

In the present study, delayed graft function occurred in 79 recipients (21%) and acute rejection in 59 recipients (15%), comparable with similar studies.[4] Very young recipient age was associated with poorer short-term graft survival, probably because of greater

technical complexity and higher incidence of vascular thrombosis and acute cellular and vascular rejection in this group.[14] The 1- and 5-year graft survival for the present patients were comparable to reported outcomes from the Collaborative Transplant Study registry (Figure 2).

In the present study, 412 patients (84%) had preemptive transplant. The frequency of preemptive kidney transplant reported in other pediatric kidney transplant centers is 35% to 86%, and this procedure avoids the risks, cost, and related problems of dialysis and is associated with better graft survival and psychological and financial benefits than transplant after dialysis.[15]

An increase in living-donor kidney transplant has been observed in some centers and has improved short- and long-term graft and patient survival.[16] The frequency of living donation varies in different regions including North America (60%), United Kingdom (25%), and Germany (18%), possibly because of variation in cultural and social attitudes and features of donation in the transplant programs.[4,17,18]

Donor nephrectomy was performed laparoscopically in 445 transplants (90%). Previous randomized and nonrandomized studies in adults showed that laparoscopic donor nephrectomy is associated with longer operative and warm ischemia times but lower duration of hospitalization and analgesic requirements than open nephrectomy. There have been no significant differences in complications between laparoscopic and open nephrectomy, and graft outcome is comparable between the 2 techniques.[19,20] In a randomized study comparing open and laparoscopic donor nephrectomy, laparoscopic donor nephrectomy resulted in better donor satisfaction, lower morbidity, and equivalent graft outcomes.[9,21]

Although the present study is a historical cohort and not a randomized study, the large number of patients is evidence that laparoscopic donor nephrectomy can be advised in pediatric kidney transplant. In the present study, we were not able to compare patient and graft survival between transplants with open and laparoscopic donor nephrectomy because most transplants with open nephrectomy were performed during the early experience with pediatric transplant and the number of patients between the 2 groups was not equal. There has been improvement in the use of immunosuppressive drugs, and more recent results

may have been improved because of the availability of stronger and safer immunosuppressive drugs. We used azathioprine in earlier transplants, and mycophenolate mofetil was used instead of azathioprine in later transplants.

The incidence of overall urologic complications after kidney transplant is 14% to 20%.[22,23] Ureteral complications such as ureteral fistula and ureteral stenosis may occur early or late after surgery and may be caused by failure to preserve ureteral blood supply during donor nephrectomy or procurement or imperfect ureterovesical anastomosis. Ureteral fistula was observed in 9 patients in the present study (Table 1); 5 patients were treated nonoperatively, and 4 other patients had open ureteral reimplant. Ureteral stenosis occurred in 8 patients, and all 8 patients were treated with open ureteral reimplant.

Lymphoceles observed were perirenal collections of lymph that may have been promoted by division of lymphatic vessels. This complication may be prevented by meticulous dissection and ligation of lymphatic ends during recipient vessel exposure and limiting unnecessary vascular dissection.[24] Symptomatic lymphocele may be treated with percutaneous catheter drainage (frequency of success, 50%) or open or laparoscopic drainage with or without marsupialization.[25] In the present study, lymphocele was diagnosed in 9 patients, and treatment included nonoperative therapy in 3 asymptomatic patients, open drainage and peritoneal window in 2 patients, and ultrasonography-guided percutaneous drainage in 4 patients.

Renal vein thrombosis was noted in 8 transplants (Table 1). Treatment included urgent nephrectomy in 2 patients because of kidney rupture in 1 patient and disseminated intravascular coagulation in 1 patient; in 2 patients, urgent thrombectomy and revision of renal vein anastomosis was performed with successful outcome. There were 2 patients who were treated nonoperatively and had subsequent graft failure.

Renal artery stenosis in the transplanted kidney may cause hypertension and graft dysfunction.[26] This complication has been reported in 5% to 15% pediatric kidney transplants and should be suspected when there is new-onset hypertension, proteinuria, or increase in serum creatinine level.[27] The detection of transplant renal artery stenosis has increased after introduction of new noninvasive diagnostic techniques. In the present study, this

complication was detected in 7 patients (1.8%) but may have been undiagnosed in other patients.

The most frequent causes of death after kidney transplant include cardiovascular disease (30%-36%), infection (24%-56%), and malignancy (11%-20%).[28] The most common causes of death in the present recipients were sepsis (52%), cardiovascular disease (38%), and malignancy (10%).

Limitations of the present study included the retrospective study design. In addition, we were not able to compare the results between open and laparoscopic donor nephrectomy because open nephrectomy was performed earlier and the number of patients having open and laparoscopic nephrectomy were not equal.

In summary, kidney transplant is available for most pediatric age groups and may provide excellent results. Overall transplant survival has increased because of improvements in techniques and advances and immunosuppressive drugs. Preemptive transplant may be advisable. The present study confirmed the results of other studies that showed that laparoscopic donor nephrectomy may provide better donor satisfaction, lower morbidity, and equivalent graft outcome compared with open nephrectomy and may encourage living donation for pediatric transplant. In adults, acceptable results have been reported with laparoscopic donor nephrectomy in many transplants, and the present study confirms these results in children.[29]

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