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KIDNEY TRANSPLANTATION IN CHILDREN WITH URINARY DIVERSION OR BLADDER AUGMENTATION

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ABSTRACT

Purpose: Urinary tract anomalies or dysfunction leaves the bladder unsuitable for urine drainage in a significant proportion of children presenting for kidney transplantation. We reviewed a multi-institutional experience to determine the ramifications of kidney transplantation in children with bladder augmentation or urinary diversion.

Materials and Methods: During a 28-year period 18 boys and 12 girls 1.7 to 18 years old (mean age 12.1) received 31 kidney transplants. Cause of end stage renal disease was renal dysplasia in 8 cases, posterior urethral valves in 5, obstructive uropathy in 5, neurogenic bladder/chronic pyelonephritis in 4, spina bifida/chronic pyelonephritis in 3, prune belly syndrome in 3 and reflux in 2.

Results: Of the patients 17 had augmented bladder (ileum 9, ureter 5, sigmoid 2 and stomach 1), 12 had incontinent urinary conduits (8 ileum, 6 colon) and 1 had a continent urinary reservoir. Surgical complications included 1 case each of stomal stenosis, stomal prolapse, renal artery stenosis, urine leak, enterovesical fistula and wound dehiscence. Medical complications included urinary tract infection in 21 cases and metabolic acidosis in 5. A bladder stone developed in 1 patient. There was no correlation between the incidence of symptomatic urinary tract infections and type of urinary drainage. Acidosis was more common in patients with augmented bladder (4 of 17 versus 1 of 14) but there was no correlation between the bowel segment used and the occurrence of acidosis. Graft survival was 90% at 1 year, 78% at 5 years and 60% at 10 years. Etiology of graft loss included chronic rejection in 6 cases, noncompliance in 4 and acute rejection in 1. There were no deaths.

Conclusions: Drainage of transplanted kidneys into an augmented bladder or urinary conduit is an appropriate management strategy when the native bladder is unsuitable or absent. Patients with kidney transplants drained into augmented bladder or urinary conduit are at increased risk for urine infection. Graft survival is not adversely affected compared to historical controls when a kidney transplant is drained into a urinary conduit or augmented bladder.

KEY WORDS: kidney transplantation, urinary diversion, bladder

A congenital or acquired genitourinary anomaly is identified as the etiology in a fifth of children with end stage renal disease,[1] and many have significant lower urinary tract dysfunction. Twelve years following the first successful kidney transplant between identical twins, this life saving procedure was offered to individuals without a functional bladder.[2] Since that initial publication several series of kidney transplants drained to incontinent urinary conduits, augmented bladders or continent urinary reservoirs have been published.[3–9] However, to our knowledge no large series of such kidney transplants in the pediatric population have been reported. The Urologic Society for Transplantation and Vascular Surgery sought to determine the success and complications of kidney transplantation in children with incontinent or continent urinary diversion or bladder augmentation.

MATERIALS AND METHODS

A total of 16 transplant centers participated in a retrospective review of 31 kidney transplants performed on 18 boys and 12 girls 1.7 to 18 years old (mean age 12.1) between December 1970 and April 1998. Of these cases 12 with incontinent urinary conduits were included in a previous report.[10] Patient characteristics, cause of end stage renal disease and allograft source are detailed in table 1. Of the patients 2 had received a previous kidney transplant, 5 were on hemodialysis and 4 were on continuous ambulatory peritoneal dialysis at the time of transplantation, and 1 had received both modalities of end stage renal therapy. Maintenance immunosuppression for the 31 kidney transplants is outlined in table 2. In 8 transplants a polyclonal (4) or monoclonal (4) antibody was used in the induction period.

The majority of the urinary tracts of patients with urinary

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TABLE 1. *Patient characteristics*

	No. (%)
Sex:	
Male	18 (60)
Female	12 (40)
Etiology of end stage renal disease:	
Renal dysplasia	8 (27)
Posterior urethral valves	5 (17)
Obstructive uropathy (not valves)	5 (17)
Neurogenic bladder/chronic pyelonephritis	4 (12)
Spina bifida/chronic pyelonephritis	3 (10)
Prune belly syndrome	3 (10)
Vesicoureteral reflux	2 (7)
Allograft source:	
Heart-beating cadaver	17 (55)
Living relative	14 (45)

TABLE 2. *Maintenance immunosuppression used in 31 pediatric kidney transplants*

	No. (%)
Prednisone, cyclosporine A, azathioprine	13 (43)
Prednisone, azathioprine	8 (27)
Prednisone, cyclosporine A	2 (6)
Prednisone, cyclosporine A microemulsion, mycophenolate mofetil	2 (6)
Prednisone, cyclosporine A microemulsion, azathioprine	2 (6)
Prednisone, tacrolimus, mycophenolate mofetil	2 (6)
Prednisone, tacrolimus	1 (3)
Prednisone, cyclosporine A, mycophenolate mofetil	1 (3)

conduits or those on clean intermittent catheterization are colonized with bacteria. Therefore, we defined urine infection not by a positive urine culture, but by a symptomatic event (fever, dysuria, abdominal pain and so forth) associated with a positive urine culture. A patient was considered to have pyelonephritis if the infection were manifest by fever and/or kidney tenderness. Patients with symptoms localized to the bladder, urethra, urinary conduit or reservoir were considered to have lower tract urine infection. Statistical analysis was performed using chi-square or Fisher's exact test.

RESULTS

Followup ranged from 1 to 171 months (average 59). The majority of transplants from the augmentation group were performed within the last decade while those in the conduit group generally were performed earlier.

Urinary drainage. Of the patients 17 had augmented bladder, 12 incontinent urinary conduit and 1 continent urinary reservoir (table 3). The urinary conduit or bladder augmentation was created and functioning for drainage of the native kidneys before kidney transplantation in 19 cases (63%). These procedures were performed between 9 and 188 months (mean 69) before kidney transplantation. The augmentation or conduit was performed specifically for a kidney transplant in 10 cases an average of 3.8 months (range 1.4 to 6) before transplantation. Bladder augmentation was performed at 36 and 45 months following transplantation in 2 patients, respectively. The transplant kidney ureter was anastomosed to the native bladder in 8 cases, to the bowel segment used for bladder augmentation in 5, to the ureteral segment of a ureterocystoplasty in 1 and to the native ureter (ureteroureterostomy) in 1. Details regarding the ureter to bladder augmentation anastomosis were not reported in 3 cases. In 16 of the 18 cases (89%) with an augmented bladder or continent reservoir nonrefluxing ureteroneocystostomy was used while in 2 a refluxing anastomosis was created.

TABLE 3. *Urinary drainage in 30 pediatric kidney transplant recipients*

	No. (%)
Bladder augmentation:	17 (57)
Ileocystoplasty	8
Ureterocystoplasty	5
Sigmoid cystoplasty	2
Ileocecocystoplasty	1
Gastrocystoplasty	1
Continent urinary reservoir	1 (3)
Urinary conduit:	12 (40)
Ileal conduit	7
Sigmoid conduit	4
Cecal conduit	1

Of the 17 patients with augmented bladder the urethra served as primary urinary drainage in 12 (71%). In 7 patients (augmentation 6 and continent urinary reservoir 1) auxiliary urinary stomas (Mitrofanoff) were created and all but 1 served as the primary urine drainage port. In 16 of the 17 cases transplants drained into an augmented bladder and in the patient with a continent reservoir clean intermittent catheterization was used. Only 1 patient voided. Of these 18 patients 17 (94%) were continent.

Survival. Graft survival is illustrated in figure 1. Of the kidneys 11 were lost, including 7 (54%) in the conduit group and 4 (22%) in the augmentation/reservoir group (p not significant). Etiology of graft loss included chronic rejection in 6 cases, noncompliance in 4 and acute rejection in 1. No graft was lost due to infection. Function of the allografts, as measured by serum creatinine, is illustrated in figure 2. All patients were alive at last followup.

Complications. Surgical: Surgical complications after 6 transplants included 1 case each of stomal stenosis, conduit prolapse, wound dehiscence, renal artery stenosis, urine leak and difficult voiding. Ureterocystoplasty was performed following transplantation for urine leak. The boy with difficult voiding following transplantation at age 21 months had a history of posterior urethral valves. Vesicostomy was created and 2 years later he underwent ileocystoplasty with closure of the vesicostomy. Recurrent febrile urine infections led to a thorough evaluation. There was no hydronephrosis or reflux. Urodynamics showed normal compliance of the augmented bladder. A small fistula between the augmentation patch and adjacent bowel was discovered at exploration, and treated with surgical closure of the fistula and excision of the ileal patch. Of the 6 surgical complications 2 (15%) occurred in the conduit group and 4 (22%) in the augmentation/reservoir group (p not significant).

Medical: Symptomatic urinary tract infections after transplantation occurred in 21 cases (68%), including 9 of 12 (69%) in the conduit group and 12 of 19 (67%) in the augmentation/reservoir group (p not significant). Pyelonephritis occurred in 17 patients, and lower urinary tract infection alone without pyelonephritis was reported in 4. Of the patients in the

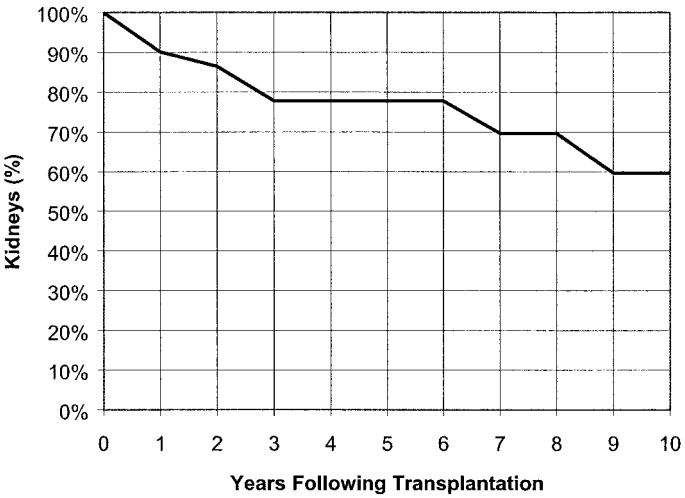

FIG. 1. Actuarial life table kidney transplant survival

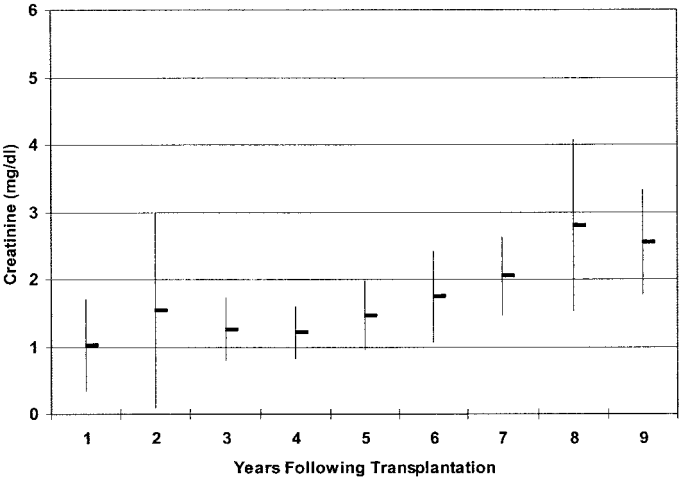

FIG. 2. Serum creatinine after renal transplantation in 31 kidney transplants.

augmentation/reservoir group 4 were given trimethoprim/sulfamethoxazole, 1 nitrofurantoin, 1 mandelamine, 1 ciprofloxacin and 1 multiple antibiotics. None of the patients in the conduit group received prophylactic antibiotics. In 1 patient a bladder stone developed following ileocystoplasty, and in 5 (16%) metabolic acidosis developed requiring treatment, including 4 of 18 (22%) in the augmentation/reservoir group and 1 of 12 (8%) in the conduit group (p not significant).

DISCUSSION

In 1966 Kelly et al reported 8 kidney transplants in 7 patients with ileal conduits.[2] Since then many centers have published experience with transplantation in patients with urinary diversion. In 1971 Tunner et al described 4 children with kidney transplants drained into incontinent urinary conduits.[11] In 1982 Marshall et al reported the first augmentation cystoplasty following kidney transplantation in a man,[12] and in 1984 Stephenson et al reported the first pediatric kidney transplants drained to augmented bladders.[3] In 1989 Heritier et al reported the first kidney transplant drained into a Kock pouch.[13] As the number of kidney transplants increases, so do reports of transplantation in children with bladder augmentation or urinary diversion.

The success of renal transplantation, as measured by allograft and patient survival, is increasing. The North American Pediatric Renal Transplant Cooperative Study reported 1 and 5-year actuarial allograft survivals of 91% and 77% for living donor kidneys and 81% and 61% for cadaver donor kidneys in pediatric renal transplant recipients.[14] Allograft survival among our patients was similar with 90% at 1 year and 78% at 5 years. As in the North American Cooperative Study series, the most common cause of graft loss among our patients was immunology. No graft was lost due to infection or complication of urinary drainage. Other recent series have shown that kidney transplantation is generally successful in patients with urinary diversion or bladder augmentation but there is a higher rate of complications among these transplant recipients.

Urine infection. As with patients in other series, our transplant recipients were at increased risk for urinary tract infection. Of those children who had urine infection two-thirds had multiple episodes of pyelonephritis. Colonization of the urinary tract with bacteria was undoubtedly present in all patients in the conduit group and the majority of those in the augmentation group. Of these 18 patients 17 drained the bladder or reservoir with clean intermittent catheterization. Only 1 boy with a gastrocystoplasty voided to completion. Regular drainage of augmented bladder and irrigation to remove mucous are recommended to prevent symptomatic urine infections. Only 8 patients received prophylactic antibiotics on a long-term basis. Perhaps broader use of low dose antibiotic prophylaxis could have reduced the incidence of urine infection. Alfrey et al reported recurrent pyelonephritis in 3 transplant recipients with augmentation cystoplasty.[7] One patient died of urosepsis and 1 allograft loss was attributed to acute urine infection. This experience led them to recommend that patients with augmentation cystoplasty should have bowel segments excised before transplantation. Although urinary tract infection was common in our patients we do not believe that our series and most other reported series justify such a conclusion.

In the late 1970s long-term followup of conduit urinary diversion showed that in a substantial proportion of diverted cases end stage renal disease developed,[15] and other series confirmed this finding.[16, 17] Urine stasis and colonization of the conduit and the collecting systems were thought to increase the risk of chronic pyelonephritis and subsequent parenchymal scarring in these patients. Despite these reports, similar kidney injury and loss have not been identified among kidney transplant recipients with conduit urinary diversion. The Urologic Society for Transplantation and Vascular Surgery reported no allograft losses due to chronic infection in 55 kidney transplants.[10] Kidney survival was comparable to other contemporary series. As in our series, the most common cause of graft loss was rejection. It is possible that immunosuppression medications diminished the inflammatory response to urine infection and, thus, decreased infection related scarring in our transplant recipients. Alternately, because of the difficulty of differentiating clearly between chronic rejection alone and chronic rejection with infection related nephropathy, it is possible that chronic infection contributed to some graft losses. Nevertheless, if infection were a significant factor, it is likely that allograft survival would have been more obviously diminished.

Surgical complications. The surgical complication rate (19%) in our patients is higher than that reported from other unselected series but not significantly different from other series of transplant recipients with urinary diversion or bladder augmentation.[8, 9] The Urologic Society for Transplantation and Vascular Surgery reported surgical complications following 10 of 55 transplants (18%) in patients with urinary conduit.[10] Of 3 patients in that series with urinary conduits created following lower urinary tract reconstruction 2 had wound complications. Both of our children who underwent bladder augmentation following transplantation had surgical complications. Urinary tract reconstruction should be performed before transplantation when possible.

Perforation of augmented bladder was reported by Rink et al in 1988.[18] This potentially fatal complication has been reported in up to 9% of patients undergoing augmentation cystoplasty.[19] We are aware of 2 perforations occurring in augmented bladder following kidney transplantation.[20, 21] In theory long-term steroid use, with attendant impairment of tissue healing, could predispose transplant recipients to perforation. In addition, patients receiving immunosuppression may not demonstrate the typical signs of peritonitis. Therefore, it is surprising, that this complication has not been reported more often. Physicians must be acutely aware of the possibility of perforation in any transplant patient with an augmented bladder or urinary reservoir.

Stones. Bladder and/or upper tract stones occur in 8% to 52% of patients with bladder augmentation.[22, 23] Only 1 girl with an ileocystoplasty and Mitrofanoff stoma had a bladder stone in our series. This low incidence could be the result of frequent followup and aggressive urinary drainage management common among kidney transplant recipients. Mucous production from bowel segments and urinary stasis are thought to increase the risk of stones in augmented bladder.[23] Irrigation of augmented bladder with saline, mucolyt-

ics or urea solution has been suggested as a means of preventing stones.

Metabolic alterations. When urine comes into contact with highly absorptive intestinal mucosa metabolic alterations occur,[24] which is a concern particularly in patients with renal dysfunction. In the series of Koo et al 11 of 13 (85%) children with urinary conduit, bladder augmentation or urinary reservoir required alkali therapy for metabolic acidosis.[9] Fontaine et al described 2 of 14 (14%) children with augmentation cystoplasty who had hyperchloremic acidosis requiring oral therapy.[8] Of 30 patients[5] (17%) in our series 1 with ileal conduit and 4 with augmentation cystoplasty required oral alkalization. Prolonged contact between urine and bowel mucosa, as occurs in patients with enterocystoplasty or intestinal urinary reservoir, appears to exacerbate metabolic abnormalities. As expected, these metabolic alterations were observed less often among patients in whom the surface area of bowel mucosa exposed to urine was low, that is those with urinary conduit.

Stomach has been recommended as the preferred bowel segment for bladder augmentation in patients with renal insufficiency. The secretion of acid into the urinary tract offsets metabolic acidosis of chronic renal failure and may decrease the risk of urine infection. However, gastric acid production can also cause problems when stomach is interposed in the urinary tract. In 1993 Nguyen et al reported dysuria and hematuria in a third of patients with gastrocystoplasty.[25] Reinberg et al reported spontaneous ulceration and perforation of a gastric augmentation segment in a child waiting for a kidney transplant.[26] Our sole transplant recipient with gastrocystoplasty voided well and had no dysuria. However, we concur with the recommendations of Rink that ureter, ileum and colon are preferable to stomach for augmentation cystoplasty.[27]

CONCLUSIONS

When possible, kidney transplant ureters should be drained to the native bladder. Dysfunctional bladder may be rehabilitated through the use of anticholinergic medications and/or clean intermittent catheterization. However, other options must be pursued for patients who have lost the bladder and those who have lost adequate storage function of the bladder. Bladder augmentation offers transplant recipients increased urinary storage capacity. When combined with clean intermittent catheterization, this option will provide urinary continence for the majority of children. When the bladder is absent, an incontinent urinary conduit or a continent urinary reservoir may be used. When possible, urinary tract reconstruction should be completed before kidney transplantation to decrease the risk of surgical complications. Infection is the most common complication following kidney transplantation in children with augmentation cystoplasty or urinary diversion. Pediatric kidney recipients with enterocystoplasty or continent urinary reservoir are at increased risk of metabolic abnormalities. They should be followed carefully to detect and treat electrolyte and acid/base imbalances. Bladder augmentation or urinary diversion does not adversely affect the function and survival of kidney transplants in children.

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