

Renal Transplant in Patients with Spinal Cord Injuries

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Abstract

Objectives: There is no knowledge on the outcome of renal transplant for end-stage renal disease secondary to neurogenic bladder caused by spinal cord injury. In this study, we evaluated the outcome of kidney allograft recipients with spinal cord injury.

Materials and Methods: We evaluated graft survival, clinical course, laboratory findings, and imaging studies in 21 men (veterans) with spinal cord injury and renal failure secondary to neurogenic bladder. They underwent renal transplant between 1990 and 2006. Bladder dysfunction was appropriately managed before or with receiving the kidney allograft.

Results: Mean ($\pm$ SD) age of patients was 43.8 ± 5.9 years. Mean glomerular filtration rate at the closing date of the study was 89.5 ± 33.6 mL/min. During follow-up (median: 6 years, range: 1-17 years), mean duration of graft survival was 15.4 ± 1.0 years (95% confidence interval, 13.2-17.5 years). Following renal transplant, mean nadir level of serum creatinine was 74.25 ± 16.79 μ mol/L (0.84 ± 0.19 mg/dL). Six patients

(28.6%) had kidney stones before renal transplant, and 2 patients (9.5%) after (1 patient with new kidney stones and 1 patient with kidney stones before and after transplant). Pyelonephritis occurred in 18 patients (85.7%) before transplant, and in 9 patients (42.9%) patients after ($P = .07$). Graft loss occurred in 2 patients (9.5%) 4 and 18 months after the transplant.

Conclusions: Spinal cord injury patients who receive allograft kidney transplants have acceptable outcomes, and transplant may reduce urolithiasis and upper urinary tract infection.

Key words: Kidney transplant, Kidney failure, Neurogenic bladder, Urinary tract infection, Urolithiasis

Neurogenic bladder is defined as bladder dysfunction resulting from disease or injury affecting the neural pathways or neuromuscular junctions controlling the function of the lower urinary tract (1). The condition often occurs following spinal cord injury. In the past, renal failure was the leading cause of death after spinal cord injury (2). Lower urinary tract dysfunction may lead to upper urinary tract deterioration and eventual renal failure in patients with spinal cord injuries. Presently, mortality from spinal cord injury has decreased dramatically, in part because of improved treatment in managing urologic dysfunction associated with spinal cord injury (3). High detrusor pressure and high intravesical pressure may result in vesicoureteral reflux. With or without detrusor-sphincter dyssynergia, vesicoureteral reflux is associated with urinary tract infection (4), ischemic injury, and upper urinary tract deterioration, leading eventually to renal scarring (5). All factors mentioned above exacerbate deterioration of renal function, leading to end-stage renal disease.

To date, the efficacy of renal transplant has been studied in patients with end-stage renal disease, yet

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not in patients with accompanying spinal cord injury. In this study, we assessed the outcome of kidney transplant in patients with neurogenic bladder dysfunction because of spinal cord injury. In addition, we compared urinary tract infection and urolithiasis before and after renal transplant.

Materials and Methods

In this retrospective study, we included 21 men (veterans) with spinal cord injury and renal failure due to neurogenic bladder dysfunction who underwent renal transplant between 1990 and 2006. The diagnosis of neurogenic bladder was confirmed through physical examination, imaging, and urodynamic studies. Imaging included voiding cystourethrogram and ultrasonography.

With the exception of neurogenic bladder, other renal failure causes were excluded from the study. Renal transplants were performed in Iran for 16 patients and in the United Kingdom for 5 patients. In this multicenter study, once patients were admitted to the hospital, pretransplant medical evaluations, laboratory tests, and imaging studies were performed. All kidneys were obtained from live donors, 3 from immediate family members and 18 from unrelated donors. For immunosuppression, triple therapy consisting of cyclosporine, azathioprine, and steroids was used by the majority of centers. After 1994, the majority of patients received mycophenolate mofetil instead of azathioprine.

All patients returned for periodic visits, and the function of the renal allografts was monitored by expert nephrologists. Glomerular filtration rates were determined using the Cockcroft-Gault equation. Patients were last seen in May 2007 on the closing date of the study and they signed written informed consent forms for participation in this research study. At that visit, patients underwent imaging and laboratory studies, and we collected the most recent information on the functional state of their renal allografts and any complications. Due to the multicenter retrospective methods of the study, we were unable to collect data on specific rejection episodes.

The Urology and Nephrology Research Center has adopted codes of ethics as a guideline for human experimentation. The study was approved by the ethics committee of the research center. Data are

presented as mean with standard deviation (SD) and 95% confidence interval (CI), median with range, or number with percentage. Statistical analyses were performed using Kaplan-Meier and chi-square tests as appropriate, with statistical significance considered at $P < .05$.

Results

No female patients were enrolled in the study. Mean age of the 21 men was 43.8 ± 5.9 years. Eighteen patients had paraplegia, and the remaining 3 patients had quadriplegia. Median duration of renal failure before transplant was 2 years (range, 0.5-25 years). Before kidney transplant, 1 patient had hypertension and hyperlipidemia, and diabetes mellitus was diagnosed after renal transplant. Except for the aforesaid patient, no patient had a systemic disease before transplant. Median follow-up after transplant was 6 years (range, 1-17 years).

Figure 1 demonstrates the cumulative survival curve of the transplanted grafts. Following renal transplant, mean nadir level of serum creatinine was $74.25 \pm 16.79 \mu\text{mol/L}$ ($0.84 \pm 0.19 \text{ mg/dL}$). On the closing date of the study, mean glomerular filtration rate was $89.5 \pm 33.6 \text{ mL/min}$, and mean serum creatinine was $106.08 \pm 31.82 \mu\text{mol/L}$ ($1.20 \pm 0.36 \text{ mg/dL}$). Among the 14 patients with more than 5 years of follow-up, no patient experienced graft failure. Mean duration of graft survival was 15.4 ± 1.0 years (95% CI, 13.2-17.5 years). Graft loss occurred in 2 patients (9.5%) 4 and 18 months after transplant. By ultrasound imaging on the closing date of the study, 2 patients (9.5%) were diagnosed

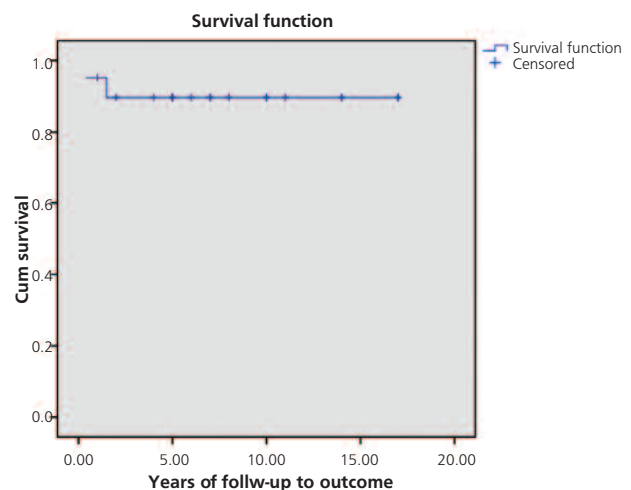


Figure 1. Cum survival of renal allograft in this study

with grade 1 hydronephrosis, and 2 others (9.5%), with grade 2 hydronephrosis. At the closing date of study, for the 2 patients with grade 1 hydronephrosis, their serum creatinine levels were 106.96 $\mu\text{mol/L}$ (1.21 mg/dL) and 159.12 $\mu\text{mol/L}$ (1.80 mg/dL), and for the 2 patients with grade 2 hydronephrosis, their serum creatinine levels were 97.24 $\mu\text{mol/L}$ (1.10 mg/dL) and 167.96 $\mu\text{mol/L}$ (1.90 mg/dL).

Regarding lower urinary tract dysfunction, 5 patients had hyperreflexic bladder, 15 patients had both hyperreflexic bladder and detrusor-sphincter dyssynergia, and 1 patient had an areflexic bladder that subsequently developed into a hyperreflexic bladder. Table 1 shows different types of management for lower urinary tract dysfunction. Five patients (23.8%) were diagnosed with bladder stones before transplant, and all underwent stone removal before receiving the allograft. One patient (4.8%) had a bladder stone after transplant; he had not had a bladder stone before transplant.

Table 1. Management of lower urinary tract dysfunction in 21 patients with spinal cord injury

	Frequency	Percentage
Cystoplasty before transplant	7	33.3
Cystoplasty and sphincterotomy before transplant	3	14.3
Sphincterotomy before transplant	5	23.8
Ileal conduit	2	9.5
Indwelling catheter after transplant	2	9.5
CIC and medical treatment	2	9.5
Total	21	100

Abbreviations: CIC, clean intermittent catheterization.

Six patients (28.6%) had kidney stones before renal transplant, while 2 (9.5%) had kidney stones after transplant. Only 1 patient experienced kidney stones both before and after transplant. Four of six patients with kidney stones underwent stone removal before renal transplant. Pyelonephritis occurred in 18 patients (85.7%) before transplant, and in 9 patients (42.9%) after transplant ($P = .07$). Eleven patients (52.4%) had orchiepididymitis before transplant, while 8 patients (38.1%) had orchiepididymitis after transplant ($P = .02$). In our study, 12 patients (57.1%) had symptomatic urinary tract infections including pyelonephritis or orchiepididymitis after renal transplant. At the final evaluation, 19 patients (90.5%) had pyuria, but none was symptomatic. The function of all allograft transplants was intact, except for the 2 graft losses previously noted. The frequency of pyelonephritis and orchiepididymitis, before and after transplant, is given in Table 2.

Table 2. Comparison of frequency of orchiepididymitis and pyelonephritis before and after transplant

	Orchiepididymitis	Pyelonephritis
No orchiepididymitis or pyelonephritis (Either before or after transplant)	9 (42.9%)	3 (14.3%)
Patients with equal number of episodes before and after transplant	7 (33.3%)	5 (23.8%)
Patients with fewer episodes after transplant	4 (19.0%)	13 (61.9%)
Patients with more episodes after transplant	1 (4.8%)	0 (0%)

Data are presented as number (percentage); episodes refer to episodes per year.

In our study, 7 of 9 patients with cystoplasty who experienced pyelonephritis before transplant had fewer episodes of upper urinary tract infection after transplant, while the remaining 2 patients had a similar number of episodes. Among the 6 patients with cystoplasty who experienced orchiepididymitis before transplant, 3 had fewer episodes and 3 had a similar number of episodes after transplant. In addition, one bladder stone and one graft loss occurred among patients with cystoplasty.

Discussion

Obtaining good outcomes after renal transplant in patients with lower urinary tract dysfunction is challenging because of posttransplant complications. Approximately 6% of patients undergoing renal transplant each year in the United States have experienced end-stage renal disease secondary to lower urinary tract abnormality (6). Patients with neurogenic bladder due to spinal cord injury are considered special cases, as they may have accompanying problems due to injury to other organs, either by trauma or due to existing paraplegia or quadriplegia, such as bedsores and related comorbidity. Renal transplant in patients with lower urinary tract dysfunction must be accompanied by bladder and urethral management. The aim of treatment is to achieve a low-pressure bladder as a urine reservoir. Treatment options include conservative modalities, such as clean intermittent catheterization and bladder relaxants, and invasive modalities, such as bladder augmentation, intestinal conduit, or external sphincterotomy. The main risk after kidney transplant in patients with spinal cord injury and neurogenic bladder is posttransplant infection, urinary tract infection in particular.

Ileal conduit can be performed in patients with end-stage renal disease due to neurogenic bladder

dysfunction using 1 of 2 methods, either performing ileal conduit surgery 2 months before renal transplant, or simultaneous with the transplant. In our study, 2 patients underwent simultaneous renal transplant and ileal conduit operation; they did not experience any significant complications, and graft survival was excellent.

Cystoplasty (bladder augmentation) can be performed before or after renal transplant (7), and each technique had both advantages and disadvantages. In our study, 10 patients underwent cystoplasty before transplant, and all had favorable graft outcomes. When cystoplasty is performed before the transplant, the healing process of the augmented bladder is not influenced by subsequent immunosuppression after the transplant. The main drawbacks of this approach included complications associated with "dry" cystoplasty and injury to vascular pedicles at the time of ureteric reimplantation, leading to cystoplasty necrosis (7).

Others have postulated that cystoplasty should be postponed until renal function has stabilized following transplant when the dosage of immunosuppressive drugs would be reduced (7). Chronic bacteriuria and urinary tract infection occur frequently in recipients with augmented bladders, as high as 52% for asymptomatic and 22% for symptomatic urinary tract infections (8, 9). Although spinal cord injury patients with renal transplant are susceptible to urinary tract infection, according to our findings, it seems that bladder augmentation may decrease the risk of urinary tract infections.

In patients with abnormal lower urinary tracts, urinary tract infection may result in severe outcomes such as graft loss, pyelonephritis, and orchiepididymitis; thus, urinary tract infection must be detected and treated vigorously. After any kidney transplant, urinary tract infection may be diagnosed in up to 40% of recipients resulting in increased mortality and morbidity. Considering our results, asymptomatic pyuria and probably urinary tract infection did not seem to affect renal transplant in patients with lower urinary tract dysfunction in general.

Most patients with suprasacral spinal cord injuries have detrusor-sphincter dyssynergia, which is probably responsible for elevated intravesical pressure, autonomic dysreflexia, and high postvoid residual urine volume that result in recurrent urinary tract infection, vesicorenal reflux, and hydro-

nephrosis. Untreated detrusor-sphincter dyssynergia and its complications may cause progressive renal damage. When alternative treatments for detrusor-sphincter dyssynergia, including clean intermittent catheterization, rehabilitation, and medical therapy, are unsuccessful at protecting kidney function, sphincterotomy as an irreversible therapeutic procedure may yield an acceptable outcome. The operation changes high-pressure incontinence into low-pressure incontinence, thereby protecting the upper urinary tract. In 8 patients in our study, sphincterotomy was performed; in 3 patients, this was combined with cystoplasty. Since all 8 patients who underwent sphincterotomy had good graft survival, in general, sphincterotomy seems to be a reliable and safe treatment to overcome detrusor-sphincter dyssynergia when all other options to restore continence have been exhausted (10).

Before 1980, only a small number of hemodialysis patients with spina bifida or traumatic paraplegia received renal allografts in the United Kingdom, possibly owing to lack of information on the part of physicians (11) as well as a shortage of resources to fund renal replacement (12). Although many patients could be treated by home dialysis and most of them are suitable candidates for renal transplant, previously evidence was lacking on the long-term outcome of renal transplant in these patients. Our findings demonstrated acceptable patient survival and long-term graft survival in veterans with renal transplant after end-stage renal disease secondary to abnormal lower urinary tract function due to spinal cord injury. These patients received appropriate management for lower urinary tract dysfunction after renal transplant. Therefore, we conclude that if spinal cord injury patients with coincidental lower urinary tract dysfunction receive appropriate management of lower urinary tract dysfunction in addition to kidney transplant, the kidney allograft has good long-term survival with a low incidence of complications. Renal transplant appears to be a reasonably promising therapeutic option for spinal cord injury patients with renal failure from neurogenic bladder.

References

1. Samson G, Cardenas DD. Neurogenic bladder in spinal cord injury. *Phys Med Rehabil Clin N Am.* 2007;18(2):255-274, vi.
2. Borges PM, Hackler RH. The urologic status of the Vietnam war paraplegic: a 15-year prospective followup. *J Urol.* 1982;127(4):710-711.

3. Hackler RH. A 25-year prospective mortality study in the spinal cord injured patient: comparison with the long-term living paraplegic. *J Urol*. 1977;117(4):486-488.
4. Esclarín De Ruz A, García Leoni E, Herruzo Cabrera R. Epidemiology and risk factors for urinary tract infection in patients with spinal cord injury. *J Urol*. 2000;164(4):1285-1289.
5. Ku JH, Choi WJ, Lee KY, et al. Complications of the upper urinary tract in patients with spinal cord injury: a long-term follow-up study. *Urol Res*. 2005;33(6):435-439.
6. Hatch D. Kidney transplantation in patients with an abnormal lower urinary tract. *Urol Clin North Am*. 1994;21(2):311-320.
7. Zaragoza MR, Ritchey ML, Bloom DA, et al. Enterocystoplasty in renal transplantation candidates: urodynamic evaluation and outcome. *J Urol*. 1993;150(5 Pt 1):1463-1466.
8. Basiri A, Otoukesh H, Simforoosh N, et al. Kidney transplantation in children with augmentation cystoplasty. *J Urol*. 2007;178(1):274-277; discussion, 277.
9. Serrano DP, Flechner SM, Modlin CS, et al. Transplantation into the long-term defunctionalized bladder. *J Urol*. 1996;156(3):885-888.
10. Fontaine E, Hajri M, Rhein F, et al. Reappraisal of endoscopic sphincterotomy for post-traumatic neurogenic bladder: a prospective study. *J Urol*. 1996;155(1):277-280.
11. Whitfield HN, Hendry WF. *Textbook of Genito-Urinary Surgery*. New York: Churchill Livingstone; 1985.
12. Wing AJ. Why don't the British treat more patients with kidney failure? *Br Med J (Clin Res Ed)*. 1983;287(6400):1157-1158.