Should a Complex Uropathy Be a Contraindication for Renal Transplantation in Children?

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ABSTRACT

Background. Anatomic and functional disorders of the lower urinary tract represent up to 40% of the causes of renal failure in children. Several centers avoid renal transplantation in these patients because of the high risk of complications and lower graft survival. The aim of this work was to determine the frequency of urinary tract abnormalities (UTAs) among our pediatric series, and to compare the frequency of complications, function, and long-term graft survival among patients without versus with UTA.

Methods. This single-center, retrospective study compared outcomes between pediatric recipients with versus without UTA. We analyzed demographic features, etiology, pretransplant protocol, urinary tract rehabilitation, incidence of complications, rejection events, as well as graft function and survival.

Results. Among 328 pediatric cases performed between 1998 and 2008, we excluded nine patients due to incomplete medical records, analyzing 319 procedures in 312 patients. Sixty-seven patients (21%) had UTA. The average age, weight, and height at the time of grafting were significantly lower in the urologic group: 11.1 versus 12.6 years, 28.8 versus 34.4 kg; 125.4 versus 138.4 cm, respectively. There were significantly higher frequencies of a transperitoneal approach and vena cavae and aortic anastomoses among patients with UTA ($P < .001$), posing a greater technical challenge in this population. No differences in creatinine levels were observed at 0.5, 1, 2, 5, and 10 years: 1.3 versus 1.6 at 5 years, and 1.4 versus 1.5 at 8 years. Urologic complications, including urinary tract infections (UTIs), occurred among 80.6% of patients with UTA versus 42.1% in the non-UTA group ($P < .001$). UTIs appeared predominantly in patients with UTA (62.7% vs 35.3%, $P < .001$), representing a 2.7-fold risk compared with those children transplanted for other reasons. Rejection incidence was similar in both groups (49.8%). There was no significant difference in 5-y (89.8% vs 85%) or 10-year (83% vs 67%) graft survivals between the groups ($P = .162$).

Conclusion. Our results demonstrated that with proper interdisciplinary care, graft and patient survivals of pediatric recipients with UTAs were not affected; therefore, these patients should not be rejected for transplantation.

URINARY TRACT ABNORMALITIES (UTAs) represent a significant percentage among the causes of end-stage chronic renal failure (ESCRF) in children. According to the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS, 2008), primary disorders associated with UTAs constitute almost 40% of

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ESCRF causes: renal aplasia, hypoplasia, or dysplasia (15.9%); obstructive uropathies (15.6%); and reflux nephropathy (5.2%).[1–3] Patients with lower UTAs who have received a renal graft have been previously reported to show higher incidence of urologic complications[4–9] that may affect long-term graft function and survival.[10–13] For these reasons, some centers do not consider these patients to be suitable candidates for renal transplantation; they consider them to be high-risk subjects.[14] However, they can successfully be transplanted if these patients receive the appropriate pre- and posttransplant interdisciplinary management by a transplant surgeon, urologist, and a nephrologist[3,15] with the fundamental and common purposes of rehabilitating the urinary tract.[16,17] The purpose of this work was to determine the frequency of UTA among our series of pediatric cases as well as their urinary rehabilitation, comparing the frequency of complications and long-term graft and patient survivals with recipients free of UTAs.

METHODS

This single-center, retrospective, comparative study compared outcomes of recipients with a pretransplant diagnosis of ESCRF secondary to a UTA versus those with no urologic etiology. We included children grafted between January 1998 and December 2008 who had complete medical records. We analyzed demographic features, ESCRF etiology, protocols for patients with UTAs, urinary tract rehabilitation, medical and surgical complications, episodes of lower urinary tract infections (UTIs), rejection events and their treatment, evolution of kidney function, as well as patient and graft survivals.

The immunosuppressive regimen was similar for both groups: from 1998 to 2001, all patients received cyclosporine, azathioprine, and prednisone. Since 2001, all patients received induction with monoclonal antibodies (basiliximab or daclizumab) and long-term immunosuppression with tacrolimus, mycophenolate mofetil, and prednisone. From June 2001 to August 2004, sirolimus was administered as part of a protocol for early steroid withdrawal.

The central tendency and dispersion measures were used to describe continuous variables. For qualitative variables, we used frequencies and proportions. To establish a relation between two nominal qualitative variables, we employed contingency tables for analysis with chi-square or Fisher exact tests, the latter in cases where the sample size was small in at least one cell. To assess graft function, serum creatinine levels were compared by analysis of variance of repeated measurements with a fixed effect factor. Estimated risks were obtained by comparing both groups with odds ratios. Actuarial graft and patient survivals constructed with the Kaplan-Meier method were compared by log-rank tests. SPSS version 15.0 was used for the statistical analysis.

RESULTS

We excluded nine patients among the series of 328, because of incomplete medical records; therefore we included 319 procedures in 312 patients. Seven patients underwent retransplantations, and four patients had been subjected to a previous procedure before 1998 or at another transplant center; consequently, second transplantations were performed in 11 recipients. The etiology in 67 patients (21%) was secondary to UTA; the remaining 252 children were transplanted due to other reasons.

Diagnoses among patients with UTA were: neurogenic bladder (NB; $n = 26$), vesicoureteral reflux (VUR; $n = 19$), posterior urethral valves (PUV; $n = 8$), urethral obstruction ($n = 7$), myelomeningocele ($n = 3$), prune belly ($n = 2$), ureteropyelic stenosis ($n = 2$). NB, VUR, and PUV represented almost 80% of the group. Among patients with no urologic disorders, an unknown etiology was predominant (75%; $n = 190$), followed by glomerulonephritis ($n = 20$), glomerulosclerosis ($n = 11$), retransplantation ($n = 6$); lupus nephropathy ($n = 4$), Alport's syndrome ($n = 4$), Wilm's tumor ($n = 3$), and other syndromes (Jeune, Finish, Fanconi, oxalosis; $n = 14$).

Forty of the 67 patients with lower UTA (59.7%) required from one to five pretransplantation urologic surgeries to rehabilitate their urinary system, depending on the complexity of the underlying pathology. Thus, in the NB cases, 10 bladder augmentations were performed; seven with ileum, two with ureter, and one with sigmoid colon. Eight cases had continent conduits and two required intermittent transurethral clean catheterization. The remaining NB patients underwent bladder neck plasty and medical management. All PUV were resected. VUR cases underwent ureteral reimplantation, endoscopic application of submeatal macroplastic treatment, or nephrectomy. Twenty-four urologic recipients (35.8%) received pretransplantation antimicrobial prophylaxis.

After comparing demographic variables, we observed that patients with UTA versus non-UTA patients were significantly younger (11.1 vs 12.6, $P = .005$), showed lower body weight (28.8 vs 34.4 kg, $P = .002$), and were of shorter height (125.4 vs 138.4 cm, $P < .001$). In both groups, a retroperitoneal approach with vascular anastomoses to the iliac vessels was used in most cases. Only those recipients whose body weight was <15 kg or who required bilateral nephrectomy underwent a transperitoneal approach; in some cases, the renal vessels were anastomosed to the vena cava and aorta. These variables showed significant predominance in the UTA compared to the non-UTA group, posing greater technical challenges: namely, recipients <15 kg (22.4% vs 3.2%, $P < .001$); transperitoneal approach (40.3% vs 9.1%, $P < .001$); and cavae-aortic anastomoses (25.4% vs 7.5%, $P < .001$), respectively.

There were no significant differences between groups when comparing the immunosuppressive regimen, preemptive transplantation or type of donor (living, cadaveric, or cadaveric en bloc). Among the total number of patients, 13.2% (42/319) underwent preemptive transplantation and 78.1% (249/319), a living donor transplantation.

Rejection events occurred in 49.8% of patients (159/319); both groups were affected similarly (49.3% vs 50%). The mean time to the first rejection event was 30.16 months in patients with UTA versus 19.76 months among the non-UTA group (P = NS). Among these events, 45.9% (73/159) were biopsy-proven; the remaining were treated as clinically suspicious. Steroid resistant rejections (31/159 or