Urologic Complications in 4000 Kidney Transplants Performed at the Saint Barnabas Health Care System

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ABSTRACT

Renal transplantation is the current standard treatment for end-stage renal disease and is associated with immunologic, vascular, and urologic complications. In this study we report urologic complications following ureteral reimplantation based on 1 urologist's experience at a single high-volume renal transplant institution.

Methods.   A retrospective review was performed on all patients who underwent ureteral reimplantation by the transplant urologist at the time of their kidney transplant between July 1, 1993, and December 31, 2016.

Results.   There was a total of 3951 ureteral reimplantations performed for 3890 renal transplants. The overall complication rate was 7% (276 patients). Vesicoureteral reflux was the most common complication (4.25%), followed by ureteral stricture (1.9%), urine leak (0.6%), and de novo ureteropelvic junction obstruction (0.25%).

Conclusion.   This study is a continuation of our previous case series. Over time, our overall rate of urologic complications has increased. Vesicoureteral reflux has remained the most common complication with increasing incidence compared with our prior reviews. One possible cause for increased incidence is our thorough longitudinal follow-up over more than 2 decades. Some patients who previously had no evidence of reflux eventually did in fact develop reflux. The incidence of ureteral stricture, urine leak, and ureteropelvic junction obstruction has overall remained stable over the past 23 years. In our program, 1 transplant urologist has performed almost all ureteroneocystostomies, leading to consistent management and generalizable results. Review of the literature shows variable rates of complications among different studies with multiple surgeons, disparate techniques, and short follow-up. Our study eliminates many of these confounding factors and provides more reliable, reproducible data.

UROLOGIC complications have been observed since the beginning of renal transplantation and have caused significant morbidity and mortality. In the early days of renal transplantation, the incidence of urologic complications was reported to be between 10% and 25% [1,2] with an associated 20% to 30% mortality rate [3,4]. This incidence has decreased significantly over the past 40 years with refinement of surgical techniques and improvement of suture materials. Current urologic complication rate has been reported to be between 2.8% [5] and 15.5% [6]. A review of literature indicates that there are many different techniques for ureteroneocystostomy. Furthermore, some

institutions use ureteral stents routinely while others use them selectively, and yet others do not use them at all. Thus, it is difficult to compare urologic complication rates among different transplant programs. In addition, most programs have multiple surgeons who perform the ureteroneocystostomy contributing to variability in results and complication rates.

In this study, we report our experience with urologic complications in almost 4000 ureteral reimplantation operations performed by 1 transplant urologist over a 23 year period. Our program has evolved from Politano-Leadbetter ureteroneocystostomy technique without the use of stent to Lich-Gregoir technique with the routine use of ureteral stent. The most unique aspect of our program is that there is 1 transplant urologist who performs almost all ureteroneocystostomies and treats all urologic complications. This allows a review of a single surgeon's complication rate in a critical manner.

PATIENTS AND METHODS

A retrospective review was performed on all patients who underwent ureteral reimplantation by the transplant urologist at the time of their kidney transplant between July 1, 1993, and December 31, 2016, at the Saint Barnabas Health Care System. The transplant urologist kept a detailed record of all urologic complications on these patients as he treated them. Between July 1993 and June 1994, most ureteroneocystostomies were performed using the Politano-Leadbetter technique without routine use of a ureteral stent. Since July 1994, the Lich-Gregoir technique was adopted with a routine use of an indwelling ureteral stent.

RESULTS

Between July 1, 1993, and December 31, 2016, the transplant urologist performed 3951 ureteral reimplant operations at the time of 3890 kidney transplants at the Saint Barnabas Health Care System. There were almost equal numbers of deceased and living donor kidney transplants (1946 deceased donor and 1944 living donor). There were 2446 male patients (62.9%) and 1444 female patients (37.1%). The average age was 47.9 years, with average age for male patients being slightly higher at 48.4 years and average age for female patients being 47 years.

A total of 3929 ureteroneocystostomies were performed, and most (3856; 98.1%) were performed using the Lich-Gregoir technique with the routine use of a ureteral stent. In 73 cases (1.9%), the Politano-Leadbetter technique was used without the use of a ureteral stent. Furthermore, there were 12 ureteroileostomies performed on 11 patients who had an ileal conduit (1 received a kidney with duplicated ureters). One patient with ileal conduit was found to have nonfunctional ileal conduit at the time of transplant and underwent a cutaneous ureterostomy. In 2 patients, ureteroneocystostomy was performed into an Indiana Pouch. In 7 patients, ureteroureterostomy between the transplant kidney and the ipsilateral native ureter was needed. There were 11 pediatric en bloc kidney transplants

Table 1. Urologic Complications in 4000 Kidney Transplants

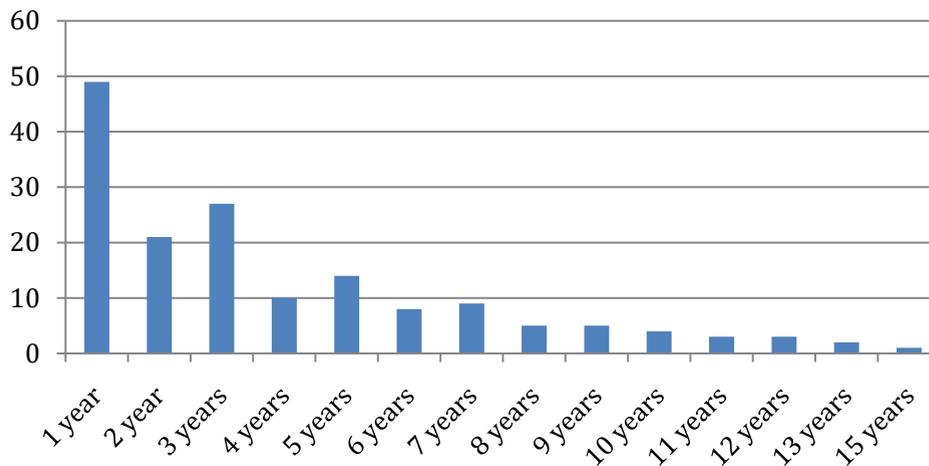| Complication	No. of Patients	%
Vesicoureteral reflux	168	4.25
Ureteral stricture	74	1.9
Urine leak	24	0.61
UPJ obstruction	10	0.25
Total	276	7.01

Abbreviation: UPJ, ureteropelvic junction.

(2 ureteroneocystostomies per transplant) and 1 had 3 total ureters between the 2 en bloc kidneys. There were 48 kidneys with duplicated ureters. After eliminating ureteroureterostomy, ureteroileostomy, cutaneous ureterostomy, and ureteroneocystostomy into the Indiana Pouch, there were 3929 ureteroneocystostomies performed by the transplant urologist. These ureteroneocystostomies were reviewed for urologic complications. There were 276 urologic complications (7.01%) (Table 1). The urologic complications included vesicoureteral reflux, ureteral stricture, urine leak, and de novo ureteropelvic junction (UPJ) obstruction.

Vesicoureteral Reflux

Vesicoureteral Reflux was the most common urologic complication occurring in 168 patients (4.25%). These patients presented with recurrent urinary tract infections (UTIs). Over half of the patients with reflux presented within the first 3 years (97; 57.7%) since the kidney transplant, but some presented as long as 15 years after the transplant (Fig 1). A voiding cystourethrogram (VCUG) was performed to evaluate the cause of the UTI and revealed the reflux. Among the reflux patients, all but 2 had a Lich-Gregoir reimplant. Nearly three-quarters of the patients with reflux were female (124; 73.8%), while the remainder (44; 26.2%) were male. The reflux occurred at similar rates in living donor (81; 48.2%) and deceased donor transplant patients (87; 51.8%). The initial treatment of reflux included no treatment in 3 (1.8%), antibiotic suppression in 31 (18.4%), hyaluronic acid/dextranome (Deflux) injection in 22 (13.1%), and surgical reconstruction in 112 patients (66.7%). None of the 22 patients who underwent hyaluronic acid/dextranome injection had a durable response for more than 1 year, and 11 patients chose to undergo surgical reconstruction, while the remaining 11 patients chose to undergo antibiotic suppression. As a result, a total of 42 patients (25%) underwent antibiotic suppression, 123 (73.2%) underwent surgical reconstruction, and 3 (1.8%) were not treated.

Of the 123 reconstructions, the surgical technique was a ureteroureterostomy between the ipsilateral native ureter and the transplant ureter in 112 patients, Politano-Leadbetter reimplant in 3 patients, repeat Lich-Gregoir reimplant in 7 patients, and ureteropyelostomy in 1 patient. Among the 123 patients, 95% had resolution of recurrent UTIs [7]. One patient developed obstruction and required a repeat ureteroureterostomy. An additional

No. of Patients With Reflux

Fig 1. Time to presentation with reflux after kidney transplant.

patient developed a urine leak and required a repeat ureteroureterostomy.

Ureteral Strictures

The second most common urologic complication was ureteral obstruction due to distal ureteral stricture observed in 74 patients (1.9%). The ureteral stricture occurred more frequently in male patients (47; 63.5%) than in female patients (27; 36.5%). It occurred at a similar rate between the deceased donor transplant recipients and living donor transplant recipients (38 and 36, respectively). These patients were initially treated with stent insertion followed by balloon dilation (43 patients) or reconstructive surgery (31 patients). Among those treated with balloon dilation, 10 (23.2%) failed to be relieved of obstruction and required reconstructive surgery. In total, 41 of 74 patients (55.4%) required surgical reconstruction for treatment of obstruction. The surgical techniques of reconstruction included 28 ureteroureterostomies between the ipsilateral native ureter and the transplant ureter, 5 ureteropyelostomies, and 8 repeat ureteroneocystostomies.

Urine Leaks

There were 24 urine leaks (0.61%). They occurred more often in male patients than in female patients (15 and 9, respectively). They were more common in living donor transplants than in deceased donor transplants (14 and 10, respectively). All but 1 occurred in Lich-Gregoir reimplantation. These patients' conditions were diagnosed and treated initially with cystoscopy and stent insertion. If the leak was very small, stent and Foley catheter drainage was attempted. If it was a larger urine leak, the patient was treated with immediate ureteral reconstruction. The most common reconstruction technique was ureteroureterostomy between the ipsilateral native ureter and transplant ureter (14 patients). In 3 patients, repeat ureteroneocystostomy

was performed. In 3 patients, stent and Foley catheter drainage resolved the urine leak. In 3 patients, there was significant necrosis of the transplant ureter and part of the kidney requiring both partial nephrectomy and ureteropyelostomy. One patient needed ureteropyelostomy without a partial nephrectomy.

UPJ Obstruction

There were 10 patients (0.25%) who developed UPJ obstruction after the transplant. These UPJ obstructions were not present in the donors. It seemed to have resulted from scarring. It was seen equally in both sexes. All but 1 required ureteropyelostomy using the ipsilateral native ureter. In 1 case, Y-V pyeloplasty was performed.

DISCUSSION

In summary, there were 276 urologic complications among 3929 ureteroneocystostomies (7.01%) performed as part of 3890 kidney transplants at St. Barnabas Health Care System (Table 1). The urologic complications included vesicoureteral reflux, ureteral stricture, urine leak, and de novo UPJ obstruction. We have previously presented similar data based on 1000 kidney transplants [8] and 2500 kidney transplants [9]. In the study with 1000 kidney transplants, we found a urologic complication rate of 4.3%, with the most common complication being ureteral stricture (2.7%), followed by urine leak (0.8%), vesicoureteral reflux (0.5%), and UPJ obstruction (0.3%).

Over 1500 kidney transplants later, we found that our complication rate has increased slightly to 5.5%, and the most common complication has changed to vesicoureteral reflux (3%), followed by ureteral stricture (1.3%), urine leak (0.9%), and UPJ obstruction (0.3%).

After nearly 4000 kidney transplants, the complications are 4.25% vesicoureteral reflux, 1.9% ureteral stricture,

Table 2. Urologic Complications Over Time

Complication	1000 Kidney Transplants, %	2500 Kidney Transplants, %	4000 Kidney Transplants, %
Vesicoureteral reflux	0.5	3	4.25
Ureteral stricture	2.7	1.3	1.9
Urine leak	0.8	0.9	0.6
UPJ obstruction	0.3	0.3	0.25
Total	4.3	5.5	7

Abbreviation: UPJ, ureteropelvic junction.

0.61% urine leak, and 0.25% UPJ obstruction. The evolution of complications over time is shown in Table 2.

It is remarkable that reflux and stricture had significant changes in their incidence, while urine leak and UPJ obstruction were stable in their incidence over a 23-year period. The fact that reflux has increased over time from 0.5% to 4.25% may be explained by our increased diligence and detection. In our program, any patient with a UTI post kidney transplant is advised to undergo a VCUG. Unfortunately, the true incidence of vesicoureteral reflux is unknown since VCUG is not routinely performed on all transplant patients but only those with recurrent UTIs.

The reflux is seen significantly more often in women then in men (73.8% vs 26.2%). It is proposed that the etiology of reflux is caused by thinner bladders in women leading to a weaker antireflux tunnel that is created at the time of reimplantation. Once diagnosed, antibiotic prophylaxis is started on these patients. We have abandoned hyaluronic acid/dextranome injection in these patients because no patient treated with hyaluronic acid/dextranome (0 of 22) achieved long-term success, and all ultimately required either antibiotic suppression or reconstructive surgery. The decision to perform surgery is based on a variety of factors, which include patient's age, current creatinine level, frequency of recurrent urinary tract infections, compliance with antibiotic suppression, and patient's overall health. The degree of reflux is not used to determine the need for reconstructive surgery. For example, if a patient's creatinine at the time of diagnosis is over 2.5, antibiotic suppression rather than surgery is recommended because the kidney has already lost significant function. If a patient is elderly or ill and does not wish to undergo a reconstructive surgery, again, antibiotic suppression is recommended. Otherwise, most patients with symptomatic reflux are recommended to undergo surgical reconstruction.

The reconstructive surgical technique depends on whether a nonrefluxing ipsilateral native ureter is available. Whenever a nonrefluxing native ureter is available ipsilateral to the transplant, we use ureteroureterostomy as the treatment technique. The ureteroureterostomy can be performed in an end-to-side fashion or an end-to-end fashion, depending on the length of the transplant ureter. Stents are inserted in both the transplant ureter and native ureter to facilitate identification of the ureters during the reconstructive surgery. When a nonrefluxing native ureter is not available ipsilateral to the transplant, a

ureteroneocystostomy is performed using the Politano-Leadbetter technique. Most of the patients (95%) who underwent reconstructive surgery were cured of symptomatic UTIs and were free of need for antibiotic suppression [7]. We, again, did not perform VCUG routinely on these patients postoperatively. Only 2 patients developed complications (1 obstruction and 1 leak) requiring exploration and repair. Thus, ureteroureterostomy and Politano-Leadbetter ureteroneocystostomy are excellent techniques to treat vesicoureteral reflux in these patients.

The second most common complication was that of ureteral obstruction in 74 patients (1.9%). Our initial report after the first 1000 transplants demonstrated a rate of obstruction of 2.7%. Our rate then decreased by 50% at the review of 2500 patients to 1.3%. It has now stabilized at a rate of 1.9% at the completion of this most recent study. This improvement may be because of a couple of factors. One may be simply that the surgeon's technique has improved over time. Another explanation may be that use of shorter segment of ureter when using Lich-Gregoir technique, compared with the Politano-Leadbetter technique, allowed a decreased stricture rate.

These patients were treated with stent insertion followed by either balloon dilation (43; 58.1%) or reconstructive surgery (31; 41.9%). Ten patients who had balloon dilation failed to be relieved of obstruction and required surgery. In total 41 patients (55.4%) required reconstructive surgery. Surgical technique was evenly divided between repeat ureteroneocystostomy and ureteroureterostomy, depending on the length of the transplant ureter after the strictured area was excised. Since the transplant ureter has a tenuous blood supply, use of the shortest possible segment of the donor ureter at the time of transplant seems to contribute to a decrease in the distal ureteral stricture rate. Butterworth et al [10] and Thrasher et al [11] have also reported similar conclusions.

The third most common complication was urine leak, which occurred in 24 patients (0.61%). Use of an indwelling stent appeared to decrease the incidence of urine leaks. This result is similar to those of others reported in the literature [8,12–14]. It was more common in female patients than in male patients (15 vs 9). It was more common in living donors than in deceased donors (14 vs 10). The fact that the incidence of urine leak did not change significantly from our first study suggests that the incidence of urine leak may depend less on the technique and more on the donor characteristics.

Ten patients (0.25%) who developed UPJ obstruction appeared to have scar tissue develop several years after the transplant. This was not a typical UPJ obstruction with a congenital obstruction. One was treated with a Y-V pyeloplasty with good result. The others underwent ureteropyelostomy using the ipsilateral native ureter with good results.

In conclusion, a review of literature suggests widely variable urologic complication rates. When reviewing reports that show a lower rate of complications, several common themes become apparent. The routine use of ureteral stent

seems to decrease risk of urologic complications. Furthermore, shortening the length of ureter with the Lich-Gregoir technique also decreases urologic complications. Finally, the surgeon's experience or skill factor must be considered. Emiroglu et al [15] stated that their low rate of urologic complications is a result of the experience of their team which "worked as a unit for 25 years." In our program, 1 urologist has performed almost all transplants and handled all complications for the past 23 years. This has led to consistent results with respect to urologic complications.

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