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Reconstruction of late-onset transplant ureteral stricture disease

Brian T. Helfand, Jessica P. Newman, Anne K. Mongiu, Parth Modi, Joshua J. Meeks and Christopher M. Gonzalez

Department of Urology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

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OBJECTIVES

To describe our experience with surgical management of transplant ureteral strictures over a 6-year period.

MATERIALS AND METHODS

The present study identified patients who underwent open reconstruction for transplant ureteral strictures between March 2002 and May 2008 after kidney or kidney–pancreas transplantation. Baseline clinical characteristics were documented, including age at transplantation and reconstruction, serum creatinine levels, immunosuppressive drug regimen, and comorbidities. Postoperative complications were noted, including urinary tract infections, stricture recurrence and graft failure. Successful reconstructions were defined as stable allograft function with unobstructed outflow not requiring repeat dilation, ureterotomy or stent placement.

RESULTS

Median age at the time of reconstruction was 51 years and the mean time from transplantation was 62 months. Seven of the 13 patients had failed previous balloon dilation. The patients were followed for a median of 41 months and a successful repair was achieved in 10 of 13 patients. Ureteral strictures recurred in two patients who received ureteroneocystostomies, which were subsequently managed with chronic stent exchanges. Another recurrence involved a 1.5-cm anastomotic stricture 6 months postoperatively, which was balloon-dilated and has remained recurrence-free for 16 months.

CONCLUSIONS

Patients who present >6 months after renal transplantation with ureteral strictures that are recalcitrant to endoscopic management can safely undergo open surgical ureteral reconstruction without subsequent renal or graft failure. Further investigation involving a larger patient cohort is required to confirm these initial results.

KEYWORDS

kidney transplant, transplant ureteral stricture, pyelovesicostomy, ureteroneocystostomy, outcomes

INTRODUCTION

Urological complications are a significant cause of morbidity after renal transplantation. In particular, ureteral strictures are one of the most common complications in transplant patients, with an incidence in the range 0.6–10.5% [1–3], and appear to be independent of whether patients undergo living or cadaveric donor transplantations [4].

Patients who present with acute renal failure or deteriorating graft function not related to immunosuppressive therapy often undergo an ultrasound of the transplant kidney and/or renogram to evaluate for mechanical obstruction. Those patients found to have ureteral strictures as the cause of obstruction may be initially treated by endoscopic or percutaneous management, including JJ stent insertion or percutaneous balloon dilatation. However, although these techniques are minimally invasive, they are often limited by their success rates, which are in the range 45–62% [5,6]. When these endoscopic options fail or are not feasible, more definitive surgical corrections are required to prevent subsequent renal failure and/or allograft loss.

Several studies have reported the efficacy of surgical repair of obstructed transplant ureters [7–10]. These reports encompass a relatively small number of patients with various causes of ureteral obstruction, including ureteral stricture disease and physical obstruction from lymphoceles, kinked or redundant ureters, and extrinsic compression from crossing blood vessels. In addition, most studies only report on the outcomes of patients at follow-up, 1–2 years after their ureteral reconstruction [9,11].

Most of the published literature reporting on ureteral obstruction after renal transplantation details the outcomes of management when performed within a few months post-transplantation. The aetiology of early stricture disease is caused by poor surgical technique or compromised ureteral blood supply during surgery. By contrast, the aetiology of late stricture disease is relatively unknown and considered to be caused by infection, fibrosis or progressive vascular disease [5,8,11–13]. The various aetiologies of stricture disease may affect the long-term outcome of surgical repair in that late strictures may not be as conducive to repair as a result of the potential chronic nature of the disease. Currently, the data on the long-term outcomes of surgical repair of transplant strictures presenting late (>6 months) after transplantation are incomplete. Therefore, the present study aimed to determine the

TABLE 1 Patient demographics

Patient number	Age at surgery (years)	Transplant type	Year of transplant	PMH	Immunosuppression
1	55	Kidney, cadaveric	1987	HTN	Azathioprine, cyclosporine, prednisone
2	53	Kidney, living, related	2003	HTN, PD × 5 years	MMF, tacrolimus
3	51	Kidney, living, related	2002	DM and HTN, HD × 7 months	Sirolimus, tacrolimus
4	57	Kidney, cadaveric	2004	PSC, secondary hepatorenal syndrome	MMF, tacrolimus
5	60	Kidney, living, unrelated	2004	DM	MMF, tacrolimus
6	18	Kidney, living, related	2004	ESRD, secondary to congenital hepatic fibrosis	Prednisone, tacrolimus
7	50	SPK, cadaveric	1997	DM	MMF, prednisone, tacrolimus
8	51	Kidney, living, unrelated	2005	IDDM, HTN	Sirolimus, tacrolimus
9	59	Kidney, cadaveric	1981	Reflux nephropathy w/ chronic pyelonephritis, HTN	Azathioprine, prednisone
10	44	Kidney, cadaveric	1997	PCKD	Prednisone, tacrolimus
11	41	Kidney, living, unrelated	2006	Pan-urethral stricture	MMF, cyclosporine
12	51	Kidney, cadaveric	2004	DM, HTN	MMF, tacrolimus
13	23	Kidney, living, related	2006	Potter's disease	MMF, prednisone, tacrolimus

DM, diabetes mellitus; ESRD, end-stage renal disease; HTN, hypertension; IDDM, insulin-dependent diabetes mellitus; MMF, mycophenolate mofetil; PCKD, polycystic kidney disease; PD, Potter's disease; PSC, primary sclerosing cholangitis.

outcomes of patients who underwent surgical reconstruction of late-presenting transplant ureteral strictures over a 6-year period.

MATERIALS AND METHODS

The Northwestern Hospital Enterprise Data Warehouse was used to retrospectively identify patients who underwent open reconstruction for late-onset transplant ureteral strictures after kidney or kidney–pancreas transplant, as performed by a single surgeon (C.M.G.) from March 2002 to May 2008. Institutional review board approval was obtained to perform the study.

The baseline clinical characteristics of the study population were documented, including age at renal transplantation, as well as age at ureteral reconstruction. In addition, serum creatinine levels, immunosuppressive drug regimen and comorbidities were documented.

All of the patients in the cohort were referred from the transplant service with higher serum creatinine levels and decreased urine output (<100 mL/day), with hydronephrosis confirmed by renal ultrasound at various time points after renal transplant. In some cases, obstruction was confirmed by renogram. Antegrade pyelography was used to diagnose and determine the location of the stenosis. All of the patients were treated initially with percutaneous nephrostomy tube placement and JJ stent placement. This does not apply for patients early in this series because balloon dilation was not widely used at our institution until 2004. The choice to use balloon dilation as a management strategy was guided by the location and length of the stricture. Pan ureteral strictures were never managed in this regard.

The choice of surgical reconstruction was determined by the surgeon based upon ureteral stricture length, allograft ureter length, the degree of peri-ureteral fibrosis and personal preference. In brief, all patients underwent general endotracheal anaesthesia and received prophylactic i.v. broad-spectrum antibiotics. A modified Gibson incision was used for all but one case where a midline incision was performed. Ureteral reconstruction was in the form of excision and ureteroneocystostomy, excision and ipsilateral ureteroureterostomy (UU), excision and direct pyelovesicostomy, and/or ureteral reconstruction using a modified Boari flap. After surgical repair, a JJ ureteral stent was placed in all patients. A Jackson–Pratt drain was placed around the anastamotic site to monitor for the presence of urine leaks. In addition, all patients had an indwelling Foley catheter both during and after the procedure. A cystogram was performed before decatheterization to evaluate for extravasation of urine. Patients were screened postoperatively for recurrence using patient history and physical examination, assessment of subjective voiding symptoms, serum creatinine levels, urine output, urine culture, and renal ultrasound and endoscopy with either antegrade or retrograde pyelogram when indicated. For the purposes of the present study, successful reconstructions were defined as stable allograft function with unobstructed outflow not requiring repeat dilation, ureterotomy or indwelling stent placement.

RESULTS

BASELINE CHARACTERISTICS

Thirteen patients (10 men and three women) who ultimately underwent surgical repair for post-transplantation ureteral stricture by one surgeon (C.M.G.) were included in the present study. The median (range) age at transplantation was 41.9 (17.0–59.7) years. Of these patients, six underwent cadaveric transplantations and seven had living donor grafts (Table 1). Reasons for renal failure requiring renal transplantation included hypertension in three patients, diabetes mellitus in two patients, both diabetes mellitus and hypertension in three patients, hepatorenal syndrome secondary to primary sclerosing cholangitis in one patient, end-stage renal disease secondary to congenital hepatic fibrosis in one patient, polycystic kidney disease in one patient, Potter's disease in one patient, and ureteral stricture disease

TABLE 2 Patient outcomes after open reconstruction of transplant ureteral strictures

Patient number	Stricture length (cm)	Stricture location	Time from transplant to reconstruction (months)	Procedure	Outcome	Postoperative UTI	Follow-up length (months)
1	3	Distal	176.1	Transplant ureteral re-implant	Success, no further stricture disease	No	16.3
2	1.5	Distal, Ureterovesical junction	8.3	Transplant pyelovesicostomy	Success, no further stricture disease	No	68.3
3	3	Distal	20.6	Ureteroureterostomy	Success, no further stricture disease	No	67.0
4	Length of ureter	Length of ureter	5.1	Transplant pyelovesicostomy	Recurrent stricture, managed with chronic stent exchange	No	63.7
5*	2.5	Distal	8.9	Transplant ureteral re-implant	Success, no further stricture disease	No	59.8
6*	1	Distal, Ureterovesical junction	11.4	Transplant pyelovesicostomy	Success, no further stricture disease	No	55.2
7*	4	Distal	91	Transplant ureteral re-implant	Success, no further stricture disease	Yes	6.8
8	2	Proximal	8.5	Boari flap of bladder to transplanted ureter	Recurrent stricture 6 months postoperatively, balloon dilated successfully	No	44.0
9*	1.3	Distal	309.7	Transplant ureteral re-implant	Recurrent stricture, managed with chronic stent exchange	Yes	35.4
10*	3	Distal	118.5	Transplant pyelovesicostomy	Success, no further stricture disease	No	34.5
11	Length of ureter	Length of ureter	6.1	Transplant pyelovesicostomy	Success, no further stricture disease	No	34.0
12*	6	Distal	27.1	Transplant ureteral re-implant	Success, no further stricture disease	No	32.0
13*	2	Distal	26	Transplant ureteral re-implant	Success, no further stricture disease	No	16.7

**Patients who failed initial management with balloon dilation.*

in one patient. Of the kidneys, eight were transplanted in the left iliac fossa, four were transplanted in the right iliac fossa, and one was transplanted intra-abdominally as a result of the large size of the graft and the small body habitus of the patient. All transplant ureteroneocystotomies were performed using a Lich–Gregoir technique. The cohort of patients was maintained on various immunosuppressive regimens according to transplant surgeon and nephrologist preference (Table 2).

The median (range) age of patients at the time of ureteral reconstruction was 51.0 (18.0–60.4) years. The mean (range) time from transplantation to diagnosis of the stricture was 62.8 (5.1–309.6) months. All patients presented post kidney transplantation with acute renal failure and decreased urine output (<100 mL/day), with hydronephrosis confirmed by renal ultrasound. All strictures were initially managed with percutaneous nephrostomy tube placement, with subsequent placement and internalization of a stent. Antegrade pyelography was used to diagnose and determine the location of the stenosis. On the basis of the year of balloon dilation availability, seven of the 13 patients underwent subsequent management with endoscopic balloon dilatation(s) of the stricture. For these patients, a mean (range) of 1.42 (1–4) endoscopic balloon dilations were performed before open surgical reconstruction.

The mean (range) length of the stricture, including the two patients with pan-ureteral strictures, was 3.3 (1.0–7.0) cm. Most patients (n = 10) had a stricture located at the distal ureter, one patient had a stricture at the proximal ureter, and two patients had a stricture along the length of the entire ureter.

Of the seven patients with viable allograft ureters, six underwent ureteroneocystostomies and one underwent ipsilateral UU. Of the six patients without adequate ureteral length, five were reconstructed using direct pyelovesicostomy and one underwent ureteral reconstruction using a modified Boari flap. The mean (range) estimated blood loss from the procedure was 354 (0–1400) mL, with two patients requiring intra-operative blood transfusions. There was no obvious association between estimated blood loss and the type of reconstruction performed. All resected ureteral segments were sent for pathological analysis and demonstrated histological evidence of fibrosis and chronic inflammation.

No patient required blood transfusion postoperatively. A single patient went into clot retention on postoperative day 9, which resolved after irrigation through the Foley catheter. One patient had a small bowel obstruction after surgery requiring re-exploration of the abdomen and lysis of adhesions on postoperative day 7. Of the 13 patients, two developed a postoperative urinary tract infection (one positive for >100 000 *Escherichia coli* and the other positive with *Pseudomonas aeruginosa*). No patient experienced a wound infection or dehiscence. Time to stent removal postoperatively was determined both by physician preference and patient compliance. The mean (range) time until stent removal was 48.2 (29–73) days, excluding the two patients who required chronic stent exchanges. The mean (range) time to removal of the Jackson–Pratt drain was 4 (2–10) days. The Foley catheter was removed after cystography had confirmed no urine extravasation, with a mean (range) time to removal of 10.2 (7–16) days.

Median (range) follow-up after surgery was 41.1 (6.8–68.4) months. All patients initially improved and had stable renal function associated with spontaneous adequate urine output. Successful reconstruction was achieved in 10 of 13 patients. Ureteral strictures recurred in two patients who had previously undergone ureteroneocystostomies, which were subsequently managed with chronic stent exchanges. Interestingly, one of these patients experienced a perioperative urinary tract infection. The third patient with a stricture recurrence underwent a Boari flap ureteral reconstruction and was found to have a 1.5-cm anastomotic stricture 6 months postoperatively. The ureteral stricture was subsequently balloon-dilated and the patient has remained recurrence-free 16 months post-procedure. During the extended follow-up, four patients had allograft failure secondary to acute rejection and were unable to be rescued by immunosuppression therapies; three of which were irreversible. There were no reported cases of BK virus or cytomegalovirus infection in this population. Two patients subsequently died of unrelated causes (myocardial infarction; sepsis secondary to neutropenia) over 6 months postoperatively.

DISCUSSION

Ureteral strictures are a relatively common complication after renal transplantation with a reported incidence of 31 per 1000 transplants [14]. Early transplant ureteral strictures, which are diagnosed within 3 months of surgery, are commonly the result of inadequate surgical technique, overdissection of the ureter, compromise of the blood supply during surgery or ischaemic fibrosis secondary to poor harvesting technique and rejection [5,11]. The aetiology of later complications may be related to repeat urinary tract infections, retroperitoneal fibrosis or vascular insufficiency [5,8,12,15]. One of the largest published series to date reported the outcomes of 1000 patients after renal transplantation and identified 36 patients (3.6%) with ureteral obstructions; 20 considered to be related to a compromised vascular supply and 16 related to a physical obstruction other than ureteral stenosis (e.g. extrinsic compression, kinked ureter) [11]. These patients presented for corrective surgery within a median of 4 months after their initial transplant surgery. By contrast, our cohort of patients had a relatively delayed presentation of ureteral stricture, including one patient with onset of renal failure/hydronephrosis over 25 years after renal transplantation. In addition, no patient in our series had an obvious physical/anatomic obstruction as a cause for the ureteral stenosis. Therefore, our patient population had ureteral obstructions solely from strictures, whereas previous series reported on all causes of obstruction that may have influenced outcomes [7,10,11].

Minimally invasive endoscopic or percutaneous management is often the first option for patients with ureteral strictures after renal transplant surgery. Percutaneous balloon dilation success rates in patients have been reported as 50% [5,6]. Prognostic factors for successful dilatation include early diagnosis after transplant, length of stricture and a previous episode of rejection [6]. However, in many patients, acute renal failure/oliguria/hydronephrosis representing stricture disease does not present early after renal transplantation, and endoscopic management is less likely to be a viable option. The findings of the present study support this notion because patients in our series presented several months after transplantation and had failed endoscopic management of transplant ureteral strictures. Ureteral strictures that fail percutaneous or endourological management require definitive surgical correction. Open surgery has the advantage of using a more proximal and healthy ureter for repair [11].

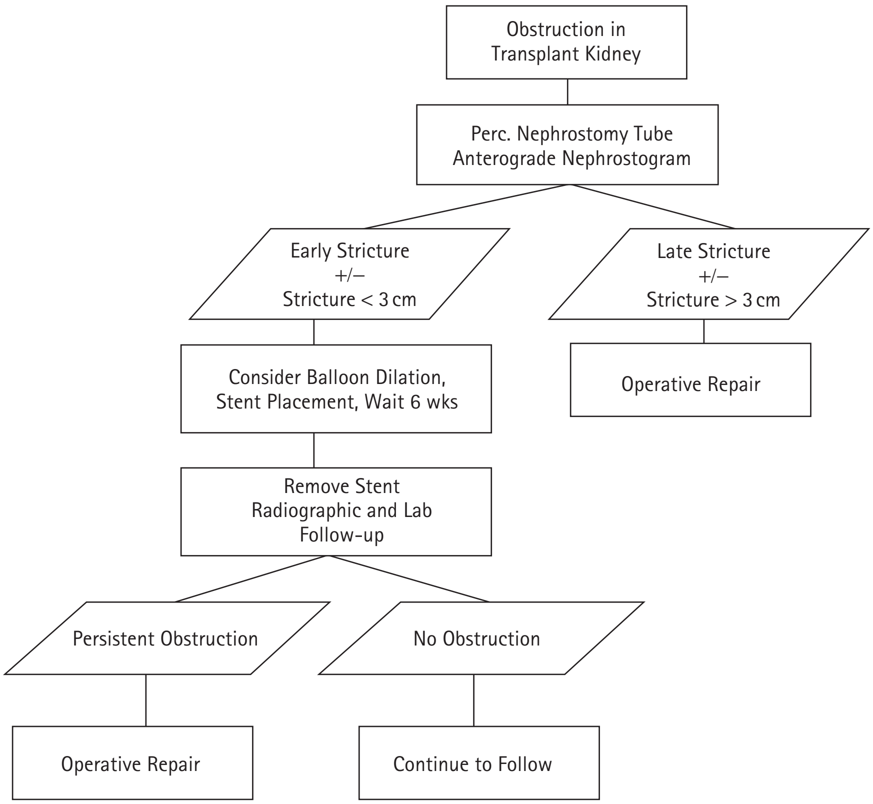
In one study of 56 patients with ureteral stenosis after kidney transplant, initial treatment with percutaenous nephrostomy followed by balloon dilatation and stenting resulted in a 45% success rate [6]. Considering patients in the same series who presented more than 5 months after initial transplant surgery, the success rate of endourologic treatment was only 11% ($P = 0.6$) [6]. In our series of late-onset ureteral strictures, none of seven patients were succesfully treated with balloon dilatation and stenting. Taken together, these data suggest that endourological management may not be effective for late-onset ureteral strictures and open repair may be the best choice for first-line therapy in these patients. Further data are needed to support this conclusion.

Options for surgical repair depend on several variables, including the length and location of the stricture, surgeon preference and degree of fibrosis surrounding the ureter. In the present study, transplant UU, pyelovesicostomy and reimplantation were all performed successfully. In our study population, two of the six ureteroneocystostomies performed for distal ureteral disease had stricture recurrence. Perhaps alternative surgical techniques such as pyeloureterostomy should be considered in this population with distal stenosis. For example, Salomon *et al.* [9] evaluated 10 patients who presented with distal ureteral stricture disease a mean of 13 months after renal transplantation. All patients were corrected with pyeloureterostomy with the patient's native ipsilateral collecting system and experienced no further ureteral complications after surgery, with a mean follow-up of 2 years. Thus, although ureteral reimplant is a useful option, other alternatives should be considered.

Pyelovesicostomy is beneficial when the native ureter is not suitable for reconstruction. This technique has an increased risk of VUR, with subsequent infection, decreased renal function and possible graft failure [16]. However, the five patients in the present series who underwent a pyelovesicostomy all did well without evidence of VUR or recurrent infections. Ureteroureterostomy with native ureter is an attractive option if there is adequate length and viable tissue remaining in the native ureter. The UU technique has been associated with a decreased risk of VUR and urinary fistulas, and also spares the ureter for further repair if recurrent complications arise [17]. In the present series, the patient who underwent UU repair with the native ureter experienced no recurrence or complications. However, it should be noted that the native ureter was rather atretic in appearance, probably related to a lack of native urine production from renal failure. In our opinion, the atretic appearance should not preclude subsequent UU repair.

The patients included in the present study were prescribed various immunosuppressive regimens after transplantation, which could have predisposed them to subsequent infection or wound dehiscence [18,19]. However, no complications of this nature were observed; therefore, the results obtained in the present study are similar to previous reports of urological surgery in immunosuppressed patients after kidney or kidney–pancreas transplants, which showed a similar incidence of postoperative morbidity

FIG. 1. Proposed alogrithm for the management of transplant ureteral strictures.



between transplant and non-transplant patients [20].

The results obtained in the present study should be evaluated within the context of the study limitations, including its retrospective nature and the relatively small patient population. In addition, it was not possible to determine the overall prevalence of ureteral stricture disease or patients who underwent a successful endoscopic management within the transplant population at our institution as a result of patient referral biases and incomplete datasets. Finally, median stricture length in this series was relatively short at 3.3 cm, which may have introduced a favourable selection bias for the outcomes reported.

On the basis of our institutional experience, we propose an algorithm for the management of transplant ureteral strictures (Fig. 1). In this algorithm, we propose that patients who are found to have hydronephrosis of the transplant kidney should undergo percutaneous nephrostomy tube placement. Endourologic management (i.e. balloon dilation) should be considered as initial therapy in a subset of patients based upon timing after nephrostomy tube placement (i.e. <3 months) and ureteral stricture length <3 cm. Finally, definitive operative repair can be considered in patients with late-onset disease and/or longer strictures.

In conclusion, the prevalence of successful endoscopic management of delayed stricture disease is unknown. However, the data obtained in the present study suggest that open surgical reconstruction is a safe procedure that does not appear to be associated with graft failure, rejection or increased morbidities. Future studies involving a larger cohort of transplant patients should be performed to confirm the success of surgical outcomes of delayed transplant ureteral strictures.

CONFLICT OF INTEREST

None declared.

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Correspondence: Chris M. Gonzalez, Department of Urology, Feinberg School of Medicine, Northwestern University, 675 North Saint Clair Street, Suite 20–150, Chicago, IL 60611, USA.
e-mail: cgonzalez@nmff.org

Abbreviation: **UU**, ureteroureterostomy