Review Article

The development and current status of minimally invasive surgery to manage urological complications after renal transplantation

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ABSTRACT

Introduction: In the past, urological complications after renal transplantation were associated with significant morbidity. With the development and application of endourological procedures, it is now possible to manage these cases with minimally invasive techniques.

Materials and Methods: A MEDLINE search for articles published in English using key words for the management of urological complications after renal transplantation was undertaken. Forty articles were selected and reviewed.

Results: The incidence of urological complications postrenal transplantation was reported to be 2–13%. Ureteric leaks occurred in up to 8.6%, and 55% were managed endourologically. The incidence of lymphocele was as high as 20%, and less that 12% of the cases required treatment. Ureteric stricture was the most common complication, and endourological management was successful in 50–70%. The occurrence of complicated vesicoureteral reflux was 4.5%, and 90% of low-grade reflux cases were successfully treated with deflux injections. Stones and obstructive voiding dysfunction occurred in about 1% of kidney transplant recipients.

Conclusion: Minimally invasive techniques have a critical role in the management of urological complications after renal transplantation. Urinary leakage should be managed with complete decompression. Percutaneous drainage should be the first line of treatment for lymphocele that is symptomatic or causing ureteric obstruction. Laparoscopic lymphocele deroofing is successful in aspiration-resistant cases. Deflux is highly successful for the management of complicated low-grade kidney transplant reflux. The principles of stone management in a native solitary kidney are applied to the transplanted kidney. Early identification and treatment of bladder outlet obstruction after renal transplantation can prevent urinary leakage and obstructive uropathy.

Key words: Minimally invasive, renal transplantation, urological complications

INTRODUCTION

The incidence of end-stage kidney disease (ESRD) in India is 151/million.[1] Management of ESRD is renal replacement therapy, and unarguably the best form of renal replacement is renal transplant in our region.[1] Urological complications postrenal transplant can cause significant morbidity and rarely mortality. Evolution of endourological armamentarium has made it first line of treatment for many such complications. We review the current status of endourological management of post renal-transplant complications.

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Access this article online	
Quick Response Code:	Website: www.indianjurol.com
	DOI: 10.4103/0970-1591.185100

How to cite this article: Sabnis RB, Singh AG, Ganpule AP, Chhabra JS, Tak GR, Shah JH. The development and current status of minimally invasive surgery to manage urological complications after renal transplantation. Indian J Urol 2016;32:186-91.

MATERIALS AND METHODS

An exhaustive MEDLINE search was undertaken using the MeSH words "post-transplant," "complications," "ureteric leak," "ureteric stricture," "lymphocele," "vesicoureteral reflux (VUR)," "dysfunctional voiding," "graft lithiasis," "endourology," and "minimally invasive." All the articles including case reports published in English were reviewed. All the data available were comprehensively analyzed.

RESULTS AND DISCUSSION

The incidence of post-transplant urological complications is highly variable (2–13%).[2] There is lack of definition of urological complications, methods of management are not standardized, and most of the published data is in the form of small cases reports/cases series.[3]

Urinary leaks

Urinary leak is an early postoperative complication, which can significantly increase the morbidity of renal transplantation.[4,5] It occurs in 1.2–8.9% of the cases.[3] Common etiologies for urinary leak are distal ureteric ischemia or poor suturing technique.[3,5]

These patients present as incision site pain (50%), dysuria, rising creatinine (71%), oliguria (43%), soakage from the operative wound, and sepsis (14%).[6] An ultrasound examination is the initial investigation of choice; magnetic resonance imaging (MRI) or computed tomography (CT) scan can help in noninvasive diagnosis.[6] Antegrade dye study may help in evaluation of the lesion.

The role of stenting the ureteric anastomosis in decreasing the rate of urinary leak is unclear with one study noting a 1.4% leak rate with stent as compared to 4.4% without stent.[5] The authors suggested that double-J (DJ) stenting should be done in high-risk patients with predisposing comorbidities.[5]

The primary management of urinary leak is placing a urethral catheter (PUC) and the endeavor should be to identify the site of leak. Minor leaks, which occur in the initial postoperative period due to delayed healing, can be managed in this manner.[7] In a series of 1200 consecutive transplants, 37 patients developed a leak, of which 6 (16.2%) could be managed only on PUC.[7]

Other studies have evaluated the role of minimally invasive surgery in managing urinary leaks and a total of 85 (55.5%) of 153 patients in these series could be salvaged using minimally invasive techniques.[2,7,8] The principle of management of post-transplant urinary leak is complete decompression that is achieved by placing a PUC, percutaneous nephrostomy, DJ stent, and drainage of urinoma.[3,7,8] The patient is followed up with serial ultrasounds, serum creatinine, and nephrostograms. Once no leak is seen on the nephrostogram, the nephrostomy is removed and the DJ stent is kept for another 4–6 weeks.[3,4] Close monitoring is essential as these patients are at high risk of developing strictures of the ureter. Patients failing this treatment require open surgical reimplantation or pyeloureterostomy with the native ureter.

Lymphocele

A lymphocele is collection of lymph in the post-transplant perigraft location. It may occur in 1–20% of renal transplants, but most are small and asymptomatic.[9] In a series published by Zietek *et al*., 12% patients developed clinically significant lymphoceles. A lymphocele may present any time from 2 weeks to 5 years after transplant and they present with retention of urine, decreased urine output, rising creatinine, iliac vein thrombosis, limb edema, wound dehiscence, graft loss, or voiding symptom.[9,10] On examination of the aspirate, a straw-colored fluid rich in lymphocytes with high protein content, and creatinine level is used to differentiate it from urine. Asymptomatic lymphoceles can be left alone.[7]

Treatment options include aspiration, percutaneous drainage, laparoscopic [Figure 1], or open marsupialization.[7,9] Aspiration alone has a near 100% chance of recurrence and percutaneous drainage has a 50% success rate as described in a series of 14 patients treated using this method by Zietek *et al*.[9] Sclerosants in form of betadine, fibringlue, and tetracycline can be used along with continuous drainage.[7] If the above methods fails, laparoscopic marsupialization of the lymphocele to the peritoneal cavity should be done; this method has a success rate of 86% in a series of 7 patients,[9] but one should not forget that this method has the potential to cause ureteric and vascular injury.

In summary, lymphoceles are common but not all of them require treatment; percutaneous drainage should be the first line of treatment failing which patients should be subjected to laparoscopic marsupialization.

Ureteral stricture/stenosis

The occurrence of post-transplant ureteric stricture varies from 2% to 7.5%.[11] Traditionally, ureteral strictures were managed surgically and had substantial morbidity.[2,12,13]

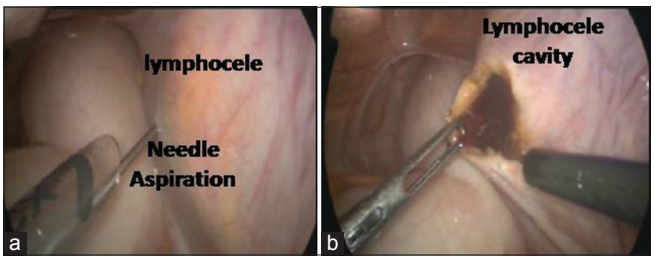

Figure 1: (a and b) Lymphocele appears as a medial bulge with a bluish hue. First a needle puncture and aspiration is done laparoscopically to confirm the position of lymphocele. After this, lymphocele wall is incised, ellipse of tissue excised, edges are everted and sutured

Ureteric strictures can present as painless, asymptomatic hydronephrosis with rising serum creatinine and patient may present with oliguria.[3] The most common cause of post-transplant obstructive uropathy is a ureteric stricture, but other possible causes are urolithiasis, blood clot, compression by lymphocele, hematoma, abscess, rarely ureteric rejection, and BK virus infection. Renal recipients should be subjected to routine ultrasound of the graft kidney; other investigations include MRI, CT scan, and radionuclide scan.[3]

Bhagat *et al.* classified ureteric strictures as Grade 1 - mild stenosis, Grade 2 - moderate to severe stenosis, and Grade 3 - complete cutoff of the contrast.[2] More recently, He *et al.* have classified ureteric strictures as Grade 1 having no obvious narrowing in ureter, probably caused by edema, blood clot, etc.; Grade 2 as narrowing <1 cm at the distal ureter or anastamotic site; Grade 3 as narrowing >1 cm, extending from distal to proximal ureter.[14] Grade 1 and 2 strictures are managed by endourological methods. Ureteric strictures can also be classified on the basis of presentation as early (<3 months post-transplant) or late (>3 months posttransplant).[15,16]

The evolution of minimally invasive treatment started with the use of percutaneous nephrostomies for decompression of pelvicalyceal system, this was followed by DJ stenting, and now various methods are available.[2,3,17] Patients diagnosed to have post-transplant obstructive uropathy should be first subjected to urinary diversion in the form of a percutaneous nephrostomy; retrograde stenting may be attempted but is technically challenging.[2,3] Endourological modalities used for management of ureteric strictures include DJ stenting, balloon dilatation, facial dilatation, and endoureterotomy.[2,3] Each of these procedures can be done in an antegrade [Figure 2] or a retrograde fashion.

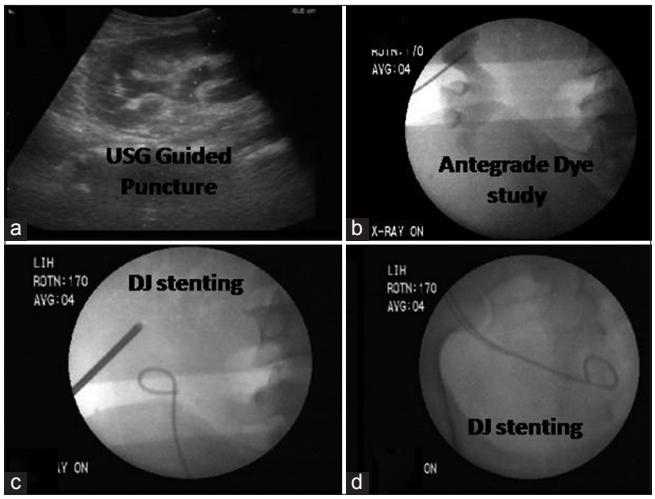

Figure 2: (a-d) On ultrasonography the kidney is visualized. Pelvicalyceal system is punctured through anterior calyx, by aligning cortex, calyx and pelvis in same line. Dye study is done to confirm the position of needle following which double J stenting; percutaneous nephrostomy or percutaneous nephrolithotomy may be done

Balloon dilatation of the stricture is the most popular procedure; in eight series, the total number of patients treated were 176, of which in 86 (48.8%) patients, the stricture could be successfully dilated and these ureters were patent over a period of at least 18 months [Table 1].[11,15,18,19] Balloon dilatation is also used in combination with endoureterotomy and, in some series, was found to have better results. In two series combining holmium YAG laser with balloon dilatation, the success rate was 100% and 67%, respectively.[19,20] Balloon dilatation has successfully been combined with cold knife and bugbee endoureterotomy.[21] The success rate of balloon dilatation is about 50%, its failures can be salvaged by endoureterotomy and the success rate is about 83%.[21] Repeat dilatation has poor results (25%).[21]

Endoureterotomy is another option for managing ureteric strictures. This can be done under direct vision using laser, cold knife, and electro cautery or an Acucise® balloon device (Applied Medical resources, Rancho SantaMargarita, CA, USA). In a series published by Katz *et al.*, 14 patients were subjected to direct vision endoureterotomy and 13 had a successful outcome (92.8%).[17] Laser endoureterotomy has a high success rate; it can be done retrograde using a semi-rigid ureteroscope and antegrade using a flexible ureteroscope in which it may be easier to approach the stricture from the dilated proximal segment.[3,19,20] Acucise® balloon endoureterotomy using a 75W cut, placed anteriorly away from vessels and bowel may have a success rate of about 67%.[22,23] It is a blind procedure and has a risk of thermal injury to adjacent organs and therefore it did not become popular.

In series which have used only a DJ stent as a modality for treatment of ureteric strictures, the overall success rate is 56%.[2] Two series have described the use of double DJ stents; one of them used two 7 fr DJ stents and the another one used two 4.8 fr stents, but the results are comparable to series using a single stent only.[18,22] The use of metallic stents such as Memokath™ and WALL STENT™ has also been described in patients with failed attempts at dilatation.[4,24]

Table 1: Management of ureteric strictures[11,15,18,19]

Procedure	Patients treated in various studies (*n*)	Successful outcome (*n*)	Success rate (%)
Double J stenting (1)*	41	23	56
Fascial dilatation (1)*	6	4	66.6
Balloon dilatation (8)*	176	86	48.8 (39-89)
Acucise endoureterotomy (3)*	16	14	87 (67-89)
Laser endoureterotomy (2)*	8	8	100
Endoureterotomy using electro cautery (1)*	14	13	92

*Figure in parenthesis indicate the number of series

In summary, post-transplant ureteric strictures are a relatively commonly occurring complication and they should be managed endourologically if they are short segment (<1 cm), Grade 1 or 2 and present early (<3 months) post-transplant.[2] Failed balloon dilatation may be salvaged with endoureterotomy failing which open surgical repair should be done. Endourological management significantly decreases morbidity in select subgroup of patients.[3]

Vesicoureteral reflux

In the renal transplant recipient, the incidence of VUR ranges from 2% to 86%.[25] Symptomatic VUR requiring hospital admission is around 4.5%.[25,26] Extravesical techniques and intentional wide anastamosis to prevent stenosis contribute to increased incidence of VUR in transplanted kidneys.[25] VUR may also result from fibrosis of the ureter secondary to rejection.[25,27] It has been shown in a 5-year follow-up study that VUR is not associated with decreased graft function or survival although it may be associated with higher incidence of hypertension and sepsis.[25]

Patients with symptomatic VUR having recurrent urinary tract infection (UTI) and reflux nephropathy should be treated.[28,29] Before treatment, a detailed evaluation of the bladder and its outlet should be done to rule out secondary reflux. A micturating cystourethrogram is obtained to establish the diagnosis and grade VUR. Treatment options for symptomatic VUR include open surgical repair with an antireflux procedure or ureteropyelostomy with the native ureter in case the native ureter is not refluxing. However, these are associated with increased morbidity and complications.[28]

Dextranomer/hyaluronic acid copolymer (Dx/HA) (Deflux™ QMed Scandinavia, Uppsala, Sweden) has been used in the management of VUR in transplanted kidneys. In three different series comprising of a total of 49 patients, the success rate was 75%, 54%, and 74%, respectively.[26,28,30] In a series published by Yucel *et al*., 26 patients were treated using deflux injections, ten patients had a low-grade (1–2) reflux, and 16 had a high-grade reflux (3–4).[26] Of the low-grade reflux, 5 were injected intraureterally and 5 subureterally and it was found that 4 of 5 patients with intraureteral injection and 5 of 5 patients with subureteral injection had resolution of reflux.[26] Overall 90% of patients in low-grade reflux responded to the treatment and the technique of injection did not alter the outcome.[26] In the high-grade reflux patients, the success rate was only 31%. Dx/HA is injected using a 3.7 fr needle intraureterally where the ureter is supported by bladder wall, injection is continued till adequate closure of orifice is achieved, if closure is not satisfactory, subureteral injection may be added.[26] In renal transplant patients, the neo orifice is at an awkward angle, the intramural portion of the transplanted ureter is sometimes so small that a mound cannot be created and the more laterally placed orifices respond poorly to treatment.[26] In another series of 19 patients with symptomatic reflux, deflux was used with the success rate of 57.9% after first and 78.9% after second injection. In the patients who responded to a single injection, the mean incidence of UTI decreased from 4.63 to 0.81.[30] In the group that required two injections, there was no decrease in incidence of UTI.[30]

Thus, VUR in transplanted kidneys is rare and it seldom requires treatment. Symptomatic VUR has to be treated, deflux is a viable option with good success rates, close to 90% in low-grade reflux. High-grade symptomatic reflux has to be managed surgically.

Urolithiasis

The incidence of graft urolithiasis varies from 0.4% to 1%, and may give rise to obstructive uropathy and graft dysfunction.[31,32] Because of their occurrence in a denervated kidney, these stones are often asymptomatic and the unusual location of the kidney makes the management of these stones challenging.

Graft lithiasis can result from *de novo* stone formation or it can be urolithiasis gifted by the donor. Graft lithiasis in the recipient have been attributed to improper drainage of urine, VUR, infection especially with organism such as *Proteus mirabilis*, retained suture material, tertiary hyperparathyroidism, hypercalcemia, hypercalciuria, hyperuricosemia, and hyperuricosuria caused by calcineurin inhibitor. Increased intake of protein, calcium, and Vitamin D may contribute to urolithiasis.[33-35] Graft urolithiasis can present with decreased graft function, UTI, hematuria, vague abdominal discomfort, anuria, and rarely pain.[31,33] The mean time of presentation after the transplant was 1.6–3.6 years.[33]

The investigations to diagnose graft urolithiasis include ultrasound examination and CT scan. Treatment of a graft urolithiasis is as in a solitary functioning kidney.[31] Once the patient is diagnosed to have graft calculi, the aim first is to stabilize the graft function by placing a nephrostomy or DJ stent. If the stone is non-obstructing, one can directly proceed for stone management.

Minimally invasive modalities used for graft urolithiasis are shock-wave lithotripsy, percutaneous nephrolithotomy (PCNL), and flexible or rigid ureteroscopy.[31,33,34,36] The use of a particular modality is dependent on the size of the stone, location of the stone, and patient characteristic. A stone <4 mm can be observed for spontaneous passage.[33,34]

Extracorporeal shock wave lithotripsy (SWL) is used for managing calculi of size <1.5 cm. SWL in these patients is done in the prone position, under fluoroscopic guidance. Localization of the stone is hindered by the bony pelvis which also causes attenuation of the shock waves. Concerns

that the position of the transplanted kidney may impair stone clearance have been unfounded.[31] In a series published by Challacombe *et al*., 13 patients were treated with SWL, in 11 patients, there was complete clearance of stone and in two patients flexible uretero-renoscopy (URS) was additionally required.[31] Pre-stenting the ureter is not a prerequisite for SWL, but stringent follow-up is mandatory.[31] In three series comprising of 23 patients, success rate >90% was obtained with SWL.[31,33,34]

URS is an effective tool to manage graft urolithiasis. It can be done both in a retrograde and antegrade fashion. The retrograde access is difficult, as the ureter does not support the scope; ureteroscopy becomes possible if the scope is passed on a wire.[31] Hyams *et al*. demonstrated antegrade URS in 5 cases and retrograde URS in 7 cases. A hydrophilic wire was initially passed which was subsequently replaced for an Amplatz super-stiff wire or a nitinol wire, which could support the scope. Stones were fragmented using holmium laser and fragments were extracted. All patients were stone-free, apart from one who had a 2 mm residual fragment.[36]

PCNL is the most effective technique to manage stones larger that 1.5 cm. PCNL in grafted kidneys is performed in the supine position; access is usually gained from anterior calyx using ultrasound and fluoroscopic guidance [Figure 2].[32] In a series published by Krambeck *et al*., 13 patients were treated with PCNL, 12 patients required single puncture, and one case required two punctures. Three patients required a relook nephroscopy after which 100% clearance was achieved. No patients had intraoperative complications related to the procedure. Mean follow-up duration of the study was 5.3 years during which one patient developed recurrence, which was managed by SWL.[32]

Voiding dysfunction post-transplant

Voiding dysfunction is reported to occur in about 1.1% of transplanted patients.[37] The incidence is high in patients older than 60 years.[38] The causes of voiding dysfunction include benign prostatic hyperplasia (BPH), bladder neck stenosis, stricture urethra, and underactive detrusor. BPH is the most common cause of bladder outlet obstruction in transplanted patients [Table 2].[6,37,38] Transurethral resection of prostate (TURP) is performed for patients not responding to medical management. In a series of 43 patients, 35 underwent TURP with a success rate of 81.5%.[38] The timing of TURP in patient developing urinary retention in the immediate post-transplant period is variable, early intervention may cause ureteric leak and infections and the complication rate may be as high as 25%. Therefore, it is advisable to wait for 4 weeks after the transplant.[38,39] The use of holmium laser enucleation of prostate in a renal transplant patient has been recently described successfully.[40]

Table 2: Management of bladder outlet obstruction[6,37-40]

Etiology	Number of series	Number of patients	Method of treatment	Complications
BPH	4	61	TURP - 53 Alpha blockers - 8	1 bladder neck leak, 1 death
Bladder neck stenosis	3	11	Bladder neck incision in all	Nil
Stricture urethra	3	12	Optical urethrotomy - 10 Dilatation - 2	Recurrence in one patient, he was subjected to repeat optical urethrotomy with dilatation

BPH=Benign prostatic hyperplasia, TURP=Transurethral resection of prostate

Bladder neck contractures can cause problems similar to BPH and should be managed with bladder neck incisions. It is a simple procedure, without many complications. Stricture urethra can also cause bladder outlet obstruction after transplant; in a series of 6 patients, all were managed with visual internal urethrotomy.[38] Patients may require repeat urethrotomy or dilatation.[6]

Bladder outlet obstruction can give rise to complications such as urinary leak, and the diagnosis are missed before a transplant surgery due to the relative oliguria/anuria. Once identified in the immediate post-transplant period, the urine should be diverted by a PUC or SPC and definitive endourological procedure performed after 1 month.[3] Procedures such as VIU and BNI can be done earlier.

CONCLUSION

Minimally invasive techniques have a critical place in the management of urological complications after renal transplant surgery. Urinary leaks should be managed with complete urinary diversion and require a stringent follow-up. Percutaneous drainage should be the first line of treatment for symptomatic lymphoceles. Grade 1–2 ureteric strictures should be initially managed endourologically. Deflux is a viable option for managing symptomatic low-grade reflux post-transplant, with high success rate. Graft lithiasis has to be treated like a solitary functioning kidney and, depending on the size and location of stone, appropriate modality of treatment should be selected. Early identification and treatment of bladder neck obstruction can prevent morbid complication of urinary leak in the post-transplant patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest

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