The Diagnosis and Management of the Urological Complications of Renal Transplantation: a series of 1100 patients

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Objective: To analyse the Urological Complications after Renal Transplantation and their management. **Material and methods:** -A retrospective analysis of 1150 consecutive live donor renal transplants was performed. The study period extended from December 1995 to December 2004. The surgical procedure for ureteral reimplantation was modified Lich anastomosis. Ultrasonography, renal scanning, antegrade pyelography, retrograde pyelography and cystography were the diagnostic tools. **Results:** -Overall, 68 primary urological complications (5.9%) were identified during the 15-year experience in 65 patients. The Urological Complications in our series included 35 ureteral obstruction (3.0%), 25 ureteral or bladder leaks (2.17%), 05 out flow obstruction, 02 cases of vesicoureteral reflux and 01 case of ureteral stone. **Conclusion:** The incidence of Urological Complications in our study is 5.9%. Early exploration of the ureteric leaks and timely intervention to obstructed kidney reduced the morbidity and improves graft survival. The causes of these complications and techniques for their prevention are discussed in this study.
Key words - Renal transplantation, Complications.

Renal transplantation is now universally accepted as the first choice of treatment for end stage renal disease. More than 95% one-year patient survival and more than 90% allograft survival is achieved in most of the centers through out the world[1]. The first successful human renal transplant was performed in 1953. Initially, radiation was used for immunosuppression (1959), followed by 6-mercaptopurine. In the early 1960_s, tissue typing was introduced to allow better donor selection. Azathioprine became available for use in human in 1961. Prednisolone became part of standard immunosuppression regimen with azathioprine in 1962. In 1967, Belzer demonstrated the feasibility of organ preservation. In 1978, cyclosporin was first used, and its significant impact on graft survival was demonstrated[2].

Urological complications, which have been observed since the beginning of renal transplantation, cause significant morbidity and mortality. In the early period of renal transplantation, the incidence of urological complications was reported to be 10% to 25% with an associated 20% to 30% mortality rate[3, 4]. This incidence has decreased significantly over the past 40 years with refinements in surgical techniques and improvement in suture material. The current urological complication rate has been reported to be between 2.9% to 9.2%[4,5]. The most frequent urinary tract complications are ureteral leaks and ureteral stenosis. A review of literature reveals many techniques of ureteroneocstostomy[3, 4,5].

Patients and methods:

Between January 1990 (when our renal transplant program was begun) and December 2004, a total of 1150 consecutive live donor renal transplants were done in1100 patients including 700 males and 400 females with a mean age of ± S.D. of 29.5 ±10.5 years (range 5-60). There were 1100 first, 48 second and 02 third transplant.

After induction of general anesthesia, the bladder was distended with 100 to 150ml of an antibiotic solution to improve intraoperative identification. A Gibson incision was made either in the right or left lower 1quadrant. The subcutaneous tissue and external oblique, internal and transverse muscles were divided with an electrocautery. The inferior epigastic vessels were divided and ligated. In women, the round ligament was divided and ligated. The spermatic cord was identified and preserved. The retroperitoneun was entered and the lymphatics over the iliac vessels were ligated and divided to prevent lymphocele. The transplanted kidney was inspected and the vessels prepared for anastomosis. Generally, the renal vein was anastomosed to the external iliac vein, then the renal artery to the internal iliac artery. The ureter was then passed behind the spermatic cord and anastomosed to the bladder by modified lich method without the use of ureteral stents. A submucsal tunnel was created by using the over lying deterusor muscle and perivesical pad of fat to prevent reflux. A Foley catheter was used to drain the bladders of all patients for at least 05 days after surgery. All patients in our series were followed for at least one year.

Renal function was monitored postoperatively by serum creatinine and urine output. In cases of early graft dysfunction, ultrasound and diethylene triaminie pentaacetic acid renal scanning were routinely performed, usually followed by a percutaneous renal biopsy. Further imaging was dependent on the findings and clinical impression but, if indicated included percutaneous nephrostomy with antegrade urography.

Results:

The urological complications in the first consecutive 1150 renal transplants are reported in our study with a minimum follow up of 12 months.

Over all, 68 primary urological complications (5.9%) were identified during the 15-year experience in 65 patients. One ureteral complication occurred after

transurethral resection to relieve bladder outflow obstruction and, although almost certainly related to the resection, that was considered as separate primary complication. There was no significant correlation between recipient age, sex, transplant number or primary renal disease and the incidence of urological complications.

The urological complications included 35 ureteral obstruction (52%), 25 ureteral or bladder leaks (including ureteral necrosis) (37%), 0.5 out flow obstruction (prostate, bladder neck, or urethra)(7%), 01 ureteral stone (01%) and 02 cases of symptomatic vesicoureteral reflux (03%) requiring correction. The urological complication was corrected after 01 procedure in 63 cases and after 2 procedures in 02. No graft was lost due to urological complications. However, 02 patients died of the complications and their cases will be discussed. The incidence of urological complication in our study is 5.9%.

Ureteral obstruction: In our series, primary ureteral obstruction was seen in 35 cases (3.0%) Table 1. he clinical presentation of ureteral obstruction was decreased urine output (oliguria), urinary tract infection progressing to sepsis, local pain over the graft site and a gradual rise in serum creatinine.

The use of imaging modalities in diagnosing these complications included ultrasonography, renal scanning, antegrade pyelography and retrograde pyelogaphy. A cause of obstruction other than ischemia was identified in 15 cases including 05 lymphoceles, 03 damaged ureters recognized during retrieval, 02 redunt and kinked ureter, 02-twisted ureter, 01 abscess, 01 ureteropelvic obstruction and 01 double renal pelvis.Among the 35 cases of uretral obstruction, the site of obstruction was upper ureter in 05 cases, middle ureter in 05 and lower ureter/vesicoureteral junction in 25. The interval of obstruction after transplantation ranged from 5 hours to 400 weeks (median 15 weeks). Initial management of uretic obstruction was PCN followed by definite procedures. The 25 cases of vesicoureteral obstruction were treated primarily by ureteral reimplantation into the bladder in 20, native uretropyelostomy in 03 and percutaneous antegrade placement of a ureteral stent in 2. Among these cases of vesicoureteral obstruction, only 01 reimplantation failed, which was then successfully managed by secondary reimplantation. The 05 cases of mid ureteral obstruction were treated by native uteteropyelostomy in 02, an antegrade stent in 01 and retrograde stent in 02. Obstruction in later cases recurred after removal of the stent but subsequent native ureteropyelostomy was successful. The 05 cases of ureteropelvic junction obstruction were treated by native ureteropyelostomy in 04 and an antegrade stent in 01. Unfortunately one of the 04 cases that underwent ureteropyelostomy died because of septicemia.

Urinary leakage: There were 25 cases of urinary leakage (2.17%) in our series. Table2: The clinical symptoms of urinary leakage which usually presented before the 5th post transplant week included fever, pain and swelling over graft site, perineum, scrotum or labia, elevated serum creatinine, cutaneous urinary leakage and sepsis.The diagnostic studies performad in these patients with urinary leakage included ultrasonography, renal scanning, antegrade pyelography, retrograde pyelography and cystography. The majority of ureteral leaks could be attributed to ischemia. Among the 25 cases of urinary leakage, 04 arising from the bladder, 04 from lower ureter and 03 from upper ureter and in 14 there was complete necrosis of the ureter.

Two of the 03 upper ureteral leaks were managed conservatively with a retrograde stent and one required surtusing of hole made at retrieval. Of the 04 lower ureteral leaks native ureteropyelostomy, 02 ureteral reimplantation and 01 reimplantation into a Bori flap treated 01. Among the patients treated by reimplantation 01 had recurrent leakage, a secondary reimplantation was successful. Two of the 04-bladder leaks required open repair and two were treated conservatively with urethral catheter drainage. Finally, of 14 ureteral uecrosis 08 were treated by simple reimplantation, 02 reimplantation with a Bori flap are 04 by native ureteropyelostomy. Table-2:

Table: 1- Ureteral obstruction: incidence and management.

Location	=n	Median wks on set (range)	Treatment
Upper/PUJ	05	55(7-228)	Native ureteropyelostomy (04) Antegracde stent (01)
Middle	05	65(9-155)	Native ureteropyelostomy (02) Antegrade stenbt (01) Retrograde stent (02)
Lower/vesic oureteral junction	25	15(0-400)	Reimplant (20) Native ureteropye-lostomy (03) Antegrade stent (02)

Bladder outflow obstruction: -There were 05 cases of outflow obstruction in the male transplant population comprising o2 bladder neck contractures, 02 urethral strictures and 01 prostatic outflow obstruction. Two cases of bladder neck obstruction, all within one month of transplant were treated successfully by endoscopic bladder neck incision. There were 02 urethral strictures requiring treatment, one developed 12 months after transplantation and was successfully treated by internal urethrotomy, while 01 occurred 03 months after transplantation in a patient with a history of recurrent urethral stricture.

One patient has significant outflow obstruction as a result of prostatic enlargement and he underwent transurethral resection at 10 months after transplantation. This patient had a bladder leak that was diagnosed 12 weeks after transurethral resection of the prostate and an

open operation was required for closure. The patient subsequently became septicemia and died 05 days later.

Table: 2 Ureteral Leakage Incidence and Management:

Location	=n	Median wks onset (range)	Treatment
Upper ureter	03	30(0-8)	Suture hole (01) Retrograde stent (02)
Lower ureter	04	3.5(02-7)	Native ureteropyelostomy (01) Reimplant (02) Bori flap (01)
Bladder	04	6.0(0-50)	Suture hole (02) & prolonged catheter drainage (02)
Ureteral necorosis	14	4.5(0-10)	Reimplant (08) Bor flap (02) & native ureteropyelostomy (04

Vesicoureteral reflux:
Two patients had persistent vericoureteral reflux in the transplant ureter resulting in recurrent pyelonephritis in the graft and ureteral reimplntation was successful.

Ureteral stone:
The one case of sympotmatic ureteral stone in the series occurred 02 years after transplantation. This patient presented with atypical abdominal pain and was treated successfully by ureteroscopic stone manipulation with no further recurred.

Discussion:
Urological complications remain a major source of morbidity and occasional mortality in renal transplantation despite a reduction in their incidence of at least half over the last 30years[3, 5, and 6]. Our urological complication rate occurring after transplantation during the last 15 years for 1150 consecutive transplants is 5.9%. Table-3: shows a comparison of the present with contemporary series including >400 transplants[5, 7-16]. The majority of urological complications encountered after renal transplantation are ureteral obstruction and leaks. Prompt diagnosis and treatment are important to prevent graft loss and to decrease morbidity and mortality. High dose steroid use is a strong risk factor for urological complications, in particular ureteral leak and stricture. It will be interesting to determine whether new immunosuppressive protocols based on FK 506 or cyclosporin that involve total steroid withdrawal will lower this complication rate further. It seems likely that ischemia of the ureter as a result of complications of the retrieval (that is division of lower polar artery or stripping of the ureter will continue to be the cause of urological complication[4, 7'17].

The majority of urological complications are technical in nature. These technical problems can occur during retrieval or reimplantation. Effective retrieval begins with a careful inspection of the donor collecting system and ureter, since congenital ureteropelvic junction obstruction or partial duplication can be missed. The importance of maintain a ureteral blood supply by not dissecting the periureteral connective tissue, and avoiding the "golden triangle" of the renal hilum, great vessels and medial lower pole is well documented and bears constant reinforcement to all those involved with organ procurement surgery. When ureteral compromise may have occurred, a ureteral stent at transplantation can be useful adjuvant. However, urolojical complications still many occur with stents is place[5, 15,18].

The techniques of ureteral reimplanatation may be open interavesical or extravesical in nature but recently extravesical techniques are gaining popularity[14, 15,16]. The advantages of extravesical techniques include decreased bladder bleeding, use of a shorter segment of ureter and decreased operating time. The disadvantages of the extravesical implantation is a grater risk of reflux but with use of extravesical techniques that create a muscular tunnel that is probably no longer important[5, 15,16].

The key to diagnosing urological complications is a high index of suspicion and the early use of imaging techniques. Ultrasound and isotope scanning are the usual first approaches in the presence of renal dysfunction[19, 20]. If any uncertainty is present as a leak or obstruction, antegrade pyelography is safe and effective and can be used as access for nephrostomy drainage in[21, 22].

In our series primary treatment for most ureteral complications remained an open operation. While endoscopic techniques are growing in popularity, the underlying cause of most transplant ureteral complications is technical, ischemic or secondary to another pathological condition (i.e. lymphocele). In case of a damaged ureter usually due to ischemia, open surgery and use of more proximal and healthy ureter improves the chance for success. For a short transplant ureter we have used with equal success native ureteropyelostomy or the Bori flap/Psoas hitch procedures. Neverthless, nephrostomy drainage can be an important adjuvant treatment[20, 21, especially for the ill patients in preparation for surgery but it seldom cures the problem alone. Although percutaneous endoscopic techniques can be used to treat a variety of urological complictions[23], long term results of dilatation for obstruction, even at specialist center, have been reported to be less than 50%[24].

The risks of transurethral resection of the prostate in the posttransplant period are highlighted by our one patient who had urinary leakage post operatively. We suggest

Table 3: Comparison of the present study with other large series of Renal Transplants (1981-2004)

Ref	Year	Number of transplants	Vesico ureteric anastomosis	Ureterc stents	Urinary leaks.%	Ureteric obstruction %
[7]	1981	1000	L-P	No	5.6	7.5
[8]	1983	505	L-P	No	2.2	1.0
[9]	1984	718	L-P	No	8.9	3.3
[10]	1988	808	Extravesical	No	1.4	0.9
[11]	1992	1000	Extravesical	No	0.9	0.3
[12]	1994	1200	Extra/transvesical	N/A	4.0	2.5
[13]	1997	534	1Extravesical	No	5.6	6.3
[14]	1998	600	Extravesical	Mixed	2.5	1.7
[15]	2000	400	Extravesical	Yes	0	0
[16]	2001	1200	Extravesical	No	3.1	1.9
[5]	2002	1128	L-P/Lich	Mixed	3.1	1.1
Present	2004	1150	Extravesical	No	2.17	3.0

that in men at risk for outflow obstruction, the urinary outflow tract should be assessed with cystoscopy and urinary flow rate, and significant outflow obstruction should be treated before transplantation. Transurthral resection of prostate done before transplantation is the procedure of choice[4]. The use of medical treatment for transplant patient with alpha-blockade is another option but its interaction with current immunosuppressive agents is not fully known.

Conclusion:

The incidence of post-transplant urological complications in our series is 5.9%. Majority of these urological complications were ureteral obstruction and urinary leakage. Early intervention was required to avoid graft loss. The key factors in decreasing the urological complications are meticulous organ procurement, complete recipient evaluation with treatment of lower urinary tract pathological conditions before transplantation, low dose steroid immunosuppressive protocols, prompt diagnosis with a high index of suspicion and a combination of endourological and open reconstructive techniques.

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