



Surgical Treatment for Ureteral Complications Following Renal Transplantations

Renal Transplantasyon Sonrası Üreteral Komplikasyonlarda Cerrahi Tedavi

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What's known on the subject? and What does the study add?

The aim of this study was to review the causes of and surgical treatment methods for ureteral complications following renal transplantations.

ABSTRACT

Objective

Ureteral stenosis and necrosis are the most common urological complications after a renal transplantation. Surgery is the treatment of choice in ureteral necrosis, whereas surgery, percutaneous approaches and laser endoureteromy may be applied in ureteral stenosis. The aim of this study was to review the causes of and surgical treatment methods for ureteral complications following renal transplantations.

Materials and Methods

One hundred sixty renal transplantations were performed from both cadaveric and live donors at our transplantation center between 2011 and 2014. Demographic features, complication types, surgical methods and the treatment results in 10 patients, who required surgical intervention due to ureteral complications, were recorded. Data was collected retrospectively through patient charts.

Results

Patients who were operated on because of ureteral complications were enrolled in the study. Six patients (3.75%) had ureteral stenosis, and 4 patients (2.5%) had ureteral necrosis. Three of these transplantations were made from living donors (2 female and 1 male) and 7 were from cadavers (1 female and 6 male). Extravasation was found in 4 patients due to necrosis, all encountered in the second week of operation. Two patients underwent native ureteropyelostomy and two underwent ureteroneocystostomy for ureteral necrosis. One patient underwent ureteroureterostomy, four had ureteroneocystostomy, and one had native ureteropyelostomy for stenosis. One patient experienced postoperative urine leakage and underwent native ureteropelvic anastomosis.

Conclusion

In our study, urological complications following renal transplantation were mostly seen after cadaveric renal transplantations. Ureteral

ÖZET

Amaç

Üreter darlığı ve nekrozu renal transplantasyon sonrası en sık görülen ürolojik komplikasyonlardır. Darlıkların tedavisinde cerrahi, perkütan girişimsel yaklaşımlar, laser endoüreterotomi gibi yöntemler uygulanabilir. Üreter nekrozlarında cerrahi tedavi ön planda yer almaktadır. Çalışmamızda yapılan renal transplantasyon sonrası görülen üreter komplikasyonlarının nedenlerini incelemek ve uygulanan cerrahi tedavi seçeneklerini değerlendirmek amaçlanmıştır.

Gereç ve Yöntem

2011 ve 2014 yılları arasında transplantasyon merkezimizde yapılan 160 kadavra ve canlı renal transplantasyon kayıtları retrospektif olarak değerlendirmeye alındı. Ürolojik komplikasyon nedeniyle cerrahi müdahale uygulanan 10 hastanın demografik özellikleri, gelişen komplikasyon türü, ürolojik komplikasyona uygulanan cerrahi yöntemler ve sonuçları kayıt edildi. Hastaların verilerine dosya taramaları ile ulaşıldı.

Bulgular

Üreter darlığı 6 hastada (%3,75), üreter nekrozu 4 hastada (%2,5) görüldü. Transplantasyonların 3'ü canlı donörden (2 kadın, 1 erkek), 7'si kadavradan (1 kadın, 6 erkek) yapıldı. İdrar kaçağı üreter nekrozundan dolayı, 4 hastada görüldü. Kaçak oluşan hastalarda kaçaklar yaklaşık 2. haftada görüldü. Üreter nekrozu nedeniyle 2 hastaya native üreteropyelostomi, diğer 2 hastaya üreteroneosistostomi uygulandı. Üreter stenozu için bir hastaya üreteroureterostomi, 4 hastaya üreteroneosistostomi, bir hastaya native üreteropyelostomi uygulandı. Native üreteropyelostomi uygulanan hastada idrar kaçağı görüldü.

Sonuç

Çalışmamızda renal transplantasyon sonrası ürolojik komplikasyonlar en sık kadavra transplantasyonlar sonrası görüldü. Üreter stenozu en sık görülen komplikasyondur. Üriner sistem enfeksiyonları üreter

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Phone: +90 506 484 58 03 E-mail: drerdaluyisal@hotmail.com Received: 17.06.2015 Accepted: 26.06.2015

ABSTRACT

stenosis was the most commonly encountered complication. Urinary tract infection levels were statistically high in patients with ureteral complications. Successful outcomes were achieved in all surgical methods. Ureteroneocystostomy and native ureteropyelostomy may be preferred for treating ureteral complications in suitable patients. Choice of treatment should be determined according to the patient and cause. Large scale studies are required in order to identify which treatment is more favorable.

Key Words

Ureteral complications, renal transplantations, surgical treatment

ÖZET

komplikasyonu gelişen grupta anlamlı olarak yüksek bulundu. Uygulanan tüm cerrahi yöntemlerde başarı elde edildi. Ancak native üreteropyelostomi uygulanan bir hastada ikinci bir girişimi gerektirmeyen geçici idrar kaçağı görüldü. Hangi yöntemin daha üstün olduğunu değerlendirmek için geniş serili çalışmalara ihtiyaç duyulmaktadır. Üreteroneocystostomi ve native üreteropyelostomi uygun hastalarda başarıyla uygulanabilir. Tedavi seçimi hasta ve nedene bağlı olarak belirlenmelidir.

Anahtar Kelimeler

Üreteral komplikasyonlar, renal transplantasyon, cerrahi tedavi

Introduction

Ureteral stenosis and necrosis are the most common urological complications following renal transplantations, with a rate of 10-25% (1,2). The most encountered complication seen in the long-term is stenosis (3). Ureteral complications may cause graft loss or even morbidity if not promptly treated (4,5). It has been reported that ureteral revisions which are performed in the first year of transplantation have no impact on the graft functions in long-term follow-up (6).

Surgery, preventative treatments and laser endoureteromy may be performed in case of a ureteral stenosis. Surgery is the first choice of treatment in ureteral necrosis. Ureteroneocystostomy and native ureteropyelostomy are the most frequently used methods in urinary tract reconstruction.

The aim of this study was to review the reasons for surgical treatment of ureteral complications following renal transplantations that were performed in our center.

Materials and Methods

One hundred sixty renal transplantations were performed from both cadaveric and live donors at our transplantation center between 2011 and 2014. Demographic features, complication types, surgical methods used, and the treatment results in 10 patients who required surgical intervention due to ureteral complications were recorded. Data from these patients were obtained through surgical operation reports and file scans.

Surgical Techniques

Donor Nephrectomy

All living donor nephrectomies were carried out through the open donor method. Cadaveric donor nephrectomies were carried out with classic open harvesting with a liver transplantation team present. All donor nephrectomies and renal transplantations were performed by two transplantation specialists.

Open Living Donor Nephrectomy

Extraperitoneal open donor nephrectomy was performed with lumbar incision with the patient in a flank position. The ureter was dissected and released until it intercrossed with the internal iliac artery. It was then tied with a surgical polyglactin suture and cut. The renal artery was tied with a single silk strand and cut. The renal vein was cut with the help of a Satinsky clamp and the stump was sutured with 5/0

polypropylene. Donor nephrectomy was completed. The kidney was removed from the abdomen and prepared on the back table.

Ureteroneocystostomy

Ureteroneocystostomy was the most commonly used method in patients with ureteral necrosis and stenosis. Ureteroneocystostomies were performed extravesically. While the urinary bladder was full, a prolapse was created at the mucosa by inserting a detrusor muscle at the upper lateral part of the ureteral hiatus with an incision of 2-3 cm. Afterwards, the urinary bladder was punctured with a 1 cm cut and an ureteral-vesical anastomosis was created using 5/0 absorbable poly (p-dioxanone) suture materials. A double-J stent was placed in all patients. The detrusor was closed by creating a tunnel.

Native Ureteropyelostomy

Native ureteropyelostomy was applied in one patient with ureteral stenosis and in two patients with ureteral necrosis. Anastomosis was performed between native ureter and graft renal pelvis by 5/0 absorbable poly (p-dioxanone) suture material. Double-J catheters were placed in all patients.

Ureteroureterostomy

Due to stenosis, an end-to-end ureteroureterostomy was performed in one patient using 5/0 absorbable poly (p-dioxanone) suture materials through double-J.

The urine volume in patients, who received surgical intervention due to ureteral complications, was monitored through a Foley catheter and a vacuumed drainage system. For the first two days following the procedure, biochemistry analyses and graft functions were observed and graft vein movements were monitored through the use of Doppler imaging. Foley catheters were routinely checked once every 5 to 7 days while double-J catheters were checked on the 45th day.

Immunosuppressant Regimen

Triple immunosuppression protocol was applied to renal transplantation recipients. Anti-thymocyte globulin (ATG) (1.5 mg/kg) induction therapy was started and continued for 5 to 7 days in all cadaver graft recipients. Tacrolimus (TAC) or cyclosporine, mycophenolate mofetil (MMF) and prednisolone were administered to maintain immunosuppression.

Triple immunosuppression protocol and basiliximab were started in living donor recipients. They also received MMF and prednisolone with TAC or cyclosporine.

The initial dose of orally administered TAC was 0.15-0.30 mg/kg daily. The medicine was administered twice a day either 1 hour before meals or 2 hours after meals. As target through blood concentration, (this phrase is unclear) 12-15 ng/mL for the first month, 8-12 ng/mL for the second month, 6-10 ng/mL for the third month and 5-10 ng/mL for the duration of the treatment.

Cyclosporine was given to four diabetic patients due to uncontrolled hyperglycemia. It was switched to cyclosporine A in 3 patients under TAC treatment due to hyperglycemia and in 2 patients due to TAC nephrotoxicity. The initial dose of cyclosporine A was 10-14 mg/kg/day for the first two weeks and 5-10 and 10-14 mg/kg/day were given as maintenance dosage. Drug dosages were adjusted according to cyclosporine A blood levels (C2) in the second hour of the drug intake. Cyclosporine target blood levels were maintained at C2>1500 ng/mL for 0-3 months, C2=1200-1400 ng/mL for 3th month; 800-1000 ng/mL for 3-12 months, and at around 800 ng/mL after 12 months.

Mycophenolate mofetil was started within the first 72 hours after renal transplantation. Mycophenolate mofetil was given at two different daily doses at a total dose of 2 g/day.

Basiliximab was introduced as 20 mg in two doses as induction therapy in living renal transplantations. The first dose was given 2 hours before renal transplantation and the second dose was applied 4 days after renal transplantation. Basiliximab was administered intravenously in 50 mL of normal saline within 20-30 minutes.

Methyl prednisolone was started at the dose of 15 mg/kg intravenously and reduced gradually. Oral prednisolone was administered orally at the dose of 1 mg/kg on the fourth day. The patients were discharged on prednisolone 20 mg/day. Five mg/day prednisolone was administered as a maintenance dosage.

The immunosuppressive agent of m-TOR inhibitory group was not used in any patient.

The mean follow-up period was 26.4±14.4 (12-40) months. All graft functions are still stable and show no signs and symptoms of deterioration.

Statistics

The data obtained via analysis of the patient files were analyzed using SPSS 16.0 for Windows statistical software. The data was presented as mean ± standard deviation (SD). A p value of less than 0.05 was considered statistically significant.

Results

Six patients (3.75%) had ureteral stenosis, and 4 patients (2.5%) had ureteral necrosis. Three of the transplantations were made from living donors (2 female and 1 male), and 7 were from cadavers (1 female and 6 male). All patients underwent double-J stenting; the bladder capacities were between 100 and 400 cc. The duration between transplantation and the manifestation of ureteral stenosis was approximately 2 months. Extravasation due to necrosis was found in 4 patients, following the second week of operation. Two patients underwent native ureteropyelostomy and two others underwent ureteroneocystostomy for ureteral necrosis. One patient underwent ureteroureterostomy, four had ureteroneocystostomy, and one had native ureteropyelostomy for stenosis. One patient, who underwent native ureteropelvic anastomosis, had a postoperative urine leak and he was followed conservatively by drainage. Ureteral complications and treatment methods in our patients are summarized in Table 1. The comparison of the characteristics between the groups of patients, who had ureteral complication and those who did not, is given in Table 2. Characteristics of patients with ureteral complication and their donors are given in Table 3. Acute rejection attack was seen once in 2 patients with ureteral complications. With proper treatment, the rejection was decreased. Graft loss was not observed in any patients in this group.

Discussion

Ureteral complications are significant causes of hospitalization within the first year following renal transplantation. Stenosis, necrosis and urine leakage may cause liquid-electrolyte imbalance, graft loss and acute renal failure. These complications have been encountered less in recent years due to the technical progression in surgical techniques. Failure of ureter vascularisation and insufficient blood supply are assumed to be responsible for these urological complications. Excessive dissections nearby renal artery and vein may cause vascular damage and subsequent ureteral necrosis (7). It has been reported that there was no association between ureteral length and complications (8). Complication rates in ureteroureterostomy has been found to be lower than that in ureteroneocystostomy (9).

The most significant risk factors for urological complications following renal transplantation have been described as follows; old

Table 1. Characteristics of the group without urological complications and the group with urological complications

Age	Sex	Ureteral complications	Treatment	Result	Living/Cadaver
38	F	Stenosis	NUP	No complications	Living
40	F	Stenosis	UNC	No complications	Living
26	F	Stenosis	UNC	No complications	Cadaver
43	F	Stenosis	UNC	No complications	Cadaver
45	M	Stenosis	UNC	No complications	Cadaver
42	M	Necrosis	UU	No complications	Cadaver
42	M	Necrosis	UNC	No complications	Cadaver
34	M	Necrosis	UNC	No complications	Living
22	F	Necrosis	NUP	No complications	Cadaver
55	F	Necrosis	NUP	Urine leak	Cadaver

NUP: Native ureteropyelostomy, UNC: Ureteroneocystostomy, UU: Ureteroureterostomy, F: Female, M: Male

recipients, old renal donors, male gender, recurrent transplantation, delayed renal function and lack of ureteral stenting (5,10,11). There were delayed graft functions in four of our patients who had ureteral complications following cadaver renal transplantations. The mean age of the recipients was 38.7 years and ureteral stents were placed in all of our patients. Therefore, these findings were not consistent with the previous reports in the literature supporting the idea that complications were caused by other factors. For example, in a study, it was discovered that ureteral stenosis was related to multiple renal arteries, delayed graft function and advanced age (12). At first, elderly patients seemed to have a higher risk for ureteral complications. However, our study showed that there was no statistically significant difference in age between the groups of patients with and without ureteral complications. Most of the patients were middle-aged. The average age of the donors was 36.1 years.

Ureteral necrosis and urinary leakage are the most common early urological complications after renal transplantation. Persistent ureterovesical stricture is the most frequent delayed complication. Stenosis usually appears in the first two months. Although surgical techniques may take part in the etiology as well as ischemia, a recent study stated that surgical methods have less influence in the development of ureteral stenosis (13).

We encountered ureteral strictures in approximately the second month and leakage in the second week in posttransplant patients. There are numerous treatment options for ureteral strictures, including surgical reconstruction and endoscopic approach. With the advances in the interventional radiology, the necessity for surgery has been reduced in recent years, but surgical revision is still needed in many patients (2).

Yag laser endoureterotomy can be used safely and successfully in patients with posttransplant ureterovesical strictures (3). There are some reports indicating that native ureteropyelostomy can effectively be used in posttransplant strictures (14,15). We successfully performed ureteroureterostomy for urethral stenosis.

The second most common complication after stricture is ureteral necrosis along with subsequent urinary leakage. These complications require reconstruction and revision. The most preferred methods are native ureteropyelostomy and ureteroneocystostomy. We performed ureteroneocystostomy in two patients with ureter necrosis which were close to ureterovesical anastomosis. In two other patients, we chose ureteropyelostomy because of widespread ureteral necrosis.

It has been shown that there are no significant differences in long-term follow-up results between reconstruction methods performed for posttransplant urological complications (16). A study revealed that pyeloureterostomy could be a favorable method compared to ureterocystostomy in ureteral complications (17). In another study, the researchers obtained positive results by performing pyeloureterostomy after ureterovesical complications (18). Reconstruction of ureteral complications due to necrosis with pyeloureterostomy is known to be a simple and safe method (19).

Ureteral complications, especially seen after cadaveric renal transplantation, are at a rate of 2-20% on average (20,21,22). However, there are studies showing that urological complications are seen in a small percentage of patients i.e. 2.8-4.9% (23,24).

In our study, the total urological complication rate was found to be 6.25%. Cadaveric renal transplantations showed higher urological complication rates than did living renal transplantations. Our total

Table 2. Characteristics of the group without urological complications and the group with urological complications

	No urological complication (n=150)	With urological complication (n=10)	p value
Cold ischemic time (hours)	18±6.2	17.4±4	>0.05*
Recipients age (years)	38.7±8.4	38.3±7.9	>0.05
Hemodialysis time (year)	7±4.4	7.8±4.6	>0.05
Acute rejection (graft loss)	3	No	
Urinary tract infection (%)	16.8%	40%	<0.001

Data was presented as mean ± Standart deviation (SD), Cadaveric renal transplantation*

Table 3. Characteristics of recipients with ureteral complications and their donors

Recipient gender	Recipient age	Living/Cadaveric	Bladder capacity (ml)	Hemodialysis Time (year)	Donor age	Donor gender
F	38	Living	100	3	44	F
F	40	Living	200	2	36	M
F	26	Cadaver	100	6	26	M
F	43	Cadaver	200	14	39	M
M	45	Cadaver	100	12	31	M
M	42	Cadaver	200	9	40	F
M	42	Cadaver	100	10	41	M
M	34	Living	100	6	33	M
F	22	Cadaver	200	2	26	M
F	55	Cadaver	100	14	45	M

F: Female, M: Male

urological complication rate was consistent with the literature data, but it was found to be a slightly higher than the average. Failure of ureteral vascularization and insufficient blood supply are assumed to be responsible for these urological complications. Excessive dissections nearby the renal artery and vein may cause vascular damage and subsequent ureteral necrosis because donors of recipients with urological complication development are advanced in age. This may be the reason for high complication rates. Keeping cold ischemia time short, not excessively dissecting especially the renal pelvis and periureteral tissue, paying attention to anastomosis technique and controlling rejections by applying suitable immunosuppressive therapy are of a great importance in reduction of urological complications (24). Placing a double-J stent also helps reduce urological complications (25).

We routinely used ureteral double-J stents in cadaveric renal transplantations. It is still a widely controversial issue whether or a not double-J stent is required in renal transplantations. We assume that the use of a double-J stent can reduce complications in cadaveric renal transplantations, kidneys with long cold ischemia times, cases of abnormal bladder, such as neurogenic, small, ureteral injury, and cases of comorbidity in the receiver.

In a study, it was stated that elongated cold ischemia duration is a high risk factor for ureteral complications in patients with diabetes mellitus (13). Another study stated that shortening the cold ischemia duration is extremely important for decreasing ureteral complications (24). In our study, no differences between the cold ischemia durations in patients with and without ureteral complications were found. Besides, no patients with ureteral complication had diabetes mellitus. These findings led us to believe that the patients in this study experienced complications for other reasons.

In our study, we have concluded that urinary tract infections were significantly common in patients with ureteral complication compared to patients without ureteral complication. Urinary tract infections may trigger an ureteral complication and ureteral complications can be results of these infections. In a study, it was concluded that urinary tract infection levels in patients with extravesical ureteroneocystostomy were high (26). When urinary infections are accompanied by urological complications, the risk of early graft loss may increase (27).

Conclusion

In our study, urological complications following renal transplantation were mostly seen after cadaveric renal transplantations. Ureteral stenosis was the most commonly encountered complication. Urinary tract infection levels were significantly high in patients with ureteral complications. Successful outcomes were achieved in all surgical methods. Ureteroneocystostomy and native ureteropyelostomy may be preferred for treating ureteral complications in suitable patients. Choice of treatment should be determined according to the patient and the cause. Large-scale studies are required in order to identify which treatment is more favorable.

Ethics Committee Approval: Ethics committee approval was not obtained due to the study was disagned as retrospectively, **Informed Consent:** Consent form was filled out by all participants., **Concept:**

Erdal Uysal, Mehmet Fatih Yüzbaşıoğlu, **Design:** Erdal Uysal, Mehmet Fatih Yüzbaşıoğlu, Mehmet Dokur, Mehmet Ali İkidağ, **Data Collection or Processing:** Erdal Uysal, Mehmet Dokur, Mehmet Ali İkidağ, **Analysis or Interpretation:** Erdal Uysal, Mehmet Fatih Yüzbaşıoğlu, Mehmet Dokur, Mehmet Ali İkidağ, **Literature Search:** Erdal Uysal, Mehmet Dokur, **Writing:** Erdal Uysal, Mehmet Fatih Yüzbaşıoğlu, **Peer-review:** Externally peer-reviewed, **Conflict of Interest:** No conflict of interest was declared by the authors., **Financial Disclosure:** The authors declared that this study has received no financial support.

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