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Management of Urological Complications After Renal Transplantation: Our Experience and Technical Alternatives: Retrospective Clinical Research

Böbrek Nakli Sonrası Ürolojik Komplikasyonların Yönetimi: Deneyimlerimiz ve Teknik Alternatifler: Retrospektif Klinik Araştırma

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ABSTRACT Objective: Renal transplantation is the primary treatment method for end-stage kidney disease. Many reasons such as surgical reasons and infection may cause urological complications after transplantation. Management of renal transplantation urinary complications requires respectable surgical experience. In this study, we aimed to present the management of patients who require surgical reconstruction after renal transplantation at our center. **Material and Methods:** The data of 16 patients who underwent reconstructive surgery after transplantation were reviewed retrospectively. The patients' demographic data were evaluated. Which reconstructive method was applied to the patients, timing of surgical correction after transplantation, pre and post-surgical glomerular filtration rate (GFR) were evaluated. **Result:** Them mean age of the patients was 35.6 years. The mean time from transplantation to reconstructive surgery was 312 days. The average postoperative hospitalization time was 11.2 days. The earliest complication was total ureteral necrosis seen on the 21st postoperative day and the latest complication was vesicoureteral reflux (VUR) in our series. In patients who developed VUR, VUR was seen more than 6 months after the operation. Nephrostomy was placed in 75% of patients. Ureteroneocystostomy was applied to 3 patients (18.7%), one was applied with Boari flap, and two were applied with modified Lich-Gregoir technique. Pre-operative GFR inter-quantile range (IQR): 35.6-70.3, postoperative first-month GFR IQR: 47.4-69.5, third postoperative months GFR IQR: 50-74.5 were detected. A significant difference was observed between preoperative GFR and postoperative third month GFR (p=0.007). **Conclusion:** Reconstructive surgery following kidney transplantation is a challenging but effective method. Even if it is performed in different centers, complications after transplantation are likely to occur.

Keywords: Renal transplantation; complications; reoperation

ÖZET Amaç: Böbrek transplantasyonu, son dönem böbrek yetersizliğinde esas tedavi yöntemidir. Cerrahi teknik, enfeksiyon gibi birçok sebep transplantasyon sonrası ürolojik komplikasyon gelişmesine sebep olabilir. Transplantasyon sonrası ürolojik komplikasyonların yönetimi iyi bir cerrahi tecrübe gerektirir. Bu çalışmada, merkezimizde böbrek transplantasyonu sonrası cerrahi rekonstrüksiyonu yapılan hastaların yönetimini sunmayı amaçladık. **Gereç ve Yöntemler:** Transplantasyon sonrası rekonstrüktif cerrahi uygulanan 16 hastanın verileri geriye dönük olarak incelendi. Hastaların demografik verileri değerlendirildi. Hastalara hangi rekonstrüktif yöntemin uygulandığı, transplantasyon sonrası cerrahi düzeltmenin zamanlaması ve cerrahi öncesi ve sonrası glomerüler filtrasyon hızı [glomerular filtration rate (GFR)] değerlendirildi. **Bulgular:** Hastaların ortalama yaşı 35,6'dır. Transplantasyondan rekonstrüktif cerrahiye kadar geçen ortalama süre 312 gündü. Operasyon sonrası ortalama yatış süresi 11,2 gün idi. Bizim serimizde en erken komplikasyon postoperatif 21. günde görülen total üreteral nekroz, en geç komplikasyon vezikoüreteral reflü (VUR) idi. VUR gelişen hastalarda VUR operasyondan 6 aydan fazla süre geçtikten sonra görülmüştür. Hastaların %75'ine nefrostomi takıldı. Bir hastaya Boari flap yöntemi, 2 hastaya modifiye Lich-Gregoir tekniği ile toplamda 3 (%18,7) hastaya üreteroneosistostomi yapıldı. Ameliyat öncesi GFR çeyrekler açıklığı [inter-quantile range (IQR)]: 35,6-70,3 ameliyat sonrası 1. ay GFR IQR: 47,4-69,5, ameliyat sonrası 3. ay GFR IQR: 50-74,5 olarak belirlendi. Ameliyat öncesi GFR ile ameliyat sonrası 3. ay GFR arasında anlamlı bir fark gözlendi (p=0,007). **Sonuç:** Böbrek nakli sonrası rekonstrüktif cerrahi zorlu ama etkili bir yöntemdir. Farklı merkezlerde yapılsa bile nakil sonrası komplikasyonların oluşması muhtemeldir.

Anahtar Kelimeler: Böbrek transplantasyonu; komplikasyonlar; reoperasyon

Renal transplantation is the primary treatment method for end-stage kidney disease. Moreover, its cost and comorbidities are pretty low compared with peritoneal dialysis or hemodialysis.[1] The most common urinary complication of kidney transplantation is ureteral complications, and it has been reported in 2.6-15%.[2-5] Immunosuppression is one of the lousy mortality reasons for kidney transplantation. It can

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cause ureteral complications as well as infectious complications. However, the reason for ureteral complications is not only infection. Moreover; surgical technique, prolonged cold ischemia time, >65 age, two or more renal arteries, and pre-operative chronic diseases can occur.

The most common underlying causes of ureteral complications are obstructive reasons (such as urolithiasis, lymphoceles, or hematoma pressure), vesicoureteral reflux (VUR), anastomosis leakage, BK polyomavirus infection, and cytomegalovirus (CMV) infection.[6] Nowadays, ureteral stent performing is a routine procedure for kidney transplantation. Historically, non-stent using techniques of the anastomosis can cause ureteral complications.

Although VUR is common after kidney transplantation, pyelonephritis associated with VUR is relatively rare in current studies (1.4%-2.8%).[7,8] Ureteral strictures are often treated with endoscopic methods, but these techniques have a high probability of recurrence. For this reason, reconstructive surgeries are the most definitive treatment methods. These surgeries vary according to the location and cause of the stenosis.[9,10]

In this retrospective series, we aimed to evaluate the patients who applied to our clinic with early and late ureteral complications after kidney transplantation. We planned to present the reconstruction technique and patient management, especially based on the patient's history.

MATERIAL AND METHODS

ETHICS APPROVAL

This study was approved by the İstanbul Prof. Dr. Cemil Taşcıoğlu City Hospital Clinical Research Ethics Committee (date: November 08, 2021, no: 391).

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study.

The work was performed at Urology Department of Şişli Hamidiye Etfal Training and Research Hospital İstanbul, Türkiye.

PATIENTS SELECTION

Patients who were detected in our clinic due to ureteral complications after kidney transplantation between June 2016 and December 2021 were retrospectively scanned. Anamnesis, kidney transplant dates, method of transplantation (living donor/cadaveric), the onset of symptoms, symptoms at admission, during postoperative first-month glomerular filtration rate (GFR), during postoperative third months GFR, management of complications data were recorded and evaluated. Definitive repair data were obtained from the electronic data system.

Transplantation was not performed by a single surgeon, as most cases were obtained from different centers. All transplantations were performed using the open technique.

STATISTICAL ANALYSIS

The SPSS program (IBM; USACorp, Armonk, NY) was used for statistical analysis. Descriptive analysis was performed for quantitative values. The normal distribution of qualitative data was evaluated with the One-Sample Kolmogorov-Smirnov test. The Friedman test was applied to more than two data that did not show the normal distribution in the related groups. If the p value was <0.05, it was considered significant. Wilcoxon test with Bonferroni correction was used in the evaluation between groups. If the p value was <0.017, it was considered significant.

RESULTS

Complications requiring surgical intervention were detected in 16 patients after transplantation. It was determined that only one of the complications was not ureteral, and this was recurrent native kidney infection which should be performed nephrectomy. Transplantation was performed in 3 of the patients followed in our center. The other 13 patients had been transplanted in other centers. VUR was detected in 3 of the ureteral complications, while ureteral necrosis and ureteral stenosis were detected in 12 patients. The mean age of the patients who underwent reconstruc-

tive surgery was 35.6. Only 2 of the patients were children. While seven patients were female, nine patients were male. The mean time from transplantation to reconstructive surgery was 312 days. 5 of 12 patients were transplanted from a cadaveric and eight from a living donor. All patients had a JJ catheter inserted at the time of transplantation. The average postoperative hospitalization time was 11.2 days. Demographic data are summarized in Table 1.

The earliest complication was total ureteral necrosis seen on the 21st postoperative day, and anastomosis (pyeloureterostomy) was performed on the native ureter. However, the latest complication was VUR observed on postoperative days 1329 and was treated with subureteric injection. Nephrostomy was placed in 75% of patients before reconstructive surgery. While VUR was observed in three of the patients who did not undergo nephrostomy placement, the only patient who was not applied was the patient who underwent native kidney nephrectomy. Ureterovesical junction (UVJ) stenosis was observed in 3 patients (18.7%), ureteropelvic junction (UPJ) stenosis was observed in 2 patients (12.5%), while both proximal ureteral stenosis and UVJ stenosis were observed in 1 patient (6.2%).

Proximal ureteral necrosis was observed in 1 of the patients with UPJ stenosis. Total ureteral necrosis in 2 patients (12.5%), proximal ureteral necrosis in 1 patient (6.2%), distal ureteral necrosis in 1 patient (6.2%) were observed. While anastomosis was performed on the right native ureter in 8 patients (50%), three were pyeloureterostomy, and five were ureteroureterostomy. Ureteroureterostomy was applied to the transplanted ureter in 1 patient (6.2%). While ureteroneocystostomy was applied to 3 patients (18.7%), one was applied with Boari flap, and two were applied with modified Lich-Gregoir technique. Right native kidney nephrectomy, right ureteroureterostomy, and ureteroneocystostomy were performed together in a patient with proximal and distal ureteral stenosis. Native kidney nephrectomy was required in this patient whose infection did not improve despite reconstructive surgery. Reconstructive treatment techniques are summarized in Table 2.

TABLE 1: Demographic data of the patients.

Parameters	Average
Age	35.6
Male/Female ratio	9/7
Rate of cadaveric transplantation	31.2%
Hospitalization time	11.2 days

TABLE 2: Patient diagnosis, surgical technique and operation timing.

Patient no	Diagnosis	Diagnosis	Surgical treatment	Days after transplantation
1	50	VUR	Subureteric injection	1329
2	52	UVJ stenosis	Ureteroneocystostomy with modified Lich-Gregoir technique	220
3	13	VUR	Subureteric injection	329
4	53	UVJ leakage+necrosis	Ureteroureterostomy on right native ureter	40
5	39	Mid-ureteral necrosis	Ureteroureterostomy on right native ureter	81
6	54	UVJ stenosis	Ureteroneocystostomy with modified Lich-Gregoir technique	280
7	37	UPJ stenosis	Pyeloureterostomy on the right native ureter	198
8	43	UPJ stenosis	Ureteroureterostomy on the right native ureter	108
9	35	Distal ureteral necrosis	Ureteroureterostomy on the right native ureter	278
10	47	Total ureteral necrosis	Pyeloureterostomy on the right native ureter	246
11	23	UVJ stenosis	Ureteoneocystostomy Boari flep	439
12	25	Proksimal+distal ureteral stenosis+ Recurrent urinary infection	Right native nephrectomy+ Right native ureteroureterostomy+ ureteoneocystostomy	433
13	52	Total ureteral necrosis	Pyeloureterostomy on the right native ureter	21
14	22	Proksimal ureteral necrosis	Ureteroureterostomy on transplanted ureter	140
15	11	Recurrent urinary infection	Nephrectomy for native kidney	197
16	14	VUR	Subureteric injection	664

VUR: Vesicoureteral reflux; UVJ: Ureterovesical junction; UPJ: Ureteropelvic junction.

Pre-operative GFR inter-quantile range (IQR): 35.6-70.3, postoperative first-month GFR IQR: 47.4-69.5, third postoperative months GFR IQR: 50-74.5 were detected (p=0.007). In the evaluation between the groups, only a significant difference was observed between the pre-operative, third-month postoperative GFR results (p=0.007).

DISCUSSION

Even in high-volume centers with good surgical techniques, surgical reconstruction may be required after transplantation.[11,12] Management of urological complications after transplantation is important for prolonging graft life and reducing mortality. For this reason, reconstructive surgeries to be applied offer a permanent solution. Furthermore, in addition to this, an experienced surgical team that can manage ureteral complications will also significantly reduce mortality and morbidity. Although JJ catheterization has been shown to reduce ureteral complications, it is not a definitive solution.[13] Infectious causes, transplantation technique, and post-transplantation follow-up are essential in preventing urological complications.

VUR is frequently observed after transplantation. The sub-ureteric injection has a high success rate in transplanted ureteric reflux as well as in primary VUR cases.[14,15] In our series, complete success was achieved with sub-ureteric injection in all patients diagnosed with post-transplant VUR. Also, all of the VURs were seen after six months post-transplantation.

Post-transplantation urine leaks and ureteric obstruction are benign conditions that can progress with graft loss. Percutaneous nephrostomy was placed as the first treatment method for all complications with ureteral obstruction and ureteral necrosis in our series. In our 2 cases with UVJ stenosis, re-anastomosis was performed with the modified Lich-Gregoir technique. In a case with necrosis in the distal ureter, anastomosis was applied to the native ureter. Boari flap was also performed on a patient with distal ureteral stenosis. In distal ureteral strictures, fibrotic areas can cause tension of the anastomosis and ureter. This situation will significantly reduce the success rate of reconstructive surgery. Boari flap is one of the technique that will significantly reduce this failure. Berli et al. also drew attention to this situation in their study presenting complication management.[16]

Two of our cases with total ureteral necrosis were transplanted at an external center and were transferred to us. One was diagnosed on the 21st postoperative day, and the other was diagnosed on the 246th postoperative day.

In UPJ stenosis, the location of the stenosis, the length of the stenosis, and the presence of accompanying necrosis are the factors affecting the treatment option. While pyeloureterostomy was performed to the right native ureter in one of our two cases with UPJ stenosis, ureteroureterostomy was performed to the right native ureter in our other case.

Two of our cases with total ureteral necrosis were transplanted at an external center and were transferred to us. One was diagnosed on the 21st postoperative day, and the other was diagnosed on the 246th postoperative day. It was revealed that the total necrosis observed on the 21st day was due to the failure to preserve the ureteral vascularization during transplantation. However, late total ureteral necrosis was found to be due to CMV. As in our case, Karam et al. reported that CMV infection is frequently observed in patients with ureteral necrosis.[17]

In our cases, pre-operative nephrostomy was essential in preserving the renal reserve and preventing infections. Moreover, it also provides convenience for leak control after reconstructive surgeries. JJ stent was applied routinely after all reconstructive surgeries, and nephrostography was taken. After confirming that there was no leakage after nephrostography, the nephrostomy was removed, and the JJ stent was removed 4-6 weeks later. In this way, anastomosis safety was ensured in a controlled manner.

According to the GFR evaluation after reconstruction surgery, there was no significant improvement in GFR in the postoperative first month, but a significant improvement was observed after the third postoperative month. This suggests that reconstructive surgeries on GFR will be beneficial in the long

term. However, multicentric studies with more extensive series are needed.

The major limitation of this study is that it did not evaluate the success of transplantations performed at only one center. However, the fact that it includes the complications of transplantations performed in many centers is a guide for studies that will show results with multi-center extensive participation. The major limitation of this study is that it did not evaluate the success of transplantations performed at only one center. However, the fact that it includes the complications of transplantations performed in many centers is a guide for studies that will show results with multi-center extensive participation. The most important aspect of this study is that it shows that the ureteral complications of kidney transplantations performed by different surgeons can be managed with an experienced team.

CONCLUSION

Reconstructive surgery following kidney transplantation is a challenging but effective method. Even if it is performed in different centers, complications after transplantation are likely to occur. The surgeon performing the transplantation surgery should have experience in ureteral complication management. As in our study, experience in managing ureteral complications will prevent graft loss and mortality, although the transplanting surgeon is different. Moreover, this prevention may improve GFR in the long term.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Mesut Demir;* ***Design:*** *Mesut Demir;* ***Control/Supervision:*** *Mesut Demir;* ***Data Collection and/or Processing:*** *Şeyma Demirci;* ***Analysis and/or Interpretation:*** *İbrahim Halil Baloğlu;* ***Literature Review:*** *Şeyma Demirci;* ***Writing the Article:*** *İbrahim Halil Baloğlu;* ***Critical Review:*** *İbrahim Halil Baloğlu.*

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