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THE EFFECT OF INTRAOPERATIVE URETERAL CATHETER USAGE ON BACTERIURIA AND COMPLICATIONS IN DECEASED DONOR RENAL TRANSPLANTATION*

KADAVERİK BÖBREK NAKLİNDE İNTRAOPERATİF ÜRETERAL KATETER KULLANIMININ BAKTERİÜRİ VE KOMPLİKASYON OLUŞUMUNA ETKİSİ

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ABSTRACT

Objective: The use of ureteral catheters in renal transplantation is controversial. We aimed to investigate the effect of intraoperative catheter use on bacteriuria and urological complications in deceased donor renal transplantation.

Material and Method: Study design is cross sectional study. A total of 150 patients who underwent deceased donor renal transplantation in the Istanbul University Istanbul Faculty of Medicine Transplantation Unit were included in the study. Ureteral catheters were used in 72 patients but not in the remaining 78. The two patient groups were compared in terms of the incidence of early postoperative urological complications and bacteriuria in the first month after transplantation.

Result: Ureteral catheter usage significantly reduced the frequency of early postoperative urological complications (p=0.004). The frequency of bacteriuria in the first month after transplantation was significantly lower in patients using ureteral catheters (p<0.001). In patients with ureteral catheters, the duration of anti-thymocyte globulin administration (p=0.003) and Foley catheter usage (p<0.001) was found to be significantly shorter than in the group without ureteral catheters.

Conclusion: The routine use of ureteral catheters results in fewer urological complications in patients with deceased donor renal transplantation. Catheter use does not increase, and even lowers, the risk of early bacteriuria. The significant reduction in early

ÖZET

Amaç: Kadaverik böbrek naklinde, intraoperatif üreteral kateter kullanımının bakteriüri ve ürolojik komplikasyonlara olan etkisini incelemeyi amaçladık.

Gereç ve Yöntem: Bu kesitsel çalışmada İstanbul Üniversitesi, İstanbul Tıp Fakültesi Transplantasyon Ünitesi'nde kadavradan böbrek nakli yapılan 150 hasta çalışmaya alındı. Üreteral kateter kullanılmayan 78 hasta ve üreteral kateter kullanılan 72 hasta olduğu tespit edildi. Bu iki hasta grubu postoperatif erken dönem ürolojik komplikasyonlar, nakil sonrası 1. ayda görülen bakteriüri varlığı açısından karşılaştırıldı.

Bulgular: Üreteral kateter kullanılan olgularda, postoperatif erken dönem ürolojik komplikasyon sıklığı anlamlı düzeyde azalmıştır (p=0,004). İlginç bir şekilde üreteral kateter kullanılan hastalarda, nakil sonrası birinci ayda görülen bakteriüri sıklığı da anlamlı düzeyde azalmıştır (p<0,001). Üreteral kateter kullanılan hastalarda, anti-timosit globulin kullanım süresi (p=0,003) ve foley kateter kullanım süresi (p<0,001) üreteral kateter kullanılmayan gruba göre anlamlı düzeyde kısa saptanmıştır.

Sonuç: Kadaverik böbrek nakli olgularında rutin üreteral kateter kullanımında ürolojik komplikasyonlar daha az görülmektedir. Kateter kullanılan grupta erken bakteriüri görülme riskinin artmadığı hatta azalmış olduğu saptanmıştır. Bu anlamlı düzeyde azalmanın, üreteral kateterli hasta grubunda anti-timosit glo-

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bacteriuria in patients with ureteral catheters is associated with significantly shorter durations of anti-thymocyte globulin and Foley catheter usage. Therefore, the routine use of intraoperative ureteral catheters is recommended in deceased donor renal transplantation.

Keywords: Bacteriuria, complications, deceased donor renal transplantation, ureteral catheter

bulin kullanım süresi ve foley kateter kullanım süresinin anlamlı düzeyde kısa olması ile ilşkili olduğu düşünülmüştür. Bu nedenle kadaverik böbrek naklinde rutin intraoperatif üreteral kateter kullanımı önerilmektedir.

Anahtar Kelimeler: Bakteriüri, komplikasyonlar, kadaverik böbrek nakli, üreteral kateter

INTRODUCTION

End-stage renal disease is an important health issue that requires resolution in both socioeconomic and medical terms. The gold standard in renal replacement therapy is renal transplantation. Renal transplantation can be performed from a deceased or living donor.

Urological complications such as urinary obstructions, urinary leakage, and urinomas may occur after renal transplantation. The frequency of these complications is 4-8% and resulting mortality is very rare (1,2). Major urological complications after renal transplantation are usually seen in the early period (first three months) after transplantation and are usually caused by vesicoureteral anastomosis (3). These complications may cause morbidity and graft loss in patients (4). Ureteral ischemia is thought to be mainly responsible for early ureteral complications in cases when there are no technical complications (5).

The use of ureteral catheters in renal transplantation, although its therapeutic benefit is controversial, is thought to be advantageous in facilitating the creation of a waterproof anastomosis between the ureter and bladder, and reducing anatomical folding (3,6). There are studies showing that the use of prophylactic intra-operative ureteral catheters positively affects the graft function by reducing urological complications in patients with deceased donor renal transplantation (7). There are reports suggesting that good vascularization and a non-tense anastomosis are effective in preventing both early and late ureteral complications. They recommend ureteral catheter usage only in difficult anastomoses or in situations where the vesicoureteral anastomotic blood supply may be compromised (8).

The most serious complication of catheter use is the possibility of an increase in the frequency and severity of UTIs. In one study, the use of ureteral catheters was associated with an increase in UTIs (9). On the other hand, there are studies arguing that the use of ureteral catheters is not associated with bacteriuria (10).

Other complications that may be caused by ureteral catheters include permanent hematuria, bladder discomfort, migration of the catheter, broken catheter, calcification of the catheter, and complications seen during removal of the catheter (7).

The aim of this study is to investigate the effect of ureteral catheter use in terms of early urinary complications, bacteriuria after renal transplantation in order to evaluate the decision to use ureteral catheters in renal transplantation due to controversial results.

MATERIAL and METHODS

A total of 151 patients who underwent deceased donor renal transplantation in the Istanbul University Istanbul Faculty of Medicine Transplantation Unit between 2006 and 2016 were retrospectively analyzed after approval of the Ethical Committee of Istanbul Faculty of Medicine was obtained (Date: 10.08.2018, No:13). Since most of the data of one of the patients were unavailable, this patient was excluded from the statistical analysis. The remaining 150 patients were included in the study.

Ureteral catheters were not used in patients with deceased donor renal transplantation in our clinic between 2006 and 2011, but have been routinely used since 2011, due to the change of the decision of the surgical team. Patients were divided into two groups depending on the use of ureteral catheters. Seventy-eight patients without ureteral catheter were defined as Group 1, and 72 patients with ureteral catheter were defined as Group 2.

All the clinical findings and laboratory results of the patients, both pre- and postoperative data, were obtained from our hospital's computer registry system, patient epicrisis, patient follow-up files, and pre-transplant patient preparation forms.

The collected data included the sex of the patients, the pre-transplant dialysis method (hemodialysis or peritoneal dialysis) used, the use of anti-thymocyte globulin (ATG) after transplantation, the length of ATG administration (days) and total dose (mg) used, the use of basiliximab, the type of calcineurin inhibitor used (cyclosporine or tacrolimus), the use of antibiotherapy, delayed graft function in the early period (whether dialysis was required in the first postoperative week), urological complications (urinary leak or urinary stenosis) in the early (first three months) postoperative period, the use of ureteral catheters, duration of Foley catheter use, whether bacteriuria was seen in the first month (early period) after transplantation, the time of bacteriuria detection (postoperative day), whether the urine culture was positive at the time

the positive urine sample was given (day), and the deceased donor kidney cold ischemia time.

Surgical procedures

All of the cadaver donor renal transplantations included in the study were performed by the same surgical team. All kidneys were transplanted extraperitoneally and heterotopically into the iliac fossa. Arterial anastomosis was performed between the renal artery and the external iliac artery; vein anastomosis was performed between renal vein and the external iliac vein as an end-to-side anastomosis. In the use of right kidneys, the renal vein was anastomosed after tubular lengthening by using the inferior vena cava. Ureteral anastomosis was performed in the form of ureteroneocystostomy using the Lich-Gregoir technique to create a submucosal anti-reflux mechanism.

The two groups were compared in terms of the immunosuppressive treatments they received after transplantation, the duration of Foley catheter usage, the rate of urological complications in the postoperative period, the rate of bacteriuria (positive urine culture), the time when bacteriuria started, the duration of deceased donor kidney cold ischemia, and postoperative delayed graft function.

Statistical analysis

Mean and standard deviation values, and minimum and maximum values were calculated for the descriptive statistics of continuous variables. Frequency distributions and ratios were calculated for the descriptive statistics of categorical variables.

The Number Cruncher Statistical System (NCSS) 2007 Statistical Software (Utah, USA) program was used for statistical analysis. While evaluating the data of the study, in addition to descriptive statistical methods (mean, standard deviation, median, frequency, ratio), the Shapiro Wilks test and box plot graphics were used to evaluate the suitability of variables to normal distribution.

Normally distributed variables were compared between the two groups using the t-test for independent groups. The Mann Whitney U test was used for non-normally distributed data. The chi-square test and Fisher's Exact test were used for the comparison of qualitative data. The results were evaluated at the 95% confidence interval, and $p<0.05$ was considered to be statistically significant.

RESULTS

Of the 150 patients included in the study, 55.3% (n=83) were female and, 44.7% (n=67) were male.

When the type of dialysis used before transplantation was examined, 80% of the patients (n=120) had hemodialysis, 12.7% (n=19) had peritoneal dialysis, and 7.3% (n=11) had hemodialysis and peritoneal dialysis at different times.

It was found that 98% of the patients (n=147) received ATG after the deceased donor renal transplantation. The duration of ATG use ranged from 2 to 23 days, with an average of 10.32±6.07 days, while the doses ranged from 50 to 3.236 mg with an average dose of 974.09±6,174.52 mg. Basiliximab was used in 38.7% (n=58) of the patients, while 146 patients received calcineurin inhibitors after transplantation. Of the latter 146 patients, tacrolimus was used in 42.5% (n=62) and cyclosporine in 57.5% (n=84).

Seventy-eight patients without ureteral catheters were defined as group 1, and 72 patients in whom ureteral catheters were used were defined as group 2. When the immunosuppressive treatment received by the patients after deceased donor renal transplantation was compared according to the patient group (use and non-use of ureteral catheters), no statistically significant difference was found between the two groups in terms of the rate of use or dose of ATG ($p>0.05$). The duration of ATG use was found to be significantly shorter in group 2 patients compared to group 1 ($p=0.003$) (Table 1).

Table 1: Immunosuppressive treatments received by patients according to use of ureteral catheters

		UC (-)	UC (+)	Test value	p-value
ATG usage	No	2 (2.6)	1 (1.4)	0.264	[c]**0.999**
	Yes	76 (97.4)	71 (98.6)		
Duration of ATG use (day)	Median (Q1-Q3)	9 (6-19)	7 (5-13)	-2.944	[b]**0.003****
ATG dose (mg)	Median (Q1-Q3)	780 (485-1460)	740 (500-1290)	-0.322	[b]**0.748**
Basiliximab	No	55 (70.5)	37 (51.4)	5.774	[a]**0.016***
	Yes	23 (29.5)	35 (48.6)		
Tacrolimus/Cyclosporine	Tacrolimus	1 (1.4)	61 (84.7)	103.819	[a]**<0.001****
	Cyclosporine	73 (98.6)	11 (15.3)		

[a]: Pearson chi-square test, [b]: Mann-Whitney U test, [c]: Fisher exact test, AGT: Anti-thymocyte globulin, Q1: First quartile, Q3: Third quartile, UC: Ureteral catheter, *: p<0.05, **: p<0.01

It was found that the rate of basiliximab use in group 2 was significantly higher than in group 1 patients (p=0.016), as was the use of tacrolimus/cyclosporine (p<0.001) (Table 1).

It was found that the rate of urological complications in the postoperative period between the groups was statistically significantly lower in group 2 patients compared to group 1 (p=0.004).

A statistically significant difference was found between the groups in terms of the Foley catheter removal time (p<0.001). The Foley catheter was removed in a shorter time in cases with ureteral catheters than in cases without ureteral catheters (Table 2).

It was observed that both groups received intravenous antibiotic prophylaxis for the first seven postoperative days. It was determined that the early period bacteriuria rate was statistically significantly lower in group 2 than in group 1 patients (p<0.001). There was no statistically significant difference between the groups in terms of the day of detection of bacteriuria (p>0.05) (Table 2).

It was determined that the duration of cold ischemia of the donor kidney groups was significantly shorter in the group 2 patients compared to group 1 (p=0.003) (Table 3).

No statistically significant difference was found between the groups in terms of delayed graft function in the early postoperative period (needing hemodialysis in the first week) (p>0.05) (Table 3).

Patients with postoperative urological complications, medical comorbidities (acute myocardial infarction, sepsis), early rejection, a second surgical intervention in the early period, early explantation, or postponed ureteral catheter intake due to positive urine culture were excluded from the statistical analyses. The catheter removal time ranged from 17 to 76 days with an average of 44.45±13.38 days.

DISCUSSION

Complications associated with ureteral-bladder anastomosis such as ureteral obstruction due to edema or stricture in the anastomosis and urinary leakage are usually seen in the first three months after renal transplantation and threaten graft survival (7).

In a Cochrane Systematic Review published in 2013 that recommends the use of prophylactic intraoperative ureteral catheters, the basis of this recommendation is the randomized controlled studies that demonstrate the use of intraoperative ureteral catheters in reducing the incidence of major urological complications. Urinary tract infections (UTI) were more common in the catheter group; however, the incidence was equivalent between the two groups if 480 mg of cotrimoxazole was used (11).

There are centers that routinely use catheters to prevent urological complications. However, the use of ureteral catheters may lead to an increase in other catheter-related complications, such as infection, persistent hematuria,

Table 2: Comparison of the two groups in terms of specified parameters

		Group 1	Group 2	Test value	p-value
Urological complication rate in the postoperative period	No	61 (78.2%)	68 (94.4%)	8.201	[a]**0.004****
	Yes	17 (21.8%)	4 (5.6%)		
The duration of Foley catheter usage (day)	Median (Q1-Q3)	10.5 (3-14.75)	8 (7-10)	-5.016	[b]**<0.001****
Bacteriuria in the early period	No	17 (21.8%)	36 (50%)	13.035	[a]**<0.001****
	Yes	61 (78.2%)	36 (50%)		
Bacteriuria detection time (day)	Median (Q1-Q3)	11 (8-15)	12 (9-16)	-0.419	[b]**0.675**

[a]: Pearson chi-square test, [b]: Mann-Whitney U test, [c]: Fisher exact test, Q1: First quartile, Q3: Third quartile, *: p<0.05, **: p<0.01

Table 3: Comparison of the two groups in terms of the duration of cold ischemia and postoperative delayed graft function in the early period

		UC (-)	UC (+)	Test value	p-value
The duration of cold ischemia	Mean±sd	17.81±5.18	15.52±3.92	3.011	[b]**0.003****
Postoperative delayed graft function in the early period	Yes	28 (35.9)	19 (26.4)	1.573	[a]**0.210**
	No	50 (64.1)	53 (73.6)		

[a]: Pearson chi-square test, [b]: Independent groups t test, [c]: Mann-Whitney U test, Q1: First quartile, Q3: Third quartile, UC: Ureteral catheter, sd: Standard deviation, **: p<0.01

bladder irritation, catheter migration, catheter break, catheter calcification, and complications during removal. There are also publications showing that the use of ureteral catheters increases the rate of urinary tract infection while decreasing that of urological complications (7). Urinary tract infections may also adversely affect graft function as a catheter-related complication. In contrast, Chordia et al. showed that the use of ureteral catheters was not associated with an increase in bacteriuria in renal transplant patients (10). It is also probable that in the presence of the ureteral catheter, the lack of resistance in the flow of urine prevents stasis and may prevent urinary infection. Our findings indicate that using a ureteral catheter did not increase the rate of bacteriuria in deceased donor renal transplantation, with the infection rate even decreasing in the catheter group. The role of antibiotic prophylaxis in preventing infection has not been evaluated, since both groups used prophylactic antibiotics.

In our study, it was determined that the routine use of ureteral catheters in renal transplantation significantly decreased postoperative urological complications. This finding is consistent with other reports. Interestingly, we found the rate of positive urine culture to be lower in patients with ureteral catheters. While this result is consistent with several reports, others have described an association between ureteral catheter usage and an increased risk of UTI (9).

In our study, we have shown that the use of ureteral catheters reduces both urological complications and bacteriuria. Consequently, the period of hospitalization after transplantation of patients with ureteral catheters was significantly shortened compared to the group in which ureteral catheters were not used. This shortening of the hospitalization period also helps to protect renal transplant recipients receiving immunosuppressive therapy from nosocomial infections, particularly those by antibiotic-resistant microorganisms. In addition, the shortening of the hospitalization periods and the significant decrease in the rate of urological complications requiring additional intervention help to reduce the burden on the health system.

Catheter insertion during renal transplantation is easily performed and does not require instrumentation or imaging. However, removal of the catheter requires an additional endoscopic procedure, which adds to additional cost and burden. Occasionally, delay or forgetting to remove the catheter can cause increased health expenses (7). Numerous centers have adopted the approach of using prophylactic ureteral catheters and endoscopic removal at a specified time after transplantation (12). Generally, ureteral catheters are removed 2-12 weeks post-renal transplantation (13).

In a prospective randomized controlled study, removal of the ureteral catheter in the first week after living-donor renal transplantation was found to reduce the risk of UTI compared to its removal at the routine fourth week; however, the complication rates were similar (14).

In a study investigating the optimal time for post-transplant prophylactic ureteral catheter removal, patients were divided into two groups in which the catheter was removed early (day 5) or late (week 6). It was found that catheter-related complications such as hematuria, migration, fragmentation, and UTIs in the first three months were less and the quality of life was improved in patients with early catheter removal (15).

In our patients, while the targeted time for ureteral catheter removal was four weeks, we found that the actual time of removal tended to be later than this due to patients not keeping appointments or delays due to non-clinical reasons. Despite this, there was no increase in the bacteriuria rate as expected.

Considering the benefit of ureteral catheters in preventing urinary complications, despite our recommendation for removing them as soon as possible, our study demonstrated that the duration of ureteral catheter use could be as long as 44.45±13.38 days. However, this prolonged duration of catheter use did not cause a significant increase in bacteriuria. Removing ureteral catheters before complete tissue healing can result in a higher risk for urinary complications.

The significantly shorter removal time for the Foley catheter in the ureteral catheter group was attributed to two reasons. First, there was a decrease in urological complications due to the application of a ureteral catheter to the ureteroneocystostomy anastomosis area. Second, the surgical team may have felt safer with using the ureteral catheter which may have led to the earlier removal of the Foley catheter and also to reduce the risk of UTIs. Publications showing that prolonged bladder catheterization is a risk factor for UTI in renal transplant recipients (16) and early removal of the Foley catheter in renal transplant patients reduces the risk of UTI (17) support this view.

The observation that the duration of ATG use was shorter in the second group and in terms of tacrolimus/cyclosporine use, tacrolimus was used predominantly in the second group with less bacteriuria, suggests that using a potent immunosuppressive such as ATG for a longer period may play a role in the development of bacteriuria.

While cyclosporine was used more frequently in the first group, tacrolimus was used predominantly in the second group. The bacteriuria rate was found to be lower in this group in which tacrolimus, a potent immunosuppressive, was used. In our opinion, however, while there are many factors responsible for the formation of infection, the use of a more potent immunosuppressive drug or prolonging the duration of ATG use (on average nine days in the first

group and seven days in the second group), although statistically significantly shorter, cannot be considered sufficient to reach a conclusion about the susceptibility to infection. In addition, it was thought that the shorter cold ischemia time in group 2 may have contributed to the a lower incidence of UTI by reducing the possibility of acute tubular necrosis. The shorter cold ischemia duration in group 2 is thought to be related to change in organ distribution system in May 2008 and fewer double transplants in group 2. Cold ischemia duration is not related to the usage of ureteral catheter.

The strengths of our study include well-matched numbers of patients with and without ureteral catheters, consistency in the surgical procedures where a team experienced in kidney transplantation performed the transplantations procedures using the same surgical technique, and the provision of detailed data on the early follow-up after transplantation.

This retrospective study showed that the routine use of ureteral catheters in deceased donor renal transplantation reduces urinary complications and shortens the time of Foley catheter removal. Although we recommend that the routine ureteral catheter used in deceased donor kidney transplantation cases be removed as soon as possible, there was no increase in the risk of bacteriuria in cases where catheter removal was delayed for non-medical reasons.

In conclusion, we recommend that the ureteral catheter should be used routinely in all deceased renal transplantations since we did not observe any adverse effects of ureteral catheterization on the incidence of infection.

Ethics Committee Approval: This study was approved by Istanbul Faculty of Medicine Clinical Research Ethics Committee (Date: 10.08.2018, No:13).

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