TRANSPLANT INTERNATIONAL

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

Ureteral length in live donor kidney transplantation; Does size matter?

Liselotte S. S. Ooms,[1] Inez K. B. Slagt,[1] Frank J. M. F. Dor,[1] Hendrikus J.A.N. Kimenai,[1] Khe T. C. Tran,[1] Michiel G. H. Betjes,[2] Jan N. M. IJzermans[1] and Türkan Terkivatan[1]

1 Division of Transplant Surgery, Department of Surgery, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands
2 Division of Nephrology, Department of Internal Medicine, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

Keywords
complications, kidney, length, transplantation, ureter, urological.

Correspondence
Türkan Terkivatan MD, PhD
Department of Surgery, Erasmus MC, University Medical Center Rotterdam, Room H-903, PO BOX 2040, 3000 CA Rotterdam, The Netherlands.
Tel.: +31 10 7040704
Fax: +31 10 7032396
e-mail: t.terkivatan@erasmusmc.nl

Conflicts of interest
The authors declare no conflict of interests.

Received: 11 April 2015
Revision requested: 7 May 2015
Accepted: 2 July 2015
Published online: 6 Aug 2015

doi:10.1111/tri.12635

Summary

The aim of this study was to evaluate the role of ureteral length on urological complications. Data were retrospective collected from the INEX-trial database, a RCT to compare the intravesical to the extravesical ureteroneocystostomy. Ureteral length was measured in 198 recipients and used to divide recipients into three categories based on interquartile ranges: short (≤8.5 cm), medium (8.6–10.9 cm) and long ureters (≥11 cm). Urological complications were defined as the number of percutaneous nephrostomy placements (PCN). Fifty recipients fell into the short, 98 into the medium and 50 recipients into the long ureter category. Median follow-up was 26 (range 2–45) months. There was no significant difference in number of PCN placements between the categories. There were 9 (18%) PCN placements in the short ureter category, 21 (20%) in medium ureter category and 10 (21%) in the long ureter category, $P = 0.886$. Risk factor analysis for gender, arterial multiplicity and type of ureteroneocystostomy showed no differences in PCN placements between the three ureteral length categories. We conclude that ureteral length alone does not seem to influence the number of urological complications.

Introduction

Reducing ureter-related complications remains one of the challenges in kidney transplantation. Major urological complications, such as urinary leakage and ureter strictures, may lead to increased morbidity and prolonged hospital stay [1,2]. They are reported with an incidence between 4.8 and 22% [3,4]. Multiple factors are presumed to contribute to the development of urological complications. The influence of donor and recipient factors is being discussed in literature and includes male gender of recipient and donor, arterial multiplicity and pre-emptive transplantation as possible risk factors for urological complication [5].

Some other factors that may contribute to the development of urological complications after kidney transplantation are graft related, such as ureteral vascularization and arterial multiplicity [6]. Diminished blood supply of the ureter can cause ischemia of the most distal part of the ureter, resulting in urinary leakage or ureter strictures. The native vascularization of the ureter is by segmental arteries derived from the renal, vesicle, gonadal, common iliac or internal iliac vessels or directly from the abdominal aorta (Fig. 1). During living donor nephrectomy, most of these segmental branches are dissected, resulting in the renal artery as the main blood supply of the ureter. Therefore, it is assumed that a shorter ureteral length is accommodated with better vascularization and may possibly cause less urological complications.

Because of the limited knowledge about the influence of ureteral length on urological complications after kidney transplantation, we have conducted this study using the available data of the recently published randomized controlled INEX-trial [7].

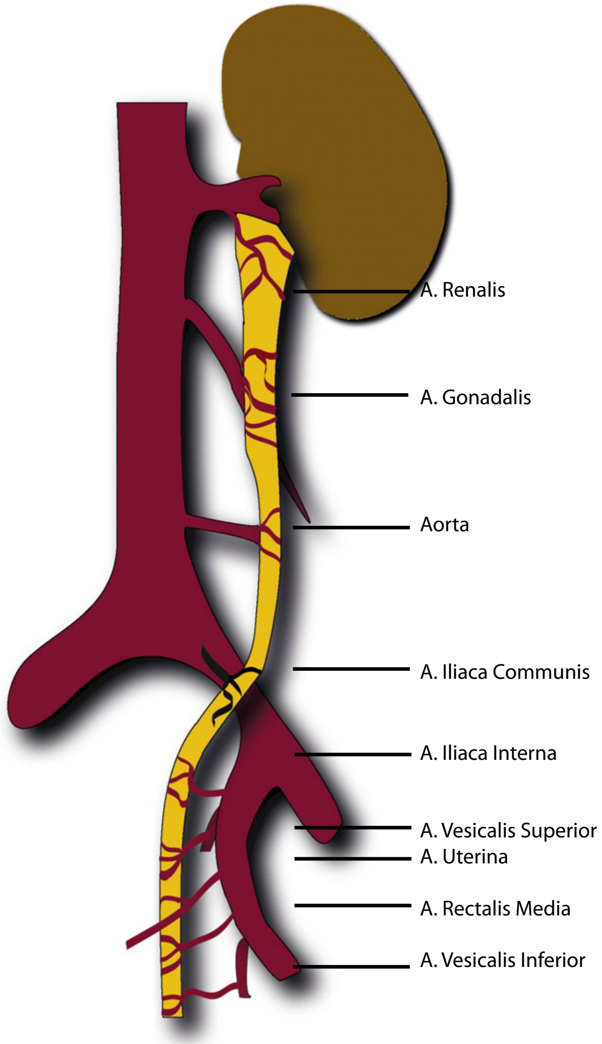

Figure 1 Vascularization of ureter.

Patients and methods

Study population and data selection

Between October 2010 and December 2012, a randomized controlled trial, referred to as the INEX-trial, was conducted in our center [7]. In this study, 200 consecutive recipients of a living donor kidney transplant were randomized to either an intravesical or extravesical ureteroneocystostomy. Exclusion criteria were age <18 years, a double ureter system of the donor kidney, robot-assisted donor nephrectomy using the DaVinci Surgical System or an absent native bladder of the recipient. During this trial, ureteral length was measured and documented prospectively in all kidney transplant recipients.

Baseline characteristics included recipient gender, age, body mass index (BMI), warm and cold ischemia time, duration of operation, number of donor renal arteries and median follow-up in months. Total ureteral length was measured intra-operatively from the center of the pyelum to the most distal part of the ureter. After the vascular anastomoses had been performed, the ureter was prepared for the ureteroneocystostomy. The kidney was placed in its preferred position before cutting the excess length of the ureter. The length of a ureter is ideal when a tension-free anastomosis can be made and the risk of ureteral rotation or kinking is minimalized. The length of the removed segment was measured and then subtracted from the total ureteral length, representing the remaining ureteral length in the recipient for this study. Recipients were divided into three categories based on the interquartile ranges of ureteral length. Patients with a ureteral length at or below the 25th percentile were placed in the lowest category (short ureter category), the ureteral lengths above the 75th percentile in the highest category (long ureter category) and the middle 50% in the moderate category (medium ureter category).

Percutaneous nephrostomy (PCN) placement during complete follow-up was used as a primary outcome for urological complications, as PCN placement is considered to be the initial treatment for major urological complications, such as urinary leakage or ureteral stenosis. The reason for PCN placement and the consecutive treatment were documented. Urinary leakage, (detected by a MAG-3 scan or proven by chemistry samples in case of extensive fluid production of the wound or by the drain) or a rise in serum creatinine level combined a hydronephrosis on ultrasound, indicated PCN placement.

Risk factor analysis

A risk factor analysis was performed to determine the relationship between the numbers of PCN placements in the three ureteral length categories by analyzing each potential risk factor separately. Based on available literature, we selected recipient gender, arterial multiplicity of the kidney graft and type of ureteroneocystostomy as potential risk factors [5,8].

Surgical technique in the recipient

The extraperitoneal approach in the iliac fossa was performed in all recipients. All kidney grafts with multiple arteries had an arterial reconstruction prior to transplantation. This was either side to end or side to side on the main renal artery. After the (end-to-side) vascular anastomoses on the external iliac vessels, a consultant transplant surgeon performed either an intravesical anastomosis described by Politano and Leadbetter [9] or an extravesical anastomosis described by Lich and Gregoir [10,11] as determined by randomization to create continuity of the urinary tract. A ureterovesical 8-French stent was used as part of our standard care and was externalized suprapubically. The stent was removed 10 days postoperatively. A urinary bladder catheter was placed and removed after 7 days.

Immunosuppressive treatment

Immunosuppressive treatment consisted of 20 mg basiliximab intravenous on the day of surgery and day 4 after transplantation. Postoperative immunosuppression consisted of tacrolimus (starting dose 3 mg/kg and titrated through a serum level of 10–15 ng/ml for the first 3 months), 2000 mg mycophenolate mofetil and prednisolone starting at 50 mg and tapered off to be discontinued at 4 months after transplantation.

Statistical analysis

Categorical variables were presented as numbers (percentage). Continuous variables were presented as means with standard deviation if normally distributed or as median with range if not normally distributed. Continuous variables were analyzed using the one-way ANOVA or Kruskal–Wallis test. Categorical variables were analyzed using chi-square test. Risk factor analysis was performed using logistic regression with PCN as outcome and the interaction of ureteral length categories and gender, type of ureteroneocystostomy and arterial multiplicity as predictors. All analyses were conducted using IBM SPSS Statistics for Windows (version 21.0. Armonk, NY: IBM Corp, USA). A *P*-value of <0.05 (two-sided) will be considered statistically significant.

Results

Baseline characteristics

Between October 2010 and December 2012, a total of 200 recipients were included in the INEX-trial [7]. Ureteral length was measured in 198 recipients. Mean ureteral length of all recipients was 9.6 cm ± 1.6 cm. Recipients were divided into three different categories. Fifty recipients were allocated to the short ureter category (≤8.5 cm), with a mean ureteral length of 7.5 cm ± 0.9 cm. Ninety-eight recipients were allocated to the medium ureter category (8.6–10.9 cm), mean ureteral length was 9.7 cm ± 0.6 cm and 50 recipients were allocated to the long ureter category (≥11 cm), mean ureteral length was 11.7 cm ± 0.6 cm. All ureters were shortened during surgery; the removed segment size had a mean of 4.7 cm ± 2.1 cm. Table 1 provides an overview of baseline characteristics of the three categories. No significant differences were found between recipient gender and age, BMI, ischemia time, duration of operation or follow-up in months. The median follow-up of all recipients was 26 (2–45) months.

Table 1. Baseline characteristics.

Variable	Short ureter (*n* = 50)	Medium ureter (*n* = 98)	Long ureter (*n* = 50)	*P*-value
Recipient age in years mean ± SD	52 ± 14	55 ± 13	55 ± 14	0.514
Recipients gender				
Male *N* (%)	29 (58)	66 (67)	34 (68)	0.469
Female *N* (%)	21 (42)	32 (33)	16 (32)	
Recipients BMI mean ± SD	26 ± 5	26 ± 5	27 ± 4	0.583
Warm ischemia in minutes mean ± SD	26 ± 7	26 ± 6	27 ± 14	0.498
Cold ischemia in minutes mean ± SD	147 ± 25	150 ± 29	149 ± 32	0.773
Duration operation in minutes mean ± SD	131 ± 25	133 ± 29	135 ± 31	0.808
Follow-up in months median (range)	29 (3–44)	25.5 (2–45)	25 (11–44)	0.235
Ureteral length in cm mean ± SD	7.5 ± 0.9	9.7 ± 0.6	11.7 ± 0.6	<0.001

SD, standard deviation; M, male; F, female; BMI, body mass index.

Urological outcome

There was no significant difference in the number of PCN placements between the three categories (Table 2 and Fig. 2).

In the short ureter category (≤8.5 cm), nine recipients (18%) were treated with a PCN. Eight recipients received a PCN due to hydronephrosis, and one recipient had urinary leakage. Median time between transplantation and PCN placement was 9 days (range 3–182 days). The recipient with urinary leakage recovered from the leakage without any other intervention. However, this recipient developed a ureter stricture 1 year after transplantation for which a ureter reconstruction was performed. Of the eight recipients with a PCN placement due to hydronephrosis, one had immediately surgical ureter reconstruction and another recipient underwent an unsuccessful percutaneous balloon dilatation of a ureter stricture followed by surgical ureter reconstruction. In six recipients, the hydronephrosis resolved without any other intervention (Table 2 and Fig. 2).

In the medium ureter category (8.6–10.9 cm), 21 recipients (21%) had a PCN placement. In 17 recipients (81%), it was because of hydronephrosis and in four recipients (19%) due to urinary leakage. Median time between transplantation and PCN placement was 12 days (range 2–86 days). All four recipients with urinary leakage recovered without any other intervention. Of the 17 recipients with

Table 2. Urological complications.

Variable	Short ureter (n = 50)	Medium ureter (n = 98)	Long ureter (n = 50)	P-value
PCN N (%)	9 (18)	21 (21)	10 (20)	0.886
Days between KT-PCN median (range)	9 (3–182)	12 (2–86)	7 (3–29)	0.367
Reason PCN	N = 9	N = 21	N = 10	
Hydronephrosis N (%)	8 (89)	17 (81)	8 (80)	0.847
Urinary leakage N (%)	1 (11)	4 (19)	2 (20)	
Treatment PCN	N = 9	N = 21	N = 10	
No N (%)	6 (67)	14 (67)	9 (90)	0.493
Balloon dilatation N (%)	1 (failed)	2 (9)	1 (10)	
Ureteral revision N (%)	3 (33)	4 (19)	–	
Nephrolithotomy N (%)	–	1 (5)	–	

KT, kidney transplantation; PCN, percutaneous nephrostomy.

PCN placement due to hydronephrosis, four recipients underwent surgical re-intervention because of a ureter stricture, two underwent successful percutaneous balloon dilatation and in 10 recipients, the hydronephrosis resolved without any other intervention. In one recipient, the hydronephrosis was due to obstruction due to nephrolithiasis in the kidney graft 9 months after transplantation. This recipient underwent percutaneous nephrolithotomy, and the PCN could be removed successfully afterward (Table 2 and Fig. 2).

In the long ureter category (≥11 cm), 10 recipients (20%) were treated with a PCN. Eight recipients had hydronephrosis (80%) and two recipients (20%) urinary leakage. Median time between transplantation and PCN placement was 7 days (range 3–29 days). There was no need for any re-intervention for the recipients with urinary leakage. In eight recipients with a hydronephrosis, one recipient with a ureter stricture underwent successful percutaneous balloon dilatation. In the other seven recipients, hydronephrosis resolved without additional intervention (Table 2 and Fig. 2).

Risk factor analysis

In total, 31 of 129 (24%) males and 9 of 69 (13%) females received PCN placement. Thirty-six of 198 patients had arterial multiplicity of the kidney graft of whom 9 of 36 (25%) received a PCN. This group contained 19 of 36 kidneys with a lower pole artery, of whom 6 of 19 (32%) received a PCN and 17 of 36 kidneys with an additional

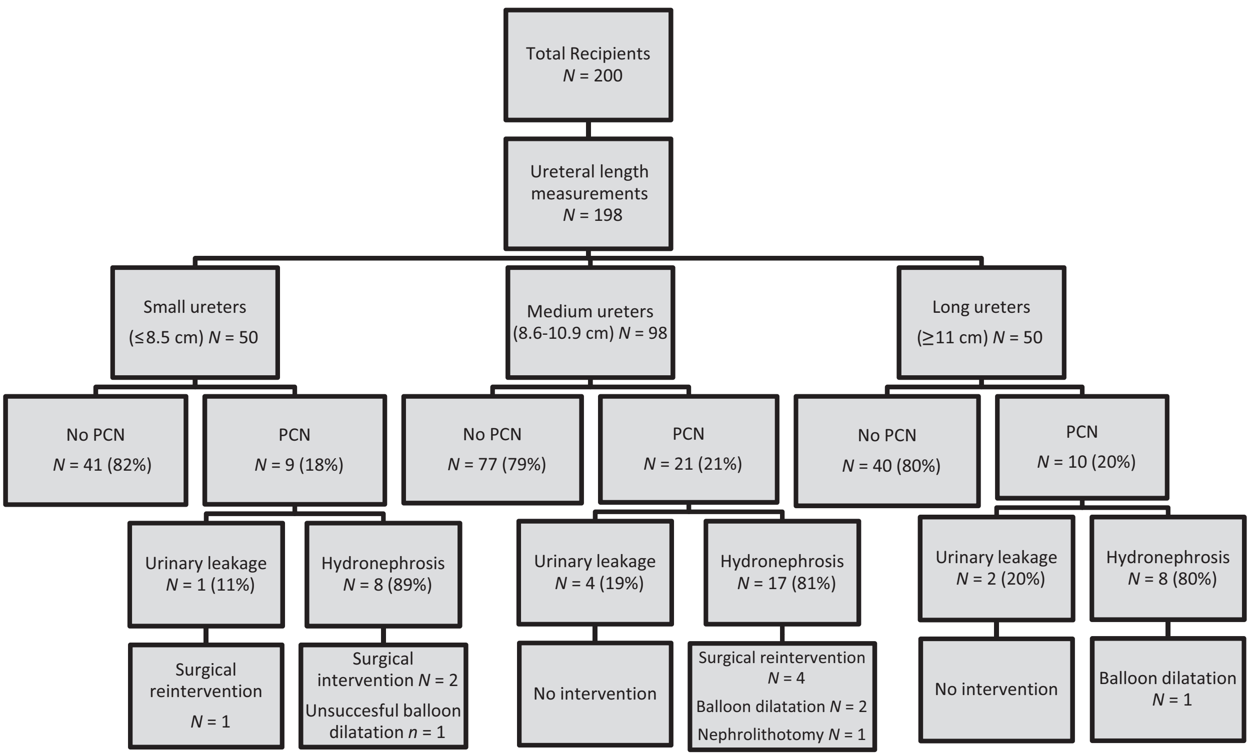

Figure 2 Flow chart.

(nonlower pole) artery, of whom 3 of 17 (18%) received a PCN. Furthermore, in 20 of 100 (20%) patients with an extravesical ureteroneocystostomy, a PCN was placed and 20 of 98 (20%) patients with an intravesical anastomosis. Risk factor analysis was performed using logistic regression with PCN as outcome and the interaction of ureteral length categories and gender, type of ureteroneocystostomy and arterial multiplicity as predictors. The interaction between gender and ureteral length category was not significant ($P = 0.355$), neither was the interaction for arterial multiplicity ($P = 0.152$), nor the interaction for the type of ureteroneocystostomy (intravesical versus extravesical) ($P = 0.239$). Therefore, we cannot conclude differential effects of the risk factors in the three categories.

Discussion

Based on the available anatomical knowledge of the ureteral vascularization, it is presumed that a shorter ureteral length is preferable to a longer ureter in kidney transplantation. However, in this study, we found that ureteral length alone does not seem to contribute to the number of urological complications. We performed a risk factor analysis for recipient gender, arterial multiplicity and for type of ureteroneocystostomy. There were no differential effects of these risk factors in the three ureteral length categories.

In a study by Ali-Asgari *et al.*, the complication rate, long-term survival and hospitalization days were not significantly different between ureters less or more than 5.5 cm. However, no information could be found on the technique of ureteral length measurement [12].

Slagt *et al.* previously analyzed risk factors for urological complications in deceased donor kidney transplantation. Multivariate analysis showed that male recipients and arterial reconstructions were independent risk factors for urological complications [5]. Carter *et al.* also stated that arterial multiplicity increases the risk of urological complications after living kidney transplantation, confirming the earlier findings by Kok *et al.* [6,8]. Unfortunately, analysis of the influence of a lower pole artery could not be performed adequately due to the limited number of patients with a lower pole artery in this series.

There are some limitations to this study. The measurements of the ureteral length were part of the earlier published INEX-trial. In this randomized controlled trial, the intravesical versus extravesical ureteroneocystostomy was compared. Therefore, our study population is not uniform. However, in the INEX-trial, the number of urological complications was the same in both groups [7]. Furthermore, different transplant surgeons measured the ureteral length and interobserver bias of a few millimeters could not be excluded.

Our number of urological complications, defined by PCN placements, is high compared to literature. We have a relatively large number of patients who received a PCN due to hydronephrosis, which resolved without any treatment 23 of 40 (58%). This is probably because in our center, PCN placement is considered to be a minimal invasive intervention and we therefore maintain a low threshold to place a PCN. A bit hydronephrosis leads to PCN placement either for therapeutic benefit but also as a diagnostic tool. If we would exclude these PCN placements due to hydronephrosis which needed no additional intervention, the short ureter category would include 3 of 50 (6%) PCN placements, the medium ureter 11 of 98 (11%) and the long ureter 3 of 50 (6%), $P = 0.423$. Therefore, still, ureteral length does not seem to influence the number of PCN placements.

If neither the ureteral length nor the technique for ureteroneocystostomy are factors that contribute to urological complications, the use of a ureteral stent may be questioned. In our institute, a ureterovesical stent is placed routinely. The Cochrane review of Wilson *et al.* reports a urological complication rate of 0–4% in the stented group versus 0–17.3% in the nonstented group. However, the number of urinary tract infections is significantly higher in the stented group and stent-related complications, such as obstruction, migration and stone formation, should not be neglected. We agree with the authors of the Cochrane review that a well-designed study of stenting versus selective stenting should be executed [13].

Additionally, more insight should be established in the microcirculation and perfusion of the ureteral blood flow. To our knowledge, only one animal study has been published about the effect of ureteral access sheath on microcirculation of the ureter. Lallas *et al.* [14] demonstrated that the use of the access sheath can cause a transient decrease in ureteral blood flow. This raises the question whether the use of a ureterovesical stent in kidney transplantation also influences the microcirculation of the ureter.

We conclude that ureteral length alone does not seem to influence the number of urological complications after kidney transplantation. Risk factor analysis for recipient gender, arterial multiplicity and for type of ureteroneocystostomy provided no differential effects between the three categories. Further research on the microvascular blood flow of the ureter and the use of a ureterovesical stent is warranted to answer more questions about risk factors for urological complications in living donor kidney transplantation.

Authorship

LSSO: participated in research design, writing of the manuscript, performance of research, collected data and participated in data analysis. IKBS: participated in research design, writing of the manuscript, collected data and performance of the research. FJMFD, HJANK and KTCT: participated in the writing of the research and performance of the research. MGHB: participate in the writing of the manuscript and performance of the research. JNMI: participated in research design, writing of the manuscript, performance of the research. TT: participated in research design, writing of the manuscript, performance of research and participated in data analysis.

Funding

None.

Acknowledgements

Our data manager J.G. Van Duuren- van Pelt.

References

1. Pleass HC, Clark KR, Rigg KM, *et al.* Urologic complications after renal transplantation: a prospective randomized trial comparing different techniques of ureteric anastomosis and the use of prophylactic ureteric stents. *Transplant Proc* 1995; **27**: 1091.
2. Neri F, Tsivian M, Coccolini F, *et al.* Urological complications after kidney transplantation: experience of more than 1,000 transplantations. *Transplant Proc* 2009; **41**: 1224.
3. Dols LF, Terkivatan T, Kok NF, *et al.* Use of stenting in living donor kidney transplantation: does it reduce vesicoureteral complications? *Transplant Proc* 2011; **43**: 1623.
4. Buresley S, Samhan M, Moniri S, Codaj J, Al-Mousawi M. Postrenal transplantation urologic complications. *Transplant Proc* 2008; **40**: 2345.
5. Slagt IK, Ijzermans JN, Visser LJ, Weimar W, Roodnat JI, Terkivatan T. Independent risk factors for urological complications after deceased donor kidney transplantation. *PLoS One* 2014; **9**: e91211.
6. Kok NF, Dols LF, Hunink MG, *et al.* Complex vascular anatomy in live kidney donation: imaging and consequences for clinical outcome. *Transplantation* 2008; **85**: 1760.
7. Slagt IK, Dor FJ, Tran TC, *et al.* A randomized controlled trial comparing intravesical to extravesical ureteroneocystostomy in living donor kidney transplantation recipients. *Kidney Int* 2014; **85**: 471.
8. Carter JT, Freise CE, McTaggart RA, *et al.* Laparoscopic procurement of kidneys with multiple renal arteries is associated with increased ureteral complications in the recipient. *Am J Transplant* 2005; **5**: 1312.
9. Politano VA, Leadbetter WF. An operative technique for the correction of vesicoureteral reflux. *J Urol* 1958; **79**: 932.
10. Gregoir W. [the Surgical Treatment of Congenital Vesico-Ureteral Reflux] Le Traitement Chirurgical Du Reflux V'esico-Ur'et'eral Cong'enital. *Acta Chir Belg* 1964; **63**: 431.
11. Lich R Jr, Howerton LW, Davis LA. Childhood urosepsis. *J Ky Med Assoc* 1961; **59**: 1177.
12. Ali-Asgari M, Dadkhah F, Ghadian A, Nourbala MH. Impact of ureteral length on urological complications and patient survival after kidney transplantation. *Nephrourol Mon* 2013; **5**: 878.
13. Wilson CH, Rix DA, Manas DM. Routine intraoperative ureteric stenting for kidney transplant recipients. *Cochrane Database Syst Rev* 2013; **6**: CD004925.
14. Lallas CD, Auge BK, Raj GV, Santa-Cruz R, Madden JF, Preminger GM. Laser Doppler flowmetric determination of ureteral blood flow after ureteral access sheath placement. *J Endourol* 2002; **16**: 583.