



Is surgical treatment necessary in all hydronephrotic kidney allografts?

Da li je hirurški pristup neohodan u svim slučajevima lečenja hidronefroze transplantiranog bubrega?

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Abstract

Background/Aim. The management of kidney graft hydronephrosis (KGH) is usually surgical, although some cases require expectant management and follow-up. The aim of the study was to discuss the criteria for expectant management or immediate surgical intervention in the series of patients with KGH. **Methods.** The paper is based on a retrospective study of 42 patients with KGH. The patients underwent kidney transplantation from January 2007 to December 2012. There were 19 cadaveric donor recipients and 23 living donor recipients. The average follow-up was 15,2 (range 12–21) months. The average recipient's age was 41,6 years. In every case study, the diagnosis of graft hydronephrosis was established using abdominal ultrasonography. The degree of hydronephrosis was estimated on the basis of measuring the maximal diameter of the pelvicalyceal dilatation (PD). **Results.** There were no patients with graft failure after the period during which they were under medical observation. Hydronephrosis resolved completely in six (14%) patients. The median maximal PD was 28 ± 9 (range 14–38) mm and the median last PD was 23 ± 11 (range 0–35) mm and they did not differ significantly ($p = 0.23$). The last serum creatinine was significantly lower than the maximal creatinine value ($p < 0.05$). In twelve (29%) patients renal function normalized. Renal function remained stable during the period of medical observation. At the end of the follow-up, all patients had sterile urine culture. **Conclusion.** The traditional doctrine, according to which KGH represents an absolute indication for surgery, can be debated; the majority of the patients observed require just active surveillance. Prompt surgical correction is recommended only in cases with increasing pelvicalyceal dilatation and the development of symptoms, progressively decreasing renal function or recurrent urinary tract infection.

Key words:

kidney transplantation; postoperative complications; hydronephrosis; kidney function tests; prognosis; conservative treatment.

Apstrakt

Uvod/Cilj. Pristup lečenju hidronefroze transplantiranog bubrega (HTB) je obično hirurški, iako neki slučajevi zahtevaju ekspektativni pristup i praćenje. Cilj rada bio je utvrditi kriterijume za ekspektativni pristup ili neposredan hirurški pristup na seriji bolesnika sa hidronefrozom transplantiranog bubrega. **Metode.** Rad se bazira na retrospektivnom istraživanju koje je obuhvatilo 42 bolesnika sa HTB. Ispitivanjem su obuhvaćeni bolesnici kod kojih je učinjena transplantacija bubrega u periodu od januara 2007. godine do decembra 2012. godine. U posmatranom periodu učinjeno je 19 kadaveričnih transplantacija i 23 transplantacije sa živog donora. Prosečno vreme praćenja bilo je 15,2 (raspon 12–21) meseca. Prosečna starost osobe koja je primila bubreg bila je 41,6 godina. Dijagnoza hidronefroze u svakom slučaju je postavljena ultrazvučnim pregledom. Stepem hidronefroze procenjivan je na osnovu merenja maksimalnih prečnika proširenih bubrežnih čašica i karlica. **Rezultati.** Tokom perioda praćenja nije bilo slučajeva nefunkcionalnosti grafta. Problem hidronefroze u potpunosti je bio rešen kod šest (14%) bolesnika. Prosečno maksimalno proširenje bubrežnih čašica i karlica bilo je 28 ± 9 (raspon 14–38) mm, a prosečna vrednosti proširenja pijelona i čašica na kraju praćenja bila je 23 ± 11 (raspon 0–35) mm. Nije postojala statistički značajna razlika ($p = 0.23$). Poslednja kontrolna vrednost serumskog kreatinina bila je značajno niža od maksimalne vrednosti kreatinina ($p < 0.05$). Bubrežna funkcija je normalizovana kod 12 pacijenata (29) i ostala je stabilna tokom perioda posmatranja. Na kraju praćenja svi bolesnici su imali sterilan nalaz urinokulture. **Zaključak.** Tradicionalan pristup, po kome HTB predstavlja apsolutnu indikaciju za operativno lečenje, može se dalje istraživati; većina bolesnika koja je ovde praćena zahtevala je samo pažljivo praćenje. Neodložna hirurška intervencija preporučuje se samo u slučajevima sa izrazitim proširenjem bubrežnih čašica i karlice kao i razvojem simptoma progresivno smanjene bubrežne funkcije ili rekurentne infekcije urinarnog trakta.

Ključne reči:

transplantacija bubrega; postoperativne komplikacije; hidronefroza; bubreg, funkcijski testovi; prognoza; lečenje, konzervativno.

Introduction

Kidney graft hydronephrosis (KGH) is an increasing problem in kidney transplant recipients. Patients with this condition show a higher prevalence for developing irreversible graft failure. The incidence of kidney transplant obstruction ranges from 2–12%¹. The presence of KGH can be due to an obstruction, or it may appear because of other reasons². Hydronephrosis alone, or associated with additional pathological conditions, can lead to irreversible damage of renal graft and graft loss³. Therefore, all factors affecting renal function have to be explored in details.

The mainstay in the management of KGH is immediate curative treatment. The most recent studies favor early surgical repair because of the adequate functional results with preservation of renal graft function^{4,5}. It is considered that urgent surgical intervention should be the first choice in managing KGH because of satisfying functional outcome coupled with low morbidity. Delayed repair may lead to prolongation of morbidity and negatively affect kidney graft function⁶. Just a small number of authors advocate delayed repair because hydronephrosis may be due to factors other than obstruction^{2,7}. In the past, a significant portion of patients with renal transplant underwent open surgical procedures for the treatment of obstruction⁸. However, with advances in technology, these complications are now treated more often by percutaneous and/or endoscopic techniques^{3,9}. No study has yet evaluated the outcome of patients with asymptomatic and non complicated KGH who underwent expectant management. However, only clinically insignificant KGH is suitable for active surveillance without the need for immediate surgical intervention. The surgical significance of KGH may be suggested with the underlying cause of hydronephrosis, a degree of pelvicalyceal dilatation and deterioration of renal function. All factors affecting renal function in addition to hydronephrosis must be explored in detail. Close monitoring of several parameters of renal function should be the basis of active surveillance of patients with KGH. Therefore, the need for routine surgery in patients with KGH may be debated. The traditional doctrine that KGH represents an absolute indication for surgery has recently been questioned. The aim of this study was to present our experience with active surveillance of clinically insignificant KGH and recommend criteria for surgical interventions in these patients.

Methods

During a 6-year period, a retrospective review of our institution kidney transplantation database was performed. All transplantations were performed at our institution, the Clinic of Urology, Clinical Center of Serbia, from January 2007 to December 2012. After institutional review board approval, 42 patients who underwent kidney transplantation were included in this retrospective study. There were 23 kidney transplants from living donors and 19 from cadaveric donors. The average age of recipients was 41,6 (range 23–54) years. Lich-Gregoire ureteral implantation was performed in all kidney recipients and the ureter was stented with

indwelling double-J catheter. The ureteral double-J catheter was removed 21 days after transplantation. After removal of the double-J catheter, ultrasonography detected hydronephrosis in all kidney grafts.

Patients had a complete follow-up at least 1-year, 15.2 months on average (range 12–21 months) and were evaluated with frequent clinical examinations. All patients were closely followed-up with serial ultrasonography (US), urine culture (UC) and serum creatinine (SCr) determination. The maximal diameter of the pelvicalyceal dilatation was used as a US parameter. SCr and UC determination as well as US were repeated every week in first 3 months, every two weeks in 3 to 6 months and after that period they were performed once a month. In the follow-up, we determined the variables for SCr level and pelvicalyceal dilatation (PD) and compared them to previous measurements. Once these values become stable, the follow-up continues for at least 2 months, and if the values remain stable over that period, the follow-up ends. SCr values are considered normal by a SCr < 115 $\mu\text{mol/L}$. Urinary tract infection (UTI) is defined as any culture that yielded $\geq 10^5$ colonies. Recipients with UTI were treated with targeted antibiotic therapy.

Additional measurements were performed during the follow-up protocol and their repetition was decided on case-by-case basis. Graft failure was defined as the date of return to chronic dialysis, graft nephrectomy or death with a functioning graft. All values are represented as the median \pm standard deviation (range). Relationship among parameters was analyzed using the unpaired *t*-test. *P* values < 0.05 were considered statistically significant.

Results

During the follow-up, the median maximal SCr level was 245.8 ± 78.6 (range 118.2–425.8) $\mu\text{mol/L}$ and the median SCr level at the end of the follow-up was 133.8 ± 58.9 (range 90.1–172.6) $\mu\text{mol/L}$. The difference was statistically significant ($p < 0.05$). Normalized renal function as defined by the SCr < 115 $\mu\text{mol/L}$ confirmed by last SCr value was found in 12 (29 %) patients. Last SCr level remained stable as constant value during the period at least 3 months, in median 6.3 ± 2.8 (range 3–10) months. US demonstrated KGH in all patients at initial presentation. The median maximal PD was 28 ± 9 (range 14–38) mm and the median last PD was 23 ± 11 (range 0–35) mm and they did not differ significantly ($p = 0.23$).

Hydronephrosis resolved completely in six (14%) patients. During the follow-up period in 34 (81%) patients associated pathological conditions were treated. These were: graft rejection, acute tubular necrosis (ATN), cytomegalovirus (CMV) infection and immunosuppression drug nephrotoxicity and UTI. Clinical rejection was reported in 16 (38%) patients. In the half of these patients, rejection was proven by biopsy. Thirteen (31%) patients with delayed graft function due to ATN required postoperative dialysis. With respect to immunosuppression nephrotoxicity the SCr levels remained stable after drug therapy which was modified in 8 (19%) patients. Specific therapy for cytomegalovirus

(CMV) infection was noted in 14 (33%) patients. UTI with positive urine culture developed in 28 (67%) patients. In 17 (40%) patients recurrent UTI was documented.

In Figures 1 and 2c and b ultrasonography images of kidney graft hydronephrosis showing stable renal function during the period of observation are given.



Fig. 1 – Ultrasonography image of kidney graft hydronephrosis in 28 years old female living-donor recipients 21 months after transplantation with pelvicalyceal dilatation 20 mm and serum creatinine 144 $\mu\text{mol/L}$ remained stable during 7 months.



Fig. 2a – Ultrasonography image of kidney graft hydronephrosis associating with biopsy proved rejection in 41 years old male cadaveric-donor recipient 3 months after transplantation with pelvicalyceal dilatation 26 mm and serum creatinine 385 $\mu\text{mol/L}$.

Discussion

Urological complications after kidney transplantation have been reported in 2–14% of patients. KGH is the most common complication¹⁰. Both obstructive and non-obstructive KGH was reported in patients who participated in this study.

The incidence of kidney transplant obstruction ranges from 0.5–10% with approximately 90% at the ureterovesical junction¹¹. The most common cause of obstructive hydronephrosis in early post-transplant period includes edema of ureteroneocystostomy. Late obstruction occurs usually as a result of ureteral fibrosis due to ischemia, rejection or in-

fection. Less common cause includes compression by pelvic fluid collection such as hematoma, urinoma, seroma or lymphocele¹². Renal stones are rare in the transplant kidney with a reported frequency less than 1%¹³.

The frequent cause of non-obstructive KGH is decreased ureteral tone from denervation which is often coupled with ischemia, rejection or infection. Because its denervation, the short ureter could be the possibility of functional hydronephrosis. Vesicoureteral reflux (VUR), with or without incomplete bladder emptying, could be a factor that influences the development of hydronephrosis in up to 86% of cases³.



Fig. 2b – US image of the same patient 14 months after transplantation with pelvicalyceal dilatation 12 mm and serum creatinine 110 $\mu\text{mol/L}$ remained stable during 5 months.

KGH is most often identified with US, but its significance should be interpreted in conjunction with renal function and clinical data (Figure 1). There are three indicators that should be considered when determining the surgical significance of hydronephrosis: the underlying cause, degree of pelvicalyceal dilatation and deterioration of renal function. Serial ultrasounds graft monitoring and control the kidney function parameters are necessary. Recipients should be carefully monitored for deterioration of renal function. Progressive SCr elevation was a strong predictor of graft dysfunction. There is no standard cut-off value of PD in predicting the need for surgical intervention. It must be in conjunction with other parameters, mainly the SCr level. However, the higher PD is, the possibility of graft failure rises and surgery will be necessary.

The cause of KGH in our analyses is likely to be multifactorial. In our series, 34 (81%) patients were treated for associated pathological conditions. Appropriate treatment of associated pathological conditions leads to the improved graft function and may potentially influence hydronephrosis (Figures 2a and 2b). Therefore, in patients with KGH we must explore all possible factors affecting renal function in details. Our analyses confirmed the causal relationship between infection and obstruction. The polyomavirus type BK has been listed as a possible reason for causing transplant ureteric stenosis¹⁴. In our study CMV infection compromised renal function in 14 (33%) patients. CMV infection, even

in the absence of systemic symptoms, could be present with ureteric damage and hydronephrosis, too¹⁵.

Another cause of decreased renal function is immunosuppression-based nephrotoxicity¹⁶. In 2–5% of immunosuppressive agent-treated patients after kidney transplantation, hydronephrosis is a possible side-effect. This occurred due to ischemic injury and edema formation in transplanted ureter. Therefore, minimizing the negative effects of immunosuppressive therapy is an important objective in a long-term management of kidney transplant recipients. In our study, the change of immunosuppressants used to treat immunosuppression-based nephrotoxicity, was done in 8 (19%) patients.

Kidney graft rejection could be associated with hydronephrosis due to local inflammation and ischemic injury leading to edema and fibrosis¹⁷. Also, the cause could be a decreased ureteral tone resulting from denervation. In our study clinical rejection was presented in 16 (38%) patients. ATN with delayed graft function is a common clinical problem occurring after cadaveric renal transplantation and occurs in more than half of the cadaver grafts¹⁸. In our study 13 (31%) patients required dialysis within the follow-up period due to ATN-caused delayed graft function. UTI is a very common condition seen in patients with KGH. Infection could cause spasm, edema formation and ischemic damage of ureter. Hydronephrosis was associated with pyelonephritis and pyelonephritis was associated with worsening renal function¹⁹. In our analyses 28 (67%) patients had UTI. In 17 (40%) patients UTI was recurrent. All our patients were treated successfully and had sterile urine culture at the end of the follow-up.

The PD values are not changed significantly during the follow-up, but the SCr levels were changed significantly with a tendency to improve renal function. Some data indicate that for the stability of renal function the correlate of long-term graft outcome is more important than the absolute level of SCr²⁰. In our study, renal function was stable in median during 6,3 (range 3–10) months. Spontaneous resolution of hydronephrosis is possible. Female patients may develop hydronephrosis after radical hysterectomy. During this pro-

cedure dissection of the ureter from its adventitia may induce ureteric obstruction resulting from local edema and lack of vascularization. Hydronephrosis disappeared spontaneously at 6 months after the operation in more than 60% of cases²¹.

Some transplant patients resolve the hydronephrosis of graft with time. In our study hydronephrosis spontaneously disappeared in 6 (14%) patients. The possible causes may be the disturbances in pelvic and ureteric peristalsis due to transient edema and ischemia. Consequently, the peristaltic waves from the pelvis cannot propagate across the ureter and result in hydronephrosis. Transient vesicoureteral reflux (VUR) and incomplete bladder emptying could be also causal.

Our study had several limitations. It included the short follow-up and retrospective design. Therefore, a randomized prospective study with longer follow-up would allow further analyses. Also, the limited number of patients in our series was an obstacle to reporting any significant prognostic factors regarding preservation graft function in our patients. The single-institutional nature of the study might have, to some degree, limited the possibility to draw general conclusions out of it. Despite these limitations, we believe our findings may offer clinicians a way to identify patients with KGH for safe and active surveillance.

Conclusion

The traditional doctrine, according to which KGH represents an absolute indication for surgery, can be debated. In our study it was shown that some patients with KGH can be safely managed expectantly with the close follow-up. Prompt surgical correction is recommended in case of increasing pelvicalyceal dilatation with symptoms develop, progressive decreasing renal function or refractory UTI. It is important to focus on the etiology of hydronephrosis and recognize and treat associated pathological conditions which could damage graft function alone. Because of an unpredictable clinical course, an individual evaluation and approach is crucial to avoid the kidney graft failure.

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