ORIGINAL RESEARCH
GENERAL UROLOGY

Doi: 10.4274/jus.2015.613
Journal of Urological Surgery, 2016; 1: 7-12

To Save or not to Save the Kidney: Relieving Unilateral Obstruction May Significantly Improve an Initially Low Split Renal Creatinine Clearance

Böbreği Kurtarmak ya da Kurtarmamak? Tek Taraflı Üreteral Obstrüksiyonun Tedavisi Erken Dönemdeki Düşük Kreatinin Klirensini Anlamlı Olarak Arttırabilir

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

This is first study that evaluated the renal function change after relief of unilateral ureteral obstruction because of ureteral stones.

ABSTRACT

Objective

The aim of this study was to evaluate the change in acute/subacute unilateral renal function after the relief of complete unilateral ureteral obstruction by nephrostomy.

Materials and Methods

Thirty patients were prospectively enrolled in the study. All had ureteral stone, which were located in the upper ureter in 24 (80%) and in the middle ureter in 6 (20%) patients. As all patients had high-grade hydronephrosis, a percutaneous nephrostomy catheter was placed for the relief of obstruction. At the first week of urinary diversion, 24-hour creatinine clearance (CC) of both affected and normal kidneys were evaluated. In order to determine the difference, same evaluation was performed on the fourth week of nephrostomy placement.

Results

The mean age of the patients was 44.6 (36-54) years. The mean CC of the affected kidney was 38.8±4.9 ml/min in the first week of urinary diversion and increased to 42.5±5.4 ml/min at the end of the fourth week ($p<0.001$). All patients showed an improvement in CC levels ranging between 2.3% and 17.3% with a mean rate of 8.5±4.7%.

Conclusion

According to our results, kidney function may improve during the first month after the relief of obstruction. This improvement may be significant for borderline renal function to determine the curative treatment of an obstructed kidney

Keywords

Creatinine clearance, nephrostomy, obstructive uropathy

ÖZ

Amaç

Çalışmamızda akut/subakut tek taraflı komplet üreteral tıkanıklığa bağlı böbrek fonksiyonlarının nefrostomi ile tedavi sonrası değişimini göstermek amaçlanmıştır.

Gereç ve Yöntem

Otuz hasta prostpektif olarak çalışmaya dahil edilmiştir. Hepsinin üreter taşı olup 24'ünde (%80) üst üreter ve 6'sında (%20) orta üreter yerleşimliydi. Tüm hastaların ileri düzeyde hidronefrozu olduğu için perkütan nefrostomi takılması planlandı. Nefrostomi takıldıktan sonra 1. haftada etkilenen böbrek nefrostomiden ve diğer böbrek üretral kreatinin klirensi ölçümü ile değerlendirilmiştir. Değişikliği saptamak için de 1. ayda nefrostomi ve üretral kreatinin klirensleri hesaplanıp 1. haftadaki sonuçlar ile karşılaştırılmıştır.

Bulgular

Hastalarımızın ortalama yaşı 44,6'dır (36-54). Etkilenen böbreğin 1. haftadaki kreatinin klirensi 38,8±4,9 ml/dak iken 1. aydaki değer 42,5±5,4 ml/dk'ya yükselmiştir ($p<0,001$). Tüm hastaların kreatini klirens analizlerinde %2,3 ile %17,3 arasında artış saptanmıştır.

Sonuç

Çalışma sonuçlarımıza göre tek taraflı komplet üreteral tıkanıklığa bağlı bozulan böbrek fonksiyonu nefrostomi takılması sonrası 1. ayda 1. haftaya göre anlamlı olarak düzelmektedir. Bu düzelme böbrek fonksiyonları sınırda olan tek taraflı tıkanıklığı olan hastalarda asıl tedaviye veya nefrektomi yapmaya karar vermede etkili olacaktır.

Anahtar Kelimeler

Kreatinin klirens, nefrostomi, obstrüktif üropati

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Introduction

Intraluminal or extraluminal ureteral obstruction is the main cause of obstructive uropathy that may lead to cell death, tissue necrosis, progressive fibrosis and loss of renal parenchyma (1,2,3,4). Glomerular filtration rate (GFR) and renal blood flow (RBF) decrease with the unilateral ureteral obstruction (UUO) and progressively worsen until the obstruction is relieved. The response of the kidney to relief of UUO is species-specific and depends on age of the patient, duration and extent of obstruction, function of the contralateral kidney, and compliance of the ureter and renal pelvis (5). UUO demonstrates a triphasic pattern of RBF and ureteral pressure changes which is different from bilateral ureteral obstruction or UUO of a solitary kidney (6).

There are several studies demonstrating the effect of ureteral obstruction on renal function and the reversibility of some changes after the relief of obstruction (6). Indeed, most of the studies were on animal models and the human studies were generally retrospective studies (5,7,8). Several renal function variables, such as GFR, serum creatinine level, renal perfusion index, renal parenchyma thickness, resistive index, and scintigraphic methods were evaluated in those studies (5,7,8,9,10). Most of the human studies evaluated a heterogeneous group with different causes of ureteral obstruction, such as ureteral or pelvic stones, ureteric stricture, bladder cancer, ureteropelvic junction obstruction, etc. These diseases have different pathophysiological properties and this heterogeneity causes difficulty to reach a clear conclusion. In this study, we tried to prospectively evaluate the reversibility of renal function after relief of unilateral obstruction caused by ureteral stone in patients with a normally functioning contralateral kidney.

Material and Methods

With the permission of the local ethics committee, a total of 49 patients with UUO related to a ureteral stone were prospectively included in the study after obtaining informed consent. These were the patients who had undergone an unsuccessful attempt for ureteral stenting with double J and were referred to our hospital for percutaneous nephrostomy (PN). All patients had acute renal colic for a minimum of 5 and a maximum of 15 days before admission to our clinic. The initial evaluation included the history, clinical examination and biochemical analysis including serum creatinine level, urine analysis and culture. Radiological evaluation was performed by plain x-ray of the abdomen and urinary ultrasonography. Any patient who had a past history of renal stone, bilateral hydronephrosis, any chronic disease (diabetes, hypertension, etc.), abnormal creatinine level and hydronephrosis less than grade 3 in the affected kidney was excluded from the study that was 13 in number.

An intravenous pyelography (IVP) was performed in the remaining patients to determine the level of obstruction and evaluate the functional capability of the contralateral kidney. As all the patients were informed about the importance of early relief of obstruction, they were given the possibility of PN and a second chance for ureteral stenting. A total of 30 patients were included in the study for the evaluation of unilateral renal function (Figure 1).

At the end of the first day, the patients were discharged and recalled one week later to evaluate 24-hour creatinine clearance (CC) of the affected kidney with nephrostomy and urethral clearance separately. The patients were re-called 4 weeks later for the same evaluation. There was no significant change in the location of the stone seen on plain abdominal x-ray and urinary ultrasonography. There was no complication or complicated urinary tract infection during this follow-up period and all the patients underwent a definitive treatment with ureteroscopic lithotripsy or extracorporeal shock wave lithotripsy (ESWL) in a maximum of 6-week period after the insertion of PN.

SPSS version 16.0 was used for statistical analysis. Data in dependent groups were analyzed for normality with the Kolmogorov-Smirnov test. As our data was distributed normally, paired t-test was performed to evaluate the mean CC rates of patients at first and fourth week of PN and urethral CC.

Results

A total of 30 patients (19 male, 11 female) with a mean age of 44.6 (36-54) years were enrolled in the study. They all had a ureteral stone located in the upper ureter in 24 and at the middle ureter in 6 patients. The mean diameter of the ureteral stone (calculated as the longest diameter of the stone) was 10.2 mm (8-13 mm) on intravenous pyelography. There was no passage of radio-opaque material in the affected system with a grade 3 hydronephrosis in 9 and grade 4 hydronephrosis in 21 patients. All patients showed an improvement in CC levels ranging between 2.3% and 17.3% with a mean rate of 8.5±4.7% (Table 1).

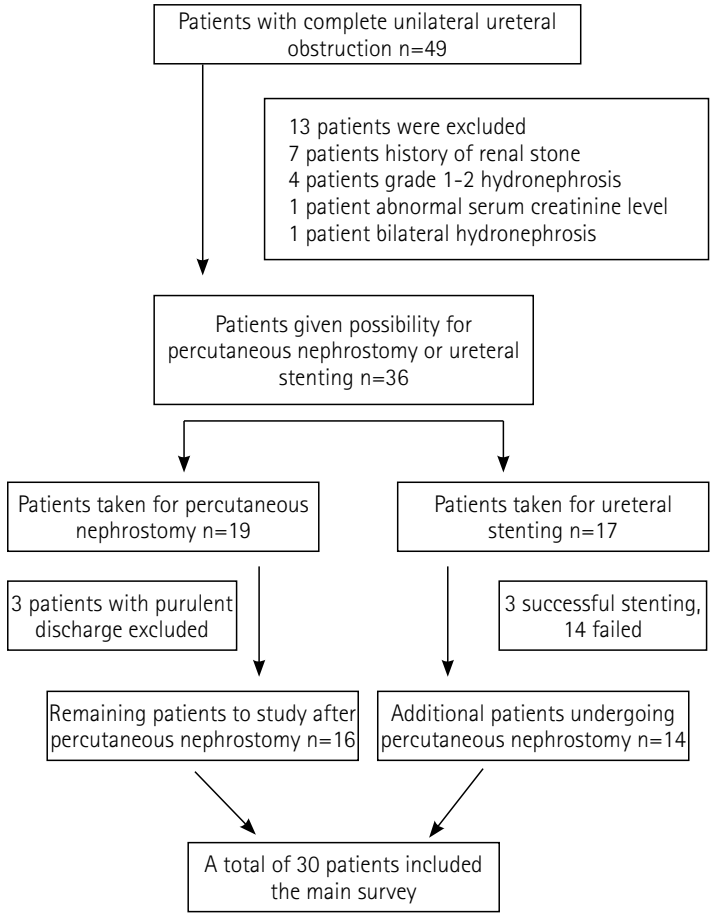

Figure 1. The diagram of study flow

There were 17 patients with CC of <40 ml/min (35.1±2.19) and 13 patients with >40 ml/min (43.6±2.74) in the first week evaluation (p<0.001). Among these groups, the mean percentage of CC improvement was 9.2±4.8% and 7.6±4.4%, respectively (p=0.339).

The mean value of separated renal function of the affected kidney was 45.94% and 48.32% in the first week and fourth week, respectively and the differences were statistically significant (p<0.001) (Table 2).

Discussion

The only way of preventing obstructive uropathy is to relieve the obstruction (8,9,10,11). Better et al. (12) evaluated the change in CC in a patient with an obstructed kidney for a duration of 3 months after relief of obstruction. The CC of the affected kidney increased from 2.6 ml/min to 10.2 ml/min at the first week after relief of obstruction and remained unchanged thereafter. Shi et al. (13) have reported the ability of a kidney to return to normal GFR 4 weeks after relief of 3-day complete UUO. However, longer obstruction might cause irreversible defects and only a partial recovery of renal function would be seen after relief of obstruction (14). In a recent experimental study, Soliman et al. (15) have reported nearly 12% increase in CC rate in dogs 32 weeks after relief of a 4-week obstruction. In another experimental study, Cochrane et al. (16) have reported that the volume density of interstitium in the renal cortex of mice with UUO for 2 and 4 weeks recovered 13% after relief of obstruction. These were all experimental animal studies. It is well-documented that the response of kidneys to UUO is species-specific and animal models may not adequately reflect the exact mechanism (6). For this reason, we tried to design a human

Table 1. The creatinine clearance rates of patients in the 1st and 4th week after relief of obstruction and the percentages of change

	Creatinine clearance in the first week (ml/min)	Creatinine clearance in the fourth week (ml/min)	The difference between the groups (ml/min)	The percentage difference between the groups (%)
Patient 1	47.8	54.1	6.3	11.6
Patient 2	32.1	33.7	1.6	4.7
Patient 3	49.3	55.7	6.4	11.5
Patient 4	43.6	48.7	5.1	10.5
Patient 5	38.5	42.5	4.0	9.4
Patient 6	33.5	39.2	5.7	14.5
Patient 7	44.7	45.8	1.1	2.4
Patient 8	38.4	40.7	2.3	5.7
Patient 9	36.7	38.1	1.4	3.7
Patient 10	32.7	39.5	6.8	17.2
Patient 11	40.7	41.6	0.9	2.2
Patient 12	36.5	39.7	3.2	8.1
Patient 13	41.6	45.7	4.1	9.0
Patient 14	36	38.5	2.5	6.5
Patient 15	45.8	52.1	6.3	12.1
Patient 16	34.1	35.7	1.6	4.5
Patient 17	44.3	50.7	6.4	12.6
Patient 18	41.6	46.7	5.1	10.9
Patient 19	35.5	40.5	5.0	12.3
Patient 20	31.5	37.2	5.7	15.3
Patient 21	42.7	43.8	1.1	2.5
Patient 22	36.4	38.7	2.3	5.9
Patient 23	36.9	38.3	1.4	3.7
Patient 24	32.5	39.3	6.8	17.3
Patient 25	40.2	41.1	0.9	2.2
Patient 26	36.5	39.7	3.2	8.1
Patient 27	41.4	45.5	4.1	9.0
Patient 28	36.2	38.7	2.5	6.5
Patient 29	33.3	39	5.7	14.6
Patient 30	44.2	45.3	1.1	2.4
Mean	38.8±4.9	42.5±5.4	3.6	8.5
		p<0.001		

Table 2. The urethral creatinine clearance and the separated function of the affected kidney rates (ratio of affected kidney creatinine clearance to total creatinine clearance) in the 1st and 4th week after relief of obstruction

	Urethral creatinine clearance in the first week (ml/min)	Urethral creatinine clearance in the fourth week (ml/min)	Separated renal function of the affected kidney in the first week (%)	Separated renal function of the affected kidney in the fourth week (%)
Patient 1	48.3	47.8	49.80	53.09
Patient 2	39.4	41.2	44.89	44.99
Patient 3	52.6	52.9	48.38	51.28
Patient 4	49.1	48.6	47.03	50.05
Patient 5	45.3	46.1	45.90	52.03
Patient 6	43.7	44.5	43.39	46.83
Patient 7	48.2	47.6	48.11	49.03
Patient 8	42.6	42.9	47.40	48.62
Patient 9	43.5	44.1	45.81	46.81
Patient 10	45.1	44.4	42.03	47.07
Patient 11	43.2	42.5	48.51	49.46
Patient 12	43.6	44.1	45.56	47.37
Patient 13	47.3	47.6	46.79	48.98
Patient 14	41.3	41.8	46.57	47.94
Patient 15	54.2	53.5	45.80	49.33
Patient 16	41.3	41.6	45.22	46.18
Patient 17	52.4	52.7	45.81	49.03
Patient 18	48.2	48.9	46.32	48.84
Patient 19	45.6	45.1	43.77	47.31
Patient 20	41.3	42.5	43.26	46.67
Patient 21	45.6	45.1	48.35	49.26
Patient 22	43.2	44.3	45.82	46.62
Patient 23	42.3	41.6	46.59	47.93
Patient 24	45.6	44.1	41.61	47.12
Patient 25	43.1	42.5	48.25	49.12
Patient 26	43.1	43.8	45.85	47.54
Patient 27	52.3	51.1	44.18	47.10
Patient 28	41.1	40.4	46.83	48.92
Patient 29	43.6	44.1	43.30	46.93
Patient 30	49.2	48.4	47.32	48.34
Mean	45.51±3.8	45.52±3.6	45.94±1.99	48.32±1.75
		p=0.909		p<0.001

study evaluating the response of kidneys to the relief of UUO. To our knowledge, this is the first study evaluating relief of acute/subacute UUO in such number of cases (30 patients) with prospective design.

Gillenwater has concluded that the best method for determining the absolute degree of injury and recoverability was to relieve the obstruction with PN and monitoring the renal function by CC (17). Hussain et al. (18) have also investigated the most reliable method for determining the future recovery of renal function after relief of obstruction and concluded that PN with CC had 97.8% accuracy for this evaluation. In the present study, the mean rate of increase in CC in this period was 8.5%. Although this improvement rate varied, all patients showed somehow an increase in the CC rate of their affected kidney. Our results are compatible with the literature. Khalaf et al. (9) have investigated the recoverability of renal function in 91 patients after relief of chronic unilateral obstruction. They have used GFR for the evaluation of renal function and found an improvement in 63.7% of patients whereas 32% of patients had further deterioration after relief of obstruction. Different from our study, the authors have evaluated a heterogeneous group of patients with ureteric stricture, renal and ureteral stones, and ureteropelvic junction obstruction. Beside this, it has been pointed out that 25 of 91 (27.5%) patients in the study group had a GFR of <10 ml/min/1.73 in whom the recovery of renal functions was rarely expected. In another study, Shokeir et al. (19) have evaluated recovery of renal functions in 32 patients with complete obstruction with a non-functioning or absent contralateral kidney. They used serum creatinine level for determining the recovery

and reported a significant decrease in creatinine levels after relief of obstruction. This was also observed in our study.

Patient age is one of the factors that was found to be related with recovery rate (20). The conclusion on the importance of patients' age for the recovery of UUO comes from the studies of the treatment of ureteropelvic junction obstruction, a congenital chronic disease. Mikkelsen et al. (21) have reported that 30 years was the limit of age to expect a significant improvement in renal functions after the treatment of ureteropelvic junction obstruction. According to our knowledge, there is no age-specific evaluation for the relief of complete obstruction related to ureteral stones. In our study, we were not able to find any significant difference in terms of recovery of renal function between patients who were <45 years and >45 years of age. Although the difference in recovery rates between these groups was not significant, we observed a higher rate of recovery in patients who were younger. Similar finding were observed between the groups who had CC rates of <40 ml/min and >40 ml/min. Patients who had a CC rate of <40 ml/min had higher percentage of clearance improvement, but it was not statistically significant. For that reason, large number of patients may be needed to make an exact evaluation of the importance of age and CC.

One of the limitations of our study was the chronicity of ureteral obstruction. We were not able to determine the exact time of obstruction, but the CC of affected kidneys was over 35 ml/min in all patients. Although we cannot make a clear conclusion, this may give an idea that the obstruction was acute or subacute in most of our patients. The second limitation was about the severity of obstruction. We could not show that the obstruction in our patients was totally complete obstruction but the radiological evaluation brought out the idea that the obstruction was severe that we could not visualize contrast in the distal ureteral segment of obstruction. In our study, since all the subjects, who were taken PN for obstruction, had other chronic severe diseases (cancer, hypertension, infection, chronic obstruction etc.), we could not make up a control group. Therefore we compared the separate renal functions with two subsequent measurements. Another limitation of our study was that we did not evaluate the immediate renal function of patients at the time of relief of obstruction and we were not able to document possible recovery after the 4th week of the obstruction. The early evaluation of CC just after relief of obstruction may cause bias due to rapid physiological changes caused by relief of obstruction. In order to avoid this possible bias, we found it more acceptable to evaluate the renal functions at the first week of relief of obstruction. All patients had curative treatment after 4 weeks, for this reason, we were not able to evaluate the CC rates of the affected kidneys after 4 weeks of follow-up. In the literature, there are some studies reporting that a 4-week follow-up might be sufficient to evaluate the recovery of renal functions. Deng et al. (22) evaluated improvement of renal function in patients with ureteropelvic junction obstruction after insertion of nephrostomy and reported that paranchymal thickness increases in 4 weeks and tubular function returns to nearly normal levels in this period. In another study, Shokeir et al. (20) evaluated renal resistive index and reported that at the first week of relief of obstruction, the mean resistive index significantly decreased and stabilized till to the 4th week. According to these studies, we believe that a 4-week follow-up was enough to document recovery of renal functions after relief of obstruction.

Conclusion

Renal function of an obstructed kidney is the main determinant of the possible treatment opportunities. In order to decide the best treatment modality, evaluation of renal functions becomes very important. Although Khalaf et al. (9) have reported that renal damage was irreversible in patients with a GFR less than 10 mL/min/1.73 m^2, there are plenty of patients with intermediate functions that may lead to unnecessary indications for nephrectomy. Similar to the limited number of human studies, we found a significant increase in functional status of an obstructed kidney after relief of obstruction. According to our results, kidney function may improve by one month after relief of obstruction, thus, it may be reasonable to wait for determining the curative treatment of an obstructed kidney.

Ethics

Ethics Committee Approval: The study were approved by the Marmara University of Local Ethics Committee, Informed Consent: Consent form was filled out by all participants. Peer-review: Internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Cenk Murat Yazıcı, İlker Tinay, Tufan Tarcan, Concept: Cenk Murat Yazıcı, Tufan Tarcan, Design: Cenk Murat Yazıcı, Tufan Tarcan, Data Collection or Processing: Cenk Murat Yazıcı, İlker Tinay, Analysis or Interpretation: Cenk Murat Yazıcı, Tufan Tarcan, Literature Search: Hasan Hüseyin Tavukçu, Writing: Hasan Hüseyin Tavukçu, Cenk Murat Yazıcı. 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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