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The Effect of Retrograde Intrarenal Surgery on Kidney Function in Renal Stone Treatment

Böbrek Taşı Tedavisinde Retrograd İntrarenal Cerrahinin Böbrek Fonksiyonuna Etkisi

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ABSTRACT

Aim: In this study, we aimed to evaluate the alteration in renal function by analyzing the estimated glomerular filtration rate after Retrograde Intrarenal Surgery, and present the factors which have an impact on alteration.
Methods: We analyzed 88 patients who underwent RIRS for renal stones between May 2018 and February 2019, prospectively. Estimated glomerular filtration rate was calculated by modification of diet in renal disease (MDRD) formula preoperatively, on the first postoperative day, on the first postoperative month and the third postoperative month. All data was recorded on the follow-up form. All procedures were performed under general anesthesia.
Results: The stone-free rate of the study was 79.5%. Preoperative eGFR was 99.86 mL/min/1.73m^2 for the study group. The eGFR was calculated 101.80 mL/min/1.73m^2 on the first postoperative day and 111.66 mL/min/1.73m^2 on the third-month follow-up. The change in eGFR was 1.94 mL/min/1.73m^2 in the early period and 11.8 mL/min/1.73m^2 in the long-term follow-up period. There was a statistically significant improvement in eGFR in the long-term follow-up period than the early period when compared to preoperative renal function.
Conclusion: On the contrary of former stone removal modalities, RIRS can stabilize postoperative kidney function. It may even help improve postoperative kidney function in patients with preoperative renal dysfunction. Urologists may keep in mind the RIRS option in patients with this condition.

Keywords: ureteroscopy, lithotripsy, kidney, function

ÖZ

Amaç: Bu çalışmada, Retrograd İntrarenal Cerrahi sonrasında eGFR'yi analiz ederek böbrek fonksiyonundaki değişikliği değerlendirmeyi ve değişikliği etkileyen faktörleri sunmayı amaçladık.
Yöntem: Mayıs 2018 ile Şubat 2019 arasında böbrek taşı nedeniyle RIRS yapılan 88 hastayı prospektif olarak analiz ettik. eGFR, ameliyat öncesi, ameliyat sonrası ilk gün, ameliyat sonrası ilk ay ve ameliyat sonrası üçüncü ayda MDRD formülü ile hesaplandı. Tüm veriler takip formuna kaydedildi. Tüm işlemler genel anestezi altında yapıldı.
Bulgular: Çalışmanın taşsızlık oranı %79,5 idi. Preoperatif eGFR 99,86 mL/dak/1.73m$_2$ idi. eGFR, postoperatif ilk günde 101.80 mL/dak/1,73m^2 ve üçüncü ay takibinde 111,66 mL/dak/1,73m^2 olarak hesaplandı. eGFR'deki değişiklik erken dönemde 1,94 mL/dak/1,73m^2 ve uzun dönem takip döneminde 11,8 mL/dak/1,73m^2 idi. Üçüncü ay takiplerinde preoperatif böbrek fonksiyonuna göre ve erken döneme göre eGFR'de istatistiksel olarak anlamlı bir iyileşme vardı.
Sonuç: Eski taş çıkarma yöntemlerinin aksine RIRS, postoperatif böbrek fonksiyonunda stabilizasyon sağlayabilmektedir. Hatta preoperatif böbrek fonksiyonu bozuk olan hastalarda operasyon sonrası böbrek fonksiyonlarında düzelmeye yardımcı olabilmektedir. Ürologlar, ameliyat sonrası böbrek fonksiyonlarında iyileşme olmasını istedikleri hastalarda RIRS seçeneğini akılda tutabilirler.

Anahtar Kelimeler: üreteroskopi, litotripsi, böbrek, fonksiyon

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INTRODUCTION

Shock wave lithotripsy (SWL), retrograde intrarenal surgery (RIRS) and percutaneous nephrolithotomy (PNL) are the recommended interventions for urinary system stones, depending on the localization and size of the stone. Beside the stone's characteristics, the anatomic features of the kidney influence the decisions regarding disease management [1]. The purpose of the treatment is to achieve high stone-free rates, avoiding surgical complications. Although SWL is a minimally invasive option, the need for multiple sessions and low success rates for the stones located in lower calyx, are the common disadvantages. Additionally, possible complications such as renal hematoma may lead to death [2].

The favourite modality for larger stones is PNL, which may lead to parenchymal damage when the surgeon has to make multiple punctures to access the collecting system during the procedure, and that may also result in a decrease in renal function. Furthermore, PNL may result in some severe surgical complications [3, 4]. As a result, RIRS has been accepted as a minimally invasive treatment for urinary system stones because of few surgical complications and the fact that these are low grade. It has therefore increased in popularity among urologists, even for larger stones, because of its high success rate and that it offers more comfort for the patients.

Several studies evaluated the glomerular filtration rate alteration after PNL or SWL. The results showed that renal functions did not deteriorate in the mid or long term after the intervention, echoing the data in the literature which revealed that resolving the obstruction in the kidney improved the renal function, when compared to preoperative status. However multiple punctures during PNL could have some adverse effects on renal functions [4-8].

Flexible ureteroscopes and laser fibers were designed for use under irrigation fluids. Ureteral access sheaths (UAS) were used to facilitate the manipulation of ureteroscopes and laser fibers, and also provide a stable fluid pressure in the renal collecting system [9]. However stone burden, residual stone fragments and hemorrhage during the procedure may reduce the discharge of the irrigation fluid, and result in higher intrarenal pressure than required. High pressure leads to renal calyceal distension which may cause renal functional deterioration [10]. The other possible reason for renal malfunction is the direct damage of the laser energy to the renal parenchyma when dusting the stone in calyces [11].

In this study, we aimed to evaluate the alteration in renal function by analyzing the estimated glomerular filtration rate (eGFR) after RIRS and present the factors which have an impact on alteration.

MATERIAL AND METHOD

After the approval from the institutional review board (Decision Number: 2017-KAEK-189_2018.05.30_13), we analyzed 88 patients who underwent RIRS for renal stones between May 2018 and February 2019 prospectively. Patients who have prior double J catheter (DJ), solitary kidney, a history of chronic renal failure, concomitant ureteral stone, ureteral stricture or urinary tract anomaly and missing data during follow-up, were excluded from the study. All patients were evaluated with non-contrast computerized tomography (CT) preoperatively and postoperatively. Patients with stones located in different sites of the kidney were investigated by complete blood count, urine analysis, urine culture, urea, creatinine and routine biochemical tests before the operation. The characteristics of the stone and the patient were recorded on the follow-up forms. The sum of all longest dimensions of all stones was recorded as the stone size in case of multiple stones. The stone density was assessed by the CT in Hounsfield Unit (HU). The time between starting endoscopy and end of DJ stent insertion was defined as operation time. Estimated glomerular filtration rate (eGFR) was calculated on the day before the surgery, by modification of diet in renal disease (MDRD) formula:

(eGFR $=175 \times (\text{Serum creatinine})^{-1.154} \times (\text{age})^{-0.203}$ x0.742 [if female]x1.212 [if Black]).

The calculation was repeated on the post-operative first day, on the post-operative first month and the post-operative third month. All data

were recorded on the follow-up form. The patients were treated with appropriate antibiotics when a urinary tract infection was diagnosed, and all interventions were performed after a sterile urine culture obtained.

Informed consent was obtained from all patients. Intravenous first-generation cephalosporin was administered 30 minutes before the surgery for the surgical prophylaxis. All procedures were performed under general anesthesia. First, the surgeon accessed the ureter by a 9.5 F ureteroscope (Karl Storz®, Tuttlingen, Germany) for a safe dilatation under the guidance of a guidewire. The 7.5 F ureteroscope was used to reach the stone in the RIRS procedure. Ureteral access sheath (Elite Flex®, Ankara, Turkey) was placed in the ureter in all RIRS cases. A 7.5 F flexible ureteroscope (Flex-X2®, Karl Storz, Tuttlingen, Germany) was used for RIRS. A 200 mm laser fiber (Ho YAG Laser; Dornier MedTech®; Munich, Germany / Dornier Med-Tech GmbH, Medilas H20 and HSolvo, Wessling, Germany) was used for laser lithotripsy. The energy of the laser was between 0,8 – 1,5 Joule and 8 – 15 Hz. At the end of the operation, a ureteral stent was placed in all patients. Operation time was defined from the beginning of cystoscopy to the end of ureteral stent placement. Intraoperative data were recorded and patients who had no complication were discharged on the postoperative first day.

All patients were checked with a complete blood count, urine analysis and biochemical tests perioperatively. On the first month follow-up, in cases of no residual stone fragments requiring auxiliary interventions, the DJ catheter was displaced after the patient was examined and checked with an X-Ray. All laboratory and screening findings were recorded in the follow-up form. The patients were monitored with CT and routine laboratory tests on the third-month follow-up. The follow-up period for all patients was a minimum of three months after surgery.

All analyses were carried out using the SPSS 25.0 statistical software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). The data distributions were evaluated using the Kolmogorov-Smirnov test. In case of discordance between the graphics and test results, skewness and kurtosis values were considered. Comparisons of preoperative eGFR and postoperative eGFR were performed by paired samples t-test. Other numerical data were analyzed using Student's t-test and for categorical data, the chi-square tests were used. The possible influencing factors (age, gender, hydronephrosis, obstruction, stone location, stone volume, stone density, preoperative creatinine level) on renal functional alterations, were analyzed with binominal regression analyses; $p<0.05$ was considered as statistically significant.

RESULTS

The study population consisted of 88 patients, 54 (61.4%) of whom were males and 34 (38.6%) were females. The mean age of the patients was 46.43 ± 14.768 years-old, and the mean body mass index (BMI) was 28.20 ± 5.64. Twenty-one patients had comorbid diseases such as hypertension, diabetes mellitus, coronary artery disease, chronic respiratory disease and others. The mean stone volume was 751.86 ± 689.00 mm3. The demographic data of the patients and stone characteristics are shown in Table 1.

The stone-free rate of the study was 79.5%. Totally 14 (15.9%) patients had surgical complications which were mostly low-grade. Only two patients required surgical intervention: one for DJ catheter migration and one for renal colic because of steinstrasse. The operation outcomes are shown in Table 1.

Preoperative mean eGFR was 99.86 ± 2.55 mL/min/1.73m^2 for the study group. Mean eGFR was calculated 101.80 ± 2.66 mL/min/1.73m^2 on the first postoperative day and 111.66 ± 2.34 mL/min/1.73m^2 on the third-month follow-up. Mean change in eGFR was 1.94 ± 15.66 mL/min/1.73m^2 in the early period and 11.8 ±14.58 mL/min/1.73m^2 in the long-term follow-up period. There was a statistically significant improvement in eGFR in the long-term follow-up period than the early period, when compared to preoperative renal function ($p=0.023$). Twenty patients had improvement and only three patients had a deterioration of their chronic kidney disease stage. The comparison of eGFR alteration and renal functional outcomes preoperative and postoperative periods are shown in Table 2 and 3.

Table 1. Characteristics Of Patients and Stones and Operation Outcomes

Parameters	n=88
Age (year)	46.43 ± 14.768
Gender (n,%) Male Female	 54 (61.4%) 34 (38.6%)
Comorbidity (n,%) Hypertension Diabetes Mellitus Coronary Artery Disease Chronic Respiratory Disease Other	 6 (6.8%) 7 (8.0%) 3 (3.4%) 1 (1.1%) 4 (4.5%)
Obstruction (+/-) (n,%)	47 (53.4%)/41 (46.6%)
Hydronephrosis (n,%) No Grade 1 Grade 2 Grade 3 Grade 4	 41 (46.6%) 13 (14.8%) 30 (34.1%) 4 (4.5%) 0 (0%)
Stone Localization (n,%) Upper Calyx Middle Calyx Lower Calyx Renal Pelvis Ureteropelvic Junction Multicaliceal	 6 (6.8%) 7 (8.0%) 18 (20.5%) 31 (35.2%) 17 (19.3%) 9 (10.2%)
Number Of Stones	1.50 ± 0.87
Stone Volume (mm^3)	751.86 ± 689.00
Operation Time (minute)	67.33 ± 34.82
Fluoroscopy time (second)	16.18 ± 12.62
Hospitalization (day)	1.44 ± 2.18
Stone-free (%)	79.5%
Complication (n,%) Grade I Grade II Grade III Grade IV Grade V	 8 (9.1%) 4 (4.5%) 2 (2.2%) 0 (0%) 0 (0%)
Mean Pre-operative eGFR (mL/min/1.73m^2)	99.86 ± 2.55
Mean Post-operative 1st Day eGFR (mL/min/1.73m^2)	101.80 ± 2.66
Mean Post-operative 3rd Month eGFR (mL/min/1.73m^2)	111.66 ± 2.34

BMI: Body Mass Index; eGFR: Estimated Glomerular Filtration Rate

The multinominal regression analysis revealed that the higher preoperative creatinine levels (p=0.001) and female gender (p=0.018) were predictive factors for improvement after RIRS. The absence of obstruction had a negative correlation with deterioration after RIRS (p=0.021).

Table 2. Comparison of eGFR Alteration During Follow-Up

	Follow-Up Period		eGFR Change	p
Mean eGFR (mL/min/1.73m^2)	Pre-operative	Postoperative 1st day		
	99.86 ± 2.55	101.80 ± 2.66	1.94 ± 15.66	0.247
	Preoperative	Postoperative 3rd month		
	99.86 ± 2.55	111.66± 2.34	11.8 ± 14.58	p=0.023

eGFR: Estimated Glomerular Filtration Rate

Table 3. Renal Function Analysis

	Preoperative	Postoperative 3rd month
Group (n,%) Stage I Stage II Stage III Stage IV Stage V	 61 (69.3%) 22 (25%) 4 (4.5%) 1 (1.1%) 0 (0%)	 74 (84.1%) 13 (14.7%) 1 (1.1%) 0 (0%) 0 (0%)
CKD Stage Improvement (n,%)		20 (22.7%)
CKD Stage Deterioration (n,%)		3 (3.4%)

CKD: Chronic Kidney Disease

DISCUSSION

There are several reasons specified for renal failure. In a meta-analysis, it is reported that urinary obstruction precipitates urinary tract infections. The harmful metabolites during infection result in damage to renal parenchyma and compromise renal function. The other point stated in the research are the effects of surgical treatment. Open surgery may directly damage the renal tissue, which deteriorates the kidney function. Endoscopic urinary system stone treatment may increase the intrarenal pressure and lead to pyelovenous reflux, which deteriorates the urine flow.

Increased intrarenal pressure may result in increased renal vascular resistance. In addition, age, gender and genetics have a role in kidney diseases [12, 13]. Urolithiasis is one of the factors leading to infection, obstruction and surgery; thus, numerous studies have evaluated the relationship between urinary system stone diseases and renal function. The other focus has been the alteration of renal function after stone treatment.

Resolving the obstruction enhances the urine flow, decreases the intrarenal pressure and improves renal function; in addition, removing the stone in the tract eliminates the obstruction and the triggered infection, thus ameliorating the kidney function [11, 14]. On the other hand, a recent study reported that there was no alteration at the molecular level after the operation [15]. One of the limited number of studies conducted for the evaluation of the relationship between flexible ureteroscopy and renal function, reported that acute kidney injury was observed in one patient (0.06%) and only 5 (3%) patients had deteriorated renal function on the first postoperative day [16]. A review about the impact of urinary stone removal on renal function reported that alteration in the early period was transient and usually negligible, however it was more evident when the patients were evaluated with molecular markers [11]. The outcomes of this study are compatible with the literature and showed no statistically significant alteration in renal function on the postoperative first day (p=0.247).

Renal functions may be more stable in the late-term evaluation because early-term evaluation may be influenced by many postoperative metabolic factors. Demirtas et al. revealed that the kidney functions decreased in the very early hours after surgery then recovered in the late-term follow-up [17]. Reeves et al. reported that kidney functions for all CKD group patients improve in long term follow-ups; however increase in CKD group II, IIIa and IIIb patients were statistically significant, but others were not [18]. Desai et al. stated that all patients in their study had a stable renal function at the three months follow-up [19]. Similar to the literature, we observed a statistically significant improvement in eGFR at the three-month follow-up, compared to preoperative levels in our study (p=0.023). Assessment of renal function after an intervention has been widely studied in the literature. Hoarau et al. stated that they encountered a change towards a better CKD stage in 23 patients (14.1%) and worse in 8 (4.9%) after stone removal. In another study, Lee et al. reported that only 5.9% of patients in their cohort had improved eGFR [20]. In this study, twenty patients (22.7%) improved eGFR and CKD stage at third month, while only three (3.4%) deteriorated and 65 (73.9%) remained stable. Although we observed three deteriorations, none of them needed dialysis and all of them were CKD stage I patients who had worsened into CKD stage II. Renal functions improvement in our study was higher than reported in the literature because previous researchers did not use UAS and place the DJ stent routinely; they also had patients with renal insufficiency and multiple procedures while we did not include these group of patients in our research.

The multinominal regression analysis revealed that preoperative renal failure and female gender were the predictive factors for improvement on renal function. On the other hand, the absence of urinary tract obstruction was negatively correlated with renal function deterioration. Piao et al. reported that female gender was a predictive factor of renal function improvement on the third month follow-up and explained this difference by stating that the female hormones had inhibitor roles during the inflammatory processes [21]. The other predictive factors reported in the literature were pre-existing chronic kidney disease, setting off multiple procedures [11, 16]. Reeves et al. stated that none of the factors such as age, preoperative eGFR, stone size and operative time were found to be significant predictors [18].

Limitations of the study: Although there is a lack of articles in the literature evaluating the renal function change in patients with urinary system stones after the intervention, we conducted this study to assess renal function. Nonetheless, our study has some limitations: single-center design of the study, a relatively small number of patients and using the only eGFR as the assessment tool of renal function. A large patient population should be evaluated with various assessment tools to

obtain more reliable results.

Conclusion: Retrograde intrarenal surgery and laser lithotripsy are safe and efficient treatment options in patients with renal stone. They allow high stone removal and low complication rates, and all patients are discharged the same day of the operation, when no complication is encountered. To the contrary of former stone removal modalities, RIRS can stabilize postoperative kidney function and it may even help improve postoperative kidney function in patients with preoperative renal dysfunction. Urologists may keep in mind the RIRS option in patients in this condition. However, multicenter, prospective randomized controlled trials with a large population are necessary to confirm the results of our study.

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