Araştırma Makalesi (Research Article)

Early and Late Effects of Percutaneous Nephrolithotomy on Renal Functions According to Basal Renal Function Reserve

Bazal Böbrek Fonksiyon Rezervine Göre Perkütan Nefrolitotominin Böbrek Fonksiyonları Üzerine Erken ve Geç Etkileri

Murat SAHAN[1], Mehmet Erhan AYDIN[2], Serkan YARIMOGLU[1], Omer KORAS[3], Salih POLAT[4], Fatih GOKALP[3], Serdar CELIK[1]

[1] HSU Izmir Bozyaka Training and Research Hospital, Department of Urology, Izmir, Turkey.
[2] Dr.Yasar Eryilmaz Dogubayazit State Hospital, Department of Urology, Agri, Turkey
[3] Hatay University Faculty of Medicine, Department of Urology, Hatay, Turkey.
[4] Amasya University Faculty of Medicine, Department of Urology, Amasya, Turkey.

Özet

Amaç: Bu çalışmada, perkütan nefrolitotominin böbrek fonksiyonları üzerindeki erken ve geç etkisini ve preoperatif glomerular filtrasyon hızı düzeylerine göre araştırmayı amaçladık.

Gereç ve Yöntemler: Ocak 2014 ve Kasım 2018 arasında perkütan nefrolitotomi uygulanan 345 hasta çalışmaya dahil edildi. Preoperatif glomerular filtrasyon hızına göre hastalar üç gruba ayrıldı: Grup-1 glomerüler filtrasyon hızı>90, Grup-2 glomerüler filtrasyon hızı=60-90, Grup-3 glomerular filtrasyon hızı <60 seviyelerindeki hastalardan oluşmaktaydı. Glomerüler filtrasyon hızı ölçümleri ameliyat öncesi, postoperatif 1. gün ve 3. ayda yapıldı.

Bulgular: Postoperatif 1. günde, ortalama glomerüler filtrasyon hızı grup 1 ve grup 2'de anlamlı olarak azalmışken, grup 3'te anlamlı olarak azalmıştı. Üçüncü aydaki ortalama glomerüler filtrasyon hızı, grup 1 ve grup 2'de preoperatif düzeylere göre anlamlı olarak artmazken, grup 3 de ortalama glomerüler filtrasyon hızı preoperatif düzeylere göre istatistiksel olarak anlamlı derecede artmıştı.

Sonuç: Glomerular filtrasyon hızı, böbrek fonksiyonlarının iyi bir göstergesidir ve perkütan nefrolitotomi prosedüründen önemli ölçüde etkilenir. Böbrek travma prosedürü nedeniyle perkütan nefrolitotomi sonrası böbrek fonksiyonu azalmış olsa da böbrek taşı nedeniyle ameliyat olan hastalarda postoperatif 3. ayda böbrek fonksiyonu iyiye gider. Bu nedenle perkütan nefrolitotomi, böbrek taşına bağlı preoperatif glomerular filtrasyon hızı<60 olan hastalarda böbrek fonksiyonlarını önemli ölçüde iyileştirir.

Anahtar kelimeler: Böbrek taşı, Glomerular filtrasyon hızı, Kreatinin klirensi, Perkutan nefrolitotomi

Abstract

Objective: In this study, we aimed to investigate the early and late effect of percutaneous nephrolithotomy on renal function based on preoperative glomerular filtration rate levels.

Material and Method: Between January 2014 and November 2018, 345 patients who underwent percutaneous nephrolithotomy were included. According to the preoperative glomerular filtration rate, patients were divided into three groups: group 1 was consist of glomerular filtration rate >90 levels; group 2 was consist of glomerular filtration rate levels between 60-90; group 3 was consist of glomerular filtration rate <60 levels. Glomerular filtration rate measurements were performed preoperatively, at post-operative 1st day and 3rd month.

Results: On postoperative 1st day, mean glomerular filtration rate was significantly decreased in group 1 and group 2, non-significantly decreased in group 3. At 3rd month, the mean glomerular filtration rate was again increased compared to preoperative levels in group 1 and group 2 but this time it was statistically non-significant. However, mean glomerular filtration rate of group 3 was statistically significantly increased compared to preoperative levels.

Conclusions: Estimated glomerular filtration rate, as a better indicator of renal function, is significantly affected by the percutaneous nephrolithotomy procedure. Although, firstly renal function decreased after percutaneous nephrolithotomy because of the renal trauma procedure, kidney function is better at postoperative 3rd month because of the disappearance of kidney stone. So percutaneous nephrolithotomy was significantly improved the renal functions in patients with preoperative glomerular filtration rate <60 due to renal stone.

Keywords: Creatinine clearance, Glomerular filtration rate, Percutaneous nephrolithotomy, Renal stone

Yazışma Adresi: Serkan YARIMOGLU HSÜ İzmir Bozyaka Eğitim ve Araştırma Hastanesi Üroloji AD, Saim Çıkrıkçı Caddesi, Posta Kodu: 35170 Karabağlar / İzmir /Türkiye

Telefon: +905558745789, **Mail:** serkanyarimoglu@gmail.com

ORCID No (Sırasıyla): 0000-0002-3528-7449, 0000-0002-3567-9987, 0000-0002-0065-4245, 0000-0001-9749-5254, 0000-0002-7580-6872, 0000-0003-3099-3317, 0000-0003-0939-9989

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INTRODUCTION

The incidence of adult renal stone disease is increasing over time, with prevalence of 2-20% worldwide (1). It is certain that urinary tract stone disease causes different degrees of renal dysfunction based on infective and obstructive mechanisms. In addition, chronic diseases such as hypertension, diabetes mellitus, and metabolic syndrome, which are associated with urinary tract stone disease, also affect renal function negatively (2). So, the treatment method for stone disease should have minimum effect on kidney function. Several studies reported that minimally invasive surgical techniques used in the treatment of kidney stones are superior to open surgical techniques due to their effect on renal function (3).

Percutaneous nephrolithotomy (PCNL) is an effective and safe, minimally invasive surgical option in patients with large and/or complicated renal calculi (4). The effect of PCNL on renal function was evaluated in many studies. However, studies about the effect of PCNL on renal function are inadequate and the results are contradictory. Although it was reported that glomerular filtration rate (GFR) may decrease during the first hours after tract dilation in animal models (5), there is insufficient data for humans. The long-term impacts of PCNL on GFR were evaluated in several studies. The hole created in the kidney, complications such as bleeding during PCNL and the removal of stones from the kidney with PCNL is not known how the effect GFR in early and late period.

In this study, we aimed to evaluate the early and late effect of PCNL on renal function based on preoperative GFR levels.

MATERIALS AND METHODS

Seven hundred and ninety-four patients undergoing PCNL at single center between January 2014 and November 2018 were retrospectively reviewed. The study was carried out at the Department of Urology, faculty of medicine, Ministry of Health University Izmir Bozyaka Training and Research Hospital. The study was approved by the Ethic Committee of Amasya University (2021/1680). Four hundred and forty-three patients under 18 years, with anatomic or functional solitary kidneys, who had bilateral kidney stones or received transfusion during surgery or after the procedure, with hemodynamic changes during operation, prescribed nephrotoxic drugs, with tubeless or double J insertion procedures or who had missing data were excluded from the study. According to preoperative GFR, patients were divided into three groups: group 1 consisted of GFR >90 ml/min; group 2 consisted of GFR levels between 60-90 ml/min; and group 3 consisted of GFR <60 ml/min.

After general anesthesia, a 5 or 6 F ureteral catheter was inserted and fixed to a Foley catheter. PCNL was performed in prone position. Access was obtained under fluoroscopy using an 18-gauge needle, and tract was dilated with Amplatz dilatators to 30 F caliber. Stone fragmentation was accomplished using a pneumatic lithotripter (Vibrolith; Elmed, Ankara, Turkey). At the end of the procedure, 14 F nephrostomy tube was inserted, and antegrade pyelography was performed. Patient demographics (age, gender, body mass index) and perioperative data were recorded by the surgeon immediately postoperatively. Perioperative data included operation side, stone burden, number of percutaneous tracts, surgery time, length of stay and estimated blood loss. Also, postoperative complications were noted according to the Clavien scoring system (6). Postoperative pain control was achieved with narcotic analgesics for all patients. Nonsteroidal anti-inflammatory drugs were not used in the perioperative and postoperative period for all patients. Ceftriaxone was given as prophylaxis before the operation and continued until the nephrostomy tube was removed. Nephrotoxic drugs were not used before, during, or after the operation in all patients.

Preoperative, postoperative at 1st day and 3rd month after operation, serum creatinine was obtained from the hospital records of the patients. Creatinine clearance was calculated with the Cockcroft–Gault formula (7).

Statistical Analysis

Data were analysed using the Statistical Package for Social Sciences, version 20.0 (SPSS, Chicago, Ill) software program. Categorical data was presented as numbers and collum percentages. Continuous data was evaluated by Kolmogorov-Smirnov test to verify the normality of distribution of variables. Not normally distributed data was presented with median and IQR (25-75th) and Kruskal-Wallis test was used for comparison of CKG groups. Pearson Chi-square and Exact test analyses were used to compare the groups. Two related non-normally distributed data were compared with Wilcoxon test. Statistical significance was defined as $p<0.05$.

RESULTS

A total of 345 cases were included in this study. The number of patients in group-1, group-2, and group-3 were 98, 172, and 75 respectively. Demographic and operation data are shown in **Table 1.** There were no statistically significant differences between demographic data, blood loss, stone burden, stone density, surgery time and numbers of access. Median (25-75th) preoperative GFR levels in group-1, group-2 and group-3 were 101.1 (96.4-111.5) ml/min/1.73 m^2, 76.1 (68.3-82.1) ml/min/1.73 m^2 and 51.2 (44.8-56.7) ml/min/1.73 m^2, respectively.

A transitional decrease in GFR was observed on the 1st day after operation, but after that it increased gradually. In group-1 and group-2, GFR decreases were statistically significant on the 1st day after operation compared to preoperative GFR values ($p<0.001$). But in group-3, GFR decrease was not statistically significant on the 1st day after operation compared to preoperative GFR values ($p=0.138$) **(Table 2)**.

In the 3rd month, mean GFR was decreased compared to preoperative levels in group 1 and group 2 but it was not statistically significant (0.074 and 0.129 respectively). However, the GFR levels rose above preoperative levels in the 3rd month postoperative after PCNL ($p=0.033$) **(Table 3)**. eGFR results of the groups were shown in **Figure 1.**

Table 1. Demographic and perioperative data				
	Group-1 (N:98)	**Group-2 (N:172)**	**Group-3 (N:75)**	***p* value^**
Age, Years	46 (34.75-56)	49.5 (40.25-57)	52 (36-60)	0.076
BMI, kg/m2	26.2 (22.6-29.4)	25.7 (22.9-29.3)	27.3 (23.0-29.4)	0.411
Gender, n (%)				
Female Male	34 (34.7) 64 (65.3)	63 (36.6) 109 (63.4)	32 (42.7) 43 (57.3)	0.538*
Metabolic Syndrome, n (%)	12 (12.2)	14 (8.1)	13 (17.3)	0.104*
No. Side, n (%)				
Left Right	50 (51.0) 48 (49.0)	83 (48.3) 89 (51.7)	31 (41.3) 44 (58.7)	0.434*
Stone Localization, n (%)				
Single Kalix or Pelvis Partial Staghorn Staghorn Multiple	36 (36.7) 18 (18.4) 12 (12.2) 32 (32.7)	65 (37.8) 28 (16.3) 24 (14.0) 55 (32.0)	22 (29.3) 17 (22.7) 14 (18.7) 22 (29.3)	0.717*
Number of Accesses, n (%)				
One Two	87 (88.8) 11 (11.2)	157 (91.3) 15 (8.7)	65 (86.7) 10 (13.3)	0.527*
Stone Burden, mm^2	314 (219-579)	345 (217-640)	392 (259-767)	0.426
Stone density, HU	1000 (800-1208)	1120 (800-1300)	1035 (800-1230)	0.103
Surgery Time, min.	100 (70-130)	90 (70-120)	95 (70-120)	0.108
Length of stay, day	3.5 (2-4)	3 (3-4)	4 (2-5)	0.498
Hg Drop, mg/dL	1.9 (0.77-2.80)	1.5 (0.80-2.20)	1.3 (0.60-2.20)	0.074
Stone free status, n (%)	68 (69.4)	113 (65.7)	50 (66.7)	0.824*
Complication grade, n (%)				
Clavian 1 Clavian 2 Clavian 3A Clavian 3B	12 (12.2) 9 (9.2) 13 (13.3) 1 (1.0)	17 (8.9) 13 (4.91) 7 (4.1) 4 (2.3)	6 (8.0) 5 (6.7) 3 (4.0) 1 (1.3)	0.125**

^Kruskall Wallis, *Pearson Chi-Square, **Exact test
Results are expressed in median (IQR (25-75th)), BMI: Body Mass Index, Hg: hemoglobin, HU: Hounsfield unit

Table 2. Comparison of preoperative GFR with postoperative 1st Day GFR			
	Mean Preoperative GFR (mL/min/1.73m^2)	**Mean Postoperative 1st Day GFR** (mL/min/1.73m^2)	***p* value^**
Group-1	101.1 (96.4-111.5)	87.3 (79.7-101.9)	<0.001
Group-2	76.1 (68.3-82.1)	64.9 (57.8-75.5)	<0.001
Group-3	51.2 (44.8-56.7)	46.3 (37.3-53.0)	0.138

^Wilcoxon test
GFR: Glomeruler Filtration Rates

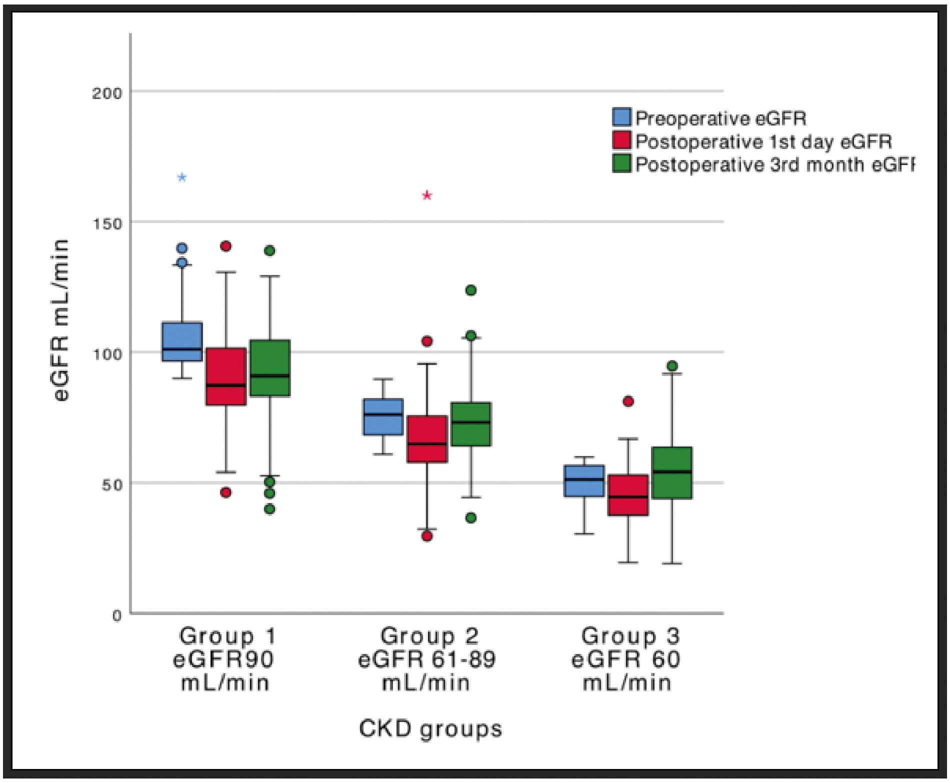

Figure 1. GFR changes within groups

Table 3. Comparison of preoperative GFR with postoperative 3rd Month GFR

	Mean Preoperative GFR (mL/min)	Mean Postoperative 3rd Month GFR (mL/min)	*p* value^
Group-1	101.1 (96.4-111.5)	101.3 (90.5-110.2)	0.074
Group-2	76.1 (68.3-82.1)	74.3 (66.1-82.7)	0.129
Group-3	51.2 (44.8-56.7)	54.2 (43.9-63.5)	0.033

^Wilcoxon test
GFR: Glomeruler Filtration Rates

DISCUSSION

PCNL is the primary treatment modality in patients with high stone burden today. Some studies reported PCNL caused scar formation after operation in animals (8,9). Percutaneous access might lead to damage of kidney parenchyma around the access point. This damage can favorably evolve with healing or progress to fibrosis, thus causing an irreversible loss of function in this location (5).

On the other hand, decline in renal function was attributed to trauma induced vasoconstriction in both kidneys based on studies such as Nazaroglu et al. (10) who demonstrated a temporary increase in resistive indices of both kidneys following unilateral SWL (shock-wave lithotripsy). The suggested mechanisms of vasoconstriction in the contralateral kidney are neural and hormonal. Efferent and afferent renal nerves contribute to renorenal reflexes that enable kidneys to have balanced and regulated function (11). Connors et al. (12) explained the role of renal nerves in renal blood flow regulation by showing that the unilateral denervation of a kidney prevented a decrease in renal plasma flow of that kidney following contralateral kidney SWL. As such, unilateral PCNL can induce vasoconstriction of the contralateral kidney through sympathetic nervous system stimulation. From the hormonal point of view, Atici et al. (13) showed a significant increase in serum renin and aldosterone levels during PCNL, which can contribute to bilateral renal vasoconstriction. These mechanisms lead to an increase in serum creatinine levels. However, glomerular filtration rate is more sensitive than serum creatinine levels. Elevation in serum creatinine levels is equivalent to a decrease in glomerular filtration rate.

Several blood and urine markers have been used to assess kidney function, but there were differences between results (14,15). The accuracy of the renal scan depends mainly on the method used to calculate clearance. Plasma clearance appears to be the most accurate; however, it necessitates multiple blood samples. In a recent study we used plasma clearance which was calculated with the Cockcroft–Gault formula (7).

Nouralizadeh et al. (16) reported that renal GFR decreases immediately after PCNL, reaches a nadir 48 h after operation, and then increases slowly in patients with preoperative normal creatinine levels. However, the late effect of PCNL on GFR changes was not investigated in that study. Handa et al. (17) reported that the drop in GFR returned to preoperative values within postoperative 72 hours. Webb and Fitzpatrick reported that renal function returned to normal values according to radionuclide imaging 2 weeks after PCNL (9). As a result of these studies, it can be concluded that GFR returns to normal values 3-14 days after PCNL. In our study, we aimed to assess the effect of PCNL on kidney functions according to basal functional reserve with repeated GFR measurements of patients on postoperative 1st day and 3rd months. Our findings were consistent with Nouralizadeh et al. (16) who reported that GFR decreased on the 1st postoperative day 1 in all groups. We evaluated GFR in the postoperative 3rd month again for late global renal function.

Nouralizadeh et al. (16) in a prospectively planned study evaluated CrCl (creatinine clearance) changes in 94 patients following unilateral PCNL, whose mean±SD creatinine clearance according to the Cockcroft-Gault equation was 87.5±32.2 ml/min before operation. They showed a decrease in CrCl in 20% of patients on the first postoperative day with an improvement trend in 72 h. Handa et al. (5) reported a decrease in bilateral renal function and perfusion following unilateral PCNL in pigs with normal renal function and also a significant increase in serum creatinine in 126 of 196 patients who underwent unilateral PCNL on the first postoperative day. In our study, a transitional decrease in GFR was observed on the 1st day after operation, but then it increased gradually. In group-1 and group 2, GFR decreases were statistically significant, although the GFR decrease was not significant in group 3, compared to preoperative GFR values on the 1st day.

Gupta et al. (18) reported that 33 patients who underwent kidney stone treatment such as PCNL, SWL, ureteroscopic stone extraction, alkalinisation and open surgery had higher serum creatinine levels of 2 mg/dl. The postoperative serum creatinine value in 32 of 33 patients was lower than the preoperative value (mean 2 vs. 3.2 mg/dl, P<0.001). Bilen et al. (19) reported significant improvement of patients with late stage renal disease who underwent PCNL; however they showed deterioration of patients with early stage renal disease. Kukreja et al. (20) reported 84 patients with kidney stone disease and impaired renal function who underwent PCNL. They showed that 33 of 84 patients had improvement of renal function according to preoperative renal function, while 24 of 84 patients had deterioration of renal function. Watts et al. (21) compared renal functional outcomes in patients with and without chronic kidney disease at a minimum of 6 months post-surgery. Patients without chronic kidney disease had an overall decrease in GFR from 105.6 to 103.3 ml/min/1.73 m^2 üst karakter olacak (p=0.494). Patients with CKD had an overall increase in mean GFR post-operatively, from 47.3 to 54.0 ml/min/m^2 (p=0.067). Etemadian et al. (22) performed PCNL on 60 patients with a creatinine level higher than 1.5 mg/dL and found that creatinine level significantly decreases after the operation. In our study, in patients with GFR<60, GFR decreased to some degree on the postoperative 1st day although it was not significant, but by the postoperative 3rd month GFR levels in this group significantly improved and exceeded preoperative GFR levels.

In a recent study, nephrotoxic drugs were not used preoperatively or postoperatively. Nephrotoxic drugs can affect the speed of GFR drop or nadir value of GFR. Handa et al. (17) reported that during PCNL applied with nephroscopy and normal saline irrigation, tract dilation, stone fragmentation caused bilateral renal vasospasm and decreasing GFR in PCNL patients with normal contralateral kidney. This is an important study to explain how the preoperative GFR values affect postoperative GFR changes in PCNL and when GFR returns to the normal value.

The main limitations of the present study are its retrospective design which could possibly cause some bias, and using serum creatinine value to calculate GFR may not be the best method. The Cockcroft–Gault formula is a widely used and shows GFR changes with appropriate error (8). However, the aim of our study was not to define the most accurate GFR measurement. We use GFR only for follow up purposes and preoperative classification. So, we think that the Cockcroft–Gault formula will not cause significant errors in the results. Our study has some potential advantages. Firstly, the same surgeons performed PCNL in our clinic with the same protocol so there was no surgery-effect bias. The other important issue is that we did not evaluate only early PCNL effects. In addition, we evaluated the impact of percutaneous surgery 3 months after PCNL because early evaluation alone may cause errors about the effect of PCNL on renal function.

In conclusion; estimated GFR, as a better indicator of renal function, is significantly affected by the PCNL procedure. Although, renal function initially decreased after PCNL because of the renal trauma procedure, kidney function is better by the postoperative 3rd month because of the disappearance of kidney stones. So PCNL significantly improved renal functions in patients with preoperative GFR <60 due to renal stone.

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Ethical Approval: The study was approved by the Ethic Committee of Amasya University (2021/1680).

Research Contribution Rate Statement Summary: The authors declare that, they have contributed equally to the manuscript.

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