Original Article

Percutaneous nephrolithotomy: Effect of unilateral procedure on contralateral kidney function

Mehrdad Mohammadi Sichani, Amir Behnamfar, Mohammad Hatef Khorami, Kia Nourimahdavi, Farshid Alizadeh, Mohammad Hossein Izadpanahi

Department of Urology, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract

Background: Although long-term effects of percutaneous nephrolithotomy (PCNL) on renal function and structure have been evaluated, knowledge regarding the immediate effects of surgery on renal function is limited. We conducted this study to evaluate the impact of unilateral PCNL on bilateral renal function during immediate post-operative period.

Materials and Methods: From April to September 2012, 40 eligible patients were enrolled in this study and underwent unilateral PCNL. During the post-operative period, creatinine clearances (CrCl) of treated and untreated sides were estimated separately and pattern of changes in bilateral renal function following this procedure was evaluated.

Results: Following the operation, CrCl of both kidneys showed a similar pattern of changes, of course more dramatic on treated side. We observed progressive decline in CrCl of both sides followed by bilateral improvement in renal function toward pre-operative values.

Conclusions: During the early post-operative period following unilateral PCNL, both kidneys experienced a temporary drop in function warranting more intensive post-operative care.

Key Words: Creatinine clearance, percutaneous nephrolithotomy, renal function

Address for correspondence:
Dr. Amir Behnamfar, Department of Urology, Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran.
E-mail: Behnamfaramir@yahoo.com
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INTRODUCTION

Since the introduction of percutaneous nephrolithotomy (PCNL) as preferred treatment modality of renal stones, a question was always asked: Does significant difference in incision size in comparison to open surgery makes it truly minimally invasive? Many investigations have been undertaken to answer this question.

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Long-term effects of PCNL on renal function and structure have been evaluated with promising results; however, our knowledge regarding the immediate effects of surgery on renal function is limited. Undoubtedly, local trauma and ischemia at the introduction site is expectable,[1] but effects of this procedure on renal units seem to be global and even bilateral. Handa *et al*. reported bilateral decrease in renal function and perfusion following unilateral percutaneous nephrostomy (PCN) in pigs and also a significant increase in serum creatinine

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in 126 of 196 patients who underwent unilateral PCNL, on the first post-operative day was shown.[1] In another study Nouralizadeh *et al*. showed a decrease in creatinine clearance (CrCl) of 20% of patients on first post-operative day.[2] As serum creatinine as a renal function index is not as sensitive as glomerular filtration rate (GFR) and CrCl estimated by Cockcroft-Gault equation is incapable of indicating effects of procedure on individual kidney, we decided to perform this study and calculate CrCl of each kidney following a unilateral procedure for the first few days following surgery.

MATERIALS AND METHODS

From April to September 2012, of proper candidates of unilateral PCNL, 45 patients who were over 18, had serum creatinine <1.5 mg/dl, had a single and simple structured stone amenable to a single tract straight forward procedure and had no evidence of obstruction (hydronephrosis and delayed excretion) or kidney damage (size, echogenicity and scar) on radiologic evaluations were enrolled in the study. Exclusion criteria for this study are: Blood transfusion during or after procedure, hemodynamic changes during operation, procedures other than uncomplicated single tract ones, procedures necessitating post-operative nephrostomy tube clamping, nephrotoxic drugs prescription, tubeless or double J placed procedures.

All patients gave their informed consent prior to their inclusion in the study and our study has been approved by Local Ethics Committee and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Pre-operative evaluations including patients history, physical examination, serum creatinine and electrolytes, urinalysis and urine culture, ultrasonography and intravenous pyelogram (IVP) were performed. As an adjuvant diagnostic modality, abdominal computed tomography scan was performed in patients who were at risk for retrorenal colon (i.e. thin or advanced age patients).

Under general anesthesia a 5-6 Fr open ended ureteral catheter was placed in the ipsilateral ureter and was secured to a Foley catheter. Patients were placed in the prone position and areas under pressure were protected with pads. Under fluoroscopic guidance, access to desired calyx was achieved using 18 gauge Chiba needle. We passed the guide wire through the needle and nephrostomy tract was dilated in a sequential manner via amplatz dilators up to 28 Fr. Having used a 24 Fr Wolf nephroscope and pneumatic lithoclast (SWISS lithoclast), target stone was fragmented and removed. At the end of the procedure, after removing ureteral catheter, proximal ureter was occluded by an 8-12 Fr closed ended nelaton catheter in antegrade fashion and occlusion was confirmed by antegrade nephrostography under fluoroscope. A 16 Fr Foley catheter was placed in renal pelvis. We placed a urostomy bag over the surgical site for maximal collection of ipsilateral kidney urine. Contralateral kidney urine was drained through urethral Foley catheter.

Post-operatively, for 3 days, collected urine from each kidney (urostomy bag and urethral catheter) was evaluated twice daily for volume and creatinine concentration. We also measured serum creatinine accordingly.

CrCls were calculated using the following equation (based on 12 h collection time):

$$\frac{\text{Urine Cr} \times \text{Urine volume}}{\text{Serum Cr} \times 720}$$

For comparison purpose, we needed pre-operative estimated glomerular filtration rate (eGFR) of each kidney. As it was not possible to be measured by the previously mentioned method, based on normal pre-operative laboratory and radiological evaluations, we assumed that GFR of each kidney is half of the whole GFR estimated by Cockcroft-Gault equation (as illustrated below). Therefore, pre-operative CrCls were estimated using Cockcroft-Gault equation and divided by 2 for estimating each kidney's eGFR.

$$\frac{(140 - \text{age})\,\text{weight}}{\text{plasma Cr} \times 72}\,(\times 0.85 \text{ in females})$$

eGFR data derived from each kidney were compared with variables from the contralateral side. We used IBM® SPSS® Statistics version 20 and *T*-paired test for statistical analysis. $P < 0.001$ was considered statistically significant.

RESULTS

Of 46 patients who were enrolled in the study, six patients were excluded, due to improper collection of samples in two patients, prescribing Amikacin for post-operative fever in 1, Dj placement in 2 and blood transfusion in 1 of them. Demographic and calculi data are summarized in Table 1.

All patients underwent a subcostal procedure except two of them for whom a supracostal approach was

Table 1: Demographic and calculi data

Demographic and calculi features	Data (%)
Mean age	50.3 years
Sex	
Male	17 (42.5)
Female	23 (57.5)
Mean stone diameter	2.5 cm
Stone composition (dominant element)	
Calcium oxalate	23 (57.5)
Struvite	1 (2.5)
Cystine	3 (7.5)
Uric acid	13 (32.5)

Table 2: Estimated glomerular filtration rate of treated and untreated kidneys

P	Untreated side	Treated side	Timing
<0.001	56/49±16/5	34/86±17/4	12 h post-operation
<0.001	59/37±18/7	35/2±17/6	24 h post-operation
<0.001	49/4±16/5	32/3±16/5	36 h post-operation
<0.001	55/33±23/3	36/13±20	48 h post-operation
<0.001	58/7±25/5	35/07±13/4	60 h post-operation
<0.001	64/33±26/6	44/1±9/8	72 h post-operation
	<0.001	<0.001	*P* value

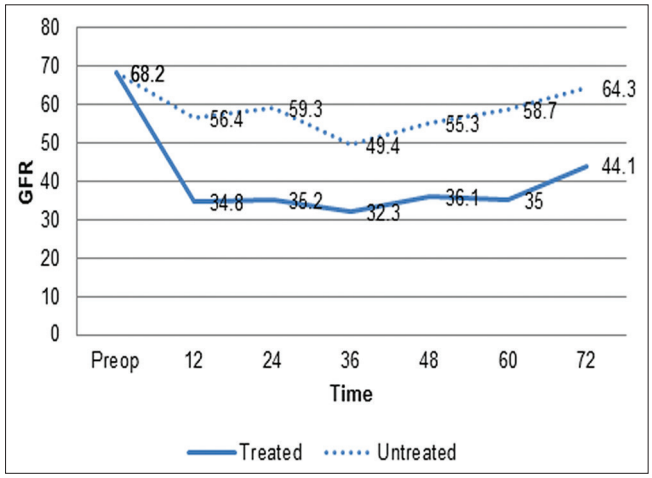

Figure 1: Pattern of changes in estimated glomerular filtration rate of both kidneys following percutaneous nephrolithotomy

used. Mean stone free rate was 94% and mean operation time was 80 min.

Mean pre-operative GFR of each kidney was estimated to be 68.2. Table 2 shows the eGFR of both kidneys for a period of 72 h post-operatively. Pattern of changes in eGFR of both kidneys are shown in Figure 1.

Following the procedure, eGFR of both kidneys changed in a similar fashion by the time; although, these changes were more dramatic on treated side. Furthermore, the eGFR of treated side was significantly lower than the opposite side during our follow-up period. Following the operation-especially after 24 h-both kidneys experienced a progressive decline in eGFR, which was more pronounced on treated side. This pattern of changes sustained for 36 h following which an improvement in eGFR of both kidneys was observed.

DISCUSSION

Our study revealed that eGFR of both kidneys was affected by PCNL in a similar fashion though in different magnitudes (i.e. a progressive decline followed by gradual recovery).

Our center is one of the major referral centers in country. In our experience, we sometimes encountered patients with mild increase in their serum creatinine level following a unilateral procedure. Hence, we decided to perform this study, which to our knowledge, is one of a kind, for evaluating bilateral renal function changes following a unilateral PCNL in a creative manner.

Several studies evaluated long-term effects of PCNL using renal scans. Dawaba *et al*. conducted a study in a group of children and reported no renal scarring on follow-up dimercaptosuccinic acid (DMSA) scans and also based on diethylenetriaminepentaacetic acid scans showed improvement in renal functions of their patients, except for one.[3] Similarly, Chatham *et al*. in their low volume study showed either preserved or improved renal function following PCNL using mercaptoacetyltriglycine renal scan; although, it was not true for 3 patients (16%) who either underwent angioembolization, post-operative shock wave lithotripsy (SWL) or had a poor functioning kidney prior to operation.[4] Using DMSA Single photon emission computed tomography (SPECT), Moskovitz *et al*. reported a slight decrease in total functional volume of treated kidney and also revealed a statistically significant decrease in the functional volume at the site of entry;[5] even though, the latter was not confirmed by Wadhwa *et al*. using non-SPECT DMSA scan.[6]

One of a kind study conducted by Handa *et al*., evaluated effects of PCN on renal function in an animal model.[1] They showed that creating nephrostomy tract in pigs using either serial dilation or balloon inflation, reduced renal perfusion and filtration by more than 50% in the treated kidney, which lasted for at least 5 h. Parallel to their study on animal model they undertook a retrospective investigation in 196 adult patients, 64% of them experienced a statistically significant increase in mean serum creatinine level (0.14 mg/dl) on the post-operative day one. Bilateral ureteral catheters used in this study provided the opportunity to evaluate contralateral kidney function after unilateral

PCN, which revealed a bilateral decrease in filtration, perfusion and excretory function. Interestingly changes in hemodynamic and excretory function of the untreated kidneys were similar to treated one. Since bilateral renal function remained unchanged in sham treated group, it can be assumed that decline in renal function to a high probability was a consequence of accessing phase of the procedure. This decline in renal function was attributed to trauma induced vasoconstriction in both kidneys based on studies such as Nazaroglu *et al*. which demonstrated temporary increase in resistive indices of both kidneys following unilateral SWL.[7] 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 of balanced and regulated function.[8] Connors *et al*. explained the role of renal nerves in renal blood flow regulation by showing that unilateral denervation of a kidney prevents decrease in renal plasma flow of that one following contralateral kidney SWL.[9] As such, unilateral PCNL can induce vasoconstriction of contralateral kidney through sympathetic nervous system stimulation. Of hormonal point of view Atici *et al*. showed a significant increase in serum renin and aldosterone levels during PCNL, which can contribute to bilateral renal vasoconstriction.[10]

Effects of tract dilation methods, numbers of tracts and simultaneous bilateral procedure on renal function have been investigated. Handa *et al*. reported similar effects of tract dilation methods (i.e. sequential dilators versus balloon inflation) on renal function.[1] It was confirmed by Unsal *et al*. using SPECT DMSA scan.[11] In another study it was shown that maximal effect on renal function was constituted with first percutaneous access and increasing the access sites in number did not lead to more declines in renal function.[12] Holman *et al*. reported similar rise in magnitude of creatinine levels following unilateral and simultaneous bilateral PCNL which was occurred in 8-11% of patients.[13] Another study, which used more reliable indices of renal function showed that bilateral renal responses following simultaneous bilateral procedure were the same extent as in unilateral procedure.[14]

Nouralizadeh *et al*. in a prospectively planned study evaluated CrCl changes in 94 patients following unilateral PCNL.[2] They showed a decrease in CrCl of 20% of patients on first post-operative day with an improvement trend in 72 h. They used Cockcroft-Gault equation to estimate CrCl, which is of course due to unchanged age and weight during the post-operative period; it is solely dependent on serum creatinine level. This matter can truly underestimate changes in eGFR, as it was shown that due to logarithmic relationship between serum creatinine level and eGFR in the presumed normal range of serum creatinine, a small change in serum creatinine would be associated with a significant change in eGFR.[15] So by keeping this fact in mind, the proportion of patients experienced the decline in CrCl might be more than 20%.

Inspired from previously mentioned studies, we planned this study to investigate effects of this modality of treatment on bilateral renal function considering limitations of former studies (i.e. using serum creatinine level as the renal function index and applying animal model results to human group). Obstructing the treated kidney ureter, enabled us to measure urine creatinine of each kidney separately and to evaluate effects of PCNL on contralateral, untreated kidney function.

In the post-operative period we observed a progressive decline in eGFR of both kidneys. Handa *et al*. reported similar changes in eGFR of both sides within 5 h of unilateral PCN using Amplatz dilators.[1] Although 5 h period seems too short, incorporation of traumata resulting from stone fragmentation and irrigation fluid pressure might change that pattern and cause the treated side GFR to decrease much more than the other side, as it is evident in our study.

Following the nadir of bilateral eGFR at 36 h post-operatively, an overall trend for improvement in bilateral renal function was noted. The difference in the patterns of this improvement can be attributed to traumatic burden of procedure on treated side, which necessitated more time for recovery. This pattern of changes in renal function has been reported previously. Using Cockcroft-Gault equation Nuralizadeh *et al*., showed a progressive decline in eCrCl post-operatively up to 48 h followed by the slight increase at 72 h.[2] Furthermore all the perfusion and filtration deficits which were mentioned in Handa's study, were normalized in 3 days following the procedure.[1] Returning of kidneys' eGFR back to pre-operative values did not happen in our study probably due to limited follow-up time, but based on the previously mentioned studies we believe that it is just the matter of time.[1,3,4]

We believe that these changes in eGFR are universal, but due to previously mentioned logarithmic relationship between serum creatinine level and eGFR, increase in serum creatinine level was observed in just a minority of patients following PCNL.

Based on the observed changes in bilateral renal function, it would be wise to avoid using nephrotoxic agents such as non-steroidal anti-inflammatory drugs and Aminoglycosides during the early post-operative period with special attention to a solitary kidney

patients and kidneys endangered by medical conditions like diabetes mellitus. Furthermore optimized replacement of volume deficits seems reasonable in supporting these susceptible kidneys. It would be beneficial to perform a follow-up renal function evaluation in patients who experience a rise in serum creatinine level following PCNL, such that CrCl estimation in 3 months seems to be appropriate.

One may consider several limitations in this study. Firstly, we could not measure eGFR preoperatively in the same manner as we did in the post-operative period. Actually it was unethical to increase the time of general anesthesia just for urine collection. Even if we collected urine for an hour, this limited time will decrease our estimation of CrCl in accuracy. So we were forced to estimate the preoperative CrCls using Cockcroft-Gault equation even though we were aware of its limitation in estimating kidneys eGFR separately. However we tried to overcome this problem by just enrolling patients with non-obstructing stones in normal appearing kidneys (based on ultrasonography and IVP) in our study. Unfortunately, evaluating preoperative GFR and differential renal function using renal scans were not possible due to ethical issues. Secondly, our method of occluding the ureter may seem unreliable but we tried to overcome this problem by confirming ureteral occlusion using antegrade nephrostography under fluoroscope. Finally, due to relatively small number of patients, our study is a preliminary one and more sophisticated results would be achieved by conducting larger trials.

Further investigation might be valuable to evaluate changes in neurotransmitters level, effect of demographic data, position type and anesthesia technique influence on eGFR and role of various vasodilators in offsetting potential hemodynamic changes following PCNL.

CONCLUSION

Safety of PCNL on long-term renal function has been proved through various methods but our study revealed that during the early post-operative period eGFR of both kidneys was affected by this procedure. It seems prudent to avoid nephrotoxic agents following a PCNL procedure.

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