

Original Article

Clinical treatment of percutaneous nephrolithotomy for patients with renal calculus

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Abstract: Objective: To explore the clinical effect of percutaneous nephrolithotomy (PCNL) on patients with renal calculus. Methods: A total of 106 patients with renal calculus were selected as research subjects and divided into the control group and the observation group according to the operation method. The control group was given open nephrolithotomy, and the observation group was given minimally invasive PCNL. The rate of stone clearance, operation time, hospitalization time, and intraoperative blood loss were statistically analyzed. The changes of kidney injury molecule-1 (Kim-1), neutrophil gelatinase-associated lipocalin (NGAL), Cystatin C (Cys-C) and high-sensitivity C-reactive protein (hs-CRP) before and after treatment and the incidence of postoperative complications were determined by immunofluorescence. The recurrence rate at 12 months after operation was recorded. Results: The stone clearance rate in the observation group was significantly higher than that in control group, while the operation time, intraoperative blood loss and hemoglobin losses were significantly lower than those in the control group (all $P < 0.05$). The levels of Kim-1, NGAL, Cys-C and hs-CRP in the observation group were significantly lower than those in control group at the same time point on the 4th day after treatment, and the difference was statistically significant (all $P < 0.05$); and they did not differ from those before operation in the observation group (all $P > 0.05$). The hospitalization time and nephrostomy indwelling timewere significantly, and the complication rate in the observation group was significantly lower than those in control group (all $P < 0.05$). Conclusion: PCNL could significantly improve the stone clearance rate and reduce postoperative inflammatory response and complications. It is worthy to promote for clinical application.

Keywords: Percutaneous nephrolithotripsy, renal calculus, open nephrolithotomy, renal injury

Introduction

Urinary calculus is a multiple disease [1]. The latest epidemiological studies showed that renal calculus accounted for more than 86% of the total incidence of urinary calculus, which is easy to relapse, seriously affecting the patient's physical and mental health and economic status [2]. Traditional open surgery is the main method for the treatment of stones >25 mm, but there is a risk of large surgical trauma and large renal injury. In recent years, with the increasing acceptance of minimally invasive surgery and the continuous improvement of equipment, percutaneous nephrolithotomy (PCNL) is widely used in the treatment of renal calculus because of its advantages of indications and high rates of stone clearance [3]. However, there will be varying degrees of complications occurring during the operation. Therefore, this research adopted open surgery and PCNL to

treat patients with renal calculus and evaluate the treatment effect, so as to provide a more effective basis for clinical application.

Materials and methods

General information

The Ethics Committee of Ningbo Yinzhou No.2 Hospital approved this research. A total of 106 cases of renal calculus treated in Ningbo Yinzhou No.2 Hospital from January 2015 to July 2016 were selected as research subjects, which were divided into the control group (48 cases) and the observation group (58 cases).

Inclusion criteria: (1) Patients' unilateral renal calculus was confirmed by B-ultrasound, abdominal plain film and angiography; (2) Stone diameter in 2.0 cm-4.0 cm, located in the renal pelvis or renal calices and other parts of the

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body; (3) The first time to receive a kidney stone surgical treatment; (4) Patients clearly understood the research purpose and signed informed consent.

Exclusion criteria: (1) Patients with serious heart, liver, kidney and other underlying systemic diseases; (2) Patients with obvious contraindications for operation; (3) Patients in severe coagulation disorders; (4) Stones located in the upper renal calyx.

Research methods

Both groups of patients were undergone primary surgery. A single dose of levofloxacin 300 mg was intravenously dripped within 30 min before operation and the preoperative preparation was completed. The control group received open surgery [3]. Patients were taken lateral recumbent position, and received general anesthesia and endotracheal intubation. A incision was made in 11 or 12 intercostal to open the renal fascia. After completion of routine exploration, the renal pelvis was longitudinally incised and the stone was removed, followed by repeated cleaning renal pelvis. Renal calyx and renal parenchyma incision were sutured and given hemostasis.

The observation group was treated with PCNL according to the report of Ozgor (2015) [3]. Under continuous epidural anesthesia, patient was placed in lithotomy position and underwent retrograde insertion of ureter. Patient then changed to prone position. The surgical film was laid on the surgical field, and gauze was placed in the drainage channel. Nephroscope was connected to the white light source, monitor and perfusion system. Under the guidance of the imaging equipment of convex array color Doppler ultrasound and other imaging devices, the best puncture site was selected by accurate locating under the 12th rib or 11 intercostal for channel expansion and a percutaneous renal access was established.

After successful insertion of the guide wire, the percutaneous renal access was expanded from stage 2 F to stage 14 F using the fascia dilator. Balloon dilator was inserted along the guide wire and helped to gradually increase atmospheric pressure; then the F24 expander with sheath was placed in close to the inflated airbag, and the balloon dilator was deflated and

pulled out. The nephroscope was inserted along the zebra guide wire into the renal pelvis or calyx. The guide wire can be pulled out after the percutaneous renal access was set up.

After locating the stone lesions, lithotripsy was carried out with the pressure ballistic or the larger stones were pinched out directly with the foreign body forceps under the condition of the direct vision of a nephroscope. Stone fragments generated during the operation can be washed out of the sheath through a pressure pump. The nephroscope was removed while after the stones were cleared in the field of vision and no other organ damage existed. A stent was built into the ureter, and a nephrostomy drainage tube was left beside the puncture channel. All patients maintained absolute repose after operation. The symptomatic treatment such as anti-infection, liver and stomach protection were given to patients, and the fistula of patients were kept unobstructed.

Observation index

Main outcome measures: 7-10 days after operation, the renal fistula was clear and had no obvious bleeding, and abdominal plain film examination was performed to determine the stone clearance rate. The operative time, hospitalization time, intraoperative blood loss and the incidence of postoperative complications were counted, and the recurrence rate within 12 months after the operation was recorded.

Secondary outcome measures: Immunofluorescence was used to determine the changes of human kidney injury molecule-1 (Kim-1), neutrophil gelatinase-associated lipocalin (NGAL), cystatin C (Cys-C) and high sensitivity C reactive protein (hs-CRP) before treatment and the 1st day, 2nd day and 4th day after treatment.

Statistical methods

SPSS21.0 software was used for statistical analysis. Measurement data is expressed by mean \pm standard deviation ($\bar{x} \pm sd$). The measurement data between two groups in line with the normal distribution was measured using a t test, expressed by t. Count data was expressed as percentage, using χ^2 test and the Fisher exact probability test, and expressed in chi-square. The difference is statistically significant when $P < 0.05$.

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Table 1. Comparison of the basic data ($\bar{x} \pm sd$)

Group	Sex (male/female)	Age (year)	Calculi diameter (cm)	Hydronephrosis (cm)
Control group (n=48)	28/20	46.97±18.68	2.87±1.58	3.04±0.47
Observation group (n=58)	31/27	52.56±20.85	3.03±1.64	3.22±0.39
t/ χ^2	0.095	0.948	0.880	1.395
P	0.696	0.174	0.192	0.085

Table 2. Comparison of the basic data ($\bar{x} \pm sd$; n, %)

Group	Multiple lithiasis	Cast stone	Staghorn calculi	Course of disease (month)
Control group (n=48)	23 (47.92)	12 (25.00)	13 (27.08)	12.35±5.87
Observation group (n=58)	29 (50.00)	17 (29.31)	12 (20.69)	11.46±7.36
t/ χ^2	0.003	0.077	0.294	0.459
P	0.848	0.667	0.495	0.328

Table 3. Comparison of the operation conditions (n, %, $\bar{x} \pm sd$)

Group	Stone clearance rate	Operation time (min)	Intraoperative hemorrhage (mL)	Loss of hemoglobin (g/L)
Control group (n=48)	38 (79.17)	157.43±59.57	222.46±59.84	13.74±4.26
Observation group (n=58)	56 (96.55)	63.27±22.28	153.87±44.28	10.86±3.45
t/ χ^2	6.270	7.039	4.129	2.463
P	0.006	<0.001	<0.001	0.009

Results

Comparison of the basic data

There was no significant difference in gender ratio, age, diameter of stone, degree of hydronephrosis and type of renal calculus in both groups of patients (all $P>0.05$). See **Tables 1-2**.

Comparison of the operation conditions

The stone clearance rate in the observation group was significantly higher than that in the control group, while the operative time, intraoperative blood loss and hemoglobin loss was significantly lower than those in the control group (all $P<0.05$). See **Table 3**.

Comparison of biochemical indexes

Before treatment, there was no difference in the expression levels of Kim-1, NGAL, Cys-C, and hs-CRP between the two groups (all $P>0.05$). On the 4th day after treatment, the indexes of the observation group were significantly lower than those of control group at the same period. The differences were statistically significant (all $P<0.05$). And the indexes of the

observation group in the 4th day had no difference compared with preoperation (all $P>0.05$). See **Figure 1**.

Comparison of postoperative situation and recurrence rate

The hospitalization time, nephrostomy indwelling time, and proportion of complications in the observation group were significantly lower than those in the control group (all $P<0.05$), while there was no significant difference in recurrence rate between two groups ($P>0.05$). See **Table 4**.

Discussion

Nephrolithiasis is a common type of calculus in urinary system, with a prevalence of 5%-10%. The number of newly diagnosed cases is 15-20/10,000 and shows an increasing trend year by year [4]. The causes of urinary calculus are complicated, but the vast majority of urinary calculus comes from the mineralization of the body's own metabolites, and is closely related to metabolic disorders, environmental conditions and dietary habits [5]. This disease can cause renal colic, urine character and paruria

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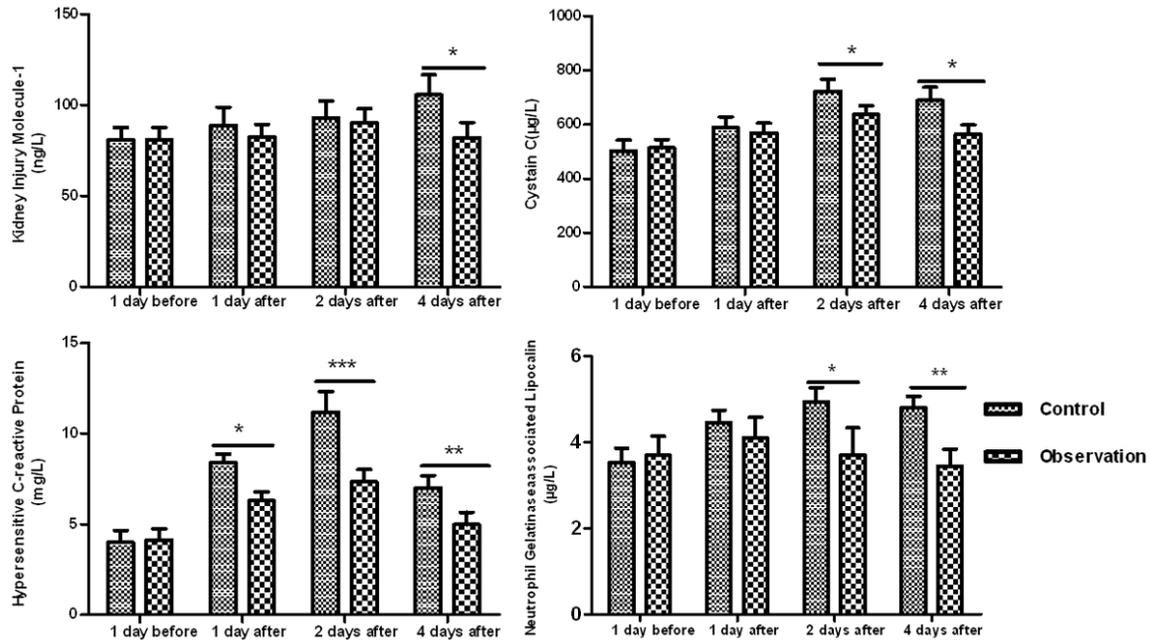


Figure 1. Comparison of biochemical indexes in two groups of patients. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Table 4. Comparison of postoperative cases and recurrence rate ($\bar{x} \pm sd$)

Group	Hospitalization time (d)	Nephrostomy indwelling time (d)	Complications rate (n, %)	Recurrence rate (n, %)
Control group (n=48)	25.75±8.25	12.77±2.02	17 (35.42)	12 (25.00)
Observation group (n=58)	18.62±6.74	8.7±1.74	9 (15.52)	6 (10.34)
t/ χ^2	3.170	11.600	4.595	3.034
P	0.001	<0.001	0.023	0.068

etc. It can also cause obstruction, infection and tumor caused by long-term friction. Thus, it seriously reduces quality of life of patients [6-8]. The calculus of urinary is usually bacterial carrier. The number of bacteria and the concentration of endotoxin are proportional to the calculus diameter [9]. After the stones have been broken, most of the bacteria or endotoxins contained in them will be released into the perfusate, which would lead to postoperative fever, bacteremia and sepsis [10, 11].

At present, conservative treatment is recommended for patients with renal stone diameter <0.4 cm; medication treatment is preferred for stone diameter <0.6 cm with smooth surface and unobstructed urinary tract; if stones are larger and the patients have severe clinical symptoms, surgical treatment is required. In the past, pen surgical lithotomy has the disadvantages such as large surgical wounds, diffi-

culty in handling calculus, low probability of one-time successful stone removal and the risk of bleeding, which in most hospitals have been nearly being eliminated [3]. The scope of clinical application of extracorporeal shock wave lithotripsy (ESWL) and PCNL is gradually become larger, which have achieved certain results, but at the same time the respective drawbacks are gradually becoming apparent [12]. ESWL has the advantages of noninvasive, high repeatability, low cost and easy operation, and it is accepted by most of the patients with renal calculus. However, with the expansion of clinical application, many studies confirmed that ESWL would cause irreversible damage to renal function and renal tissue, and the treatment outcome was easily affected by the location, shape, number of stone and the vital signs of patients and so on [13]. Naderi et al. reported, the flush perfusion pressure in ureteroscopic lithotripsy surgery can reach a maximum of

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410 mmHg, resulting that intrapelvic pressure exceeded the physiological pressure by dozens of times; therefore, the urine volume decreased, and the risk of liquid reflux appeared, thus blood circulation disorders were increased, which led to ischemic lesion of the kidney parenchyma and abnormal renal function [14].

Since PCNL launched in 1976 by Fernstrom and Johansson, its technology and equipment have been continuously improved and enhanced. With the continuous accumulation of surgical experience, PCNL has become the gold standard for the treatment of large volume, complex components and staghorn calculus [15-17]. PCNL includes standard channels, minimally invasive channels and large channels to meet the needs of different patients [18, 19]. The size of standard channel is 20-26 F, which allowed the stones to be punched out of the channel sheath without crushing the stone completely. The flow speed is fast, which is beneficial to the discharge of stones, shortening the operative time and reducing the probability of postoperative infection.

The size of minimally invasive channel is 14-18 F, which has the advantages of less injury and less bleeding. While for larger calculus, the channel is relatively small, which leads to higher relative perfusion pressure in the renal tissue during operation, and increases the chance of infection after invasion of bacteria. The large channel is usually larger than 28 F, which has a wider field of vision and larger operation space to meet the requirements of high-speed and low-pressure perfusion, thus effectively reducing renal pressure and reducing the risk of infection [20]. However, the damage to the kidneys increases, and the risk of bleeding is high. Hence, it is necessary to design an appropriate surgical plan according to the physical quality of the patient, and minimize the patient's injury and adverse reaction.

In the past, laboratory indicators such as urea nitrogen and creatinine were used to evaluate renal function; but they were susceptible to age, gender and dietary habits, and were not ideal for detection of early renal impairment [21]. In recent years, the newly discovered protein markers have higher sensitivity. The expression of Kim-1 shows tissue-specific, and its expression level will increase significantly after ischemic injury. Kim-1 will continue to

express before epithelial cell recovery, which is directly proportional to the degree of renal function damage [22]. NGAL is transferrin produced after injury. Its main role is to promote iron transport to the proximal tubule cells, to avoid cell apoptosis and thus protect renal tubular cells. Therefore, the expression in renal tubular epithelial cells after injury significantly increases [23]. Cys-C is a cysteine protease inhibitor C; kidney is the only organ in the body that can remove Cys-C. Its expression level was significantly negatively correlated with the ability of glomerular filtration rate of the body. Even if the kidney is slightly injured, Cys-C increases rapidly after 3 hours, and the degree of increase is closely related to the injury [24].

In addition, with the improvement of the overall quality requirements for surgery, the evaluation of postoperative outcome is no longer limited to stone clearance and complications, but falls on the effect of lithotomy on the overall function of the body. Stress hormones and inflammatory markers are important markers for the stress level of the body, which can effectively evaluate the adverse effects of surgery. At the same time, it can also help to better understand the speed of body rehabilitation and the effect of treatment. Therefore, this research took the above indicators as an evaluation index for postoperative effect, so as to more effectively evaluate the two groups of surgical methods.

The results of this research confirmed that the stone clearance rate in the observation group was higher than that in control group, while the operative time, intraoperative blood loss and hemoglobin loss were significantly lower than those in the control group. On the 4th day after treatment, the indexes in the observation group were significantly lower than those in the control group in the same period. The difference was statistically significant. The indexes in the observation group on the 4th day had no difference from those before operation. The hospitalization time, nephrostomy indwelling time and complication rate in the observation group were significantly lower than those in control group.

PCNL has many unparalleled advantages, and it has become the first choice for clinical treatment of complex calculus. Nevertheless, we need to consider whether we can make accu-

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rate judgment of the structure of the pelvis and calyx, the condition of hydronephrosis, and the nature and location of the stone before operation, whether the hospital's equipments meet the standards, and whether the doctor can make the best PCNL plan. All of these would have an impact on the effect of the entire operation.

In this research, there are some problems such as a small number of research populations, short follow-up time, as well as economic conditions of individual patients which limited them to choose open surgery but not PCNL, poor clinical expectation and so on. In the future, we will focus on improving the stone clearance rate in small calyx, which cannot be observed by rigid ureteroscopy, and reducing the incidence of postoperative secondary bleeding and recurrence, in order to develop more advanced methods to better serve the patients. Currently, there are a variety of methods for the treatment of calculus, but none of the methods can be applied to all types of calculus, all of which have some limitations. The general trend of renal calculus surgery in the future is minimally invasive, combined treatment with complementary advantages. However, open surgery is still the preferred method for patients with anatomic abnormalities and failure of minimally invasive surgery in some areas where medical technology and equipment are outdated.

In summary, PCNL for the treatment of complex calculus has the advantages of fewer traumas, lower risk, shorter operative time and less postoperative complications, which has better effect than open lithotomy. Therefore, PCNL is worth further clinical promotion and application.

Disclosure of conflict of interest

None.

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References

[1] Schulsinger DA. Urinary tract stones: from the invisible to the clearly distinct and discernible stone. *Kidney Stone Disease* 2014; 35-41.

- [2] Mitsuzuka K, Nakano O, Takahashi N and Sa-toh M. Identification of factors associated with postoperative febrile urinary tract infection after ureteroscopy for urinary stones. *Urolithiasis* 2016; 44: 257-262.
- [3] Ozgor F, Kucuktopcu O, Sarilar O, Toptas M, Simsek A, Gurbuz ZG, Akbulut MF, Muslum-anoglu AY and Binbay M. Does previous open renal surgery or percutaneous nephrolithotomy affect the outcomes and complications of percutaneous nephrolithotomy. *Urolithiasis* 2015; 43: 541-547.
- [4] Turk C, Petrik A, Sarica K, Seitz C, Skolarikos A, Straub M and Knoll T. EAU guidelines on interventional treatment for urolithiasis. *Eur Urol* 2016; 69: 475-482.
- [5] Laube N, Berg W, Bernsmann F, Gravius S, Klein F, Latz S, Mallek D, Porowski T, Randau T, Wasilewska A and Fisang C. Induced urinary crystal formation as an analytical strategy for the prediction and monitoring of urolithiasis and other metabolism-related disorders. *EPMA J* 2014; 5: 13.
- [6] Abeywickrama B, Ralapanawa U and Chandrajith R. Geoenvironmental factors related to high incidence of human urinary calculi (kidney stones) in Central Highlands of Sri Lanka. *Environ Geochem Health* 2016; 38: 1203-1214.
- [7] Daudon M, Frochot V, Bazin D and Jungers P. Drug-induced kidney stones and crystalline nephropathy: pathophysiology, prevention and treatment. *Drugs* 2017; 78: 163-201.
- [8] Cheungpasitporn W, Rossetti S, Friend K, Erickson SB and Lieske JC. Treatment effect, adherence, and safety of high fluid intake for the prevention of incident and recurrent kidney stones: a systematic review and meta-analysis. *J Nephrol* 2016; 29: 211-219.
- [9] Lalueza A, Sanz-Trepiana L, Bermejo N, Yaiza B, Morales-Cartagena A, Espinosa M, Garcia-Jimenez R, Jimenez-Rodriguez O, Ponce B, Lora D, Orellana MA, Fernandez-Ruiz M, Bermejo S and Aguado JM. Risk factors for bacteremia in urinary tract infections attended in the emergency department. *Intern Emerg Med* 2016; 13: 41-50.
- [10] Pan GQ, Liang YF, Lin BB, Tang ZH, Chen X, Wang LX and Chen MG. NGAL, KIM-1 and IL-18 three injury early diagnostic value in children with acute kidney. *China Modern Doctor* 2015; 53: 67-69.
- [11] Dağgüllü M, Sancaktutar AA, Dede O, Utangaç MM, Bodakçi MN, Penbegül N, Hatipoğlu NK and SÇ. Minimally invasive percutaneous nephrolithotomy: an effective treatment for kidney stones in infants under 1 year of age. A single-center experience. *Urolithiasis* 2015; 43: 507-512.

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- [12] Ichiyanagi O, Nagaoka A, Izumi T, Kawamura Y and Kato T. Age-related delay in urinary stone clearance in elderly patients with solitary proximal ureteral calculi treated by extracorporeal shock wave lithotripsy. *Urolithiasis* 2015; 43: 419-426.
- [13] Cecen K, Karadag MA, Demir A, Bagcioglu M and Kocaaslan R. Erratum to: flexible ureterorenoscopy versus extracorporeal shock wave lithotripsy for the treatment of upper/middle calyx kidney stones of 10-20 mm: a retrospective analysis of 174 patients. *Springerplus* 2016; 5: 484.
- [14] Naderi G, Latif A, Tabassomi F and Esfahani ST. Failure of isolated kidney transplantation in a pediatric patient with primary hyperoxaluria type 2. *Pediatr Transplant* 2014; 18: E69-73.
- [15] Bozzini G, Verze P, Arcaniolo D, Dal Piaz O, Buffi NM, Guazzoni G, Provenzano M, Osmolorskiy B, Sanguedolce F, Montanari E, Macchione N, Pummer K, Mirone V, De Sio M and Taverna G. A prospective randomized comparison among SWL, PCNL and RIRS for lower calyceal stones less than 2 cm: a multicenter experience: a better understanding on the treatment options for lower pole stones. *World J Urol* 2017; 35: 1967-1975.
- [16] Sakr A, Salem E, Kamel M, Desoky E, Ragab A, Omran M, Fawzi A and Shahin A. Minimally invasive percutaneous nephrolithotomy vs standard PCNL for management of renal stones in the flank-free modified supine position: single-center experience. *Urolithiasis* 2017; 45: 585-589.
- [17] Zhu W, Liu Y, Liu L, Lei M, Yuan J, Wan SP and Zeng G. Minimally invasive versus standard percutaneous nephrolithotomy: a meta-analysis. *Urolithiasis* 2015; 43: 563-570.
- [18] De S and Monga M. Percutaneous management of large renal calculi (percutaneous nephrolithotomy). *Minimally Invasive Urology* 2014; 169-176.
- [19] Yang H, Li J, Long G and Wang S. The application of a novel integrated rigid and flexible nephroscope in percutaneous nephrolithotomy for renal staghorn stones. *BMC Urol* 2017; 17: 67.
- [20] Huang JR, Song LM, Xie DH, Li MN, Deng XL, Hu M, Peng ZF, Liu TR, Du C, Yao L, Liu SF, Guo SL and Zhong JQ. A randomized study of minimally invasive percutaneous nephrolithotomy (MPCNL) with the aid of a patented suctioning sheath in the treatment of renal calculus complicated by pyonephrosis by one surgery. *BMC Urol* 2016; 16: 71.
- [21] Calice-Silva V, Raimann JG, Wu W, Pecoits-Filho R, Kotanko P and Levin N. Salivary urea nitrogen as a biomarker for renal dysfunction. *Biomarkers in Kidney Disease* 2016; 9: 647-665.
- [22] El-Ashmawy NE, El-Zamarany EA, Khedr NF, El-Fattah AIA and Eltoukhy SA. Kidney injury molecule-1 (Kim-1): an early biomarker for nephropathy in type II diabetic patients. *International Journal of Diabetes in Developing Countries* 2015; 35: 431-438.
- [23] Ebrahimi T, Pirasteh H, Rezakhaniha B, Dormanesh B, Rabati RG, Yahaghi E and Mokarizadeh A. Retracted article: the value of U-NGAL expression as a potential prognostic biomarker in patients with renal cancer after neoadjuvant chemotherapy with cisplatin. *Tumour Biol* 2016; 12: 16377.
- [24] Lezaic V, Dajak M, Radivojevic D, Ristic S and Marinkovic J. Cystatin C and serum creatinine as predictors of kidney graft outcome. *Int Urol Nephrol* 2014; 46: 1447-1454.