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Clinical Assessment of Risk Factors for Renal Atrophy After Percutaneous Nephrolithotomy

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Background: This study explored the risk factors for renal atrophy after percutaneous nephrolithotomy (PCNL), and provides a reference for clinical prevention of renal atrophy after PCNL.

Material/Methods: According to the inclusion and exclusion criteria, the clinical data of 816 patients who underwent PCNL in our hospital from May 2013 to February 2018 were retrospectively collected. Depending on whether the patient had kidney atrophy, they were divided into a renal atrophy group and a non-renal atrophy group. We collected and analyzed data on patient sex, age, kidney location, duration of disease, stone size, hydronephrosis, renal calculus position (renal ureteral junction or multiple pyelonephritis-associated stones), operation time, intraoperative blood loss, perfusion pressure, and pyonephrosis. The indicators with statistically significant differences were selected and multivariate logistic regression analysis was carried out to determine the risk factors for renal atrophy.

Results: Among 816 patients, 49 had renal atrophy and the incidence rate was 6.01%. Univariate analysis and multivariate logistic regression analysis showed that independent risk factors for renal atrophy after PCNL were: duration of the disease longer than 12 months (OR=4.216, P=0.003, 95% CI: 1.714, 7.354), perfusion pressure >30 mmHg (OR=3.895, P=0.001, 95% CI: 1.685, 8.912), moderate and severe hydronephrosis (OR=5.122, P<0.001, 95% CI: 1.847, 9.863), stones located at the junction of the renal pelvis (OR=3.787, P=0.001, 95% CI: 1.462, 7.654), stones located in multiple calyces (OR=4.531, P=0.014, 95% CI: 1.764, 8.196), and pyonephrosis (OR=10.143, P<0.001, 95% CI: 2.214, 16.248).

Conclusions: The main risk factors for renal atrophy after PCNL are: course of disease more than 12 months, moderate and severe hydronephrosis, pyonephrosis, multiple calyceal stones, stones at the junction of the renal pelvis, and intraoperative high perfusion pressure.

MeSH Keywords: Kidney • Kidney Calculi • Patient Compliance • Risk Factors

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Background

Kidney stones are caused by abnormal accumulation of crystalline substances (e.g., calcium, oxalic acid, uric acid, and cystine) in the kidneys. The incidence rate is 10.34% among males and 6.62% among females [1–3]. At present, the pathogenesis of kidney stones has not been fully elucidated, and may be related to genetics, metabolism, infection, environment, diet, anatomy, and drugs [2–8]. PCNL has become an important minimally invasive method for the treatment of renal calculi because of its minor trauma, rapid recovery, and ability to perform repeated lithotripsy [9,10]. However, PCNL technology is difficult to use, and it is greatly affected by the composition, size, and location of the stones, and it is difficult to avoid damage to the structure and function of the kidneys. Severe cases are often complicated by septic shock and renal failure [8–10]. Recent clinical studies have reported complications such as bleeding, infection, residual stones, and renal atrophy after PCNL [8–11]. Many studies have reported the causes and risk factors of postoperative bleeding and infection in PCNL, but the causes and risk factors of renal atrophy after PCNL have rarely been reported. This study retrospectively analyzed the clinical data of patients with renal atrophy after PCNL, and then explored the possible risk factors of renal atrophy after PCNL, and provides references for the prevention and treatment of renal atrophy after PCNL.

Material and Methods

Clinical data

The clinical data of 816 patients who underwent PCNL in our hospital from May 2013 to February 2018 were retrospectively analyzed. The follow-up period was 2 years. According to the occurrence of renal atrophy, patients were divided into a renal atrophy group and a non-renal atrophy group. Inclusion criteria were: (1) underwent a PCNL operation, (2) normal results of creatinine and urea before operation, (3) signed informed consent, and (4) complete medical record information. Exclusion criteria were: (1) history of malignant tumors and neuropsychiatric disorders in the past; (2) hypertensive nephropathy, diabetic nephropathy and other kidney atrophy diseases in the past; (3) severe heart, liver, or kidney insufficiency in the past; (4) hematological diseases; (5) hypercalcemia or parathyroid dysfunction and other metabolic diseases; and (6) serious chronic infectious diseases. This study was approved by the Ethics Committee of Chongqing Traditional Chinese Medicine Hospital. All the patients in the study and their families provided signed informed consent.

Judgment of renal atrophy

According to the literature [11-13], normal renal size (long axis) ranged from 11 to 13.5 cm on the left (average 12.2 cm) and from 10.8 to 13 cm on the right (average 11.9 cm). It is generally believed that a difference of 1.5 cm in length (long axis) between the 2 kidneys (preoperative and postoperative) is of diagnostic significance. Computed tomography (CT) was used to diagnose renal atrophy if it was first shown by ultrasonography. Renal atrophy was assessed by the ratio of renal cortical area to lumbar 1 vertebral body area, as follows. (1) For measurement of the area of renal cortex, several consecutive oblique coronal images were reconstructed parallel to the main renal vein. The maximum reconstructed plane was obtained. The contour of the renal cortex including renal column was drawn by two-dimensional image contour extraction method (slice method), and the area of the renal cortex was calculated. (2) Measure the area of the lumbar 1 vertebral body at the level of the pedicle in transverse image and get the maximum value. (3) The ratio of the maximum cortical area of kidney to the maximum lumbar vertebral area was calculated after and before surgery. The grading criteria were: ratios less than 50% were considered severe renal atrophy, ratios between 51% and 75% were considered moderate atrophy, and ratios between 76% and 100% were considered mild atrophy. The renal cortical area and lumbar vertebra area were measured with Image J software.

Research methods

The follow-up data of the patients within 2 years were collected. Doppler ultrasound was the main method of follow-up and was performed every 6 months to determine whether kidney atrophy had occurred. Doppler ultrasound was performed to assess renal atrophy in patients with kidney CT to determine the size of the kidney and to confirm renal atrophy. We recorded data on patient sex, age, kidney position (left, right), medical history including the time of back pain or discovery of kidney stone (≤12 months, >12 months), stone size (≤3 cm, >3 cm), and the degree of hydronephrosis. Mild hydronephrosis was defined as the separation of the renal sinus and enlargement of calices by interconnected areas filled with sonolucent urine, with the preservation of renal papillae. Moderate hydronephrosis was defined as the blunting or rounding of the calices or the obliteration of renal papillae without affecting the cortical thickness. Severe hydronephrosis was considered to be present if caliceal ballooning and cortical thinning were found [14]. We also collected data on stone location (calculus at the junction of the renal pelvis, multiple renal pelvis stones), operation time (>60 min, ≤60 min), intraoperative bleeding (>100 ml, ≤100 ml), intraoperative perfusion pressure (≤30 mmHg, >30 mmHg), and pyonephrosis.

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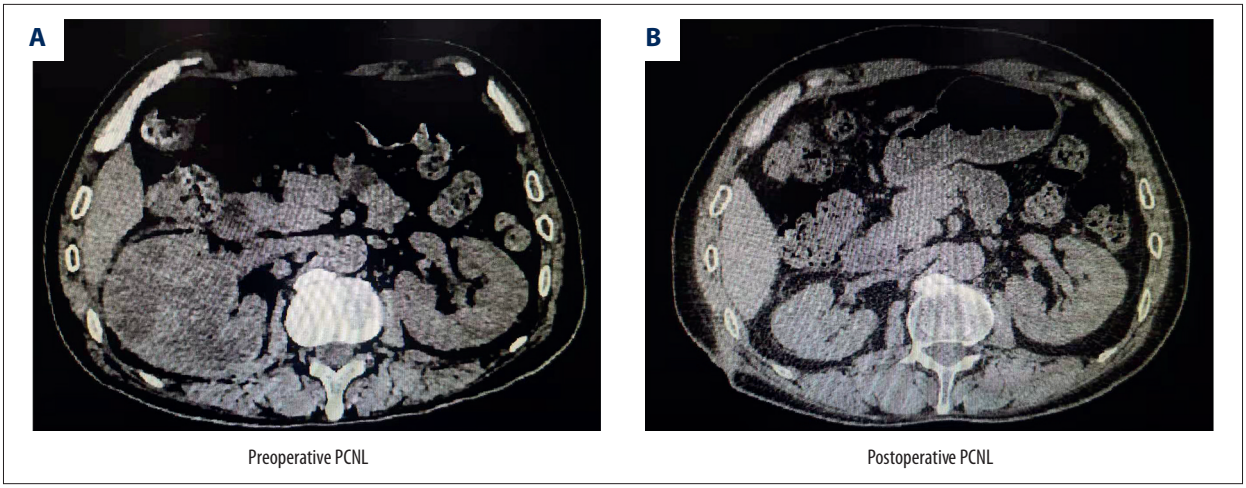

Figure 1. An example image of atrophied kidney after PCNL before/after surgery. A is a renal CT scan of a patient with pyonephrosis before PCNL. B is a renal CT scan of a patient with pyonephrosis after PCNL.

PCNL procedure

PCNL surgery has been described in previous reports [15]. Before the operation, patients were routinely disinfected and sheeted, and indwelling ureteral catheters were placed to produce artificial hydronephrosis. The patient was placed in the prone position, and under the guidance of B-ultrasound, an 18G puncture needle was targeted into the fornix of the middle calyx of the kidney. The guide wire was inserted and fixed. The fascial dilator was used for continuous expansion to 24F, and the 24F sheath was retained. We used pneumatic ballistic gravel. A ureteral stent and an 18F nephrostomy tube were placed at the end of surgery.

Statistical analysis

SPSS 20.0 software was used for data analysis. Measurement data are expressed as mean±standard deviation ($\chi \pm s$) and were assessed by *t* test. The Kolmogorov-Smirnoff single-sample test was used to calculate the normal distribution of continuous variables before doing further comparisons. The chi-square test was used to compare the 2 groups. When P was <0.05, the difference was regarded as statistically significant. Multivariate logistic analysis was used to analyze the statistical significance of the indicators. When P<0.05, the difference was regarded as significant.

Results

Changes in the incidence of renal atrophy after PCNL

In this study, 816 patients met the inclusion and exclusion criteria, 49 of whom had renal atrophy, and the incidence was 6.00%. Among them, 8 patients had renal atrophy 6 months after the operation, 30 had renal atrophy 1 year after the operation, and 11 had renal atrophy 2 years after the operation. Figure 1 is an example of an atrophied kidney image after PCNL before/after surgery. There were 15 cases (30.61%) of mild renal atrophy (cortical area: 14.85±3.59 mm, vertebral area: 18.06±4.11 mm, cortical area/vertebral area: 0.78±0.16) and 34 cases (69.38%) of moderate (cortical area: 10.21±3.07 mm, vertebral area: 17.96±4.09 mm, cortical area/vertebral area: 0.61±0.12) and severe (cortical area: 7.31±2.85 mm, vertebral area: 18.26±3.89 mm, cortical area/vertebral area: 0.37±0.13) renal atrophy.

Univariate analysis of risk factors for renal atrophy after PCNL

The results (Table 1) showed that there were no significant differences in age (P=0.185), sex (P=0.168), location of affected kidney (P=0.555), stone size (P=0.721), and operation time (P=0.601) between the renal atrophy group and the non-atrophy group. However, there were significant differences in duration of disease (P=0.007), intraoperative bleeding volume (P=0.010), perfusion pressure (P=0.001), hydronephrosis degree (P<0.001), calculi at the junction of pelvis and ureter (P=0.002), multiple calyx calculi (P=0.001), and pyonephrosis (P<0.001) between the 2 groups.

Multivariate logistic regression analysis of risk factors for renal atrophy after PCNL surgery

Multivariate logistic analysis (Table 2) showed that intraoperative bleeding was >100 ml (P=0.071), which was insufficient to determine that it was an independent risk factor for renal atrophy after PCNL. However, duration of disease >12 months (P=0.003), renal perfusion pressure >30 mmHg (P=0.001), moderate-to-severe hydronephrosis (P<0.001), stones located

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Table 1. Risk factors of renal atrophy after PCNL (n=816).

Parameter		Renal atrophy group	Non-renal atrophy group	χ^2/t value	P value
Age	Year	49.73±8.78	47.13±9.78	1.492	0.185
Gender	Male	30	541		
	Female	19	226	1.900	0.168
Location of affected kidney	Left	28	405		
	Right	21	362	0.348	0.555
Medical history (month)	>12	28	289		
	≤12	21	478	7.345	0.007
Stone size (cm)	>3	26	427		
	≤3	23	340	0.127	0.721
Intraoperative bleeding volume (ml)	>100	27	281		
	≤100	22	486	6.683	0.010
Perfusion pressure (mmHg)	>30	29	261		
	≤30	20	506	11.67	0.001
Operation time	>60	27	393		
	≤60	22	374	0.275	0.601
Degree of hydronephrosis	Moderate to severe	35	348		
	No or mild	14	419	10.699	<0.001
Calculi at the junction of pelvis and ureter	Yes	32	328		
	No	17	439	9.493	0.002
Multiple calyceal stones	Yes	34	350		
	No	15	417	10.433	0.001
Pyonephrosis	Yes	28	196		
	No	21	571	19.425	<0.001

Table 2. Multivariate logistic regression analysis of risk factors for renal atrophy after PCNL (n=816).

Risk factors	β	P value	OR value	95% CI
Medical history >12 months	1.076	0.003	4.216	1.714, 7.354
Intraoperative bleeding >100 ml	0.106	0.071	2.418	0.918, 5.879
Perfusion pressure >30 mmHg	1.418	0.001	3.895	1.685, 8.912
Moderate to severe hydronephrosis	2.174	<0.001	5.122	1.647, 9.863
Calculi at the junction of pelvis and ureter	1.214	0.001	3.787	1.462, 7.654
Multiple calyx stones	1.856	0.014	4.531	1.764, 8.196
Pyonephrosis	2.502	<0.001	10.143	2.214, 16.248

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at the junction of the pelvis (P=0.001), multiple calyx stones (P=0.014), and pyonephrosis (<0.001) were independent risk factors for renal atrophy after PCNL and are important indicators for clinical treatment.

Discussion

In the past, the treatment of renal calculi mainly used drug lithotripsy, extracorporeal shock wave lithotripsy, and nephrolithotomy. These methods have some shortcomings, such as low efficacy of lithotripsy, large incision, slow recovery, many complications, and difficulty in performing a second operation [16]. In 1976, Fernstrom and Johannson first used PCNL to remove pelvic calculi and created the PCNL method [17]. PCNL is an effective method for the treatment of upper urinary tract stones. With laser and ultrasound lithotripsy tools, kidney stones can be quickly broken and removed, and the stone clearance is better than 2 cm [18]. PCNL, as a minimally invasive operation, can perform repeated lithotripsy because of its small trauma and rapid recovery, and has become an important type of kidney stone surgery [19]. Although PCNL has obvious advantages in the treatment of renal calculi, complications such as bleeding, infection, residual stones, and renal atrophy after PCNL cannot be ignored [17–20]. At present, there are few reports on the causes and risk factors of renal atrophy after PCNL. This study summarized and analyzed the clinical data of 816 patients to determine the risk factors of renal atrophy and to provide a reference for clinical prevention. Kidney atrophy is a pathological and anatomical phenomenon that causes loss of nephrons or insufficient blood supply to the kidneys, resulting in shrinkage of kidney volume and decrease of physiological function. Renal atrophy is a serious late complication after renal calculi surgery. Some studies have reported that the incidence of renal atrophy after PCNL is 8.6% [21]. In the present study, we followed up PCNL patients in our hospital for 2 years and found that 49 of 816 patients (6.01%) had renal atrophy more than 1 year after surgery. The results of the present study are lower than those reported in previous studies, perhaps due to the maturity of PCNL technology and the improvement of the efficiency of lithotripsy equipment.

In this study, we found that there were no significant differences in age, sex, location of affected kidney, size of calculi, and operation time between the renal atrophy group and the non-atrophic group (P>0.05). However, there were significant differences in intraoperative blood loss, duration of disease, intraoperative renal perfusion pressure, degree of hydronephrosis, stones at the junction of renal pelvis, multiple renal pelvis stones, and renal empyema (P<0.05). Multivariate logistic regression analysis showed that intraoperative bleeding of more than 100 ml was not an independent risk factor for renal atrophy after PCNL. However, independent risk factors for renal atrophy after PCNL included duration of disease longer than 12 months, intraoperative perfusion pressure >30 mmHg, moderate-to-severe hydronephrosis, location of stones at the junction of pelvis and ureter, multiple calyxes, and pyonephrosis. The mechanism of renal atrophy after PCNL is still unclear. It has been found that bacterial infections caused by calculi can release many oxygen free radicals from mitochondria, lead to destruction of renal parenchymal cells, and aggravate renal damage, which may be one of the risk factors for renal atrophy [22,23]. In the present study, pyonephrosis was found to be caused by infection and contained many bacteria that release a large amount of oxygen free radicals and inflammatory factors, leading to renal parenchyma destruction and kidney atrophy. Secondly, hydronephrosis caused by kidney stones can cause renal artery vasoconstriction changes, and the intima of the blood vessels is irregularly thickened, which changes the blood supply to the kidney, which may be another risk factor affecting renal atrophy [22–24]. Studies have found that after complete ureteral obstruction in mice, renal tubular epithelial cell apoptosis and fibrosis can occur, and kidney atrophy occurs in mice at 2-4 weeks, which may be another factor affecting renal atrophy [22–25]. The present study found that risk factors for PCNL were duration of disease longer than 12 months, moderate-to-severe hydronephrosis, and location of calculi at the junction of the pelvis and ureter. Moderate-to-severe hydronephrosis can damage renal vessels and renal parenchyma, leading to renal atrophy. The prolonged course of disease and the location of stones at the junction of the renal pelvis can aggravate urinary tract obstruction and hydronephrosis, aggravate renal parenchyma injury, and further induce renal atrophy. Under the condition of high-pressure perfusion during PCNL, the structure of nephrons gradually changes with increased pressure, with diffuse exfoliation and flattening of calyceal urothelium, submucosal edema and congestion, and vacuolation of renal tubules, which further impair renal function [26,27]. The present study found that intraoperative perfusion pressure >30 mmHg was an independent risk factor for renal atrophy in PCNL, which suggests that strict control of intraoperative perfusion pressure is an important measure to avoid intraoperative renal injury and postoperative renal atrophy. In this study, we also found that multiple calyceal stones are an independent risk factor for renal atrophy after PCNL, perhaps because the Peel-Away sheath torque needs to be expanded to remove stones during surgery. This process can lead to renal parenchymal tearing, perfusion leakage, renal interstitial swelling, inflammatory cell infiltration, and other changes. These factors may induce renal atrophy after PCNL.

This study has some limitations. Firstly, the study sample was relatively small, it was not a prospective randomized controlled trial, and the follow-up time was relatively short.

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Further larger-sample long-term follow-up is needed to obtain more accurate clinical data for in-depth analysis. Secondly, the pathophysiology of renal atrophy after PCNL has not been elaborated and explored in detail. In addition, this was a single-center regression study, and multi-center studies can obtain more accurate clinical reference data. In conclusion, renal atrophy is one of the complications after PCNL for renal calculi, and its incidence is low.

Conclusions

Independent risk factors for renal atrophy after PCNL include longer duration of disease, moderate-to-severe hydronephrosis, location of stones at the junction of the pelvis, multiple calyx stones, and pyonephrosis. Early identification of the risk factors for renal atrophy after PCNL and formulation of reasonable preventive measures are needed to control the occurrence of renal atrophy.

Conflict of interest

None.

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