

Original Article

Multiple linear regression model for predicting functional recovery in obstructive uropathy due to stones

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Received December 17, 2015; Accepted May 5, 2016; Epub June 15, 2016; Published June 30, 2016

Abstract: This study aimed to develop a mathematical model for predicting recovery potential of an obstructed kidney with poor function by a noninvasive method. We analyzed a cohort study of 93 patients who suffered from unilateral renal or ureteral stones with hydronephrosis and renography showing an ipsilateral glomerular filtration rate (GFR) <15 ml/min. We recorded clinical parameters, including age, sex, body mass index, residual renal volume (RRV), unilateral GFR, and split renal function (SRF) before percutaneous nephrostomy (PCN). After 38.16 ± 5.87 days of drainage. Renal function was re-evaluated by renography. Almost all of the kidneys showed changes in GFR and SRF. Univariate and multivariate analysis showed that the patient's age, RRV, pre-GFR, and pre-SRF were significant factors associated with recoverability of renal function. A multiple linear regression model was developed to predict the recovery potential of the obstructed kidney.

Keywords: Urolithiasis, ureteral obstruction, renal function, linear models, percutaneous nephrostomy

Introduction

Urolithiasis can result in hydronephrosis and impairment of renal function, eventually leading to atrophy of the kidneys [1]. Management of poorly functioning kidneys due to obstruction by calculi still remains debatable. Some urologists prefer nephrectomy, especially when split renal function (SRF) is <10%. While others favor renal salvage by drainage and observation because predicting the potential functional recovery of an obstructed kidney after relief from obstruction is difficult and inaccurate [2-4]. Several methods or indices have been used to assess renal function, including serum creatinine levels, glomerular filtration rate (GFR), excretory urography, computed tomography (CT), and magnetic resonance imaging [5]. Currently, radionuclide renography is one of the most popular methods to evaluate overall and split renal function, but it is useless for prediction of functional recoverability [3].

Percutaneous nephrostomy (PCN), first described by Goodwin et al. [6], has been performed

to gain temporary relief of obstruction of the kidneys worldwide. Some researchers have used PCN as an effective means of determining recoverability of renal function in ureteropelvic junction obstruction (UPJO) [7, 8], the finding shows improved function in a large proportion of kidneys in both children and adults. However, there are limited data on the outcome of PCN in obstructed kidneys with urinary stones. If renal functional recoverability following PCN could be predicted, this would be helpful for choosing a treatment method.

This study aimed to develop a mathematical model for predicting the recovery potential of an obstructed kidney with poor renal function following PCN.

Materials and methods

Patients

The present study was approved by the Ethical Committee of Tongji Hospital of Tongji Medical College of Huazhong University of Science and

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Table 1. Demographics of the patients

Characteristic†	(n=93)
Sex	
Male	39 (41.94)
Female	54 (58.06)
Age, year	47.80±13.72
BMI	23.41±3.58
Affected side	
Left	48 (51.61)
Right	45 (48.39)
Pre-GFR‡, ml/min	8.14±3.55
Pre-SRF‡, %	12.61±5.42
RRV§, ml	42.15±17.44
Hydronephrosis, ml	1542.38±796.43
PCN duration, day	38.16±5.87
Post-GFR¶, ml/min	13.90±7.14
Post-SRF¶, %	19.25±8.74

†Data are shown as mean ± SD or n (%). ‡Pre-GFR/pre-SRF, ipsilateral GFR/SRF before PCN drainage. §RRV, residual renal volume. ¶Post-GFR/post-SRF, ipsilateral GFR/SRF after PCN drainage.

Technology. Between March 2013 and February 2015, all patients who suffered from unilateral renal or ureteral stones with severe hydronephrosis were evaluated preoperatively with urinalysis, urine culture, a complete blood count, serum biochemistry, coagulation tests, abdominal ultrasonography and three-dimensional CT (3D-CT) image reconstruction software (GE workstation 4.6, Fairfield, CT) was used to calculate the residual renal volume (RRV). Technetium-99m diethylenetriamine pentaacetic acid (^{99m}Tc DTPA) was used for diuretic renography to assess the GFR and SRF. We applied the criteria introduced by Lee et al. [9] to categorize the degree of hydronephrosis as severe, moderate, or mild. Patients who had ipsilateral GFR <15 ml/min and contralateral GFR >40 ml/min were included in this study. Exclusion criteria included infection, UPJO, and compression of the ureter. Finally, 93 patients were included in this study.

Surgical procedures

With the patient in the prone position under local or general anesthesia, PCN was performed in the affected side. The dilated collecting system was punctured by a 4F puncture needle under ultrasound guidance. A guide wire was then inserted and fixed. The puncture nee-

dle was withdrawn and dilation of the percutaneous tracts were performed serially over the guidewire with a fascial dilator to 14F. At the end of the procedure, a 12F nephrostomy tube was left in place.

Outcomes evaluation

Drainage was maintained for approximately 1 month. Changes in hydronephrosis and renal function were re-evaluated with abdominal ultrasound and radionuclide renography.

Statistical analysis

All of the data were analyzed using the SPSS version 17.0 statistical software package (SPSS Inc., Chicago, IL). Analysis of variance of repeated measurement design was performed to evaluate the between-group differences of continuous variables. Levene's tests were computed to examine the homogeneity of variance. Correlations of changes in GFR with various variables were examined by Pearson correlations. A multiple linear regression model using the stepwise method was performed to predict the relationships between renal functional recoverability and the selected variables. All *p* values were two-tailed and *P*<0.05 was considered as statistically significant.

Results

The patients' demographics are shown in **Table 1**. The mean age and body mass index were 47.80±13.72 years (range, 18-78 years) and 23.41±3.58, respectively. The sex distribution was slightly skewed toward women (58.06% vs. 41.94%). The left to right side ratio was 48:45. Before PCN, the mean GFR (pre-GFR) was 8.14±3.55 ml/min and SRF (pre-SRF) was 12.61%±5.42%. PCN tubes were successfully placed in all patients and none of the patients had bleeding or urinary tract infection. The mean volume of urine that was drained from the nephrostomy tubes was 1542.38±796.43 ml, which indicated the volume of hydronephrosis.

After a mean of 38.16±5.87 days of PCN drainage, almost all kidneys showed changes in GFR and SRF on radionuclide renography. In 39 male patients, the mean GFR and SRF of affected kidneys before PCN were 8.10±3.97 ml/min and 14.14%±8.05%, and these values increased to 12.87±6.24 ml/min and 19.83%±

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Table 2. Comparison of changes in GFR and SRF among different subgroups of variables

	n	Pre-GFR, ml/min	Post-GFR, ml/min	P value	Pre-SRF, %	Post-SRF, %	P value
Sex				0.879			0.624
Male	39	8.10±3.97	14.14±8.05		12.87±6.24	19.83±10.26	
Female	54	8.17±3.25	13.72±6.47		12.41±4.80	18.83±7.53	
Age, year				0.008*			0.147
≤30	14	10.23±3.06	19.79±7.01		14.05±5.09	23.81±8.56	
30~60	62	7.62±3.71	12.82±7.12		11.95±5.64	18.08±9.06	
>60	17	8.32±2.75	12.95±4.87		13.81±4.68	19.73±6.58	
BMI				0.160			0.449
≤18.5	9	9.77±2.26	18.43±4.93		13.93±3.79	23.36±6.00	
18.5-24.9	54	8.09±3.76	13.77±7.60		12.63±5.69	19.05±9.35	
>24.9	30	7.75±3.42	12.77±6.44		12.18±5.42	18.37±8.15	
Affected side				0.383			0.257
Left	48	8.46±3.70	14.51±8.10		13.25±5.78	20.21±9.51	
Right	45	7.80±3.39	13.24±6.38		11.93±4.99	18.22±7.81	
RRV, ml				0.000*			0.000*
≤30	31	4.47±2.35	5.95±3.26		7.70±4.54	9.81±5.67	
30-60	45	9.43±2.47	16.45±4.54		14.55±4.08	22.77±5.60	
>60	17	11.45±1.70	21.62±3.47		16.43±3.45	27.11±4.43	
Pre-GFR, ml/min				0.000*			0.000*
≤5	21	3.40±1.21	4.43±1.47		5.84±2.40	7.34±2.64	
5-10	42	7.62±1.54	12.98±3.76		12.34±3.44	19.14±5.43	
11-15	30	12.20±1.38	21.80±3.05		17.72±3.51	27.72±4.16	
Pre-SRF, %				0.000*			0.000*
≤10%	33	4.51±1.88	6.67±3.83		6.74±2.39	9.56±4.21	
10-20%	54	9.80±2.38	17.38±5.10		15.04±2.80	23.63±4.69	
>20%	6	13.22±1.10	22.30±2.38		22.96±1.45	33.11±1.47	

*p<0.05 was considered statistically significant.

10.26%, respectively, after drainage (**Table 2**). Similar findings were observed in women, but there were no differences between the two groups (P>0.05). The side of the affected kidney and body mass index also had no effect on renal functional recoverability (i.e., changes in GFR and SRF).

When comparing changes in GFR among the different age groups (≤30, 30-60, >60 years), we found that younger adults received better results than elderly patients (P=0.008). However, no significant difference in changes in SRF was observed among the age groups. RRV was divided into three categories (≤30, 30-60, >60 ml). The pre-GFR and pre-SRF were also categorized according to pre-PCN renography into three groups (≤5, 5-10, 10-15 ml/min; ≤10%, 10-20%, >20%, respectively). As presented in **Table 2**, statistical analysis showed distinct differences in RRV, pre-GFR, and pre-

SRF groups, regardless of changes in GFR or SRF (all P<0.05).

There was a significant negative correlation between renal GFR recoverability and the patient's age (r=-0.34, P=0.001, **Figure 1A**). RRV (r=0.89, P<0.001), pre-GFR (r=0.89, P<0.001), and pre-SRF (r=0.72, P<0.001) maintained positive associations with restoration of renal function (**Figure 1B-D**).

After stepwise multiple linear regression analysis, only the patient's age (X₁), RRV (X₂), pre-GFR (X₃), and pre-SRF (X₄) remained in the regression equation (**Table 3**). The multiple regression equation with a high adjusted R² value of 0.975 is shown below:

$$\Delta\text{GFR} = -0.354X_1 + 0.623X_2 + 0.995X_3 - 0.336X_4$$

Using standardized coefficients, we found that pre-GFR was the first factor affecting renal

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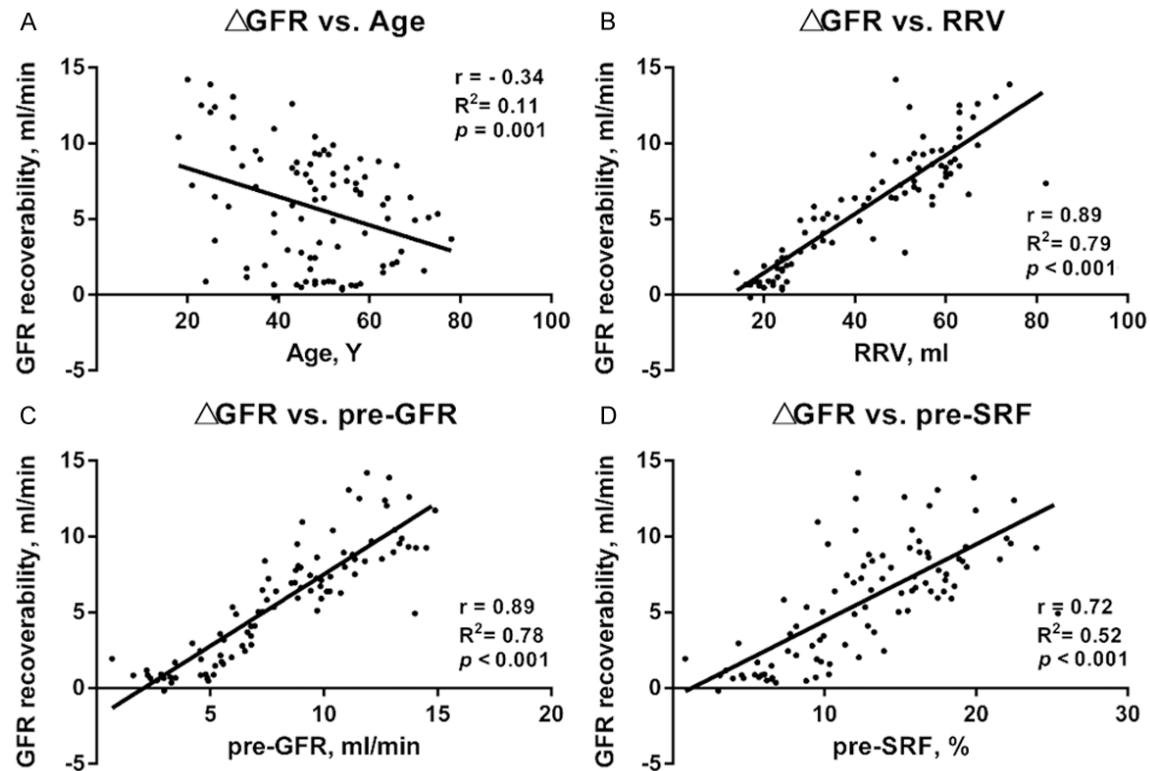


Figure 1. Correlations between renal GFR recoverability and different variables. There was a significant negative correlation between renal GFR recoverability and the patient's age (A). RRV, pre-GFR, and pre-SRF maintained positive associations with restoration of renal function (B-D).

Table 3. Multiple linear regression analysis of the factors affecting recoverability of GFR

Variables	Unstandardized coefficients	Standardized coefficients	t value	P value	Adjusted R ²
Age	-0.049	-0.354	-9.716	0.000*	0.975
RRV	0.094	0.623	9.166	0.000*	
Pre-GFR	0.771	0.995	9.595	0.000*	
Pre-SRF	-0.168	-0.336	-3.489	0.001*	

* $p < 0.05$ was considered statistically significant.

functional improvement in our study, followed by RRV, pre-SRF, and the patient's age.

Discussion

Upper urinary tract stones are a major contributory factor to worsening renal function. These patients can have severe hydronephrosis and dramatically decreased renal function [10]. Treatment of a patient with severe renal functional impairment resulting from obstruction of stones can be challenging and irrefutable. This is because doctors find it difficult to decide on whether they should perform nephrectomy directly or provide temporary relief

from obstruction and secondary surgery, owing to the fact that functional recovery cannot be well predicted.

Preservation and salvage of an obstructed kidney is indicated when there is evidence for good functional recoverability. If urologists are able to accurately predict the recovery potential of an obstructed kidney, this would be helpful for making relevant clinical decisions [3]. Common renal functional tests, such as blood urea nitrogen, serum creatinine, and the creatinine clearance rate, are of little use in a normal contralateral kidney [11, 12]. Renography is widely used to assess SRF, but it is also helplessness for accurate prediction of recovery [2, 7]. Moreover, reduced kidney function due to obstruction may decrease the sensitivity and specificity of renography in assessing GFR. During obstruction, elevated intrapelvic pressure reduces the effective glomerular filtration pressure. Additionally, because of an obstructed urinary tract, ^{99m}Tc DTPA may be trapped in the collecting system and this could

affect radiologists in identifying the region of interest.

Goodwin et al. [6] first described using PCN for relief of an obstructed kidney and for assessment of renal function to perform reconstructive surgery in optimal conditions. Some researchers have reported the use of PCN as an effective means to determine the recoverability of renal function in children or adults with UPJO [7, 12]. They showed improved function in a large proportion of kidneys, even with an SRF <10%. However, there are limited studies on the outcome of PCN in obstructed kidneys with urinary stones. Obstruction from calculi is different from UPJO, which usually comprises partial obstruction and has a longer duration in adults.

We evaluated renal functional recovery following PCN in 93 patients with severe hydronephrosis due to stone obstruction. The GFR of the affected kidney was less than 15 ml/min. The majority of the patients obtained a certain extent of renal functional recovery after drainage for approximately 1 month. We found that four factors were significantly associated with the improvement of renal function: patient's age, pre-GFR, pre-SRF, and RRV. Patients with larger residual renal tissue before PCN appeared to be more likely to obtain improvement in kidney function. Mibu et al. [13] reported that renal volume is closely related to renal function. In addition, better GFR and SRF of an affected kidney are also beneficial for functional recovery. A young age showed a markedly protective effect on recoverability of GFR, but there was no significant difference in a change in SRF among the three groups (≤ 30 , 30-60, >60 years). A reasonable explanation for this finding is that young patients often have a higher contralateral GFR than elderly patients. Therefore, on the same level of improvement in SRF, younger patients always have better GFR recoverability than older patients. Our study showed a similar conclusion by univariate analysis.

Multiple linear regression analysis showed that the patient's age, RRV, pre-GFR, and pre-SRF remained significant as independent risk factors for renal functional recovery. Automated curve fitting yielded quality of fit statistics that uniformly converged to coefficient of determination values ($R^2=0.975$), indicating a good

quality of curve fit to the datasets. The variables adopted in the mathematical model need to be assessed before the surgical procedure. Our findings suggest that urologists can use these noninvasive test results to predict the recoverability of an obstructive kidney according to the regression equation.

Examples of using this equation in clinical practice are as follows: A 39-year-old patient suffers from severe hydronephrosis due to stone obstruction. The residual renal volume calculated based on 3D-CT is 40 ml, and renography shows that the individual GFRs of two kidneys are 10 ml/min and 60 ml/min. The following equation can be adopted: $\Delta GFR = -0.354 \times 39 + 0.623 \times 40 + 0.995 \times 10 - 0.336 \times [10/(10+60) \times 100] = 16.26$ ml/min. However, for a 70-year-old patient, whose RRV is 40 ml, and the GFRs of two kidneys are 10 ml/min and 45 ml/min, the predictive ΔGFR would be 3.98 ml/min.

Hussain and colleagues [12] predicted renal functional recovery in obstructive renal failure due to stones. They found that a pre-operative DTPA scan was correlated with a post-operative decrease in serum creatinine levels. Moreover, a urine pH of 6 or less, post-PCN diuresis, and natriuresis were good prognostic indicators. Additionally, they found that PCN was the most reliable method of predicting future recovery of renal function after relief of obstruction, with 97.8% accuracy. However, in our study, some invasive test results, including drainage urine volume, pH, natriuresis, and urine specific gravity, were excluded. These factors were excluded because we wanted to develop a mathematical model for predicting recovery potential using simple clinical data only by a noninvasive method, which might be helpful in making decisions and saving time for waiting and observation. Moreover, in contrast to other reports [14, 15], routine biochemistry measurements, such as serum creatinine, urea, and potassium levels, were not chosen as variables in our research because their collinearity with GFR on renography might have reduced the efficacy of the regression equation. To the best of our knowledge, no studies to date have directly predicted the recovery potential of an obstructed kidney by a noninvasive method.

Because our data were developed from a single institution, our research has limitations. The

observation time (38.16 ± 5.87 days) was not long. Patients, especially those who had lithotripsy performed after PCN, should be carefully evaluated in the postoperative follow-up period. Additionally, we excluded kidneys with infection. Further prospective studies with these patients are necessary in future. We anticipate that other researchers will test our model and add other factors from their own clinical practice.

In conclusion, our study shows that patients with larger residual renal tissue, and better GFR and SRF of the affected kidney before PCN are more likely to obtain improvement in kidney function. Young age shows a markedly protective effect on renal functional recoverability. We have developed a mathematical model for predicting the recovery potential of an obstructed kidney using noninvasive parameters. This will be helpful for surgeons in making decisions regarding the management of hydronephrosis due to urinary calculi with poor renal function.

Acknowledgements

We wish to thank Dr. Shuping Sang (School of Medicine, Yunnan University, Kunming, P. R. China) for her excellent statistical support.

Disclosure of conflict of interest

None.

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References

- [1] Iravani O, Tay EW, Bay BH, Ng YK. Unilateral ureteric stone associated with gross hydronephrosis and kidney shrinkage: a cadaveric report. *Anat Cell Biol* 2014; 47: 267-70.
- [2] Bansal R, Ansari MS, Srivastava A, Kapoor R. Long-term results of pyeloplasty in poorly functioning kidneys in the pediatric age group. *J Pediatr Urol* 2012; 8: 25-8.
- [3] Zhang S, Zhang Q, Ji C, Zhao X, Liu G, Zhang S, Li X, Lian H, Zhang G, Guo H. Improved split renal function after percutaneous nephrostomy in young adults with severe hydronephrosis due to ureteropelvic junction obstruction. *J Urol* 2015; 193: 191-5.
- [4] Ransley PG, Dhillon HK, Gordon I, Duffy PG, Dillon MJ, Barratt TM. The postnatal management of hydronephrosis diagnosed by prenatal ultrasound. *J Urol* 1990; 144: 584-7; discussion 593-4.
- [5] O'Reilly PH. Role of modern radiological investigations in obstructive uropathy. *Br Med J (Clin Res Ed)* 1982; 284: 1847-51.
- [6] Goodwin WE, Casey WC, Woolf W. Percutaneous trocar (needle) nephrostomy in hydronephrosis. *J Am Med Assoc* 1955; 157: 891-4.
- [7] Wagner M, Mayr J, Hacker FM. Improvement of renal split function in hydronephrosis with less than 10 % function. *Eur J Pediatr Surg* 2008; 18: 156-9.
- [8] Gupta DK, Chandrasekharam VV, Srinivas M, Bajpai M. Percutaneous nephrostomy in children with ureteropelvic junction obstruction and poor renal function. *Urology* 2001; 57: 547-50.
- [9] Lee YH, Tsai JY, Jiaan BP, Wu T, Yu CC. Prospective randomized trial comparing shock wave lithotripsy and ureteroscopic lithotripsy for management of large upper third ureteral stones. *Urology* 2006; 67: 480-4; discussion 484.
- [10] Huang TY, Lin JP, Huang CN. Dyspnea as an unexpected presentation of huge hydronephrosis. *Iran J Kidney Dis* 2014; 8: 25.
- [11] Wimpissinger F, Springer C, Kurtaran A, Stackl W, Turk C. Functional aspects of silent ureteral stones investigated with MAG-3 renal scintigraphy. *BMC Urol* 2014; 14: 3.
- [12] Hussain M, Ali B, Ahmed S, Zafar N, Naqvi SA, Rizvi SA. Prediction of renal function recovery in obstructive renal failure due to stones. *J Pak Med Assoc* 1997; 47: 159-61.
- [13] Mibu H, Tanaka N, Hosokawa Y, Kumamoto H, Margami N, Hirao Y, Fujimoto K. Estimated functional renal parenchymal volume predicts the split renal function following renal surgery. *World J Urol* 2015; 33: 1571-7.
- [14] Teenan RP, Ramsay A, Deane RF. Percutaneous nephrostomy in the management of malignant ureteric obstruction. *Br J Urol* 1989; 64: 238-40.
- [15] Watkinson AF, A'Hern RP, Jones A, King DM, Moskovic EC. The role of percutaneous nephrostomy in malignant urinary tract obstruction. *Clin Radiol* 1993; 47: 32-5.