Original Article

What Factors Impact Stone-Free Rate after Retrograde Intrarenal Surgery for Large Renal Calculi?

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Objective: To investigate the outcomes of retrograde intrarenal surgery (RIRS) for large renal calculi, and to identify factors that influence the stone-free rate after RIRS for renal stone burden greater than 2 centimeters.

Materials and Methods: This retrospective chart review included patients who underwent RIRS for renal calculi greater than 2 centimeters in size during January 2015 to December 2016 at Siriraj Hospital Thailand's largest national tertiary referral center. Data were collected and compared between those having and not having residual stones greater than 2 cm in diameter.

Results: The present study included 100 eligible cases. The most common site was at lower calyces (42%). The mean stone burden size was 31.43 mm (range: 20 to 140). The average operative time was 62 minutes (range: 20 to 150), and the mean hospital length of stay was 2.7 days (range: 1 to 22). The most common stone composition was calcium oxalate monohydrate (37%), followed by calcium phosphate (23%). The success rate was 84% and 94% after the 1st session and 2nd session of RIRS, respectively. The factors that were found to predict residual stone after RIRS were stone burden greater than 35 mm in size (odds ratio [OR]: 5.86, 95% confidence interval [CI]: 1.77 to 19.57; $p = 0.004$) and lower pole location (OR: 1.97, 95% CI: 1.039 to 3.742; $p = 0.038$). Sepsis was found in 6 patients, all of whom were successfully treated with intravenous antibiotic, except for one mortality in an immunocompromised patient.

Conclusion: RIRS is a promising treatment option for renal calculi with large stone burden. Large kidney stones (>2 cm) can be treated with high success rate and low morbidity. The most significant predictors of residual calculi are stone burden more than 35 millimeters in size and lower pole location.

Keywords: Flexible ureterorenoscopy, Large renal stones, Nephrolithiasis, Retrograde intrarenal surgery, Stone-free rate

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A recent meta-analysis by De, et al[1] reported that retrograde intrarenal surgery (RIRS) was found to be the standard treatment for renal calculi size <2 cm, whereas percutaneous nephrolithrotripsy (PCNL) remains the standard therapy for large renal calculi of >2 cm in size[2,3]. However, the high stone-free rates from PCNL for the management of large stones were at the expense of a higher rate of complications, greater blood loss, and longer length of hospital stay. Another meta-analysis was conducted to evaluate the efficacy of RIRS for management of renal calculi greater than 2 cm in size; however, debate continues regarding whether or not RIRS should be considered as an alternative option to PCNL for the treatment of large renal calculi[4]. The aims of the present study were to investigate the outcomes of RIRS for large renal calculi, and to identify factors that influence the stone-free rate after RIRS for renal stone burden greater than 2 centimeters.

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Materials and Methods

The present study was approved by the Ethics Committee of the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (protocol number 186/2559[EC1]). Clinical data of patients with renal calculi, who underwent RIRS at Siriraj Hospital during the period January 2015 to December 2016, were included in this study. Study periods were screened from our institutional database. Only patients who had renal calculi with stone burden size of greater than 2 cm were included in this study. Exclusion criteria were patients with staghorn renal calculi which stone burden were too large for RIRS. The following data were collected: characteristics of patients (age, body mass index [BMI], preoperative glomerular filtration rate [GFR], underlying disease, and previous treatment), stone characteristics (size, number, location, and major composition)

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and perioperative outcomes (operative time, complications, length of stay, and residual fragments). The success rate was evaluated by surgeon at 1 month using plain film of the urinary system or ultrasonography. Stone fragments less than 4 mm without associated symptoms were determined to be clinically insignificant, and the treatment was considered to be successful.

The primary objectives of the present study were to evaluate the success rate of RIRS and determine factors related to success of RIRS for treatment of renal calculi larger than 2 cm. The secondary outcome was morbidity related to RIRS.

Statistical analysis

Number and percentage were used to describe categorical data, and mean plus/minus standard deviation and median range were used to express continuous data. Comparisons of categorical variables were performed using contingency Chi-square test. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cut-off value of stone burden size for further analyses. Patients were then divided into 2 groups, with one above and the other below the optimal stone burden size. Predictive factors for stone free status were evaluated with univariate and multivariate analysis. The confidence interval was set at 95%, and a difference with a *p*-value <0.05 was considered statistically significant. Statistical analysis was performed with Statistical Package for the Social Sciences 18.0 program (SPSS, Inc., Chicago, IL, USA).

Results

Our initial screening revealed 275 patients who underwent RIRS during the study period. Of those, 158 patients had stone burden less than 20 mm, and 11 patients had staghorn stone. All of those 169 patients were excluded. Of the remaining 106 patients, 6 were excluded due to having incomplete data. The remaining 100 patients were enrolled and their data were included in our analysis (Figure 1).

The characteristics of both patients and renal calculi were shown in Table 1. The mean age of patients was 57.73±12.78 years, and the mean pre-operative GFR was 72.46±25.35 ml/min. Prior to RIRS, 28 patients had history of previous treatment for renal calculi, and 17 patients had preoperative stenting. The most common stone location was at the lower calyces (42%), and the most often observed stone composition was calcium oxalate monohydrate (37%). The mean operative and fluoroscopic times were 61.87±28.73 minutes and 35.48±27.16 seconds, respectively. Ninety-six patients had postoperative ureteral stenting.

The optimal cut-off value of stone burden for determining residual fragment from ROC curve was 35 mm, with 63% sensitivity and 82% specificity (Figure 2). Using this value, 75 and 25 patients had stone burden size of ≤35

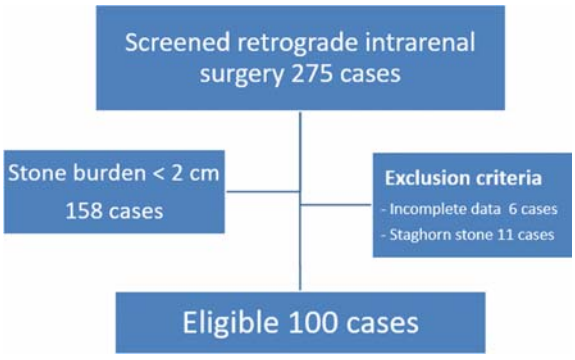


Figure 1. Flow diagram describing the patient enrollment process.

Table 1. Characteristics of patients and renal calculi

Patient characteristics	
Age (mean ± SD, years)	57.73±12.78
Gender, n (%)	
Male	56 (56.0)
Female	44 (44.0)
Body mass index (mean ± SD, kg/m^2)	26.47±5.88
Underlying disease, n (%)	
Diabetes mellitus	25 (25.0)
Hypertension	39 (39.0)
Ischemic heart disease	3 (3.0)
Chronic kidney disease	9 (9.0)
Gout	6 (6.0)
Preoperative GFR (mean ± SD, ml/min)	72.46±25.35
History of prior surgery (ESWL, URSL, PCNL, or open surgery)	28 (28.0)
Preoperative stenting	17 (17.0)
Clinical presentation (n = 100), n (%)	
Flank pain	32 (32.0)
Urinary tract infection	12 (12.0)
Hematuria	10 (10.0)
Residual stone	19 (19.0)
Lower urinary tract symptoms	2 (2.0)
Asymptomatic	25 (25.0)
Stone characteristics	
Stone burden (mean ± SD, mm)	31.43±16.47
Number of stones, median (range)	1 (1 to 5)
Localization of stone, n (%)	
Upper calyx	35 (35.0)
Middle calyx	23 (23.0)
Lower caly	42 (42.0)
Major stone composition, n (%)	
Calcium oxalate monohydrate	37 (37.0)
Calcium oxalate dehydrate	11 (11.0)
Calcium phosphate	23 (23.0)
Uric	19 (19.0)
Struvite	5 (5.0)
Cystine	1 (1.0)
Missing	4 (4.0)

SD = standard deviation, GFR = glomerular filtration rate, ESWL = extracorporeal shock wave lithotripsy, URSL = ureteroscopic lithotripsy, PCNL = percutaneous nephrostolithotomy

mm and >35 mm, respectively. As shown in Table 2, a significantly lower stone-free rate (SFR) was found in the larger stone burden >35 mm group (92% vs. 60%, respectively) (odds ratio [OR]: 7.67, 95% confidence interval [CI]: 2.41 to 24.36; $p = 0.001$). The authors also found that lower calyceal location negatively affects the success of RIRS (OR: 5.40, 95% CI: 1.60 to 18.23; $p = 0.005$). No statistically significant association was found between stone composition and residual fragment ($p = 0.583$). Multivariate analysis revealed size of stone burden of >35 mm (OR: 5.86, 95% CI: 1.77 to 19.57; $p = 0.004$) and lower calyceal stone location (OR: 1.97, 95% CI: 1.039 to 3.742; $p = 0.038$) to be statistically significant factors associated with residual fragment; thus, these factors significantly negatively affect SFR after RIRS.

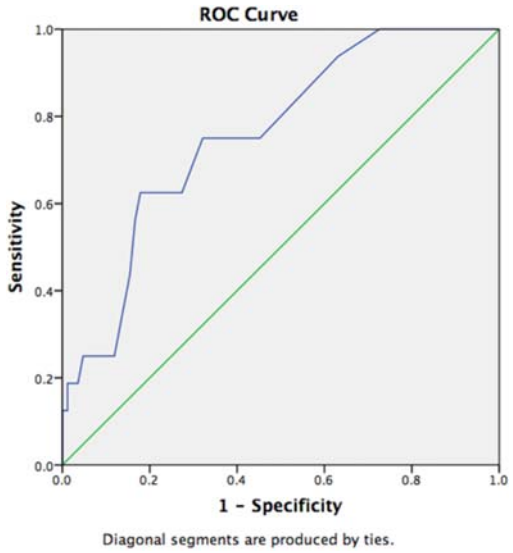


Figure 2. Receiver operating curve (ROC) curve analysis to identify the optimal cut-off value of stone burden to determine residual fragment.

Success rate was 84%. After the first session of RIRS,16 patients had residual stones with fragment size within the range of 6 to 45 mm (mean: 17.56 mm). All of those patients underwent further procedures, including 12 patients who underwent a second session of RIRS, 3 patients who underwent PCNL due to unfavorable anatomy (such as narrow infundibulopelvic angle and short infundibular length) and 1 patient who underwent ureteroscopic lithotripsy due to Steinstrasse. Following the 2nd session of RIRS, 10 patients achieved stone-free status, and the remaining 2 patients underwent subsequent PCNL due to unfavorable anatomy (Figure 3).

The mean length of hospital stay (LOS) was 2.7 days (range: 1 to 22). Overall, 12 patients developed perioperative complications, including sepsis in 6 patients, and fever with negative hemoculture in 6 others. All of those patients, except for one immunocompromised patient who died, were successfully treated with intravenous antibiotics.

Discussion

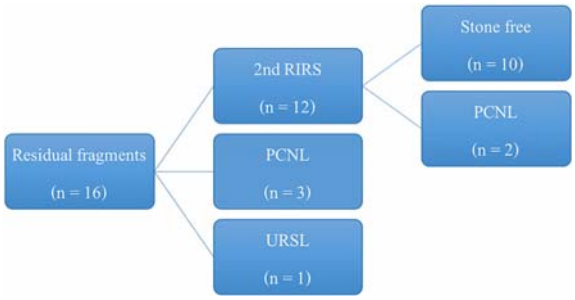
PCNL has been the standard treatment for large renal calculi >2 cm in size[2, 3], whereas RIRS has been considered the standard therapy for renal stones of <2 cm[1]. Although the successful application of RIRS for treatment of large renal calculi was reported by many studies[5-17], a meta-analysis showed that it remains unclear whether RIRS should be considered as an alternative option in large stones[4].

In the present study, RIRS had an overall success rate of 84% and 94% after the 1st and 2nd procedure,

Table 2. Stone outcome data

Parameters	Residual stone			
	No	Yes	OR (95% CI)	*p*-value
Stone burden size				
≤35 mm (n = 75)	69 (92.0%)	6 (8.0%)	7.67 (2.41 to 24.36)	0.001
>35 mm (n = 25)	15 (60.0%)	10 (40.0%)	1	
Stone location				
Lower pole (n = 42)	30 (71.4%)	12 (28.6%)	5.40 (1.60 to 18.23)	0.005
Non-lower pole (n = 58)	54 (93.1%)	4 (6.9%)	1	
Stone analysis (n = 96)				
Calcium oxalate monohydrate (n = 37)	31 (83.8%)	6 (16.2%)	n/a	0.583
Calcium oxalate dihydrate (n = 11)	10 (90.9%)	1 (9.1%)		
Calcium phosphate (n = 23)	21 (91.3%)	2 (8.7%)		
Uric (n = 19)	16 (84.2%)	3 (15.8%)		
Struvite (n = 5)	3 (60.0%)	2 (40%)		
Cystine (n = 1)	1 (100%)	0 (0.0%)		

A *p*-value <0.05 indicates statistical significance
OR = odds ratio, CI = confidence interval



RIRS = Retrograde intrarenal surgery, PCNL = Percutaneous nephrolithotripsy, URSL = Ureterorenoscopic lithotripsy

Figure 3. Further treatment procedures in patients with residual stones.

respectively, and these rates are comparable with those reported by other studies (Table 3). The parameters that strongly affect SFR of RIRS were found to be stone burden >35 mm and lower pole location. Similar to previous reports[18-20], location of stone(s) at the lower calyces remains an independent factor that influences the outcome. This factor is also important for determining treatment options after the 1st attempted RIRS since 5 out of 16 patients with unfavorable anatomy required PCNL for successful stone removal. In contrast, stone composition was not found to significantly influence the outcome, and stone-free status could be achieved in more than 80% of patients in each stone composition group, except struvite stones in which only 60% of patients succeeded. Since distinguishing stone composition is difficult due to the existence of stone heterogeneity and insufficient information from non-contrast computed tomography, this result supports the application of RIRS regardless of stone composition. Concerning morbidity, the rate of sepsis was slightly higher in the present study than in other studies; nevertheless, the overall complications were comparable. According to our results, the indication for RIRS should be extended for larger stone or considered as an alternative option to PCNL. Comparing the two procedures, both PCNL and RIRS offer good outcomes for management of larger renal calculi. However, the higher SFR of PCNL has to be at the expense of higher blood loss and longer length of stay, whereas RIRS may require multiple sessions to achieve an SFR that is comparable to that of PCNL. Determination of a treatment option between PCNL and RIRS in large renal stones should be based on consideration of these disadvantages.

Limitations

The present study has some limitations. First, the retrospective nature of this study renders it vulnerable to missing or incomplete data. For example, 4 patients could not afford stone analysis, so their stone composition data were not included in our analysis. Second, we collected and included data from a single center. Third, our center is a national tertiary referral center that is often referred complicated cases. It is, therefore, possible that our results may not be generalizable to other care settings. Fourth and last, our relatively small sample size and the disparity in group size could have adversely affected our study's ability to identify all significant differences and associations.

Conclusion

RIRS is a promising treatment option for renal stones. Large kidney stones of >2 cm can be treated with high success rate and low morbidity. The most significant predictors of residual stones are stone burden more than 35 millimeters in size and lower pole location.

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What is already known on this topic?

Retrograde intrarenal surgery (RIRS) is standard treatment in small renal calculi size less than 2 centimeters. Percutaneous nephrolithotripsy (PCNL) remain the major treatment in larger renal calculi more than 2 centimeters with higher stone-free rates and higher rates of complications, greater blood loss, and longer length of hospital stay.

What this study adds?

RIRS is the alternative option for management in large kidney stones size more than 2 centimeters with high success rate and low morbidity. The significant predictors of residual stones are stone burden more than 35 millimeters in size and lower pole location.

Funding disclosure

This was an unfunded study.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Table 3. Literature review: success rates and complications of retrograde intrarenal surgery (RIRS)

Authors	Year	Size of stone (cm)		Stone location	Renal units (n)	Success rates				Complications						Endpoint of outcomes
		Overall	Mean			1st	2nd	3rd	Overall	Fever	Urinary retention	UTI	Sepsis	Hematuria	Overall	
Grasso[5]	1998	2 to 6	2.21	All	45	75.6%	91.1%	93.3%	93.3%	-	-	2.2%	-	2.2%	-	<2 mm
El-Anany[6]	2001	>2	n/a	All	30	76.7%	-	-	76.7%	6.7%	-	-	-	3.3%	-	<2 mm
Mariani[7]	2007	>4	6.5	All	17	23.5%	58.8%	88.0%	88.0%	17.6%	-	-	-	-	-	No stone fragment
Ricchiuti[8]	2007	>2	3.37	All	23	56.5%	73.9%	-	73.9%	-	-	-	-	-	-	<2 mm
Breda[9]	2008	2 to 2.5	2.2	All	15	60.0%	86.6%	93.3%	93.3%	6.7%	-	-	-	13.3%	-	<1 mm
Mariani[10]	2008	2 to 9.7	4.4	All	63	-	-	-	95.0%	8.5%	-	-	5.1%	-	-	No stone fragment
Breda[11]	2009	2 to 15	6.6	All	27	52.0%	85.1%	-	85.1%	n/a	n/a	n/a	n/a	n/a	n/a	<1 mm
Hyams[12]	2009	2 to 3	2.4	All	19	94.7%	-	-	94.7%	n/a	n/a	n/a	n/a	n/a	n/a	<2 mm
Riley[13]	2009	2.5 to 5	3	All	22	22.7%	86.4%	90.9%	90.9%	-	-	-	4.5%	-	-	<2 mm
Akman[14]	2012	2 to 4	n/a	All	34	73.5%	88.2%	-	88.2%	2.9%	-	-	2.9%	-	-	No stone fragment
Takazawa[15]	2012	2 to 5	3.1	All	20	65.0%	85.0%	90.0%	90.0%	15.0%	-	-	5.0%	-	-	<4 mm
Koyuncu[16]	2015	>2	2.3	Lower pole	32	90.6%	100%	-	100%	-	-	-	-	-	-	No stone fragment
Zengin[17]	2015	2 to 3	2.3	n/a	80	-	-	-	80.6%	n/a	n/a	n/a	n/a	n/a	13.5%	<2 mm
Varat, et al	2017	>2	3.15	All	100	84.0%	94.0%	-	94.0%	6.0%	1.0%	-	6.0%	-	13.0%	<4 mm

UTI = urinary tract infection, n/a = not available

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ปัจจัยใดที่มีผลต่ออัตราหายของนิ่วหลังการผ่าตัดด้วยวิธีส่องกล้องรักษานิ่วในไตขนาดใหญ่

วรัชญ์ วรนิสรากุล, ศุภฤกษ์ โลหะสัมมากุล, ไชยยงค์ นวลยง, ธวัชชัย ทวีมั่นคงทรัพย์, กานติมา จงจิตอารี, กิตติพงษ์ พินธุโสภณ, ศิรส จิตประไพ, ชลัยรัชฎ์ สุขอวยชัย, ศุภชัย สถิตมั่งคั่ง, เอกรินทร์ โชติกวาณิชย์

วัตถุประสงค์: เพื่อศึกษาอัตราการการหายของนิ่ว (stone-free rate) หลังการรักษาด้วยวิธีส่องกล้องในไต (retrograde intrarenal surgery; RIRS) สำหรับผู้ป่วยที่มีนิ่วในไตขนาดมากกว่า 2 เซนติเมตรและศึกษาปัจจัยร่วมที่มีผลต่ออัตราการหายของนิ่ว

วัสดุและวิธีการ: ศึกษาทบทวนผู้ป่วยที่ได้รับการรักษาด้วยวิธีส่องกล้องในไต สำหรับนิ่วในไตที่มีขนาดมากกว่า 2 เซนติเมตร ระหว่างเดือนมกราคม พ.ศ. 2558 ถึง เดือนธันวาคม พ.ศ. 2559 โดยรวบรวมข้อมูลผลการรักษาและวิเคราะห์ปัจจัยที่เกี่ยวข้องกับอัตราการหายของนิ่ว

ผลการศึกษา: จากผู้ป่วย 100 ราย ตำแหน่งนิ่วในไตที่พบบ่อยที่สุดคือที่ ขั้วล่างของไต (42%) ขนาดนิ่วโดยเฉลี่ย 31.43 มม. (20 ถึง 140 มม.) ระยะเวลาผ่าตัดเฉลี่ย 62 นาที (20 ถึง 150 นาที) ค่าเฉลี่ยเวลาพักรักษาในโรงพยาบาลคือ 2.7 วัน (1 ถึง 22 วัน) องค์ประกอบสำคัญของนิ่วที่พบคือแคลเซียมออกซาเลตโมโนไฮเดรต (37%) และแคลเซียมฟอสเฟต (23%) อัตราการหายของนิ่วเท่ากับ 84% และ 94% หลังจากการผ่าตัดส่องกล้องครั้งที่ 1 และ 2 ตามลำดับ ปัจจัยร่วมที่มีผลต่ออัตราการหายของนิ่วหลังจากการผ่าตัด คือนิ่วขนาดใหญ่กว่า 35 มม. (OR = 5.86, 95% CI: 1.77 ถึง 19.57, p = 0.004) และตำแหน่งนิ่วในขั้วล่างของไต (OR = 1.97, 95% CI: 1.039 ถึง 3.742, p = 0.038) พบการติดเชื้อในผู้ป่วย 6 ราย ซึ่งทั้งหมดได้รับการรักษาด้วยยาปฏิชีวนะทางหลอดเลือดดำได้สำเร็จ ยกเว้นการเสียชีวิตหนึ่งรายในผู้ป่วยที่มีภาวะภูมิคุ้มกันบกพร่อง

สรุป: การรักษาด้วยวิธีส่องกล้องในไต (RIRS) เป็นตัวเลือกที่น่าสนใจสำหรับนิ่วในไตขนาดใหญ่ (>2 ซม.) โดยมีอัตราความสำเร็จสูงและภาวะแทรกซ้อนต่ำ ปัจจัยร่วมที่มีผลต่ออัตราการหายของนิ่วหลังจากการผ่าตัด คือนิ่วขนาดใหญ่กว่า 35 มม. และตำแหน่งนิ่วในขั้วล่างของไต