

Efficacy Of Retrograde Intra-Renal Surgery For The Treatment Of Large Renal Stone Burdens: A Single-Center Experience

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Abstract:

Background: Retrograde intra-renal surgery (RIRS) has gained popularity as a result of technological advances. Although widely used, the literature on its feasibility for the treatment of large renal stone burdens is limited. This study aimed to assess the efficacy of RIRS for the treatment of large renal stone burdens.

Materials and Methods: Fifty-five patients with stone burdens ≥ 21 mm and treated with RIRS between November 2019 and October 2021 were evaluated for patient demographics, stone characteristics, and stone-free rates (SFR). Patients were divided into three groups according to stone burdens (21–30 mm, 31–40 mm, and >40 mm). A standard protocol for surgery and chemoprophylaxis was followed. The SFR was determined if there were no residual stones or fragments on follow-up images. All these patients were followed up on for a minimum of 3 months.

Results: The mean age of patients was 54.11 ± 11.75 years. The mean stone burden and mean stone density were 32.36 ± 10.20 mm and 966 ± 337 HU, respectively. The mean cumulative endoscopy time was 142.0 ± 74.7 minutes per case. Endoscopy time was longer for stone densities >1000 HU. The overall SFR was 78.2%, with an average of 1.58 sessions of RIRS. SFRs for 21–30 mm, 31–40 mm, and >40 mm groups were 92.9%, 68.8%, and 54.5%, respectively.

Conclusion: RIRS is an effective therapeutic option for treating stone burdens of 21–30 mm with overall SFR of 92.9%. When the stone burden exceeds 30 mm, RIRS should only be offered to individuals who are not candidates for other therapeutic options. To better counsel the patient for a staged approach, stone hardness (HU-Hounsfield units) should be considered in surgery planning

Keyword: Retrograde intra-renal surgery; Flexible ureteroscopy; Large renal stone burden; Holmium laser lithotripsy; Stone-free rate.

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I. Introduction

In patients presenting to urology clinics, urolithiasis is one of the most prevalent diseases. The prevalence has increased in the last two to three decades. The widespread use of imaging modalities may partly explain the increase in the prevalence of urolithiasis due to incidental calculi⁽¹⁾. Renal calculi make up 80% to 90% of all urinary calculi⁽²⁾. Renal calculi are commonly treated with retrograde intra-renal surgery (RIRS) or percutaneous nephrolithotomy (PCNL). However, application of these methods has to be carefully selected. RIRS is less invasive, has fewer complications, and is especially useful in patients with complex anatomical kidneys and patients on anticoagulants or with bleeding diathesis⁽³⁾. Although it has been reported that PCNL has a high success rate in terms of stone-free rates (SFR) ($>95\%$), there are still several significant complications associated with this procedure^(4, 5). RIRS is a procedure that has been considered in the management of smaller stones since the procedure is associated with longer learning curves, long operative time, and the high cost of the procedure. Due to the advancements in RIRS technology (deflection mechanisms, ergonomics, and miniaturised laser fibers), growth in surgical expertise and compliance, and high success rates, RIRS has also been frequently considered as a PCNL substitute for the treatment of larger renal calculi^(6, 7).

Despite the technological improvements in RIRS, there is a lack of adequate clinical data assessing the efficacy of RIRS for treating large renal stone burdens. This study aimed to prospectively evaluate the SFRs of RIRS in treating large renal stone burdens.

II. Material And Methods

A total of 55 cases with large renal stone burdens (≥ 21 mm) were treated by RIRS with Holmium:Yttrium-Aluminum-Garnet (Ho:YAG) laser lithotripsy between November 2019 and October 2021. Patients' ≥ 18 years of age that consented to RIRS were included in the study. Co-morbidities, bleeding diathesis, and patient preference were the common indications for RIRS. Data was collected after obtaining approval from the hospital ethics committee. Patients with a history of failed extracorporeal shock wave lithotripsy (ESWL), failed PCNL, or solitary kidney were also included. Patients with renal anomalies (Horseshoe kidney, ectopic kidney, polycystic kidney, etc.) or complete stag-horn stones were excluded. Patients were divided into three groups according to stone burdens (21–30 mm, 31–40 mm, and >40 mm).

Surgical technique

Preoperative antibiotics were given according to the urine culture and sensitivity if a prior report was available, or Cefoperazone (1 g) with Sulbactam (0.5 g) intravenously 30 minutes before surgery. Pre-stenting was done only in cases of pyelonephritis, acute kidney injury, or when difficult ureteral anatomy does not allow ureteral access sheath (UAS). The procedure was performed under general or spinal anaesthesia with the patient in the dorsal lithotomy position.

Formal cystoscopy was done to visualise the ureteral orifice. The ureter was cannulated with a hydrophilic guide-wire (0.038 inches, PTFE-nitinol) under fluoroscopy guidance. The bladder was continuously drained with an infant feeding tube (8 or 9 Fr) during the surgery. Ureteroscopy was done with semi-rigid ureteroscope (4.5 Fr. or 6 Fr. tip). By this way, the ureter can be evaluated for a co-incident ureteral stone or a stricture, and the ureter can be dilated mechanically (optical dilatation). Ureteral compliance can also be assessed to select the appropriate UAS and determine the best position for the UAS tip.

Once the renal pelvis reached, the semi-rigid ureteroscope was removed, and the flexible ureteroscopy (fURS) (tip/shaft; 4.9/7.95 Fr) was advanced through an UAS (9.5/11.5 Fr. or 12/14 Fr.). All calyces were inspected. Sometimes, fluoroscopy guidance or a retrograde pyelogram can facilitate access to the calculus. The laser fiber (272 microns) was advanced, and the calculi were fragmented with the Ho:YAG laser. During the procedure, the pulse energy and frequency of pulsation were adjusted based on stone hardness and size. Three methods were used to fragment the stones, as mentioned in Table no 1. A double-J ureteric stent was placed once the RIRS was completed. Stent was removed 2-4 weeks post-RIRS, once SFR was confirmed on follow-up USG or X-ray KUB.

Table no 1: Laser settings for different methods

Method	Settings	Definition	Energy	Frequency
Fragmentation	High Energy, Low Frequency	Fragments needs to be removed with a basket	1.0-1.5 J	5-12 Hz
Dusting effect	Low Energy, High Frequency	Fragments smaller than 1-2 mm	0.2-0.4 J	20-25 Hz
Popcorn effect	High Energy, High Frequency	Break large fragments into tiny bits	0.6-1.0 J	12-20 Hz

Methodology

Each patient was educated about the study, and an information sheet was provided. Patient's demographic and clinical data were recorded. Stone burden was defined as the cumulative linear diameter of the stones, measured on the pre-operative computed tomography (CT) or X-ray. A standard protocol for anesthesia and chemoprophylaxis regimen was followed. They were followed up to 3 months after surgery. SFR was defined as the absence of residual stone or fragments (>2 mm) by endoscopic inspection at the end of RIRS procedure and also in the postoperative images (X-Ray/ultrasound, or CT) on follow-up. Primary outcomes were overall SFR, SFR in relation to stone burden and stone density. Secondary outcomes were number of RIRS sessions, auxiliary procedures required (ESWL/PCNL), days of hospital stay, and endoscopy time.

Statistical analysis

The statistical analysis was performed by IBM SPSS version 20. Categorical variables were described as frequency and percentage, while continuous variables were described as mean \pm SD, and normality was checked by the Kolmogorov-Smirnov test. Independent samples by the Kruskal-Wallis H test and Mann-Whitney U test were used to test the significance of the non-parametric data. Pearson's chi-square test and Fisher's exact test were used to find the association between categorical variables. A P value of <0.05 was considered statistically significant.

III. Result

Fifty-five patients with a large renal stone burden (≥ 21 mm) underwent RIRS from November 2019 to October 2021. The mean age of patients was 54.11 ± 11.75 years. The demographic data and stone characteristics are presented in Table no 2. Thirty-nine of 55 cases (70.9%) had CT-KUB prior to RIRS as a part of the evaluation. Parameters with reference to stone hardness were analysed separately in these 39 cases (Table no 4). The mean stone density on CT-KUB was 966 ± 337 HU (340 to 1504 HU). Pre-stenting was required in 14 cases (25.5%) for different indications (pyelonephritis in 7 cases, acute kidney injury in 4, infected hydronephrosis in 1, post URS in 1, and routinely while performing RIRS on the contra lateral side in other 1 case).

Table no 2: Demographic data and stone characteristics

Variables	Group	Frequency	Percentage
Age	18-55 years	26	47.0%
	>55 years	29	53.0%
Sex	Male	35	64.0%
	Female	20	36.0%
Co-morbidities	Present	31	56.3%
History of urolithiasis	Present	16	23.0%
Presenting symptoms	Pain	38	69.1%
	Fever	8	14.5%
	Hematuria	6	10.9%
	Burning urination	2	03.6%
	Incidental	11	20.0%
Laterality	Right	26	47.0%
	Left	29	53.0%

The mean cumulative endoscopic time was 142.0 ± 74.7 minutes per case. The average endoscopic time per session of RIRS was 88.3 minutes. The mean endoscopic time for stone densities >1000 HU was higher but not statistically significant (Table 4). The mean cumulative hospital stay was 2.24 ± 1.29 days. The average hospital stay per session of RIRS was 1.4 days.

The overall success rate in terms of SFR after a minimum of 3 months of follow-up was 78.2%, with an average of 1.58 sessions of RIRS per patient. SFR after the first session of RIRS was only 41.8% (23/55). The second session of RIRS raised the overall SFR to 76.4%. A third session of RIRS was required in four cases. In 12 of the 55 cases (21.8%), RIRS was unable to completely remove the stone burden, necessitating either an auxiliary procedure or medical expulsive therapy. SFR for different groups of stone burden and stone hardness are presented in Table no 3 and Table no 4.

Table no 3: SFR and stone burden

Stone Burden	No.	SFR	P-Value
21-30 mm	28	26/28 (92.9%)	0.007*
31-40 mm	16	11/16 (68.8%)	0.300
>41 mm	11	6/11 (54.5%)	0.049**
≥ 21 mm	55	43/55 (78.2%)	

SFR, stone-free rate; RIRS, retrograde intra-renal surgery.
 *: P-Value 0.007, significantly high SFR (92.9%) for 21-30 mm stone burdens compared to overall SFR (78.2%).
 **: P-Value 0.300, low SFR (68.8%) for 31-40 mm stone burdens compared to overall SFR (78.2%) but not statistically significant.
 ***: P-Value 0.049, significantly low SFR (54.5%) for >41 mm stone burdens compared to overall SFR (78.2%).

Table no 4: SFR and stone hardness

Stone Hardness	≤ 1000 HU	>1000 HU	P-Value
No. of patients	21/39	18/39	-
Overall SFR	18/21 (85.7%)	14/18 (77.8%)	0.682
Endoscopy time	141.43 \pm 63.17 min	150.29 \pm 92.12 min	0.720

SFR, stone-free rate; HU, Hounsfield units.

IV. Discussion

PCNL and open surgery were the only treatments available for addressing large stone burdens prior to the invention of semi-rigid and flexible scopes. The first use of ureteroscopy for treating renal pelvic calculus goes back to 1983 by Huffman and associates⁽⁸⁾. Since then, a number of technological and treatment

developments have been described for the minimally invasive treatment of renal calculi. In patients with comorbidities who were unfit for PCNL, Grasso et al.⁽⁹⁾ reported using RIRS to treat large lower pole renal calculi and achieved an excellent SFR that was comparable to PCNL.

One major concern with RIRS is increased operative duration. Fragmenting a stone in the lower calyx or mid calyx is time-consuming and puts strain on the deflection mechanism of the scope, which can even cause laser fiber breakage and scope damage. These can be overcome by some simple techniques like repositioning the lower calyx calculi to a favorable upper calyx with a basket, continuous irrigation, and employing the popcorn method, etc. The use of small laser fibers is now possible thanks to recent developments in laser technology, particularly the thulium fiber laser (TFL), which has advantages for irrigation and scope deflection.

The efficacy of RIRS in treating renal calculi less than 20 mm has been demonstrated in a handful of studies to be comparable to PCNL⁽¹⁰⁻¹²⁾. Grasso et al. reported an SFR of 94% and 95% for renal calculi of ≤10 mm and 11–20 mm, respectively.⁽¹³⁾ With time and technological advancements, RIRS has taken over as the standard of care for the treatment of renal calculi smaller than 20 mm. At the same time, technical advances in PCNL have made mini-PCNL and ultra mini-PCNL (UMP) relatively less invasive options with lower complications. Despite having a good SFR, PCNL does have some drawbacks, including being an invasive surgery with a high complication rate, morbidity, longer radiation exposure, a longer hospital stay, and vascular or renal parenchyma injury. Studies reported a 11.2–17.5% transfusion rate, 21-32% fever, 0-4% pneumothorax, 0.25–1.5% urinary tract infection and sepsis, and <1% colonic injury with PCNL.⁽¹⁴⁾

Over the past few years, RIRS has been frequently employed for the treatment of large stone burden (≥20 mm) due to its minimally invasive nature. However, there haven't been many studies lately that evaluated the efficacy of RIRS for large stone burden. For renal calculi > 20 mm, the overall SFR of RIRS after repeated sessions has been reported as 77%–93%.^(1, 15-17) In our study, the overall SFR was 78.2%, with an average of 1.58 RIRS procedures per patient. SFRs with respect to stone burden from different studies are presented in Table 5. In a retrospective study, Orhan Karakoc et al.⁽¹⁸⁾ reported an overall SFR of 87.7%, while Bai Y et al.⁽¹⁹⁾ achieved an overall SFR of 82.1% for renal stones >20 mm in patients with solitary kidneys.

In contrast to the aforementioned literature, a meta-analysis by Zhu M et al.⁽²⁰⁾ published significantly lower SFR with RIRS as compared with PCNL. Similarly, a systematic review and meta-analysis by Jiang H, You Z, et al.⁽²¹⁾ concluded that mini-PCNL, with its high SFRs, is the first-line choice for treating large renal calculi. Although a few recent studies have suggested that UMP can reduce the incidence of complications, Schoenthaler et al.⁽²²⁾ reported that the complications rate in UMP and RIRS was comparable, and the prone position of UMP can still result in cardiovascular insult in high-risk patients with obesity, obstructive lung disease, congestive heart failure, or cardiovascular accidents.

Table no 5: SFRs with respect to stone burden in different studies

Study	Stone burden	SFR after 1st RIRS	Overall SFR	Average sessions
Breda et al. ⁽⁷⁾	20-25 mm	-	93.3%	2.3
Riley et al. ⁽¹⁵⁾	~30 mm	-	90.9%	1.82
Grasso et al. ⁽¹³⁾	>20 mm	45%	82%	-
Demetrius et al. ⁽²³⁾	>20 mm	-	>90%	1.2-2.3
Breda A et al. ⁽²⁴⁾	~29 mm	-	89.3%	1.6
Richiuti et al. ⁽²⁵⁾	30.9±14.2 mm	-	73.9%	-
Our Study	32.36±10.20 mm	41.8%	78.2%	1.58

SFR, stone-free rate; RIRS, retrograde intra-renal surgery.

Our results are close to those of the Richiuti DJ et al.⁽²⁵⁾ study, which reported 87.5% SFR for 20–30 mm, 60% for 30–40 mm, and 40% for >40 mm stone burden. In our study, the stone burden is inversely related to the overall SFR. Table no 6 displays SFRs in various studies in relation to specific stone burdens.

Table no 6: SFRs with respect to specific stone burden in different studies

Stone Burden	Study	SFR after 1st RIRS	Overall SFR
20-30 mm	Aboumarzouk et al. ⁽²⁶⁾	-	95.7%
	Richiuti et al. ⁽²⁵⁾	-	87.5%
	Our study	60.7%	92.9%
20-40 mm	Karaoke et al. ⁽¹⁸⁾	66.6%	87.7%
	Akman et al. ⁽²⁷⁾	73.5%	91.2%
	Takzawa R et al. ⁽²⁸⁾	-	100%
	Our Study	52.3%	84.1%
>30 mm	Aboumarzouk et al. ⁽²⁶⁾	-	84.6%
	Cheng-Fenglin et al. ⁽²⁹⁾	45%	76.5%
>40 mm	Takzawa R et al. ⁽²⁸⁾	>40%	67.0%
	Richiuti et al. ⁽²⁵⁾	-	40.0%
	Our Study	0%	54.5%

SFR, stone-free rate; RIRS, retrograde intra-renal surgery.

Xue et al.⁽³⁰⁾ demonstrated that stone composition is one of the important factors in predicting the outcome of RIRS. Ito et al.⁽³¹⁾ showed that stone density (HU) has a higher potential for predicting stone hardness than stone composition. The overall SFR (85.7% versus 77.8%) was more in the ≤ 1000 HU group. The mean endoscopic time for cumulative sessions of RIRS was less in ≤ 1000 HU group (141 \pm 63 vs. 150 \pm 92 min, P-value: 0.720). These findings indicate that not only stone size but also stone hardness play a role in determining the surgical outcomes of RIRS, including operating time, number of sessions, and SFR.

Limitations

The limitations of our study are the small study group, possible selection bias as there was no randomization and no direct comparison with PCNL, and single-center study. Further multi-centre studies with prospective, double-blind randomised trials with larger series of cases would be better to demonstrate the role of RIRS in the treatment of large renal stone burden

V. Conclusion

To the best of our knowledge, RIRS is an effective therapeutic option for treating stone burdens of 21–30 mm with an overall SFR of 92.9%. For stone burdens >30 mm, only individuals who are deemed unsuitable for other therapeutic options should be considered for RIRS, as the SFRs are poor even when the RIRS is staged. This can include patients with bleeding diathesis, morbid obesity, and multiple comorbidities. To better counsel the patient for a staged approach, stone hardness (HU) should be considered in RIRS planning. With the use of contemporary laser technologies, such as new-generation pulse modulation in Ho:YAG lasers and super-pulsed thulium fibre lasers, the indications of RIRS may further increase.

Abbreviations

RIRS: Retrograde Intra-renal Surgery
SFR: Stone-Free Rate
HU: Hounsfield units
PCNL: Percutaneous nephrolithotomy
Ho:YAG: Holmium: Yttrium-Aluminum-Garnet
ESWL: Extracorporeal shock wave lithotripsy
UAS: Ureteral Access Sheath
fURS: Flexible ureteroscopy
UMP: Ultra-mini percutaneous nephrolithotomy
CT: Computed tomography
TFL: Thulium Fiber Laser

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