DOI: *10.4081/aiua.2026.15733*

ORIGINAL PAPER

Clinical impact of stone multiplicity on outcomes of retrograde intra-renal surgery

Ahmed M. Abdel Gawad [1], Tamer A. Abouelgreed [2], Mohamed Rehan [1], Esam A. Elnady [1], Maha M. Elzamek [2], Ahmed E. Refaei [2], Hesham Saad Ahmed [3], Tarek M. Abuelazayem [3], Osama I. Obeidat [4], M. Abdelwadood [5]

[1] Department of Urology, Faculty of Medicine, Al-Azhar University, Damietta, Egypt;
[2] Department of Urology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt;
[3] Department of Urology, Faculty of Medicine, Al-Azhar University, Asyut, Egypt;
[4] Department of Urology, Burjeel Royal Hospital, Abu Dhabi, UAE;
[5] Department of Urology, Faculty of Medicine, Ain shams University, Cairo, Egypt.

Summary *Objective: To evaluate the impact of stone multiplicity on stone-free rates (SFR), complication rates, and perioperative outcomes following retrograde intra-renal surgery (RIRS) for renal calculi.*
Materials and methods: A retrospective cohort study on 198 patients who underwent RIRS with holmium laser lithotripsy at a tertiary center from January 2020 to December 2024. Patients were stratified into single-stone (n = 100) and multiple-stone (n = 98) groups. The primary outcome was stone-free status on postoperative imaging. Independent predictors were assessed using Firth's penalized logistic regression to account for low event rates.
Results: The overall SFR was 93.0% (184/198), with comparable rates between the single-stone and multiple-stone groups (94.0% vs. 91.8%, p = 0.591). Residual fragments (> 4 mm) were more frequent in the multiple-stone group (8.2% vs. 3.0%, p = 0.132), although this did not reach statistical significance. The overall complication rate was low (4.5%) and comparable between groups (6.0% vs. 3.1%, p = 0.498). On multivariate analysis, stone multiplicity was not an independent predictor of stone-free status (OR 0.521; p = 0.334).
Conclusions: RIRS demonstrates comparable efficacy and safety for single and multiple renal stones, supporting its use on a viable treatment option in patients with stone multiplicity. While statistical significance was not observed, the study was adequately powered (> 80%) only to detect absolute differences of approximately 15% or greater. Therefore, the absence of statistical significance should not be interpreted as evidence of clinical equivalence, and larger adequately powered studies are warranted to determine whether smaller between-group differences exist.

KEY WORDS: *Flexible ureteroscopy; Renal calculi; Retrograde intra-renal surgery; Stone-free rate; Stone multiplicity.*

Submitted 8 June 2026; Accepted 24 July 2026

INTRODUCTION

Urolithiasis represents a significant global health burden, with a lifetime prevalence approaching 15% in developed nations. Its rising incidence has been attributed to dietary changes, increasing obesity rates, and climate-related factors (1). Retrograde intra-renal surgery (RIRS) has emerged as a cornerstone in the management of renal calculi, offering a minimally invasive alternative that avoids the morbidity associated with percutaneous access (2). Advances in flexible ureteroscope technology, digital optics, and holmium laser platforms have substantially expanded the indications for RIRS, including stones previously considered amenable only to *percutaneous nephrolithotomy* (PCNL) (3). Current *European Association of Urology* (EAU) and *American Urological Association* (AUA) guidelines recommend RIRS as a first-line or alternative treatment for renal stones up to 20 mm (4). The 2025 AUA/Endourological Society guidelines conditionally recommend mini-PCNL over ureteroscopy for 1-2 cm kidney stones, citing higher single-session stone-free rates (SFR), while acknowledging the lower complication profile of RIRS (5). Notably, these guidelines do not specifically address the impact of stone multiplicity on treatment selection, representing a gap in current evidence-based recommendations. Several predictive scoring systems, including the R.I.R.S. scoring system (6) and the *Resorlu-Unsal Stone Score* (RUSS) (7), incorporate stone burden and calyceal involvement as determinants of RIRS success. Existing literature consistently identifies stone size, lower pole location, and stone density as independent predictors of stone-free status (8). However, the specific impact of stone multiplicity, as distinct from total stone burden remains incompletely characterized. Prior studies have yielded conflicting results: *Ozgor et al.* reported significantly lower single-session SFR for multiple stones (75.7% *vs.* 82.9%), whereas *Lv et al.* found no significant overall difference after propensity-matching for stone burden (9, 10).The clinical relevance of this issue extends beyond academic interest. Multiple renal stones pose unique surgical challenges, including the need to access multiple calyces, longer operative times, and potential fragment migration. Whether these challenges translate into meaningfully different outcomes in the era of modern laser technology – particularly with standardized dusting techniques – remains uncertain and clinically important (11). This study aims to evaluate the impact of stone multiplicity on SFR, complication rates, and perioperative outcomes in a contemporary cohort of patients undergoing RIRS at a single tertiary center, with the hypothesis that modern holmium laser lithotripsy with a systematic dusting approach achieves comparable outcomes regardless of stone number.

Materials and methods

This retrospective cohort study was conducted at our urology Department, following institutional review board approval. We reviewed the records of all consecutive patients who underwent RIRS for renal calculi between January 2020 and December 2024. Given the retrospective design and use of de-identified routine clinical data, the Institutional Review Board waived the requirement for informed consent. The study was reported in accordance with the *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE) guidelines (12). Inclusion criteria were: (1) age ≥ 18 years, (2) documented renal calculus on preoperative imaging *(non-contrast computed tomography* [NCCT] and/or ultrasonography), and (3) complete operative and follow-up data. Exclusion criteria included: (1) diagnostic RIRS without therapeutic intent, (2) concomitant ureteral stone as the sole indication, and (3) incomplete medical records. Of 212 initially screened patients, 201 met inclusion criteria after exclusions, and 198 were classifiable into single or multiple stone groups (Figure 1).

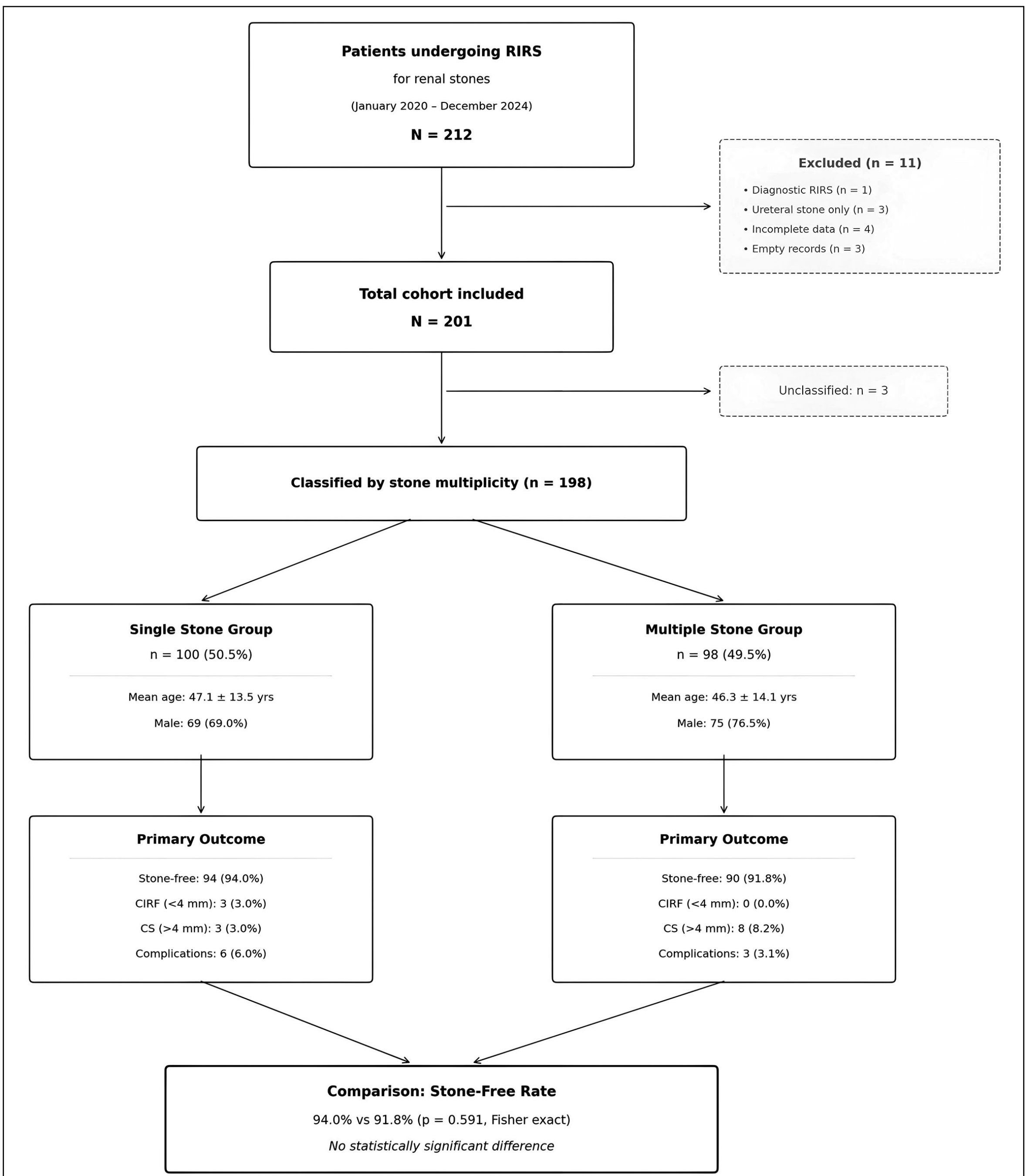


Figure 1.
Study flow diagram. RIRS: retrograde intra-renal surgery; SFR: stone-free rate; CIRF: clinically insignificant residual fragment.

Group assignment

Patients were classified into two groups based on preoperative imaging: (1) Single Stone Group (n = 100): patients with a solitary renal calculus, and (2) Multiple Stone Group (n = 98): patients with two or more renal calculi. Three patients with ambiguous classification were excluded from the comparative analysis.

Preoperative assessment

All patients underwent standardized preoperative evaluation including complete blood count, renal function tests, urine analysis with culture and sensitivity, and cross-sectional imaging. Non-contrast CT was the preferred imaging modality, supplemented by ultrasonography when CT was contraindicated. Stone characteristics including size (largest diameter in mm), density (*Hounsfield units* [HU]), number, and anatomical location (upper pole, middle pole, lower pole, renal pelvis) were recorded. Renal anatomy was documented as normal or anomalous (horseshoe kidney, duplex system, ectopic kidney, malrotated kidney). Preoperative double-J stenting was performed when clinically indicated, including failed initial access, staged procedures, symptomatic obstruction, or prior emergency stenting.

Surgical technique

All procedures were performed under general anesthesia (97.0%) or spinal anesthesia (3.0%) in the lithotomy position. A standardized technique was employed by experienced endourologists. Cystoscopy was performed first, followed by guidewire placement under fluoroscopic guidance. A *ureteral access sheath* (UAS) was deployed in all cases to maintain low intra-renal pressure and facilitate fragment extraction. Semirigid ureteroscopy was performed before flexible ureteroscopy when indicated (21.2% of cases). Flexible ureteroscopy was performed using either a single-use or a reusable digital flexible ureteroscope. Holmium:YAG laser lithotripsy was the energy source in all cases, with dusting as the predominant technique (99.5%). A combination of dusting and popcorning was utilized in 97.5% of procedures. Basket extraction of residual fragments was performed selectively (5.6%). A ureteral stent was placed at the conclusion of the procedure per the operating surgeon's discretion.

Outcome measures

The primary outcome was stone-free status, defined as the absence of residual fragments or the presence of clinically insignificant residual fragments (CIRF, < 4 mm) on postoperative imaging. Residual fragments > 4 mm were classified as *clinically significant* (CS) (13). Postoperative imaging was performed at 4-6 weeks using NCCT, plain radiography, and/or ultrasonography. Secondary outcomes included: postoperative complications graded by the Clavien-Dindo classification, hospital length of stay, day-surgery rate, and re-intervention rate and modality (14).

Statistical analysis

Continuous variables were expressed as mean ± standard deviation and compared using the Mann-Whitney U test after assessing normality with the Shapiro-Wilk test. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test with Yates' correction or Fisher exact test as appropriate (expected cell count < 5). A two-sided p-value < 0.05 was considered statistically significant. Multivariable analysis was performed using Firth's penalized maximum likelihood logistic regression, chosen a priori given the anticipated low event rate (non-stone-free cases). Standard maximum likelihood logistic regression is known to produce biased estimates when the *events-per-variable* (EPV) ratio falls below 10; Firth's method corrects this small-sample bias by incorporating a Jeffreys invariant prior into the likelihood function, producing less biased coefficient estimates and more reliable confidence intervals (15). The model included five clinically selected covariates: stone multiplicity, lower pole location, stone density, pre-stenting status, and recurrent stone former status. Results were reported as *odds ratios* (OR) with 95% Wald-based confidence intervals (16). Post hoc power analysis was performed to assess the study's ability to detect clinically meaningful differences in SFR between groups. All analyses were performed using Python 3.12 (*SciPy 1.12*) and a custom Firth implementation based on *Heinze and Schemper* (2002).

Results

Baseline demographics

A total of 198 patients were included in the comparative analysis, comprising 100 patients (50.5%) in the single-stone group and 98 patients (49.5%) in the multiple-stone group (Table 1). The two groups were well-matched for age (47.1 ± 13.5 *vs*. 46.3 ± 14.1 years, p = 0.673) and sex distribution (male: 69.0% *vs*. 76.5%, p = 0.303). Multiple stone patients were significantly more likely to have recur-

Table 1.
Baseline demographics and clinical characteristics.

Variable	Overall (n = 198)	Single (n = 100)	Multiple (n = 98)	p-value
Age, years (mean ± SD)	46.6 ± 13.8	47.1 ± 13.5	46.3 ± 14.1	0.673
Male sex, n (%)	144 (72.7)	69 (69.0)	75 (76.5)	0.303
First-time stone, n (%)	101 (51.0)	60 (60.0)	41 (41.8)	0.011*
Recurrence, n (%)	97 (49.0)	40 (40.0)	57 (58.2)	0.011*
Recurrent stone former, n (%)	93 (47.0)	37 (37.0)	56 (57.1)	0.005*
Elevated creatinine, n (%)	37 (18.7)	14 (14.0)	23 (23.5)	0.087
Incidental finding, n (%)	35 (17.7)	17 (17.0)	18 (18.4)	0.801
Fever at presentation, n (%)	22 (11.1)	11 (11.0)	11 (11.2)	0.960
Hematuria only, n (%)	4 (2.0)	3 (3.0)	1 (1.0)	0.621
Pain only, n (%)	131 (66.2)	70 (70.0)	61 (62.2)	0.249
Hematuria + pain, n (%)	12 (6.1)	7 (7.0)	5 (5.1)	0.576

*SD: standard deviation. Continuous variables compared by Mann-Whitney U test; categorical variables by chi-square (Yates' correction) or Fisher exact test. *Statistically significant (p < 0.05).*

Table 2.
Stone characteristics.

Variable	Single (n = 100)	Multiple (n = 98)	p-value
Stone size, mm (mean ± SD)	10.3 ± 3.4 [a]	N/A [b]	–
Stone density, HU (mean ± SD)	1137 ± 368 (n = 90)	1192 ± 346 (n = 90)	0.312
Multiple > 3 stones, n (%)	–	81/95 (85.3)	–
Stone location, n (%)			
Upper pole	10 (10.0)	46 (46.9)	< 0.001*
Middle pole	18 (18.0)	57 (58.2)	< 0.001*
Lower pole	17 (17.0)	70 (71.4)	< 0.001*
Renal pelvis	55 (55.0)	52/97 (53.6)	0.958
Kidney anatomy, n (%)			
Normal	95 (95.0)	97 (99.0)	0.212
Anomalous	5 (5.0)	1 (1.0)	0.212

*HU: Hounsfield units. [a] Stone size recorded only for single stones. [b] Cumulative stone burden not separately recorded. *p < 0.05.*

rent disease (58.2% *vs.* 40.0%, p = 0.011) and to be classified as recurrent stone formers (57.1% *vs.* 37.0%, p = 0.005). Fever at presentation was comparable between groups (11.0% *vs.* 11.2%, p = 0.960). There were no significant differences in presentation patterns, elevated creatinine, or incidental detection rates. Stone characteristics are summarized in Table 2. Mean stone density was comparable between groups (1137 ± 368 *vs.* 1192 ± 346 HU, p = 0.312; data available for 90 patients per group). Among patients with multiple stones, the vast majority (85.3%) had more than three stones. The most striking differences were in calyceal involvement: patients with multiple stones had significantly higher rates of upper pole (46.9% *vs.* 10.0%), middle pole (58.2% *vs.* 18.0%), and lower pole (71.4% *vs.* 17.0%) involvement (all p < 0.001), reflecting multi-calyceal distribution (***Supplementary Figure S1***). Renal pelvis involvement was similar (53.6% *vs.* 55.0%, p = 0.958). Normal renal anatomy was present in 97.0% of the cohort, with no significant difference between groups (95.0% *vs.* 99.0%, p = 0.212).

Table 3.
Operative details.

Variable	Single (n = 100)	Multiple (n = 98)	p-value
Pre-stented, n (%)	28/99 (28.3)	41/97 (42.3)	0.052
General anesthesia, n (%)	98 (98.0)	93 (94.9)	0.277
Spinal anesthesia, n (%)	2 (2.0)	5 (5.1)	0.277
Semirigid URS before RIRS, n (%)	17 (17.0)	25/96 (26.0)	0.171
Dusting technique, n (%)	99 (99.0)	98 (100.0)	1.000
Combination technique, n (%)	97 (97.0)	96 (98.0)	1.000
Fragmentation, n (%)	1 (1.0)	0 (0.0)	1.000
Basket extraction, n (%)	6 (6.0)	5 (5.1)	1.000
Day surgery, n (%)	98 (98.0)	98 (100.0)	0.498
Hospital stay, days (mean ± SD)	1.1 ± 0.8	1.0 ± 0.0	0.163

URS: ureteroscopy; RIRS: retrograde intrarenal surgery. Categorical variables compared by chi-square or Fisher exact test.

Operative details

Operative parameters are presented in Table 3. General anesthesia was employed in 97.0% of cases. Preoperative ureteral stenting was more frequent in the multiple-stone group (42.3% *vs.* 28.3%, p = 0.052), approaching statistical significance. The dusting technique was universally employed (99.5%), and a combination of dusting and popcorning was utilized in 97.5% of procedures. Day surgery was achieved in 99.0% of patients, with a mean hospital stay of approximately one day in both groups.

Primary and secondary outcomes

The overall SFR was 93.0% (184/198). The single stone group achieved an SFR of 94.0% compared with 91.8% in the multiple stone group, with no statistically significant difference (p = 0.591, Fisher exact test; Table 4, ***Supplementary Figure S2***). Clinically insignificant residual fragments were observed in 3 patients (3.0%) in the single stone group and none in the multiple stone group (p = 0.246). Clinically significant residual fragments (> 4 mm) were numerically more common in the multiple stone group (8.2% *vs.* 3.0%), though this did not reach statistical significance (p = 0.132). The overall complication rate was 4.5% (9/198), with no significant difference between groups (single: 6.0% *vs.* multiple: 3.1%, p = 0.498). Postoperative fever was the most common complication, occurring in 6 patients (6.0%) in the single-stone group and 1 patient (1.0%) in the multiple-stone group (p = 0.118). Sepsis occurred in 2 patients (2.0%), both in the single stone group. All complications were

Table 4.
Primary and secondary outcomes.

Outcome	Single (n = 100)	Multiple (n = 98)	p-value
Stone-free rate, n (%)	94 (94.0)	90 (91.8)	0.591
CIRF (< 4 mm), n (%)	3 (3.0)	0 (0.0)	0.246
CS residual (> 4 mm), n (%)	3 (3.0)	8 (8.2)	0.132
Any complication, n (%)	6 (6.0)	3 (3.1)	0.498
Fever, n (%)	6 (6.0)	1 (1.0)	0.118
Sepsis, n (%)	2 (2.0)	0 (0.0)	0.498
PCS bleeding, n (%)	0 (0.0)	1 (1.0)	0.495
Ureteric injury, n (%)	0 (0.0)	0 (0.0)	–
Clavien-Dindo grade			
Grade I	3	2	0.498
Grade II	1	0	
Grade III	2	1	
Re-intervention: RIRS, n (%)	2 (2.0)	4 (4.1)	0.442
Re-intervention: PCNL, n (%)	0 (0.0)	1 (1.0)	0.495

SFR: stone-free rate; CIRF: clinically insignificant residual fragment; CS: clinically significant; PCS: pelvi-calyceal system. All comparisons by Fisher exact test.

Clavien-Dindo grade I-III, with no grade IV-V complications or mortality. Re-intervention was required in 7 patients (3.5%), with no significant intergroup difference.

Exploratory multivariable analysis

Firth's penalized logistic regression was performed on 178 patients with complete data for all covariates (Table 5; Figure 2). The model included 5 clinically selected variables with 12 non-stone-free events, yielding an events-per-variable ratio of 2.4. Firth's penalized maximum likelihood estimation was used to mitigate small-sample bias inherent to this low EPV. Stone multiplicity was not an independent predictor of stone-free status (OR 0.521; 95% CI 0.138-1.958; p = 0.334). No covariate was statistically significant at the p < 0.05 level. Recurrent stone former status demonstrated a non-significant trend (OR 2.869; 95% CI 0.837-9.840; p = 0.094), suggesting that patients with recurrent stone disease may paradoxically achieve higher SFR, potentially reflecting greater clinical familiarity, optimized surgical pathways, or more favorable stone composition in this population. Importantly, these regression results should be interpreted as exploratory rather than confirmatory, given the low EPV ratio. The high overall SFR (93.0%) creates a statistical ceiling effect that limits the discriminative ability of any regression model, regardless of the estimation method employed.

Table 5.
Exploratory firth's penalized logistic regression: Predictors of stone-free status.

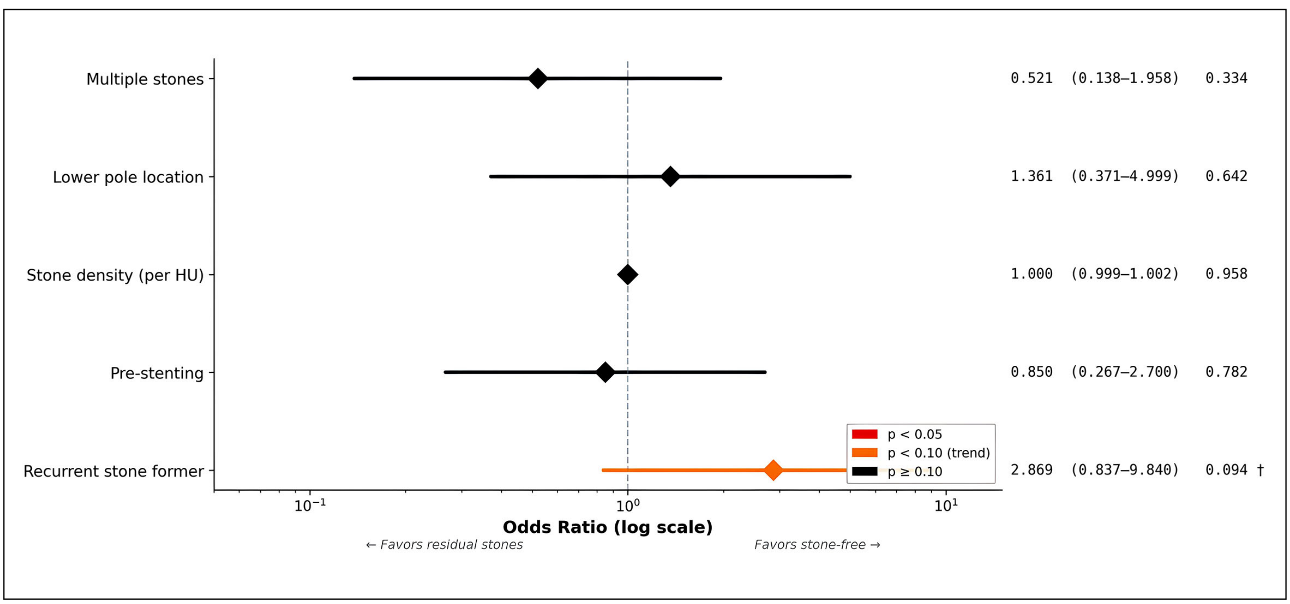
Variable	OR	95% CI	p-value
Multiple stones	0.521	0.138-1.958	0.334
Lower pole location	1.361	0.371-4.999	0.642
Stone density (per HU)	1.000	0.999-1.002	0.958
Pre-stenting	0.850	0.267-2.700	0.782
Recurrent stone former	2.869	0.837-9.840	0.094

OR: odds ratio; CI: confidence interval; HU: Hounsfield units. Model: Firth's penalized maximum likelihood. N = 178 (complete cases); events = 12 (non-stone-free); EPV = 2.4. Penalized log-likelihood = -31.68. Results are exploratory due to the low EPV ratio.

Post-hoc power analysis

Post hoc power analysis indicated that the study had only 9.3% statistical power to detect the observed 2.2% absolute SFR difference (94.0% *vs.* 91.8%) at $\alpha = 0.05$ (***Supplementary Figure S3***). The study achieved 62.3% power for a 10% difference and 88.4% power for a 15% difference. Approximately 2,140 patients per group would be required to achieve 80% power for the observed 2.2% difference. Conversely, with the current sample size of approximately 100 per group, the study was adequately powered (> 80%) only to detect SFR differences of approximately 15% or greater. This finding underscores that the non-significant p-value should not be interpreted as evidence of equivalence, but rather as insufficient evidence to demonstrate a difference given the available sample size.

Figure 2.
Forest plot of Firth's penalized logistic regression. Diamonds represent odds ratios; horizontal bars represent 95% confidence intervals. Dashed line at OR = 1.0 indicates null effect. N = 178; 12 events; EPV = 2.4.



Discussion

This study demonstrates that RIRS achieves comparable SFR and safety profiles in patients with single and multiple renal stones in a contemporary single-center cohort. The overall SFR of 93.0% is consistent with published benchmarks, and the small absolute difference between groups (94.0% *vs.* 91.8%) suggests clinically comparable outcomes. However, post-hoc power analysis indicated limited power (9.3%) to detect small differences; therefore, the absence of statistical significance should be interpreted in this context rather than as definitive evidence of equivalence. Our findings align with those of *Lv et al.*, who reported no significant overall difference in SFR between single- and multiple-stone groups after propensity-matching for stone burden in patients with 1-2 cm stones (10). However, our results contrast with the propensity-matched study by *Ozgor et al.*, who observed significantly lower single-session SFR for multiple stones (75.7% *vs*. 82.9%, p = 0.02) (9). This discrepancy may reflect differences in surgical technique and case selection: our cohort was treated with a consistent dusting approach (99.5%) using contemporary holmium laser settings, whereas earlier series employed variable fragmentation techniques. The near-universal adoption of dusting in our practice may have mitigated the challenges traditionally associated with multi-calyceal stone treatment by reducing fragment size and facilitating spontaneous passage. The overall SFR of 93.0% compares favorably with published benchmarks. A recent Italian multicenter series of 571 RIRS patients reported an SFR of only 69.6% for multiple stones. Our substantially higher SFR for multiple stones (91.8%) may reflect differences in technique, patient selection, or follow-up imaging protocols (17). Several methodological factors may contribute to the high SFR observed in our cohort, including the universal use of UAS, standardized dusting technique, and the surgeon's experience at a high-volume tertiary center.

On Firth's penalized regression, stone multiplicity was not an independent predictor of stone-free status (OR 0.521; 95% CI 0.138-1.958; p = 0.334). Standard maximum-likelihood logistic regression was not employed because the low event count (12 non-stone-free events across 5 covariates; EPV = 2.4) violates the well-established events-per-variable rule, which recommends at least 10 events per covariate. Firth's penalization corrects the small-sample bias inherent to standard logistic regression through a Jeffreys invariant prior, producing less biased coefficient estimates (18). Despite this methodological improvement, the regression results remain exploratory due to the low overall event rate; the confidence intervals are wide and the model's discriminative ability is inherently limited by the high baseline SFR (19). This finding warrants contextualization against the broader literature. *Yildirim et al.* reported that multiple stones carried the strongest negative predictive value (OR 0.254; p < 0.001) in their 642-patient analysis, and a 2025 study identified multiplicity as the only significant independent predictor of SFR (p = 0.002). The discrepancy with our findings may relate to differences in surgical technique, stone burden distribution, and the statistical power limitations of our cohort (20, 21). Our study was primarily powered to detect larger differences in SFR (approximately ≥ 15%), and smaller effect sizes – such as a modest 5-10% reduction – may require substantially larger cohorts for confirmation. The significantly higher rates of multi-calyceal involvement in the multiple stone group (upper pole: 46.9% *vs*. 10.0%; middle pole: 58.2% *vs*. 18.0%; lower pole: 71.4% *vs*. 17.0%; all p < 0.001) confirm that multiple stones impose substantially greater anatomical complexity. Despite this complexity, the comparable SFR suggests that systematic calyceal inspection and dusting – facilitated by the routine use of ureteral access sheaths – can effectively address these anatomical challenges. The trend toward higher pre-stenting rates in the multiple stone group (42.3% *vs*. 28.3%, p = 0.052) may also have contributed to outcomes by facilitating passive ureteral dilation.

The complication profile was excellent and consistent with established safety benchmarks. Our overall complication rate of 4.5% aligns with the CROES Global Study finding of 3.5% for flexible ureteroscopy (22). The low sepsis rate (1.0%) compares favorably with the systematic review estimate of approximately 5% for post-RIRS sepsis. The numerically higher fever rate in the single stone group (6.0% *vs*. 1.0%, p = 0.118) was unexpected and may reflect chance variation given the small absolute numbers (23). Several clinical implications emerge from our findings. First, the comparable outcomes suggest that RIRS can be considered in patients with multiple renal stones without routine escalation to PCNL, particularly when total stone burden is manageable, and the patient prefers a less invasive approach. Second, the high day-surgery rate (99.0%) and short hospital stay underscore the ambulatory potential of RIRS for both single and multiple stones. Third, our data may help inform ongoing discussions regarding stone multiplicity thresholds in clinical decision-making (24).

Declarations

Ethical approval and consent for participate: *This retrospective cohort study was approved by the Institutional Review Board (DFM-IRB 00012367-25-04-008) of Al-Azhar University. The study was conducted in accordance with the principles of the Declaration of Helsinki. Given the retrospective nature of the study and the use of de-identified routine clinical data, the IRB waived the requirement for written informed consent. No identifiable patient information is included in this manuscript.*

Consent for publication: *Written informed consent obtained from all participants.*

Availability of data and material: *The data that support the findings of this study are available from the corresponding author upon reasonable request.*

Competing interests: *The authors have no competing interests to declare.*

Funding: *The authors have no financial interests linked to this work.*

Authors' contributions: *AM, TA, MR: manuscript preparation, protocol, data collection and management, manuscript editing. EA, MM, AE: Data acquisition, data analysis and management, manuscript editing. HS, TM, OI, MA: Manuscript editing, project development, data analysis, and project development. All the authors have read and approved the manuscript.*

Provenance and peer review: *Not commissioned, externally peer-reviewed.*

Acknowledgments: *None.*

Limitations

This study has several limitations. First, its retrospective single-center design introduces potential selection and information biases. Second, cumulative stone burden was not systematically recorded for the multiple stone group, precluding burden-matched comparisons. As emerging evidence suggests that stone volume outperforms linear diameter in predicting SFR, the absence of this metric represents a limitation (25). Third, operative time data were incomplete, limiting assessment of procedural complexity. Fourth, the high overall SFR (93.0%) may have reduced the ability to detect small differences in outcomes, as reflected in the post-hoc power analysis indicating that only larger differences (approximately ≥ 15%) could be reliably identified. Fifth, follow-up imaging was not standardized across modalities, introducing potential variability in outcome assessment. Sixth, surgeon experience and case volume were not formally evaluated and may represent unmeasured confounders. Finally, long-term stone recurrence and functional outcomes beyond the initial postoperative imaging assessment were not captured.

Conclusions

RIRS with holmium laser lithotripsy using a standardized dusting technique achieved high SFR for both single and multiple renal stones, with comparable complication rates and hospital stay. Stone multiplicity was not identified as an independent predictor of residual stones on Firth's penalized regression analysis. These findings support RIRS as an effective and safe treatment option for patients with multiple renal calculi, reinforcing its role as a reliable treatment strategy in cases of stone multiplicity. Further prospective, adequately powered multicenter studies are warranted to validate these findings and to better define stone multiplicity thresholds for treatment algorithms.

References

1. Scales CD, Smith AC, Hanley JM, Saigal CS. Prevalence of Kidney Stones in the United States. Eur Urol. 2012; 62:160-165.

2. Ferraro PM, Bargagli M, Trinchieri A, Gambaro G. Risk of Kidney Stones: Influence of Dietary Factors, Dietary Patterns, and Vegetarian-Vegan Diets. Nutrients. 2020; 12:779.

3. Alenezi H, Denstedt JD. Flexible ureteroscopy: Technological advancements, current indications and outcomes in the treatment of urolithiasis. Asian J Urol. 2015; 2:133-141.

4. Türk C, Petrík A, Sarica K, et al. EAU Guidelines on Diagnosis and Conservative Management of Urolithiasis. Eur Urol. 2016; 69:468-474.

5. Mahmood SN, Ahmed CJ, Tawfeeq H, et al. Evaluation of mini-PCNL and RIRS for renal stones 1-2 cm in an economically challenged setting: A prospective cohort study. Ann Med Surg (Lond). 2022; 81:104235.

6. Xiao Y, Li D, Chen L, et al. The R.I.R.S. scoring system: An innovative scoring system for predicting stone-free rate following retrograde intra-renal surgery. BMC Urol. 2017; 17:105.

7. Resorlu B, Unsal A, Gulec H, Oztuna D. A New Scoring System for Predicting Stone-free Rate After Retrograde Intra-renal Surgery: The "Resorlu-Unsal Stone Score." Urology. 2012; 80:512-518.

8. Verma RP, Yadav A, Kumar V, et al. Surgical Outcomes and Predictive Factor Analysis for Facial Nerve Preservation in Patients With Cerebellopontine Angle (CPA) Tumors: A Ten-Year Single Institutional Study. Cureus (Internet). 2024 (cited 2026 Feb 3);

9. Ozgor F, Kucuktopcu O, Ucpinar B, et al. Is there a difference between presence of single stone and multiple stones in flexible ureterorenoscopy and laser lithotripsy for renal stone burden <300 mm^2? Int Braz J Urol. 2016; 42:1168-1177.

10. Lv G, Zhou Y, Qi W, et al. Comparison of flexible ureteroscopy in the treatment of 1-2 cm single nephrolithiasis and multiple nephrolithiasis. Front Surg. 2023; 10:1114206.

11. Matlaga BR, Chew B, Eisner B, et al. Ureteroscopic Laser Lithotripsy: A Review of Dusting vs Fragmentation with Extraction. J Endourol. 2018; 32:1-6.

12. Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007; 370:1453-1457.

13. Kingma RA, Voskamp MJH, Doornweerd BHJ, et al. Intraoperative cone beam computed tomography for detecting residual stones in percutaneous nephrolithotomy: a feasibility study. Urolithiasis. 2021; 49:551-557.

14. Dindo D, Demartines N, Clavien P-A. Classification of Surgical Complications: A New Proposal With Evaluation in a Cohort of 6336 Patients and Results of a Survey. Ann Surg. 2004; 240:205-213.

15. Peduzzi P, Concato J, Kemper E, et al. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol. 1996; 49:1373-1379.

16. Firth D. Bias reduction of maximum likelihood estimates. Biometrika. 1993; 80:27-38.

17. Maugeri O, Dalmasso E, Peretti D, et al. Stone free rate and clinical complications in patients submitted to retrograde intra-renal surgery (RIRS): Our experience in 571 consecutive cases. Arch Ital Urol Androl. 2021; 93:313-317.

18. Heinze G, Schemper M. A solution to the problem of separation in logistic regression. Stat Med. 2002; 21:2409-19.

19. Vittinghoff E, McCulloch CE. Relaxing the Rule of Ten Events per Variable in Logistic and Cox Regression. Am J Epidemiol. 2007; 165:710-718.

20. Yildirim Ü, Ezer M, Uslu M, et al. Can additional variables be used to predict stone-free rates following retrograde intra-renal surgery? Anticoagulants and parenchyma thickness: a detailed examination. Urolithiasis. 2023; 51:30.

21. Raj KK, Adiga KP, Chandni Clara D'souza R, et al. Assessment of Factors Responsible for Stone-Free Status After Retrograde Intra-renal Surgery. Cureus (Internet). 2024 (cited 2026 Feb 3);

22. De La Rosette J, Denstedt J, Geavlete P, et al. The Clinical Research Office of the Endourological Society Ureteroscopy Global Study: Indications, Complications, and Outcomes in 11,885 Patients. J Endourol. 2014; 28:131-139.

23. Corrales M, Sierra A, Doizi S, Traxer O. Risk of Sepsis in Retrograde Intra-renal Surgery: A Systematic Review of the Literature. Eur Urol Open Sci. 2022; 44:84-91.

24. Constantinou BT, Benedicto BC, Porto BC, et al. PCNL vs. two *staged RIRS for kidney stones greater than 20 mm: systematic review, meta-analysis, and trial sequential analysis. Minerva Urol Nephrol (Internet). 2024 (cited 2026 Feb 3); 76.*

25. Geraghty R, Pietropaolo A, Tzelves L, et al. Which Measure of Stone Burden is the Best Predictor of Interventional Outcomes in Urolithiasis: A Systematic Review and Meta-analysis by the YAU Urolithiasis Working Group and EAU Urolithiasis Guidelines Panel. Eur Urol Open Sci. 2025; 71:22-30.

Correspondence

Ahmed M. Abdel Gawad (Corresponding Author)
ahgawad84@gmail.com

Mohamed Rehan
mrehan4040@gmail.com

Esam A. Elnady
esammohsen78@gmail.com

Department of Urology, Faculty of Medicine, Al-Azhar University, Damietta, Egypt

Tamer A. Abouelgreed
dr_tamer_ali@yahoo.com

Maha M. Elzamek
maha_201001@yahoo.com

Ahmed E. Refaei
El3ameed.ae@gmail.com

Department of Urology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

Hesham Saad Ahmed
hishamsad1985@gmail.com

Tarek M. Abuelazayem
dr_tareq2010@hotmail.com

Department of Urology, Faculty of Medicine, Al-Azhar University, Asyut, Egypt

Osama I. Obeidat
osamah929292@gmail.com

Department of Urology, Burjeel Royal Hospital, Abu Dhabi, UAE

M. Abdelwadood
wadoodaref@gmail.com

Department of Urology, Faculty of Medicine, Ain shams University, Cairo, Egypt.