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ORIGINAL ARTICLE

Outcomes and lessons learnt from practice of retrograde intrarenal surgery (RIRS) in a paediatric setting of various age groups: a global study across 8 centres

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Abstract

Purpose To analyse and report the practice, outcomes and lessons learnt from a global series of retrograde intrarenal surgery (RIRS) in a paediatric multicentre series.

Methods A retrospective review of anonymized pooled data gathered globally from 8 centres in paediatric patients (≤ 18 years of age) who had renal stones and underwent RIRS from 2015 to 2020 was performed. Patient demographics, perioperative parameters, stone characteristics, complications and stone-free rate (SFR; defined as endoscopically stone free and/or residual fragments < 2 mm on follow up imaging) were analysed. The cohort was stratified into 3 groups by age: < 5 years (Group A), 5–10 years (Group B) and > 10 years (Group C). Overall, post-operative complication rate was 13.7%. Chi-square comparisons were used for categorical variables; analysis of variance (ANOVA) or Kruskal–Wallis tests were used for continuous variables.

Results 314 patients were analysed. The mean age was 9.54 ± 4.76 years. Groups A, B and C had 67 (21.3%), 83 (26.4%) and 164 (52.2%) patients, respectively. Mean stone size was 10.7 ± 4.62 mm. Pre-stenting was performed in 155 (49.4%) of patients, ureteral access sheaths (UAS) was used in 54.5% of patients with majority (71%) utilizing holmium laser for stone fragmentation. All complications were minor (Clavien–Dindo grade 1 and 2). SFR was 75.5%.

Conclusions RIRS is acceptable as a first-line intervention in the paediatric population with reasonable efficacy and low morbidity. Complications are slightly higher in patients < 5 years of age, which should be taken into account while counselling patients.

Keywords Paediatric · Renal stone · Retrograde intrarenal surgery · Ureteroscopy · Renal calculi

Introduction

Indications for minimally invasive treatments for paediatric urolithiasis are currently extrapolated from the adult population. Existing literature has demonstrated that complication rates among all three modalities shock wave lithotripsy (SWL), percutaneous nephrolithotomy (PCNL), and retrograde intrarenal surgery (RIRS) [1]. We aim to analyse and report the practices and outcomes of RIRS from a global series to add in evidence of management of paediatric renal urolithiasis management.

Methods and materials

Anonymized pooled retrospective data gathered from 8 centres of paediatric patients (< 18 years of age) who had only renal stones and underwent RIRS was done from Jan 2015 to Dec 2020. Exclusion criteria included patients with ureteric stones, and/or undergoing bilateral procedures. Institutional ethics board committee or audit board approval was obtained

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and data was anonymized before pooled analysis. Patient demographics such as age, gender, height and weight, perioperative outcomes (pre-stenting, ureteral dilation), stone characteristics, operative time, complications and stone-free rate (SFR) were analysed. Residual fragments (RF) were defined as > 2 mm or multiple fragments of any size. The cohort was stratified by age into 3 groups: < 5 years (group A), 5–10 years (group B) and > 10 years of age (group C). SFR and postoperative complication rates were analysed between these three groups. Outpatient follow-up visits were scheduled between 4 and 6 weeks, and at 3 months postoperatively to assess for early complications and SFR. Factors influencing outcomes were analysed via univariate and multivariate analysis with generalized linear models. Chi-square comparisons were used for categorical variables; analysis of variance (ANOVA) was used for normally distributed continuous variables while the Kruskal–Wallis test was used for non-normally distributed continuous variables. Statistical analyses were performed using R-4.0.2 statistical software (R Foundation for Statistical Computing, Vienna, Austria) with $P < 0.05$ indicating statistical significance.

Results

314 patients had complete data for analysis. Table 1 shows demographics and perioperative characteristics. The age of the cohort was 9.54 ± 4.76 years (range 5 months–16 years). The number of patients in groups A, B and C were 67 (21.3%), 83 (26.4%) and 164 (52.2%), respectively. A higher

Table 1 Demographics and perioperative characteristics of study cohort, stratified age group

	Total (*N* = 314)	< 5 years (*N* = 67)	5–10 years (*N* = 83)	> 10 years (*N* = 164)	*P* value
Sex, *n* (%)					
Female	129 (41.1%)	17 (25.4%)	37 (44.6%)	75 (45.7%)	0.013
Male	185 (58.9%)	50 (74.6%)	46 (55.4%)	89 (54.3%)	
Height (cm)					< 0.001
Mean (SD)	125 (29.4)	86.5 (15.0)	115 (12.2)	145 (20.1)	
Median [IQR]	129 [102–150]	85.0 [80.0–96.0]	115 [110–122]	149 [140–160]	
Weight (kg)					< 0.001
Mean (SD)	34.5 (19.9)	13.4 (5.40)	22 (6.98)	49.3 (15.3)	
Median [IQR]	31.0 [17.0–48.0]	13.0 [10.3–14.5]	20.2 [18.0–25.1]	47.7 [40.5–56.9]	
Symptomatic at presentation, *n* (%)	252 (80.3%)	51 (76.1%)	62 (74.7%)	139 (84.8%)	0.028
Hematuria	66 (21.0%)	9 (13.4%)	22 (26.5%)	35 (21.3%)	0.174
Pain	179 (57.0%)	25 (37.3%)	47 (56.6%)	107 (65.2%)	< 0.001
Fever	51 (16.2%)	21 (31.3%)	9 (10.8%)	21 (12.8%)	< 0.001
Recurrent stone former, *n* (%)	38 (12.1%)	6 (9.0%)	9 (10.8%)	23 (14.0%)	0.495
Elevated serum creatinine, *n* (%)	6 (1.9%)	5 (7.5%)	0	1 (0.6%)	< 0.001
Positive urine culture, *n* (%)	53 (16.9%)	21 (31.3%)	15 (18.1%)	17 (10.4%)	< 0.001
Kidney anatomy, *n* (%)					
Normal	291 (92.7%)	63 (94.0%)	73 (88.0%)	155 (94.5%)	0.155
Malrotated	7 (2.2%)	2 (3.0%)	0	5 (3.0%)	0.276
Horseshoe	8 (2.5%)	0	6 (7.2%)	2 (1.2%)	0.006
Duplex	6 (1.9%)	2 (3.0%)	3 (3.6%)	1 (0.6%)	0.204
Ectopic	2 (0.6%)	0 (0%)	1 (1.2%)	1 (0.6%)	0.652
Stone size (mm)					
Mean (SD)	10.7 (4.62)	9.94 (4.09)	10.6 (3.79)	11.1 (5.15)	0.390
Median [IQR]	10.0 [8.00–12.0]	9.00 [8.00–11.0]	10.0 [9.00–12.0]	10.0 [8.00–14.0]	
Stone Houndsfield Unit > 1000, *n* (%)	56 (17.8%)	4 (6.0%)	12 (14.5%)	40 (24.4%)	0.003
Pre-stented, *n* (%)	155 (49.4%)	45 (67.2%)	38 (45.8%)	72 (43.9%)	0.004
Tamsulosin given, *n* (%)	13 (4.1%)	0	2 (2.4%)	11 (6.7%)	0.044
Stone type, *n* (%)					
Single	187 (59.6%)	37 (55.2%)	51 (61.4%)	99 (60.4%)	0.708
Multiple	127 (40.4%)	30 (44.8%)	32 (38.6%)	65 (39.6%)	

Height, weight and stone size were non-normally distributed

IQR interquartile range; *SD* standard deviation

proportion of males was seen in groups A and B (74.6% and 55.4%) compared to group C (54.3%, $p = 0.013$). Mean stone size was 10.7 ± 4.62 mm (range 1–30 mm). There were two patients with stone size 1 mm, both in Group B. Both were symptomatic, presenting with fever and pain, hence surgical intervention was offered. Stone size was not significantly different between the three age groups (9.94 ± 4.09, 10.6 ± 3.79 and 11.1 ± 5.15 mm in groups A, B and C, respectively). Tamsulosin was given in only 13 (3.1%) children, all above the age of 5 years. Of the 155 (49.4%) children who were pre-stented, 68.3% were male ($p < 0.001$), 86.5% were symptomatic ($p < 0.001$) with 67.2% in Group A ($p = 0.004$). Table 2 shows intra-operative parameters. 41 male patients (13.1%) received urethral dilation, of which 14, 9 and 18 were in groups A, B and C, respectively. Ureteral access sheaths (UAS) was used in 54.5% of patients with majority (87.5%) performing holmium laser lithotripsy. Respiratory control was utilized in 46 patients (14.6%). Overall SFR was 75.4% (237 patients; Table 3). Single RFs were commoner in Group C ($p = 0.005$), multiple RFs were commoner in Group A ($p = 0.006$). 43 cases (13.7%) of post-operative complications, all modified Clavien–Dindo (CD) 1 and 2;

Table 2 Intra-operative parameters of study cohort

	Total (*N* = 314)	< 5 years (*N* = 67)	5–10 years (*N* = 83)	> 10 years (*N* = 164)	*P* value
Urethral dilation, *n* (%)	41 (13.1%)	14 (20.9%)	9 (10.8%)	18 (11.0%)	0.146
Ureteral dilation, *n* (%)	88 (28.0%)	27 (40.3%)	27 (32.5%)	34 (20.7%)	0.070
UAS used, *n* (%)	171 (54.5%)	35 (52.2%)	42 (50.6%)	94 (57.3%)	0.030
UAS size > 8 Fr, *n* (%)	134 (42.7%)	18 (26.9%)	34 (41.0%)	82 (50.0%)	< 0.001
Laser used, *n* (%)					
Holmium	275 (87.5%)	42 (62.7%)	58 (69.9%)	123 (75.0%)	0.229
Thulium	39 (12.4%)	12 (17.9%)	8 (9.6%)	19 (11.6%)	
Respiratory control, *n* (%)	46 (14.6%)	4 (6.0%)	3 (3.6%)	39 (23.8%)	< 0.001
Stone removal method, *n* (%)					
Dusting only	152 (48.4%)	38 (56.7%)	34 (41.0%)	80 (48.8%)	0.085
Popcorning only	2 (0.6%)	0	2 (2.4%)	0	
Dusting + popcorning	135 (43.0%)	26 (38.8%)	40 (48.2%)	69 (42.1%)	
Fragmentation time (min), median [IQR]	15.0 [6.90–37.5]	15.0 [8.25–16.2]	18.5 [12.0–36.0]	15.0 [6.35–42.8]	0.381
Total operation time (min), median [IQR]	60.0 [45.0–90.0]	70.0 [40.0–90.0]	60.0 [45.0–90.0]	60.0 [45.0–85.0]	0.864

Fragmentation time and total operation time were non-normally distributed

Fr French; *IQR* interquartile range; *UAS* Ureteral Access Sheath

Table 3 Post-operative outcomes of study cohort

	Total (*N* = 314)	< 5 years (*N* = 67)	5–10 years (*N* = 83)	> 10 years (*N* = 164)	*P* value
Residual fragment, *n* (%)	77 (24.5%)	19 (28.4%)	18 (21.7%)	40 (24.4%)	0.639
Single	41 (13.1%)	5 (7.5%)	8 (9.6%)	28 (17.1%)	0.005
Multiple	36 (11.5%)	14 (20.9%)	10 (12.0%)	12 (7.3%)	0.006
Intraoperative bleeding, *n* (%)	5 (1.6%)	2 (3.0%)	0	3 (1.8%)	0.328
Pelvicalyceal system injury, *n* (%)	5 (1.6%)	5 (7.5%)	0	0	< 0.001
Ureteric injury, *n* (%)	5 (1.6%)	3 (4.5%)	0	2 (1.2%)	0.080
Fever, *n* (%)	20 (6.4%)	4 (6.0%)	3 (3.6%)	13 (7.9%)	0.419
Haematuria, *n* (%)	11 (3.5%)	4 (6.0%)	2 (2.4%)	5 (3.0%)	0.449
Sepsis, *n* (%)	2 (0.6%)	0	0	2 (1.2%)	0.398
Postoperative imaging, *n* (%)					
Combination	98 (31.2%)	17 (25.4%)	25 (30.1%)	56 (34.1%)	0.006
CT only	3 (1.0%)	1 (1.5%)	0	2 (1.2%)	
US only	113 (36.0%)	29 (43.3%)	37 (44.6%)	47 (28.7%)	
XR only	66 (21.0%)	8 (11.9%)	10 (12.0%	48 (29.3%)	

CT computed tomography; *US* ultrasound; *XR* X-ray

Two cases of sepsis were managed conservatively with antibiotics (Group C, CD2). Stone sizes ≥ 10 mm was associated with higher rates of intraoperative haematuria compared to stone size < 10 mm (5.7% versus 0.7%, $p = 0.036$); other post-surgical complications did not yield any significant differences. Univariate analysis showed that patients who were symptomatic (OR 0.34 95% CI 0.18–0.65, $p < 0.001$) or had multiple stones (OR 3.57 95% CI 2.10–6.17, $p < 0.001$) were associated with RF (Table 4). Multivariate generalized linear model incorporating pre-operative and intraoperative characteristics found that ureter dilation was associated with lower SFR and longer fragmentation time was associated with a higher SFR (Table 5).

Table 5 Multivariate analysis for associations of study variables with residual fragments

Factor	OR (95% CI)	*P* value
Intercept	0.64 (0.01–15.9)	0.793
Male sex	0.94 (0.20–4.59)	0.939
Age category (compared to < 5 years)		
5–10 years	0.77 (0.06–7.80)	0.825
> 10 years	1.43 (0.22–9.95)	0.704
Stone size ≥ 10 mm	0.37 (0.04–2.95)	0.360
Symptomatic presentation	0.62 (0.08–5.90)	0.647
Presence of normal kidney	0.65 (0.06–16.9)	0.751
Prestented	0.28 (0.06–1.19)	0.092
Urethral dilation	13.0 (1.39–341)	0.051
Ureter dilation	0.05 (0.00–0.60)	0.037
UAS used	0.43 (0.07–2.43)	0.341
Fragmentation time	1.07 (1.02–1.14)	0.015

UAS Ureteral Access Sheath

Discussion

According to European Association of Urology (EAU) paediatric urology guidelines, SWL is the primary treatment option for renal stones up to 20 mm [2]. Introduction of a small calibre endoscopes has, however, made endoscopic approach an appealing choice, even with early

Table 4 Univariate analysis for associations of study variables with residual fragments

Factor	OR (95% CI)	*P* value
Male sex	0.69 (0.41–1.15)	0.154
Age category (compared to < 5 years)		
5–10 years	0.70 (0.33–1.48)	0.347
> 10 years	0.81 (0.43–1.57)	0.531
Height (cm)	0.99 (0.98–1.01)	0.306
Weight (kg)	1.00 (0.99–1.02)	0.658
Symptomatic at presentation	0.34 (0.18–0.65)	< 0.001
Hematuria	0.98 (0.51–1.83)	0.956
Pain	0.39 (0.23–0.67)	< 0.001
Fever	0.82 (0.38–1.66)	0.603
Recurrent stone former	1.51 (0.70–3.11)	0.275
Elevated serum creatinine	0.61 (0.03–3.85)	0.652
Positive urine culture	1.33 (0.68–2.51)	0.388
Normal kidney anatomy	0.58 (0.24–1.50)	0.239
Prestented	0.81 (0.48–1.36)	0.430
Tamsulosin given	All had no residual fragment	NA
Multiple stone (compared to single)	3.57 (2.10–6.17)	< 0.001
Stone size (mm)	1.07 (1.01–1.13)	0.012
Stone Houndsfield Unit > 1000	0.33 (0.12–0.82)	0.024
Urethral dilation	0.57 (0.22–1.27)	0.195
Ureteral dilation	0.28 (0.12–0.58)	0.001
UAS used	0.76 (0.42–1.38)	0.362
UAS size > 8 Fr	13.22 (2.70–239.13)	0.012
Thulium laser (compared to Holmium laser)	0.05 (0.00–0.25)	0.004
Fragmentation time	1.03 (1.00–1.06)	0.020
Respiratory control	0.38 (0.13–1.02)	0.063

Fr French; *UAS* Ureteral Access Sheath

series reporting that in up to 50% of cases, inability to attain ureteral access was the major deterrent [3–5]. Our study pointed out three important findings.

First, we demonstrated that RIRS is safe and effective procedure with a single stage SRF of 75.4% across all age groups with an acceptable rate of low-grade complications of 10.8%. Our results reflect real-world data and outcomes of paediatric ureteroscopy with all age groups of patients. Arguably, the failure to access rates and complications are higher with patients < 6 years of age; It is well known that patients under the age of 6 have a higher rate of complications (up to 24%) compared to those > 6 years (7%); and failure to access of up to 4.4% in < 6 years compared to 1.7% for those > 6 years [6]. The complications were defined as per the CD classification [7], and one of the reason for higher complications were the inclusion of all age group of patients. With the exception of 2 septicaemia cases, the remaining were all minor CD I and II complications. In all 5 cases in Group A with pelvicalyceal injury, reporting authors confirmed that this was only noted at the end of surgery based on radiological findings on retrograde pyelography and were managed with a post-operative JJ stent. We hypothesize that it could be attributed to the extremely limited pelvicalyceal space particularly vulnerable to fluctuations in intrarenal pressure. Azili et al. reported a series of 47 children who underwent RIRS for renal stone [8] and showed that complications were low grade and transient (14.9%) with an overall SFR of 50.9% after the first session. We found no differences with regard to height and weight of the patients in relation to outcome or safety of the surgical technique nor stone size.

Second, greater stone burden and Hounsfield Units (HU) units > 1000 was a definitive risk factor for postoperative RFs. In comparison, Ozkent et al. showed on multivariate analysis that stone size, lower pole and multiple stones of any size were predictors of RF and significantly affected SFR [9]; Khraman et al. demonstrated that there was a higher SFR for stones where HU was < 700 units [10].

Third, we showed that there was no evidence that the use of UAS improves SFR in children. Ureteral dilatation, either performed using sequential ureteral dilators or semi-rigid ureteroscopy, was required mainly in group A. Despite this, children in group A did not demonstrate a significantly higher rate of RF as compared to older children. The tendency to decrease the need for this step during URS or RIRS in children is clear due to reports of vesicoureteral reflux and ureteral stricture after balloon dilation or ureteral dilators [11]. EAU guidelines do not state a definitive position regarding pre-stenting, and that in at least half of the cases of RIRS in children access fails, so leaving a ureteric stent for passive dilation and re-do RIRS is an option [2]. Our ability to perform RIRS in half the cohort without pre-stenting is a point in favour of reaffirming that RIRS is a safe and viable alternate to ESWL.

Lastly, although proven safe and efficacious in adults, information is lacking on the ideal laser settings in the paediatric age groups, an important area of further research. Our analysis shows the use of thulium fibre laser (TFL) in 39 patients was associated with better SFR compared to conventional holmium laser. Traxer et al. demonstrated that TFL was superior to conventional holmium laser in ablation and dusting [12]. Albeit a small series, our study is novel in reporting use of TFL in the paediatric population.

To our knowledge, our study is the first large volume retrospective multinational study that reports real-world clinical outcomes from a pooled global cohort of paediatric patients who underwent RIRS for renal calculi in high-volume institutions. We assessed and compared trends and outcomes in our series with available literature about RIRS for paediatric and adult patients (Table 6). Despite the advantage of a multinational cohort, this study is limited by its nature with inherent bias associated with any retrospective

Table 6 Comparison of practices in our study with literature RIRS in adults and the paediatric population

Literature for RIRS	Adults	Paediatric	Our series
Safety of RIRS	✓	✓	✓
Pre-stenting	Not routine	No definite guidelines	Mainly for symptomatic and younger /shorter kids
Tamsulosin pre-op	✓	No definite guidelines	In 13 patients of Group B and C only
Urethral dilatation	×	Currently being practised in some	Few patients in all groups
Ureteral dilatation	×	Not a mandate in all ages as per EAU	Maximum in group A
UAS use	Surgeon choice	No definite guidelines	✓
Laser lithotripsy modes (dusting/ fragmentation/ combination)	✓	✓	✓
Use of gated respiration	✓	No definite guidelines	Limited in only aged > 10 years
TFL use	✓	×	✓

RIRS retrograde intrarenal surgery; *TFL* thulium fibre laser; *EAU* European Association of Urology

analysis. The authors acknowledge that an additional limitation was lack of robust data regarding stone localization limiting purposeful analysis, mainly due to heterogeneity in reporting across the multicentre cohort. Additionally, differences in institutional guidelines, surgeon preferences and endourological techniques may have led to heterogeneity within our cohort. Nonetheless, the data was subject to rigorous statistical analysis in an effort to minimize the effect of heterogeneity and reflects real-world data.

Conclusions

RIRS in the modern era is safe, efficacious and acceptable minimally invasive procedure for paediatric urolithiasis, as demonstrated in our cohort. While the overall morbidity was low, we found a higher incidence of complications in children aged 5 years or less and this should be taken into account while counselling parents. As technological advancements bring in smaller ureteroscopes, thinner laser fibres, improved image quality and greater deflection capacity, the utilization of RIRS will continue to increase in the paediatric population.

Author contributions Authors whose names appear on the submission have contributed sufficiently to the scientific work and, therefore, share collective responsibility and accountability for the results. EJL: project development, data analysis, manuscript writing. OT: protocol/project development, and manuscript editing. YQM: data collection, manuscript writing, DC: data analysis, manuscript writing, KYF: data analysis and manuscript writing. VWSC: data management and manuscript writing. ABT: protocol/project development. AP: data management and manuscript writing. DR: data management and manuscript writing. AS: data collection. CMV: data management and manuscript writing. TPB: data management and manuscript writing. MM: data collection and manuscript writing. PJJ: data collection and manuscript writing. SG: data collection and manuscript writing. EGR: data collection and manuscript writing. MC: data collection and manuscript writing. CAS: data collection and manuscript writing. YT: protocol/project development and manuscript writing. JYCT: protocol/project development and manuscript writing. VG: protocol/project development and manuscript writing. BKS: protocol/project development and manuscript writing.

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Declarations

Conflict of interest The authors declare no conflict of interests.

Ethical approval This research study was conducted retrospectively from data obtained for clinical purposes. Institutional ethics board committee or audit board approval was obtained by individual institutions and data were anonymized before pooled analysis.

Informed consent Informed consent was obtained from all individual participants included in the study.

Financial interest The authors have no relevant financial or non-financial interests to disclose.

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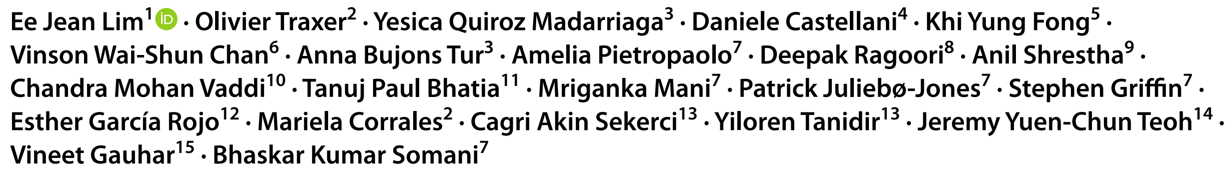
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