Real-world Global Outcomes of Retrograde Intrarenal Surgery in Anomalous Kidneys: A High Volume International Multicenter Study

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OBJECTIVE To analyze the trends and outcomes of retrograde intrarenal surgery for treatment of urolithiasis in anomalous kidneys in a large international multicenter series.

MATERIALS AND METHODS We designed a multicentric retrospective study. Nineteen high-volume centers worldwide were included. Pre-, peri- and postoperative data were collected, and a subgroup analysis was performed according to renal anomaly.

RESULTS We analyzed 414 procedures: 119 (28.7%) were horseshoe kidneys, 102 (24.6%) pelvic ectopic kidneys, 69 (16.7%) malrotated kidneys and 50 (12.1%) diverticular calculus. The average size (SD) of the stone was 13.9 (±6) millimeters and 193 (46.6%) patients had a pre-operative stent. In 249 cases (60.1%) a disposable scope was used. A UAS (ureteral access sheath) was used in 373 (90%) patients. A Holmium laser was used in 391 (94.4%) patients. The average (SD) operating time was 65.3 (±24.2) minutes. Hematuria, caliceal perforation and difficulty in stone localisation were mostly seen in diverticular stones and difficulty in UAS placement and lithotripsy in the cases of renal malrotation. The overall complication rate was 12%. Global stone-free rate was 79.2%. Residual fragments (RF) were significantly lesser in the pre-stented group ($P < .05$). Diverticular calculi was the group with more RF and needed ancillary procedures ($P < .05$).

CONCLUSION Retrograde intrarenal surgery in patients with anomalous kidneys is safe and effective with a high single-stage stone-free rate and low complication rate. There is a trend toward using smaller and disposable scopes and smaller UAS. Diverticular stones can still be challenging with higher rates of intraoperative hematuria, caliceal perforation and RF. UROLOGY 159: 41–47, 2022. © 2021 Elsevier Inc.

Congenital anomalies of the kidney and upper urinary tract arise from problems in the embryonic development and can occur due to abnormal ascent, fusion of both kidneys, abnormal rotation, a duplex collecting system or a combination of these.[1,2]

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The most common renal anomaly is horseshoe kidney (HSK), with an incidence of 1 in 400 births and a prevalence of 0.25% among the general population[3] and includes the fusion of the lower poles, resulting in an abnormal position of the ureter in the renal pelvis, malrotation with anterior displacement of the collecting system and highly placed ureteropelvic junction.[4] The incidence rate of ectopic kidney is of 1 in 3000 births. Malrotated kidneys are less frequent as an isolated finding.[1] Calyceal diverticula are rare outpouchings of the upper collecting system that likely have a congenital origin. Stones can be found in up to 50% of calyceal diverticula, although, over the combined reported series, 96% of patients presented with stones.[5]

Anomalous renal anatomy often results in compromised urine drainage, increasing the risk of developing urinary tract infection and urinary lithiasis.[6,7] Increased metabolic alterations predisposing to stone formation have been observed in these patients.[8] In the most common renal anomaly that is HSK in adults, there is an overall incidence of kidney stones of about 36%.[3]

In the past, open surgery was considered as the standard treatment for urolithiasis in anomalous kidneys such as HSK or pelvic kidneys but it has now become almost obsolete.[7] Small and uncomplicated stones could be treated by extracorporeal shockwave lithotripsy (ESWL),[9] however for larger stones, the stone-free rate (SFR) of ESWL is much less than that of percutaneous nephrolithotomy (PCNL) because of the difficulty in drainage of stone fragments through malformed structures[10-12] making PCNL the preferred choice.

Technological and technical advances in retrograde intrarenal surgery (RIRS), with the development of smaller calibre instruments, better deflection capability and the advent of modern-day lasers[13] have expanded RIRS indications for the treatment of lithiasis in anomalous kidneys and although endoscopic access can be challenging, it is now a generally well-accepted as a first-line treatment option.

Several papers reported small single-center series outcomes of RIRS in anomalous kidneys, with complications and stone-free rates (SFR) that are variable across the reported studies[2,7,14] probably due to differences in levels of experience and number of reported cases.

The aim of this study is to analyze what are the preferences, trends and outcomes of RIRS with regard to SFR, complications and the need to perform ancillary procedures for the treatment of lithiasis in anomalous kidneys. The data comprised of a large international multicenter retrospective case series and previously unpublished pooled data only involving expert endourologists from high-volume centers.[15]

MATERIALS AND METHODS

Study Design and Patients

We designed a multicentric, retrospective study to investigate RIRS outcomes in patients with anomalous kidneys.

Expert surgeons in endourology (>500 RIRS) from high-volume centers were invited for collaboration.[15] Patients with anomalous kidneys (horseshoe kidney, ectopic, malrotated, crossed fused renal ectopia, polycystic kidney or with duplex collecting system or pelvic-ureteric junction obstruction or with diverticular calculi) who had undergone RIRS between 2017 and 2021 were included. The authors completed an Excel datasheet and sent it back for analysis. Nineteen high-volume centers worldwide were included. Patients with incomplete data were excluded for analysis. Further, each author was asked to re-

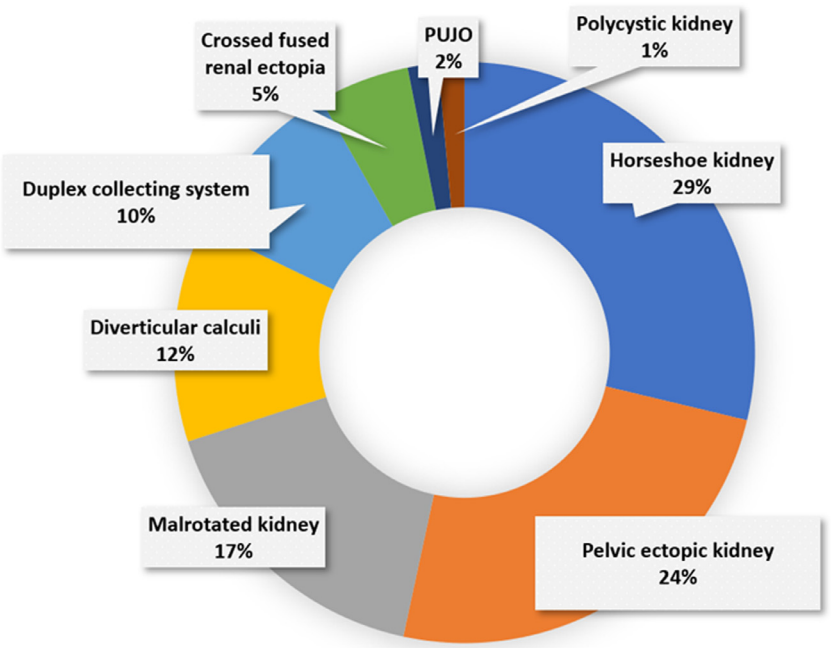

Figure 1. Subgroups of kidney alterations in the global series.
PUJO, pelvi-ureteric junction obstruction. (Color version available online.)

check that only unpublished data was provided. Any published data were then excluded, and pooled data were anonymised.

Patient Assessment: Variables and Measurement Methods

For all patients, the authors recorded gender, age and comorbidities (hypertension, Diabetes Mellitus, and cardiovascular disease. Preoperative variables like first episode of urolithiasis or recurrence, the indication for surgery (pain, urinary tract infection, hematuria), the size and number of stones and their density measured in Hounsfield Units (HU)[16] were also assessed.

Variables concerning the instruments were recorded (type of scope, use of ureteral access sheath (UAS) and their sizes, type of laser, its energy and settings).[17] Surgical times, intraoperative difficulties or complications arising during the surgery were categorised.

Single-stage stone-free rate (SFR) was defined as the absence of fragments or fragments ≤ 2 mm at the first imaging study[18] (based on either non-contrast computed tomography or ultrasound, X-ray or combination depending on local protocols). Post-surgical evaluation imaging tests were performed 1 to 3 months after surgery. Presence of residual fragments (RF), surgical and post-surgical complications and need of additional ancillary treatments (ESWL, RIRS, PCNL) were also evaluated.

Surgeons were asked to qualify their opinion for each case, if RIRS was a right first approach or if endoscopic combined intrarenal surgery (ECIRS) might have been a better approach to improve these outcomes.

Statistics

Statistical analysis was performed with IBM SPSS Statistics (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.).

The categorical variables were described as frequencies and percentages, while the quantitative variables were presented as means and standard deviations (SD). A chi-squared test was performed for categorical variables. ANOVA analysis was used to compare subgroups. A *P*-value of <.05 was considered statistically significant.

RESULTS

Global Series

Of the dataset on 481 patients, 67 were excluded for incomplete or previously published data and 414 were eventually analyzed. The mean (SD) age was 42.3 (±14.8) years. 277 were male patients (66.9%) and 137 (33.1%) females. From data available in 397 patients, 85 (20.5%) had hypertension, 95 (22.9%) had Diabetes Mellitus and 10 (2.4%) had cardiovascular disease.

The main two anomalies were horseshoe kidneys (119; 28.7%) and pelvic ectopic kidneys (102; 24.6%). Sixty-nine (16.7%) had a malrotated kidney, 50 (12.1%) had diverticular calculus, 40 (9.7%) had a duplex collecting system (partial or complete), 21 (5.1%) had crossed fused renal ectopia, 7 (1.7%) had polycystic kidney and 6 (1.4) had pelvic-ureteric junction obstruction (PUJO) (Figs. 1 and 2).

Two hundred fifty-two (56%) patients presented with a first episode of lithiasis and 182 (44%) were recurrent stone formers. Two hundred ninety-five (71.2%) were symptomatic with pain, 134 (32.4%) had signs of upper urinary tract obstruction, 65 (15.7%) had a urinary infection and 56 (13.5%) had hematuria.

The mean stone diameter (SD) was 13.9 (±6) millimeters with a mean stone density (SD) of 1051.12 (±274.19) HU. Three hundred seven (74.14%) had a single stone while 107 (25.8%) patients had multiple stones (mean 3.33 ± 3.49 stones).

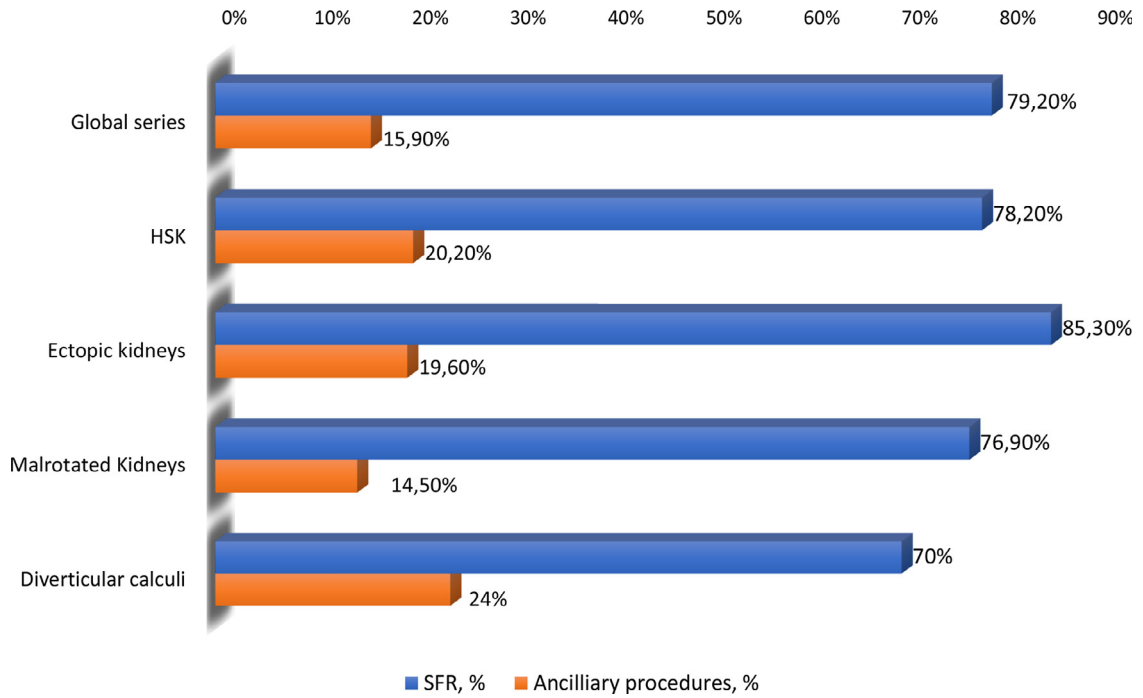

Figure 2. SFR and ancillary procedures in global series and subgroups. HSK, horseshoe kidney; SFR, stone free rate. (Color version available online.)

Table 1. Comparative analysis in main subgroups

	Global Series	HSK	EctopicKidneys	MalrotatedKidney	Diverticular Calculi	*P*
Cases, %	414 (100%)	119 (28.7%)	102 (24.6%)	69 (16.7%)	50 (12.1%)	
Age, Me (SD)	42.33 (14.86)	42.81 (16.43)	41.94 (13.16)	45.89 (17.24)	39.02 (10.41)	.093
Gender, N (%)	Male 277 (66.9%)	88 (73.9%)	69 (67.6%)	47 (68.1%)	29 (58%)	.093
	Female 137 (33.1%)	33 (32.4%)	31 (26.1%)	22 (31.9%)	21 (42%)	.44
Stone size, Me (SD)	13.94 (6.01)	12.70 (6.49)	13.76 (5.49)	13.24 (5.15)	15.84 (4.89)	.23
Stone density in HU, Me (SD)	1051 (274.2)	883.46 (228.01)	1134.74 (268.21)	1121.78 (324.77)	1005.95 (200.18)	**<.001**
Pre-stented, N (%)	193 (46.6%)	72 (60.5%)	45 (44.1%)	37 (53.6%)	7 (14%)	**<.001**
SURGICAL TIMES						
Total Time, Me (SD)	65.35 (24.27)	74.49 (22.84)	57.92 (22.29)	73.02 (29.42)	56.79 (16.54)	**<.001**
Laser Time, Me (SD)	27.46 (12.23)	29.09 (11.1)	27.78 (14.79)	27.48 (13.17)	26.44 (12.76)	.73
COMPLICATIONS						
Hematuria, N (%)	45 (10.9%)	10 (8.4%)	5 (4%)	1 (1.4%)	18 (36%)	**<.001**
Perforation UUT, N (%)	8 (1.9%)	2 (1.7%)	1 (1%)	2 (2.9%)	3 (6%)	**<.01**
Ureteric injury, N (%)	7 (1.7%)	2 (1.7%)	0	2 (2.9%)	0	**<.01**
Postoperative fever, N (%)	42 (10.1%)	8 (6.7%)	12 (11.8%)	8 (11.6%)	7 (14%)	.58
INTRAOPERATIVE DIFFICULTIES						
UAS placement, N (%)	40 (10.4%)	12 (10.1%)	9 (8.8%)	9 (13%)	4 (8%)	**<.01**
Litotripsy, N (%)	50 (12.1%)	12 (10.1%)	8 (7.8%)	12 (17.5%)	7 (14%)	**<.01**
Visualization, N (%)	66 (15.9%)	16 (13.4%)	7 (6.9%)	8 (11.6%)	19 (38%)	**<.001**
Residual fragments, N (%)	86 (20.8%)	26 (21.8%)	15 (14.7%)	16 (23.2%)	15 (30%)	**.001**
Ancillary procedures,N (%)	66 (15.9%)	24 (20.2%)	20 (19.6%)	10 (14.5%)	12 (24%)	**<.001**
— ESWL	10 (2.4%)	8 (6.7%)	0	0	2 (4%)	**<.001**
— RIRS	33 (7.9%)	8 (6.7%)	11 (10.7%)	7 (10.1%)	7 (14%)	**<.001**
— PCNL	13 (3.1%)	4 (3.3%)	7 (6.8%)	1 (1.4%)	1 (2%)	**<.001**
— - ECIRS	10 (2.4%)	4 (3.3%)	2 (1.9%)	2 (2.9%)	2 (4%)	**<.001**
Surgeon subjective opinion: RIRS right option, N(%)	332, 80.19%	101 (84.9%)	70 (68.6%)	53 (76.8%)	45 (90%)	**<.001**

ECIRS, endoscopic combined intrarenal surgery; ESWL, extracorporeal shockwave lithotripsy; HSK, horseshoe kidney; HU, hounsfield units; ME, median; N, number of cases; PCNL, percutaneous nephrolithotom; RIRS, retrograde intrarenal surgery; SD, standard deviation; UAS, ureteral access sheaths; UTT, upper urinary tract.
Boldface highlights statistically significant comparisons.

One hundred ninety-three (46.6%) patients were pre-stented before surgery. The distribution of these amongst anomalies is highlighted in Table 1. Of these patients, the majority of the pre-stented patients were in HSK group (60.5%) as the commonest presentation in these was obstruction, whilst the least stented patients were those with diverticular stones (14%). Significant differences between groups were found in stone density (P <.001) and pre-stented patients (P <.001).

Operative Parameters and Outcomes

Surgeries were performed according to surgeons' own preferences and available equipment in their centers. In 249 cases (60.14%) a disposable scope was used, and a reusable scope in 165 (39.85%) cases. The diameter of the ureteroscopes was diverse, with devices ranging between 5.3 Fr and 11.5 Fr. The most preferred flexible ureteroscopes were 7.5 Fr (110, 26.6%), 8.5 Fr (86. 20.8%) and 9.5 Fr (74, 17.9%).

A ureteral access sheath (UAS) was used in 383 (92.5%) patients with diameters between 9 and 14 Fr. A UAS ≤11 Fr was used in 253 (66.05%) patients and a UAS ≥12Fr in 130 (33.9%).

A Holmium: YAG laser was used in 391 (94.4%) patients and a thulium fiber laser in 23 (5.6%). The combination of dusting and pop-corning was the preferred mode for lithotripsy[16] and was used in 254 patients (61.35%). In 110 (26.6%) patients a pure dusting mode was used and in only 50 (12%) patients, fragmentation was the choice of lithotripsy. Even though the stone fragments were extracted in 168 (40.6%) patients, the majority of the surgeons preferred to allow spontaneous passage after in situ lasering (246 patients, 59.4%).

The mean operating time was 65.3 (±24.27) minutes with a mean laser time of 27.4 (±12.23) minutes. Total time was significantly higher in malrotated kidney and HSK (P <.001).

The difficulties and complications, immediate SFR and the need for ancillary procedures are summarized in Table 1. In 50 (12%) patients there was a surgical complication,

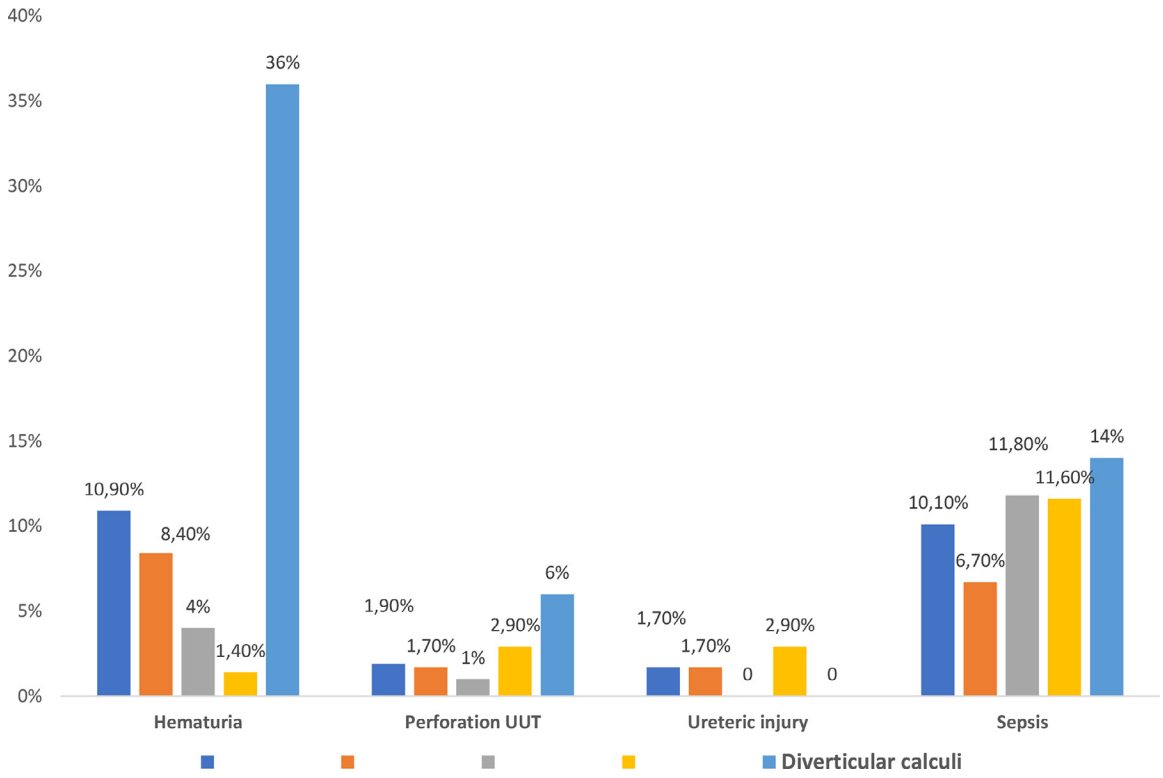

Figure 3. Complications in global series and subgroups.
HSK, horseshoe kidney; UUT, upper urinary tract. (Color version available online.)

hematuria being the most prevalent surgical problem (45, 10.9%). An upper urinary tract perforation or a ureteral injury were observed in only 1.9% and 1.7% respectively. Surgery had to be abandoned due to the occurrence of one or more of these problems in 18 patients (4.3%). A ureteral stent was placed at the end of surgery in 392 (94.7%) patients even though it was an uncomplicated ureteroscopy (364 ureteroscopes without surgical complications, 88%), probably to facilitate spontaneous passage of dust and fragments. Only 42 patients (10.1%) experienced fever in the immediate postoperative period (<30 days).

Our series had a single-stage SFR of 79.2% Fig. 2 SFR and ancillary procedures in global series and subgroups. (Fig. 3) and of the 86 (20.8%) patients with RF, retreatment was performed in only 66 (15.9%) patients of which majority patients were in HSK group. Relook RIRS was the preferred retreatment choice.

Pre-stented patients had significantly lower RF (37, 43%) than those without pre-stent (49, 57%). No relationships were found between pre-stented and complications.

Subgroup's Analysis

Comparative analysis between the following subgroups was done, with most cases being horseshoe kidneys (28.7%), pelvic ectopic kidney (24.6%), malrotated kidneys (16.7%) and diverticular calculi (12.1%).

No statistical differences noted for age, sex, and stone sizes, but most of the patients in the HSK group had a mean HU of 883.46 the least of all subgroups (Table 1).

Statistically significant differences were found in favor of cases of ectopic pelvic kidneys and diverticular calculi in the total operative time; however, no differences were found in terms of the time of laser used between the groups.

The diverticular calculi sub-group had most patients with RF and needed ancillary procedures (Fig. 3).

Intraoperative complications and difficulties encountered are summarized in Table 1 and Fig. 3 SFR and ancillary procedures in global series and subgroups. Higher rates of hematuria, caliceal perforations and difficulty in stone localization was noted in patients with diverticular stones, and greater difficulty in UAS placement and lithotripsy in cases of renal malrotation. Data points toward surgeons facing the most challenges in tackling diverticular stones, with the need for ancillary procedures in almost 30% (highest in the subset).

More than 80% of the surgeons did not feel that ECIRS would have helped them achieve a better outcome overall in all cases and despite the difficulties in RIRS for diverticular stones, a majority (90%) did not advocate ECIRS as an alternative primary choice.

DISCUSSION

The incidence of anomalous kidneys is relatively low, but the incidence of stones in patients with anomalous kidney is much higher than reported in the general adult population.[3,19]

Small and uncomplicated stones can be successfully treated by ESWL[9] or RIRS,[3] however in patients treated with ESWL, retreatment and auxiliary interventions are often needed due to impaired drainage with poor passage of fragments due to anatomic abnormalities.[19,20] For larger stones, the SFR of PCNL seems to be higher[10-12,21] but sometimes requires more than one stage to achieve a good overall stone clearance rate.[22] Laparoscopic techniques have been also described for the treatment of large stones in these patients.[23] ECIRS as a primary modality to treat renal stones

since its introduction in 2008[24] has over time proven to be safe and effective even in larger stones.[25]

Global Series Outcomes vs Other Series

The published SFR in ESWL series managing urolithiasis in anomalous kidneys is around 60%, varying from 20% to 80%,[20,26-28] PCNL has been the treatment of choice for the management of large calculi with rates of SFR around 70%-85%, although major complications such as haemorrhage, nephron-pleural fistula, and pneumothorax have been described.[8,11,21,28]

Previously published series of RIRS classically showed lower resolution rates than PCNL, but modern series (due to the advent of lasers, flexible ureterorenoscopes, and nitinol baskets that have allowed access to stones in difficult locations) reported a stone clearance rate comparable to PCNL (around 80%) and better than ESWL with minimal complication rate.[24,25]

In order to gain a global, homogeneous true representation of the SFR, complications and intraoperative preferences of RIRS in anomalous kidneys, robust data were obtained from 468 cases from 16 countries, of which only unpublished data from 414 patients were analyzed making this the largest series published. All cases were managed only by RIRS and were performed at high volume centers in the last 5 years by experienced endourologists. Furthermore, our series had patients with a good number of cases of all anomalies, stones of diverse sizes, including diverticular stones which makes it more realistic data for analysis across the anomalies for comparison.

In our series, the global SFR, defined as the absence of fragments or fragments ≤2 mm at the first postoperative control imaging study (based on either non-contrast computed tomography or ultrasound, X-ray or combination depending on local protocols), was 79.2%, highest (85.3%) in the pelvic ectopic kidney group and lowest (70%) in the diverticular calculi group. We found a mean surgical time of 65.35 (±24.27) in the global series, which is similar to 61.3 minutes reported in the systematic review by Lavan et al.[6]

Statistically significant differences between the subgroups, with longer surgical times on average (74.49 and 73.02 minutes) in the HSK and malrotated kidney groups respectively were noted. This has not been stratified and compared systematically in any study before. Furthermore, our results point out that RIRS is a challenging procedure in HSK and malrotated kidneys, even in expert hands.

In our series, we were able to compare and contrast across the different anomalies what were the intraoperative difficulties and postoperative complications, something which has not been well documented before. An important finding is that although a UAS was placed in 92.5% of patients in our series, difficulty in its placement reported in just 10.4% of the cases who were not prestented and only 1.7% cases had a ureteric injury. Disposable scopes were used in a high percentage of cases in our study (60.14%), which represents a changing trend in modern endourology.

In our series there are a significant percentage of prestenting (46.6%). Although it seems that preoperative ureteral stenting do not affect operative outcomes, it can increase the success rate of access sheath placement.[29]

The increased use of modern disposable scopes, that allow excellent deflection and vision, and the high use of UAS (92.5%), may influence the excellent SFR results obtained, although there is currently insufficient data to support this statement. The group with the lowest rate of preoperative stenting is the diverticular stone group (14% vs 44%-60%), probably due to the surgeon's expectation of easier ureteral access compared to the other groups, where access is often more difficult.

The retrospective systematic review on 14 retrospective studies published by Lavan et al[6] is the most comprehensive review to date and very nicely described the tips and tricks to perform RIRS in anomalous kidneys. In that paper, patients treated between 2005 and 2017 were included, of which 10% had semirigid ureteroscopy (URS) as primary management and the rest had flexible ureteroscopy (FURS). Mean stone diameter was 16 mm, mostly single stones and 60% of the patients were contributed by two series. The cumulative initial SFR was 76.6% (URS + FURS) but 6/16 had no data on this including the two largest series. The overall complication rate was 17.2%, much higher than our series. Heterogeneity of the data was not a true representation at all of the efficacy of RIRS as a primary treatment modality.

However, congenital anomalies of the kidney and upper urinary tract are uncommon and a prospective study with large number of patients might be difficult to set up; indeed, our study is the largest study that includes high-volume centers, showing actual practices from around the world. Moreover, our series is the first large modern (from 2017) study with a global representation of only RIRS outcomes in different anomalous kidneys. Although randomized trials between treatment modalities would be difficult to perform, large prospective multi-centric studies with long-term follow-up and standardized references would be useful to provide higher quality data.

Due to its retrospective nature we were limited in not having the complications graded as per Clavien-Dindo Classification as well as lacking in information of the position and composition of the stones to make suitable comparisons. The question of whether ECIRS could have been a better approach to improve these outcomes is a subjective opinion provided by the surgeons that is also answered retrospectively. The intent of this question was that, given that the literature has favored RIRS, PCNL and, more recently, ECIRS in the treatment of urolithiasis in normal kidneys, many patients would benefit from either treatment modality depending on the surgeon's experience and the availability of expertise at the center where they are treated.[30]

CONCLUSION

Although RIRS in patients with anomalous kidneys can be technically challenging, we highlighted that RIRS is a safe and effective treatment with acceptable complication rate in experienced hands. The SFR is expected to be high when careful case selection is made and when patients are treated in high volume centers with experienced surgeons. Diverticular stones can be challenging with possible higher rates of intraoperative complications and lower SFR. RIRS can be offered as first-line approach and treatment tailored depending on the complexity of anatomical anomaly.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

Supplementary figure 1. Country participation and contribution to the study.

Acknowledgment. To everyone who has made this work possible and has actively collaborated obtaining data.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urology.2021.10.003.

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