

Stone free rate and clinical complications in patients submitted to retrograde intrarenal surgery (RIRS): Our experience in 571 consecutive cases

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Summary

Introduction: The purpose of this study is to report the stone free rate (SFR) and clinical complications in patients submitted to retrograde intrarenal surgery (RIRS).

Materials and methods: A total of 571 procedures of upper urinary stones treated using flexible ureteroscopy and holmium laser lithotripsy from January 2014 to February 2020 have been analyzed. Overall SFR was evaluated after 3 months following the procedure by means of a non-contrast computed tomography. Success was considered as stone-free status or ≤ 0.4 cm fragments.

Results: The overall SFR was 92.3% in group 1 (stone size: < 1 cm), 88.3% in group 2 (stone size: $> 1 \leq 2$ cm), 56.7% in group 3 (stone size: 2-3 cm) and 69.6% in group 4 (multiple stones). Post-operative complications, according to the Clavien-Dindo (CD) classification system, were recorded in 32 (5.6%) procedures. The major complications recorded were: one case of subcapsular hematoma (SRH) associated with pulmonary embolism two days after the procedure (CD Grade IIIa) treated conservatively and one case of hemorrhagic shock 2 hour with multiple renal bleedings requiring urgent nephrectomy (CD Grade IVa).

Conclusions: The RIRS is an effective and safe procedure with a high SFR significantly correlated with the stone size; at the same time, RIRS could be characterized by severe clinical complications that require rapid diagnosis and prompt treatment.

KEY WORDS: RIRS; Complications; Stone free rate.

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INTRODUCTION

The retrograde intrarenal surgery (RIRS) was introduced in 2008 as an alternative to extracorporeal shock wave lithotripsy (ESWL) and percutaneous nephrolithotomy (PNL) in patients with ESWL-refractory and lower pole stones; today, according to the more recent *European Guidelines* (EAU guidelines), RIRS represents one of the first line treatments for < 2 cm renal stones (1, 2). In fact, in 2013 EAU guidelines RIRS has been reported as an effective and definitive therapeutic option for renal stones with higher stone free rate (SFR) and low rate of complications (3). Many studies have compared RIRS to percutaneous surgery (PNL) with results that seem to be similar even

for larger volume stones, but with few severe complications (4, 5); on the other hand, other studies described also life threatening complications of RIRS.

In every day practice is RIRS a really uncomplicated technique? What are the real risks?

The purpose of this study is to report the stone free rate (SFR) and clinical complications in patients submitted to RIRS.

MATERIALS AND METHODS

Outcomes of 514 (mean age was 55 yrs; range: 24-84) consecutive patients (313 males and 201 females) who underwent RIRS for renal stones from January 2014 to February 2020 have been retrospectively analyzed. 213 (41.4%) vs 301 (68.6%) stones were located in the right and left kidney; in detail, 213 (41.3%) vs 101 (19.5%) vs 75 (10.6%) vs 239 stones (46.6%) were located in the lower pole vs the middle pole vs the upper pole vs the renal pelvis, respectively. The median stone size was 1.3 cm (range 0.6-3 cm), in 128/514 (24.9%) cases the stones were multiple; CT stone density (HU) 859 (range 436 - 1674). Preintervention double-J stenting was performed in 208/571 (36.5%) cases.

Overall SFR was evaluated after 3 months following the procedure by means of a non-contrast computed tomography (N-CCT). Patients who were not considered stone free at the end of the procedure were rescheduled for second look. Success was considered as stone-free status or ≤ 0.4 cm fragments *Clinically Insignificant Residual Fragments* (CIRF). The 30 days complication rate was classified according to the *Clavien-Dindo* (CD) classification system (6).

Surgical technique

All patients were operated in the standard lithotomy position, under general or spinal anesthesia according to anesthetist-patients counseling. Preliminary semirigid ureteroscopy (using a 6.5-7 F. ureterorenoscope) was performed to observe the ureter and obtain a preconditioning ureteral dilation.

A ureteral access sheath (UAS) was positioned (10/12 or 12/14 F - *Retrace*[®] *Coloplast*; 9.5/11.5 or 10.7/12.7 F - *Flexor*[®] *Cook Urological*) depending on the ureteral diam-

eter and compliance. The length of the UAS inserted was 35 cm for women, 45 cm for men. Fluoroscopy was always performed in all cases for instrumentation and control.

A 7.5 F flexible fiberoptic ureteroscope and a 200 or 272 micron fiber were used depending on the type of laser.

Stone treatment consisted in fragmentation and/or dusting, performed by *Sphinx*[®] Jr 30W Ho:YAG laser system (LISA laser) (412 cases; 72.1%), or 120-W high-power Ho:YAG laser system (*Lumenis*[®] Ltd.) (104 cases; 18.2%) or Dornier Medilas H Solvo 30 Watt Holmium:YAG laser (*Olympus*[®]) (55 cases; 9.6%), depending on the availability of the different lasers case by case.

The most appropriate setting and technique depended on stone size and hardness and on the laser used (Table 4).

For stone size < 1 cm the treatment of choice was fragmentation and complete extraction of the fragments using a zero tip 1.9 Fr nitinol basket.

For stone size > 1 or ≤ 3 cm RIRS procedure was composed by 3 phases:

- 1) First phase: stone dusting using low energy, high frequency and long pulse width with a persistent contact between laser fiber and stone.
- 2) Extraction of fragments: the major fragments derived from stone dusting were extracted using a zero tip 1.9 Fr nitinol basket. All fragments were conserved for stone analysis.
- 3) Second stage: "popcorn effect": high energy, high frequency and short pulse duration.

Continuous irrigation with gravity drainage (40 to 50 cm H₂O) and syringe-based systems were gently applied to obtain and sustain a clear the operative field.

At the end of the procedure a 4.8-6 Fr double J stent was placed in radiology, with or without strings depending removal time (cut-off was 7 days).

In 48 procedures (9.3%), UAS could not be applied and consequently the procedure was performed without access sheath.

We used: UAS 9.5 Fr (n = 33), 10-12 Fr (n = 158), 10.7-12.7 Fr (n = 43), 12-14 (n = 195).

RESULTS

RIRS was performed in 514 patients for a total of 571 procedures (54 second look and 3 third look); preoperative assessment included physical examination, routine urine culture, and N-CCT. RIRS was performed on standard antibiotic prophylaxis (according to local guidelines) or on targeted antibiotic therapy in case of preoperative positive urine culture (in this case therapy was started 5 days before surgery and continued for 3 more days). Preoperative urine cultures were positive in 103 patients (20%). All the infections were treated by specific antibiotic therapy.

Mean operative time was 67 minutes (range: 17-172); 351 (61.4%) patients underwent RIRS under spinal anesthesia, while 220 (38.5%) patients were operated under general anesthesia. The median period between intervention and JJ stent removal was 7 days (Interquartile range

Table 1.

Stone free rate in the 514 patients submitted to RIRS.

Number of stone	Single < 1 cm	Single 1-2 cm	Single 2-3 cm	Multiple
Number of patients	202	247	37	128
Overall Success rate, pt (%)	186 (92.3%)	130 (88.3%)	21 (56.7%)	89 (69.6%)
Overall Stone free rate, pt (%)	175/186 (94%)	89/130 (68.4%)	14/21 (66.6%)	67/89 (75.2%)
Overall CIRF rate, pt (%)	11/186 (5.9%)	41/130 (31.5%)	7/21 (33.3%)	22/89 (24.7%)
Stone free rate after I look pt (%)	158/175 (90.2%)	71/89 (79.7%)	6/14 (42.8%)	44/67 (65.6%)
Stone free rate after II look pt (%)	17/175 (9.7%)	18/89 (20.2%)	8/14 (57.1%)	23/67 (34.3%)
Stone free rate after III look pt (%)	-	-	-	-
CIRF rate after I look pt (%)	11/11 (100%)	35/41 (85.3%)	5/7 (71.4%)	21/22 (95.4%)
CIRF rate after II look pt (%)	-	6/41 (14.6%)	-	-
CIRF rate after III look pt (%)	-	-	2/7 (14.2%)	1/22 (4.5%)

- IQR 1-66). Median post-operative stay was 1.8 days (IQR 1-19). At 3 months N-CCT, the overall success rate was 82.8% (426/514 cases); after the first RIRS 345/514 patients were completely free from urolithiasis (SFR: 67.1%), while 72/514 patients had ≤ 4 mm stone fragments in the same renal localization of previously treated lithiasis (CIRF rate: 14%). 54 patients had residual stones requiring second-look and three needed a third-look for significant residual fragments.

Table 1 shows success rate, stone free rate and CIRF after first treatments according to stone volume and number; the stone composition by spectrophotometric analysis is reported in Table 2.

Intraoperative complications were reported in 4 patients:

- Intraoperative bleeding: one during laser lithotripsy and one after placement of the UAS. In both cases bleeding led to poor visibility and abortion of the procedure that was rescheduled.
- Two ureteral wall injuries secondary to UAS placement: a grade 2 lesion according to Traxer classification (6) were treated with a double J stent for a long period; a grade 3 lesion required percutaneous draining of the kidney. No subsequent strictures were noted during follow up (13 and 18 months).

Post-operative complications were recorded in 31 (5.4%) procedures (Table 3):

Table 2.

Stone composition to spectrophotometric analysis.

Stone composition. no. (%)	Value
Calcium oxalate monohydrate	194 (37.7%)
Calcium oxalate dihydrate	102 (19.8%)
Uric acid	88 (17.1%)
Mixed	87 (16.9%)
Calcium oxalate and phosphate	(68)
Calcium oxalate and uric acid	(19)
Carbapatite	17 (3.3%)
Brushite	4 (0.7%)
Urate ammonium	6 (1.1%)
Cystine	4 (0.7%)
Struvite	2 (0.3%)
Various types	10 (1.9%)

Table 3.
Clinical complications following RIRS classified according to Clavien-Dindo Grading System.

Clavien-Dindo Grade System	N° of patients	Description	Treatment
Grade I	12	11 nausea and vomiting 1 cefalea	Anti-emetics and supportive care
Grade II	14	12 urosepsis 2 haematuria	Antibiotic therapy Bladder irrigation and prolonged catheterization
Grade III a	4	3 urosepsis with double J displacement 1 subcapsular renal haematoma (SRH) associated with pulmonary embolism	Antibiotic therapy + double J substitution Selective artery embolisation + inferior vena cava filter and anticoagulation therapy
Grade III b	-	-	-
Grade IV a	1	Multiple subcapsular haematoma	Urgent left nephrectomy

Table 4.
Setting laser.

	Energy (Joule)	Frequency (Hertz)	Pulse width
30W Ho:YAG laser system Sphinx® Jr (LISA laser)			
Fragmentation	0,8/1J	10/15 Hz	Short pulse (300 µs)
Dusting	0,5/0,8 J	18/20 Hz	Long pulse (650 µs)
Pop com	0,8/1J	15/18 Hz	Short pulse (450 µs)
120-W high-power Ho:YAG laser system (Lumenis®)			
Fragmentation	1J/1,5 J	25/30 Hz	Long Pulse (650 µs)
Dusting	0,2/0,5 J	50/70 Hz	Long Pulse (1000 µs)
Pop-dusting	0,5 J	80 Hz	Short Pulse (300 µs)
30 W Ho:YAG laser Medilas H Solvo (Dornier, Olympus®)			
Fragmentation	0,8/1J	10/15 Hz	-
Dusting	0,5/0,8 J	18/20 Hz	-
Pop com	0,8/1J	15/18 Hz	-

- one patient (0.1%) had a cerebrospinal fluid leak after spinal anesthesia causing headache (CD Grade I) treated with bed rest and paracetamol/caffeine;
- eleven patients (1.9%) had post-operative nausea and vomiting requiring specific therapy;
- fifteen patients (2.6%), developed urosepsis, defined as clinical signs of bacterial infections with positive blood culture (CD Grade II-IIIa). Among them, twelve (2.8%) required antibiotic therapy (CD Grade II), while in three (0.5%) double J was replaced due to concomitant hydronephrosis with double J displacement (CD Grade IIIa);
- two patients (0.3%) on antiplatelet therapy had post-operative hematuria which required bladder irrigation and prolonged catheterization (CD Grade II).
- two patients had hemorrhagic events (0.3%) at the second look of complex multiple kidney stones: 1) Subcapsular hematoma (SRH) associated with pulmonary embolism two days after the procedure (CD Grade IIIa). Treatments consisted in two blood unit transfusion and angiography, which did not show any blood spill. Inferior vena cava filter was placed and anticoagulant therapy was continued for 6 months. 6 months follow up CT scan shows a complete reabsorption of the hematoma (Figure 1).

2) Hemorrhagic shock 2 hour after RIRS due to massive renal bleeding (CD Grade IVa) (Figure 2). CT scan and angiography showed multiple renal bleedings requiring urgent nephrectomy;

- Eight patients complained severe pain and/or urinary urgency probably as a double J related side effect.

DISCUSSION

In the last years, RIRS has become increasingly popular and probably the more common procedure for kidney stones up to 2 cm (7); the high SFR with minimal invasiveness and the outpatient setting have been pointed out as specific benefits by several authors (8, 9). Standard success rates range between 65% and 92%. In our study SFR was 86% with a mean operative time of 72 minutes.

Figure 1.
Subcapsular hematoma (SRH) of left kidney (a: CT axial evaluation) (b: CT coronal evaluation).

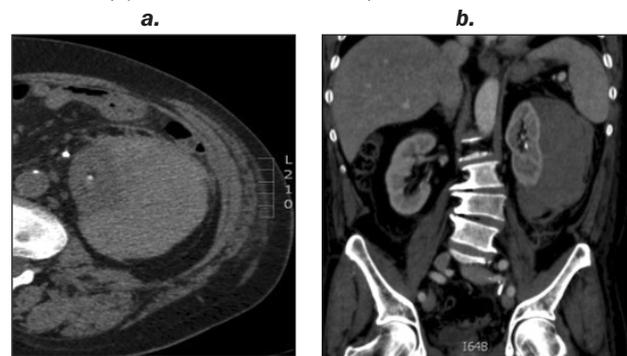
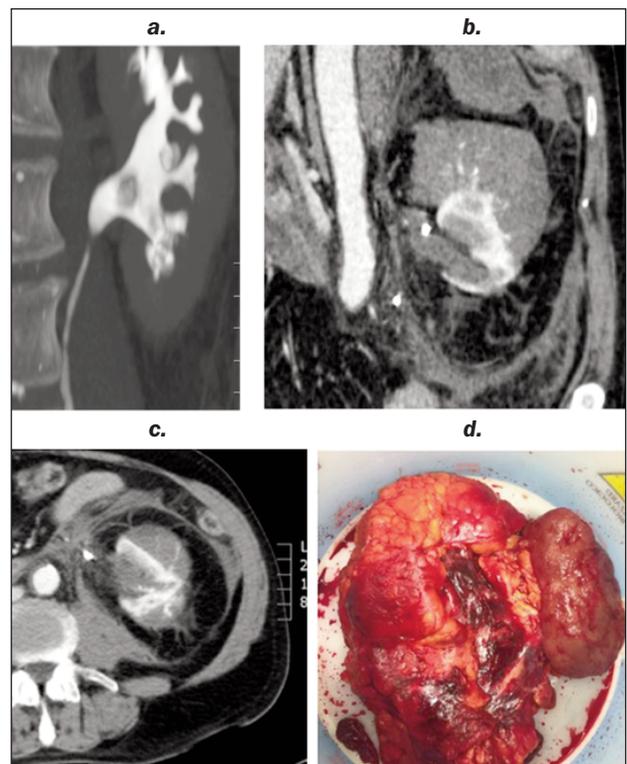


Figure 2.
Kidney hematoma with multiple renal bleedings following RIRS. a: multiple stones of left kidney (preoperative CT evaluation); b: hematoma of left kidney (CT evaluation); c: rupture of left kidney (CT evaluation); d: kidney specimen.



These results are comparable to the main previous literature (10-12).

Even if RIRS is generally considered a safe procedure, a wide spectrum of intra and mostly post-operative severe events must be considered.

Literature is weak about detailed analysis of complications even if some reports deal with serious and life threatening complications. Cindolo *et al.* in 2016 (13) in a multi-institutional study reporting fatal cases after RIRS, highlighted how this “safe” procedure hides potentially dramatic and fatal complications and the need of a careful post-operative patient monitoring: four patients died for septic complications, one for a cardiac event and one due to hemorrhagic complication. Cindolo *et al.* (14) evaluated life-threatening complications after ureteroscopy for lithiasis, reporting 12 cases of serious complications requiring urgent treatment and even one fatal case.

Ureteral injury is the most common intraoperative complication; beneficial effects and convenience of using access sheaths have been debated. UAS main purpose is to facilitate reentries into renal collecting system, theoretically reducing possible injuries to ureter and urethra. In recent studies, the routine intraoperative use of UAS during RIRS was recommended because it decreases duration of the interventions, with a minimal morbidity associated (14, 15). In our series, we used ureteral access sheaths for nearly all patients, recording two significant ureteral damage correlated to UAS (16). Proper management of such complications is crucial to avoid further short- and long-term complications.

The urinary tract infection is the most common event (2-28% of the cases) (17); in our study, 15 (2.6%) patients experienced these clinical complications; all the cases required specific antibiotic therapy with no need of intensive care support (CD II and IIIa). Double J displacement, noted in three patients, could have been the reason of post-operative infection. We suggest to check its position by X ray in case of infection, especially when antibiotic therapies are not effective. Bleeding and renal rupture are less frequent but could lead to serious consequences. In our series two patients had serious hemorrhagic complications; subcapsular hematoma after RIRS is rarely described in the literature and its etiology is not perfectly known (18).

Various authors have tried to understand what is the cause of subcapsular renal hematoma: increase intrarenal pressure leading to rupture of the fornix and separation of the capsule from the parenchyma, urinary infection and infiltration of leukocytes into the parenchyma which can be damaged by irrigation, laser and guide wires (19-22). The sudden expansion and rupture of renal parenchyma is probably the most likely explanation of our cases. Chronic hydronephrosis was present in our two haemorrhagic cases; sudden increase in intrarenal pressure was showed to cause twisting, stretching and/or obstruction of the main intrarenal vessels (23).

It is remarkable that retrograde pyelogram performed at the end of the procedure didn't show any leak or renal absorption of contrast dye; clinical complications were suspected for an uncontrolled renal pain, hypotension and hemoglobin drop.

In conclusion, RIRS should be considered an effective

and safe procedure in the treatment of renal stones, but a wide spectrum of complications must be considered. Even if rare, complications could lead to life-threatening conditions requiring quick diagnosis and prompt treatment.

Intraoperative signs of possible post-operative complications may be missing and a careful monitoring is crucial to recognize these events as early as possible.

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