Retrograde intrarenal surgery for renal stones – Part 2
Böbrek taşlarında retrograd intrarenal cerrahi – 2. bölüm

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ABSTRACT
Retrograde intrarenal surgery (RIRS) has become an effective and safe treatment modality in the management of urinary system stone disease. Recent developments and innovations in the flexible ureterorenoscope and auxiliary equipment have made this procedure easier and more effective with increased success rates. RIRS can be used as a primary treatment in patients with renal stones smaller than 2 cm, prior unsuccessful shock wave lithotripsy, infundibular stenosis, renoureteral malformation, skeletal-muscular deformity, bleeding diathesis and obese patients. In the second part of this detailed review for RIRS, effect of stone composition on success rate, preoperative assessment of stone-free rate, the cost of this modality, education for RIRS, fluoroscopy use, the current role of RIRS in the treatment of various urolithiasis types and special conditions, and combined treatment methods are discussed with up-to-date literature.

Keywords: Flexible ureteroscopy; kidney stone; laser lithotripsy; retrograde intrarenal surgery; ureteral access sheath.

Effect of Stone Composition on RIRS
Only laser lithotripters are used for stone fragmentation during retrograde intrarenal surgery (RIRS). Although holmium laser can be used for every type of stone, the fragmentation time is variable. Xue et al.[1] retrospectively evaluated the results of RIRS performed in 74 patients with stones ranging from 1 cm to 3 cm. Calcium oxalate monohydrate and calcium phosphate stones were found to be fragmented slower than calcium oxalate dehydrate, magnesium ammonium phosphate and uric acid stones, where this finding was especially significant in stones larger than 2 cm.

Preoperative Assessment of the Stone-Free Rate for RIRS
Three important studies have been published for predicting the surgical success after RIRS. Resorlu et al.[2] searched for the prognostic factors related to success of RIRS, and then developed a scoring system - named Resorlu-Unsal stone scoring-to predict stone-free rate (SFR) after RIRS. With the assessment of 207 patients, stone dimension, localization and
Table 1. Resorlu-Unsal Stone Score

<table>
<thead>
<tr>
<th>Weight</th>
<th>Clinical Condition</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Stone size &gt;20 mm (one point per 10 mm)</td>
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<tr>
<td>1</td>
<td>Lower pole stone location and IPA &lt;450</td>
</tr>
<tr>
<td>1</td>
<td>Stone number in different calyces &gt;1</td>
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<tr>
<td>1</td>
<td>Abnormal renal anatomy (horseshoe kidney or pelvic kidney)</td>
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Similarly, Jung et al.\[^2\] developed another scoring system for RIRS called the Modified Seoul National University Renal Stone Complexity (S-ReSC) scoring system. This scoring system is based on the number of sites of renal stones involved. The anatomical sites are classified into 9 subgroups, such as the renal pelvis (#1), superior and inferior major calyceal groups (#2-3), and anterior and posterior minor calyceal groups of the superior (#4-5), middle (#6-7), and inferior calyces (#8-9). If the stone is located in the inferior calyceal area (#3, #8-9), one additional point per site is added to the original score. The modified S-ReSC score, which differs between 1-12, is classified into low (1-2 points), intermediate (3-4) or high (>4) groups, where SFRs are 94.2, 84 and 45.5% for these groups respectively. The advantage of this scoring system is that it was externally validated for the first time and its predictive accuracy was shown to be better than that of the Resorlu-Unsal Stone Scoring system.

Ito et al.\[^3\] have developed a new nomogram by using 5 preoperative parameters, namely stone volume and number, presence of stone in lower calyx and hydronephrosis, and experience of the surgeon (>50 flexible ureteroscopy [fURS]). The maximum score can be 25, and the authors have stated that the success of the fURS would be higher as the patient’s score gets closer to the maximum.

Cost of RIRS

Although RIRS is an effective treatment modality with lower complication rates, it can be an expensive procedure. Flexible ureteroscope, laser lithotripter, guidewire, and ureteral access sheath (UAS) and stone basket (on the discretion of the surgeon) can be used. Gurbuz et al.\[^4\] evaluated the cost analysis of RIRS in 302 patients. In this analysis, the cost of flexible ureteroscope was found $118, laser lithotripter $156, guidewire $38 and UAS $231, where the overall cost was calculated $543 per case. They reported the cost of a stone basket as $611, which increased the overall cost significantly when used. It should be kept in mind that this analysis was performed in a high volume center, which probably had reduced overall expenditures. It should be also remembered that flexible ureteroscopes are very delicate devices and can be broken even after 1 or 2 cases if not used properly, where the cost reaches to very high values at that time.

RIRS and Education-How to Improve Surgical Techniques

There is only one study that shows the learning curve for RIRS. Cho et al.\[^5\] evaluated retrospectively 100 patients with middle sized stone and undergone RIRS for single session. They identified the learning curve by using cumulative sum analysis for monitoring change in fragmentation efficacy. The study revealed that 56 cases were required for reaching a plateau in the learning curve, and the acceptable level of fragmentation was 25 mL/min. Stone multiplicity and localization were found to be significant predictors for SFR in RIRS.

RIRS and Fluoroscopy

Fluoroscopic imaging plays an important role in endourology. Fluoroscopy is generally used for insertion of guidewire, UAS and double-J (DJ) stent, determination of stone localization, identification of renal anatomy, and ureteral balloon dilatation during ureteroscopy (URS) (either semi-rigid or flexible). With the increase in the endourological interventions, radiation exposure of surgeons, patients and operating room staff have also increased. Although the exposed dosage is low during URS, the cumulative radiation dosage theoretically has a potential to increase the risk of cancers. For this reason, in order to decrease the exposed dosage, decreased use of fluoroscopy or fluoroscopy-free techniques have been reported.

Peng et al.\[^6\] evaluated the fluoroscopy-free RIRS in 144 patients with a mean stone dimension of 1.4±0.4 cm. They required fluoroscopy in only 1 patient who had a duplicated collecting system. Stone-free status was achieved in 134 patients (95.7%), where no major complication was observed besides a minor complication rate of 3.6%.

Kirac et al.\[^7\] performed RIRS with a reduced fluoroscopy dosage in 76 patients with a stone dimension of 14.1±4.1 mm, in which single-shot fluoroscopy was used for only insertion of guidewire. Additional fluoroscopy use was required in only 4 patients (5.2%) for localization of stone in 2 patients and identification of collecting system anatomy in 2 patients with a history of prior operation. They reported a SFR of 82.9% and a complication rate of 6.6% without any major complications.
As a result, for protection against the harmful effects of radiation, RIRS with the guidance of reduced fluoroscopy or without any fluoroscopy can be performed easily and efficiently by experienced surgeons.

**The Current Role of RIRS in the Treatment of Urolithiasis**

In various studies, it has been emphasized that RIRS is an effective and reliable method in the treatment of kidney stones. The success rates of RIRS range between 65% and 92%.

**Treatment of intrarenal stones less than 2 cm**

With the technological improvements, RIRS has become a routine option in the treatment of stones <2 cm. In the past, fURS was classified as a secondary treatment after shock wave lithotripsy (SWL) for the stones <2 cm; however, in the new revised version of European Association of Urology (EAU) Guidelines, with the increased success of RIRS, fURS and SWL are regarded as the first line treatment options, especially for the stones with a diameter of 11-20 mm.

In 1990s, successful results have been published for fURS in the treatment of urolithiasis from centers with high caseloads. Grasso and Ficazzola reported a SFR of 94% and 95% for stones of ≤10 mm and 11-20 mm, respectively.

In the studies comparing fURS with SWL and/or percutaneous nephrolithotripsy (PCNL), it has been reported that fURS had a higher success rate than SWL, and a comparable success rate with lower morbidity when compared to PCNL (or MicroPerc). As the time passes, fURS will probably take the place of SWL in symptomatic stones of <2 cm.

**Treatment of intrarenal stones larger than 2 cm**

Recent guidelines recommend PCNL as the first-line treatment for stones >2 cm. Although the success rates in PCNL can be as high as 95%, it has some main complications and disadvantages such as urinary extravasation (7.2%), hemorrhage requiring blood transfusion (11.2%-17.5%), postoperative fever (21%-32.1%), septicemia (0.3%-4.7%), colon injury (0.2%-0.8%), pleural injury (0%-3.1%), and prolonged hospitalization and convalescence. For this reason, alternative options with less morbidity are more advantageous especially for patients with high risk.

First published reports regarding the use of fURS go back to 1990s. As electrohydraulic lithotripter was the only available instrument for fURS at that time, fURS was not an acceptable treatment option for large stones because of its high complication rates. Grasso et al. published the results of fURS with holmium:YAG laser in 45 patients in whom PCNL was contraindicated due to their comorbidities. They reported SFR after first session as 76%, while it rose up to 91% after retreatment with fURS with an overall postoperative complication rate of 2%, where they defined success as residual stone fragments smaller than 2 mm. These results have been encouraging for the use of fURS in the end of 1990s.

Aboumarzouk et al. published a meta-analysis of 9 studies performed between 1990-2011, which included 445 patients (460 renal units) with big kidney stones, and they found median stone diameter as 2.5 cm, median SFR as 93.7% after a median of 1.6 procedures, and general complication rate as 10.1% (major 5.3%, minor 4.8%). Major complications were defined as steinstrasse, subcapsular hematoma, obstructive pyelonephritis, cerebrovascular accident, acute prostatitis and hema-turia causing clot retention; where minor complications were hematuria recovering spontaneously and postoperative fever.

In subgroup analysis, SFR was 95.7% and minor complication rate was 14.3% without any major complication for stones with a dimension of 2-3 cm; where SFR was 84.6%, and minor and major complication rates were 15.4% and 11.5% respectively for stones larger than 3 cm. The authors concluded that fURS for stones larger than 2 cm could be performed with lower complication rate and high SFRs in experienced hands.

UAS has enabled multiple accesses and increased the image quality; which contributed to achievement of successful results.

In a matched-pair analysis, Akman et al. evaluated fURS and PCNL groups, each including 34 patients. After first procedure, SFR was found 91.2% for PCNL and 73.5% for fURS with a significant difference in PCNL. However, this significant difference disappeared after the second fURS where SFR rose to 88.2% in fURS group. While PCNL was superior for operation time, fURS was superior regarding hospitalization time. Two patients in PCNL group needed blood transfusion, but no significant difference was found for complication rates.

Requirement of more than one session to achieve successful results for big kidney stones with fURS is the main concern; but this issue can be tolerated with lower complication rates, and by this way, fURS can be a good and valuable alternative to PCNL especially for patients with high risk.

**RIRS for lower pole stones**

The limited spontaneous drainage of stone fragments after SWL due to the position of lower pole causes a dilemma in the treatment of lower pole stones. Additionally, due to the anatomy, lower pole stones can be reached more difficultly with fURS compared to middle and upper pole stones. In 1999, Grasso and Ficazzola reported a failure rate of 7% to access lower pole with the first generation devices that had limited deflection. They reported a success rate of 95, 94 and 45% for stones <1 cm, >1 cm and ≥2 cm, respectively. After a second session, the overall success was 91% and 82% for stones ≥2 cm.
Anatomical factors that affect the failure to access lower pole in fURS were evaluated. Although acute IPA <30° and length of infundibulum >3 cm were found to be associated with lower SFRs, while width of infundibulum had no effect. Increase in deflection with technological developments and improvements in surgical technique have led flexible ureteroscopes to reach lower pole more easily. Repositioning lower pole stones with tipless nitinol baskets to other calyces that are accessed easily has increased the treatment success of fURS in the management of lower pole stones. Schuster et al. published that SFR has increased for lower pole stones after repositioning when compared to in situ lithotripsy, in which the difference was more pronounced for stones of >1 cm (100% for repositioning vs. 29% for in situ). With improvements in surgical technique, similar SFRs both for repositioned and non-repositioned stones was published.

In their randomized study, Lower Pole Study Group published that fURS was not superior to SWL for stones <1 cm; however, more recent studies reported the superiority of fURS. In a matched-pair analysis for lower pole stones ranged between 11-20 mm by El-Nahas et al., fURS was found to have significantly higher SFR (86.5% vs. 67.7%) and a lower re-treatment rate (8% vs. 60%) than SWL. In retrospective studies success and complication rates of fURS were found to be similar to that of PCNL or mini-PCNL for lower pole stones of ≤20 mm. Operation time was shorter in PCNL and mini-PCNL groups, while fluoroscopy and hospitalization times were longer than fURS. These results show us that fURS has a potential to be a significant procedure in the treatment of stones smaller than 2 cm.

**RIRS in pediatric patients**

Urinary stone disease is seen in a rate of 1%-2% in pediatric population (<18 years). The treatment of stone disease in pediatric age group has a significant importance, as recurrence rate is higher in this group. The first high-volumed series was published by Cannon et al. in 2007. The SFR was reported as 76% in 21 children (with an upper age limit of 20), where no intra- and postoperative complications were seen. Passive dilatation with preoperative stenting was performed for 38% of the patients, while UAS was used in 43%. Smaldone et al. reported that they performed passive and active dilatation in 54% and 70% of the patients respectively, and used UAS in 24% of patients. In this series of 100 patients, SFR was noted as 91%, and 5 perforations were encountered, in which 1 of them needed a re-implantation.

In their series of 50 kidney stones in children with an age range of 1.2-13.6 years, Tanaka et al. achieved SFR with a single session in 58% and needed an additional procedure in 36% of the patients. They found that success rates were correlated with stone dimension, where need for additional procedure was correlated with both stone dimension and patient age. In a series of 167 patients with a mean age of 62.4 months, Kim et al. reported a SFR of 100% and 97% in stones smaller and bigger than 10 mm, respectively, without any intraoperative and postoperative complications. Insertion of a stent was required in 57% of the patients in whom an access was not achieved.

The largest series in preschool children was published by Erkurt et al. including 72 renal units in 65 children. For the stones ranging between 7-30 mm, they reported a SFR of 83% after first session, and 92.3% after the second session. Complications, including hematuria, urinary tract infection with fever and ureteral wall injury were seen in 18 patients (27.7%), and they concluded that RIRS was an efficient and reliable treatment modality in the treatment of kidney stones in preschool children.

In a multi-centered comparative study by Resorlu et al. including 72 renal units in 65 children. For the stones ranging between 10-30 mm, they reported a SFR of 83% after first session, and 92.3% after the second session. Complications, including hematuria, urinary tract infection with fever and ureteral wall injury were seen in 18 patients (27.7%), and they concluded that RIRS was an efficient and reliable treatment modality in the treatment of kidney stones in preschool children.

**RIRS in obese patients**

Obesity has negative effects on stone formation and treatment in upper urinary tract stone disease. Risk of uric acid and calcium oxalate stone formation has increased in obese patients. Success of SWL is lower in obese patients. Longer tract (stone-to-skin distance) and prone position in PCNL are associated with higher anesthesia risk in obese patients. The efficiency of fURS for obese and morbidly obese patients has been evaluated in various studies, and SFR and complication rates were found to be not affected by body mass index.
As a conclusion, it should be kept in mind that access to collecting system in the first session can be difficult in pediatric age group due to relatively narrower ureteral calibration, but this problem can be overcome by preoperative stenting. RIRS is a successful treatment option in pediatric age group, but stone dimension should be taken into consideration for indication.

**RIRS in solitary kidney**

After a good preoperative planning, complete stone removal with a minimal morbidity is crucial in patients with solitary kidney. PCNL and SWL were first-line treatment options for stones larger and smaller than 2 cm, respectively. Although PCNL has a high rate of stone clearance and treatment efficiency, it has a high morbidity rate, especially hemorrhage. SWL has a lower SFR compared to PCNL and RIRS, thus re-treatment is required more often. Indications of RIRS in solitary kidneys include previous unsuccessful SWL, patients for whom PCNL is contraindicated, and patient preference. Contraindications are severe hydronephrosis and big staghorn stones.[36]

Gao et al.[36] performed 68 procedures in 45 patients with a mean stone dimension of 18.4±1.9 mm, and noted a SFR of 64.44% and 93.33% after the first and last procedures respectively. No difference was found between stones larger and smaller than 2 cm regarding the number of procedures performed for each patient. Complications were seen in 26.6% of patients, of which 20% was grade 1, 4.4% was grade 2, and 2.2% was grade 3 (urgent intervention for anuria due to steinstrasse) according to Clavien-Dindo classification.

Atis et al.[37] published SFRs of 83.3% and 95.8% after first and second procedures in their series of 24 patients with an average stone dimension of 19.8±1.9 mm. They did not find any difference in creatinine levels measured preoperatively and 2 weeks after removal of the stent. Minor complications were observed in 16.6% of the patients, while no major complication was noted.

**RIRS in patients with spinal deformities**

In the series of 8 patients with stones ranging between 9-20 mm, Resorlu et al.[38] reported a SFR of 75%. No severe complications regarding anesthesia or surgery were observed, and the authors concluded that RIRS was a reliable and efficient procedure in patients with spinal deformities.

**RIRS in patients with isolated renal rotation anomalies**

Rotation anomalies occur during the branching of the budding ureteral tree. Increase in fibrotic tissue in upper ureter and ureteropelvic junction causes urinary obstruction and stasis. Clearance of fragments after SWL can be unsuccessful in kidneys with isolated renal rotation anomaly because of the obstruction. Tunc et al.[39] evaluated SWL in 150 kidneys with anomalies, where SFR was found to be 56.7% that was lower than in normal kidneys.

Oğuz et al.[40] published a SFR of 75% after first session and a final SFR of 83.3% after additional procedures without any major complications in 24 patients with malrotated kidneys. No difference was found in patients’ characteristics when the patients with and without successful results were compared. As a result, RIRS is an efficient treatment method without any major complications in patients with isolated renal rotation anomalies.

**RIRS in pelvic kidneys**

SWL has a lower success rate in pelvic kidneys due to both difficult clearance of fragments and inhibition of shock waves to reach the stone. PCNL also confronts difficulties in gaining intrarenal access because of pelvic bones and neighboring organs. For this reason, ultrasound- or laparoscopy-assisted access can be used. A retrograde pyelography prior to fURS would help to evaluate the anatomy, and a safety guidewire can be used. Due to abnormal ureteral tract, and tortuous and short ureter, it is much safer not to use a UAS. High ureteral insertion and lower pole localization complicate the operation.[41] Binbay et al.[42] had achieved a SFR of 70.8% after first procedure without any major complications. Bozkurt et al.[43] reported a success rate of 84.7% after single session with a minor complication rate of 19.2%. As a result, it can be concluded that fURS is an efficient and reliable treatment option for small and medium sized stones in pelvic ectopic kidneys.

**RIRS in horseshoe kidneys**

Kidney stones are seen in 20% of horseshoe kidneys, and impaired urinary drainage, recurrent urinary tract infections and metabolic abnormalities are the major risk factors for stone formation. Weizer et al.[44] had a SFR of 75% in patients with horseshoe kidney with a kidney stone smaller than 2 cm, while Molimard et al.[45] reported that SFR was 53% after first session and added that this SFR rose to 88% after an average of 1.5 procedures in 17 patients. Atis et al.[46] found a SFR of 70% at postoperative 1st month in 20 horseshoe kidneys, while 2 of the 6 patients with residual stone became stone-free after SWL. As a result, it can be concluded that RIRS is a treatment option with minimal morbidities and high success rates for patients with horseshoe kidneys.
patients, and had success in 35 patients (81.4%) after the first session. Five of the remaining 8 patients were stone-free after the second session, and they reported an overall SFR of 93% without any major complication. The success rate after the first session in lower pole calyx group was found to be significantly lower compared to other localizations.

With these results, RIRS seems to be a highly efficient treatment modality with low morbidity for stones in calyx diverticulum.

**RIRS in patients with a history of open renal stone surgery**

Endoscopic stone treatment is more difficult in patients with a history of open surgery due to anatomic distortion. Osman et al.\[48\] reported SFRs of 79.2% and 92.4% after first and second procedures in 53 patients with an average stone diameter of 14.3 mm. They noted 2 (3.7%) intraoperative complications, including a ureteral perforation and extravasation, and a hemorrhage not requiring blood transfusion; while 9 postoperative complications (18%) were noted.

Alkan et al.\[49\] compared 32 and 38 patients with and without a history of open renal stone surgery, respectively. SFRs were 100% and 95% after second procedure, and clinically insignificant residual fragment (≤4 mm) rates were 29% and 20% for patients with and without history of surgery, respectively. Seven minor complications were observed in each group, while no major complication was reported. These results show us that RIRS is a reliable option with a high success rate in patients with a history of open renal stone surgery.

**RIRS in multiple unilateral stones**

Multiple unilateral stones are seen 20%-25% of the urolithiasis patients. Alkan et al.\[50\] published their results for 173 stones in 48 patients with multiple unilateral stones. RIRS was performed as a primary procedure in 81.2%, after SWL in 14.6% and after PCNL in 4.2% of the patients. SFRs in patients with a stone ≤2 cm (23 patients) and >2 cm (25 patients) were 100% and 84%, respectively. Residual stones ≥4 mm were seen in 4 patients of whom all had a single stone of >2 cm.

RIRS can be concluded as an efficient treatment for multiple unilateral stones, especially for those ≤2 cm.

**RIRS as a second-line therapy**

Stav et al.\[51\] reported a SFR of 67% in 81 patients with a history of unsuccessful SWL. Holland et al.\[52\] compared 93 patients, whom were divided into two groups of 42 patients with primary treatment and 51 patients with secondary treatment (92% after SWL, 8% after PCNL). Success rates were 80% and 67% for first- and second-line treatment groups, respectively. As a result, RIRS has a lower SFR when performed after an unsuccessful SWL, as the negative factors affecting the success of SWL also affect the SFR after RIRS.

Yuruk et al.\[53\] found no difference in SFR for patients with primary RIRS and after SWL treatment (82.5% vs. 86.9%). In a similar way, Pillippou et al.\[54\] found no difference for SFR, complication rate, and operation and hospitalization times for the patients with or without a prior SWL. It seems that prior SWL does not affect the success and complication rates of RIRS.

**RIRS for simultaneous bilateral stones**

Bilateral kidney stones are detected in 20%-25% of urolithiasis patients. Alkan et al.\[55\] treated simultaneously 201 bilateral stones in 44 patients, and found an overall SFR of 88.6%. When the patients grouped according to stone burden, SFR was 100% and 80% for stones smaller and larger than 25 mm, respectively. They concluded that a simultaneous bilateral approach had advantages of decrease in total procedure time, anesthesia count and recovery time, while risk of bilateral ureteral injury was the disadvantage.

In a matched-pair analysis of 59 patients with simultaneous bilateral RIRS and 59 patients with unilateral RIRS, no significant difference was observed in SFRs (84.7% vs. 91.5%, respectively) and overall complication rates.\[56\] The authors concluded that bilateral RIRS was as efficient and reliable as unilateral RIRS.

Simultaneous bilateral RIRS is an efficient and reliable treatment option in selected patients. Stone burden should be taken into consideration when estimating the SFR, and at least one side should be stented after the operation.

**Combined Treatment Methods**

Use of RIRS with PCNL or SWL at the same session has been a new treatment modality recently. This combination has been developed to reduce access tract numbers and complications in the management of complex renal stones.

Hamamoto et al.\[57\] compared the results of combined RIRS and mini-PCNL with those of only mini-PCNL and standard PCNL in the treatment of patients with high stone burden. All procedures were performed in prone position; and decreased operation time, increased SFR, and a slight decrease in hemoglobin were observed in the combined therapy group.

In another study comparing standard PCNL in supine position with combination of supine PCNL and RIRS, no difference was observed for complication rate and hospitalization duration, while success rate was higher in the combination group.\[58\]

Traxer et al.\[59\] reported their first experience of RIRS combined with SWL as a very new treatment modality. Stone fragmentation was achieved in 100% of 6 patients, while SFR was 50%. Remaining 50% of the patients required a second intervention.
They did not observe any injury in digital ureteroscope as well as in laser probe. Although this new modality can be a promising option for the patients who have the risk of failure after RIRS alone, the complexity and cost of the procedure should be kept in mind.

In conclusion, RIRS has gained an increasing popularity recently, and in parallel to this, our knowledge and experience have increased. This treatment modality is an efficient and reliable method with lower complication, and higher success rates. Intrarenal access via a natural route without penetrating the parenchyma is its major feature. The length of this route as well as the delicacy and cost of the equipment are the major issues that should be overcome.

In the light of recent data, RIRS seems to be an ideal treatment modality in the management of patients with stones smaller than 2 cm, serious comorbidities, renal anomalies and bleeding disorders. High success rates can be achieved by only repeating sessions or combined treatments in patients with high stone volume.

If the problematic issues can be overcome with the ongoing technological developments, RIRS has a potential to be the first-line treatment option in the management of kidney stones.

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