Review Article

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Current status of flexible ureteroscopy in urology

Sung Yong Cho

Department of Urology, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, Seoul, Korea

Retrograde intrarenal surgery (RIRS) is being performed for the surgical management of upper urinary tract pathology. With the development of surgical instruments with improved deflection mechanisms, visuality, and durability, the role of RIRS has expanded to the treatment of urinary calculi located in the upper urinary tract, which compensates for the shortcomings of shock wave lithotripsy and percutaneous nephrolithotomy. RIRS can be considered a conservative treatment of upper urinary tract urothelial cancer (UTUC) or for postoperative surveillance after radical treatment of UTUC under an intensive surveillance program. RIRS has a steep learning curve and various surgical techniques can be used. The choice of instruments during RIRS should be based on increased surgical efficiency, decreased complications, and improved cost-benefit ratio.

Keywords: Laser lithotripsy; Surgical equipment; Transitional cell carcinoma; Urolithiasis

INTRODUCTION

1. The expanding role of retrograde intrarenal surgery in upper urinary tract pathology

Retrograde intrarenal surgery (RIRS) refers to the surgical management of upper urinary tract pathologies with a retrograde ureteroscopic approach. With the development of new surgical instruments, the deflection mechanism, visuality, and durability of RIRS have improved. Recently, the role of RIRS has expanded to the treatment of urinary calculi and urothelial malignancies in the upper urinary tract.

2. History and recent developments of flexible ureteroscopic devices

The first flexible ureteroscopic procedures were introduced in the 1960s [1-3]. However, these flexible ureteroscopes had no integrated deflecting systems or working channels. Flexible ureteroscopes were not widely utilized until the introduction of the new flexible ureteroscope and the holmium:yttrium aluminium garnet (YAG) laser system in the 1990s [4-8]. Flexible ureteroscopes basically consist of the optical system of the fiberoptic image and light bundles, a deflection mechanism, and a working channel [9]. However, recently developed digital flexible ureteroscopes are expected to provide improved image quality and durability because they do not require a separate light cable or camera head [10,11]. Narrow-band imaging digital flexible ureteroscopes are expected to increase the detection rate of upper urinary tract urothelial malignancy [12]. Deflecting mechanisms have been greatly developed as well. Deflection angles have recently been extended to 275 degrees, which enables ureteroscopic tips to access the entire renal collecting system, including the lower minor calices. Almost all flexible ureteroscopes currently available have working channels of at least 3.6 Fr in size,

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Corresponding Author: Sung Yong Cho
Department of Urology, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, 20 Boramae-ro 5-gil, Dongjak-gu, Seoul 07061, Korea
TEL: +82-2-870-2394, FAX: +82-2-870-3863, E-mail: kmoretry@daum.net

which permits adequate irrigation and insertion of stone retrieval devices. Dual-channel flexible ureteroscopes with smaller working channel diameters of 3.3 Fr have tried to overcome the limitation of a single channel to acquire better visual fields and surgical outcomes. However, the diameter of the outer sheaths was increased to 9.9 Fr [13]. With advances in the technical aspects of flexible ureteroscopes, laser lithotripsy systems, ureteral access sheaths, guidewires, highly flexible stone baskets, and flexible forceps, these instruments have become the requisites of RIRS. Table 1 lists the various flexible ureteroscopes that are currently widely used. Surgeons should know the advantages and disadvantages of the equipment to guarantee the best surgical outcomes.

CURRENT ROLE OF FLEXIBLE URETEROSCOPY

1. Active removal of renal stones and surgical options

Recently, the European Association of Urology guidelines for urolithiasis showed a broad spectrum of indicators for the active removal of kidney stones, such as stone growth, stones in patients at high risk of stone formation, obstruction caused by stones, infections, symptomatic stones with pain or hematuria, stones >15 mm, patient preference, comorbidity, and patients' social situation concerning profession or amount of travel [14]. In these cases, observation is not the option of choice. Rather, shock wave lithotripsy (SWL), percutaneous nephrolithotomy (PCNL), and RIRS are the available treatment options for active treatment of renal calculi [14].

Until now, SWL remained the first choice for the treatment of renal stones <20 mm in size [14]. However, many investigators have shown the disadvantages of SWL for treating renal stones. Previous investigations demonstrated inverse correlations between stone-free rates (SFRs) and stone sizes [15-18] and reported on the risk of ureteral obstruction with the need for additional procedures [15]. Unfavorable factors for success of SWL include SWL-resistant stones, steep infundibular-pelvic angles, a long lower pole calyx (>10 mm), and a narrow infundibulum (<5 mm) [19-23]. Furthermore, SWL often requires multiple treatments and longer treatment periods than other surgical methods in patients with multiple stones. In these cases, surgeons should consider RIRS or PCNL to treat renal and upper ureter stones.

PCNL should be the first treatment choice for stones >20 mm [14]. RIRS cannot be recommended as the first

Table 1. Characteristics of the widely used flexible ureteroscopes

Characteristic	Gyrus ACMI			Olympus		Karl Storz		Richard Wolf		Striker
	DUR-8	DUR-8 Elite	DUR-D (digital)	URF-P5,6	URF-V2	Flex-X2	Flex-Xc (digital)	Viper	Cobra	Flexvision U500
Tip and shaft diameter (Fr)	6.75/10.1	8.7/10.1	8.7/9.3	4.9/7.95 (P6)	8.4/8.5	7.5	8.5	6/8.8	6/9.9	6.9/*
Working length (mm)	650	640	650	670	670	670	700	680	680	*
Channel size (Fr)	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.3 (dual)	3.6
Deflection angle (°)	170/180	170/180, secondary defection	250	180/275 (P5), 275 (P6)	275	270	270	270	270	275
View angle (°)	80		80	90	80	88	90		85	*

*No information shown in the brochure.

treatment option for stones >20 mm. PCNL has generally been considered to be a safe surgical method with overall low postoperative complication rates and the highest SFR compared with other surgical methods [24,25]. Although serious complications such as perioperative massive bleeding, urine leakage, bowel injury, hemothorax, and fistula are rare [26], increasing attention has been paid to the need for other minimally invasive surgical options to compensate for the shortcomings of PCNL.

2. RIRS for renal and upper tract calculi

Recently, technological advances in flexible ureteroscopy, coupled with the development of novel endoscopic baskets and flexible lithotrites, have allowed the role of RIRS to expand to the treatment of renal and upper tract calculi. Definite indications for RIRS have not yet been established. However, the possible indications for RIRS for renal stones are as follows:

- Midsized renal stones not appropriate for SWL or PCNL
- Failed SWL or SWL-resistant stones
- Radiolucent stones
- Anatomical abnormalities, e.g., steep infundibular-pelvic angle, long lower pole calyx, or narrow infundibulum
- Concomitant renal and ureter stones
- Complete removal of bilateral stones in a single session
- Multiple renal stones including nephrocalcinosis
- Bleeding disorders
- Need for complete stone removal, e.g., pilot
- Percutaneous antegrade approach for ureter stones in patients who underwent urinary diversion
- Combined or ancillary procedures following PCNL
- Patient habitus, e.g., obesity, unfit for anesthetic position

1) Stone size

As mentioned above, SWL remains the first choice for renal stones <20 mm [14]. However, we should consider the inverse correlation between the SFR and stone size [15-18]. The European guidelines recommended a lower cutoff level of 15 mm [14,27]. However, this is an arbitrary level and not a definite cutoff. The cutoff can be affected by many different factors, e.g., stone multiplicity, resistance to SWL, and patient need. The lower cutoff level for consideration of RIRS usually ranges from 10 to 15 mm. The upper cutoff level of stone size has been expanded to 30 to 35 mm in previous investigations [28-30], which implies that RIRS can be a viable option for patients with renal stones >20 mm depending on the operator's skills.

2) Stone multiplicity

Concomitant renal and ureter stones or bilateral renal stones can be efficiently and safely removed by RIRS in a single session [31,32]. This combined approach is expected to reduce the need for future procedures and seems to be more cost-effective.

3) Lower pole stones

Unfavorable factors for SWL include a steep infundibular-pelvic angle, a long lower pole calyx, or a narrow infundibulum in patients with a lower pole stone [14,19-22]. PCNL is the first treatment option for lower pole stones along with a surgical procedure [33-35]. However, RIRS has shown comparable surgical efficacy and safety as well in these investigations.

4) Bleeding disorders

Because RIRS does not require a percutaneous procedure and has little probability of vessel injury during the surgical procedure, RIRS seems to be superior to PCNL or SWL for patients who take anticoagulant therapy. Until now, the ureteroscopic procedure including RIRS has shown its safety in patients with bleeding disorders with an acceptable level of increase in complications [36-38].

The presence of a bleeding disorder is one of the contraindications to SWL and patients who are scheduled to undergo PCNL are usually recommended to discontinue anticoagulant therapy. However, some studies showed that continuing aspirin therapy is safe during PCNL [39,40]. Further studies are needed to prove the safety of PCNL in patients with bleeding disorders.

5) Percutaneous antegrade approach

When patients with ureteral strictures, urinary diversion of ileal conduits, or orthotopic neobladders have ureter stones, a retrograde approach is sometimes difficult. In these cases, a percutaneous antegrade approach using a flexible ureteroscope would be appropriate [41,42]. The percutaneous procedure has proven efficacy and safety with a high SFR and minor complications [41,42]. Furthermore, if migration of fragmented small stones into the ureter occurs during PCNL, a flexible ureteroscope would be helpful to remove the stones by use of laser lithotripsy or a stone basket. The percutaneous approach can be available by use of a ureteral access sheath or a small-sized balloon catheter.

6) Contraindications

More importantly, RIRS can be performed in all patients without any specific contraindications as shown in the European guidelines [14]. The first step is that each

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treatment should be considered with regard to the clinical situation, and clinicians should determine whether RIRS is the most appropriate surgical option.

3. RIRS for upper urinary tract urothelial cancer

Endoscopic surgery began with the treatment of upper urinary tract urothelial cancer (UTUC) in the 1980s [43-45]. Currently, RIRS can be considered a conservative treatment of UTUC or for postoperative surveillance after radical treatment of UTUC [46,47]. The smooth muscle of the ureter and the renal pelvis is thinner than the bladder wall, which implies that UTUC can penetrate the wall earlier than the bladder tumor [48]. Ureteroscopic treatment of UTUC is usually based on ablation and resection using holmium:YAG lasers [47]. However, undergrading and understaging of UTUC lesions can have severe consequences. In one study, up to 25% of patients had missed UTIC lesions, and nearly 50% had a missed carcinoma in situ lesion [49]. Therefore, endoscopic management should only be considered for patients with low-grade, low-stage UTUC under an intensive surveillance program. Recently, narrow-band imaging digital flexible ureteroscopy has been developed and is expected to increase the detection rate of UTUC [12]. Narrow-band imaging is a new diagnostic approach to visualize angiogenesis in the superficial malignancy. However, further studies of this diagnostic technique are needed.

PERIOPERATIVE ASSESSMENT AND MANAGEMENT

1. Preoperative assessment of the SFR

To predict surgical success following RIRS, two well-validated tools have been introduced [50,51]. Resorlu et al. [50] investigated the prognostic factors associated with RIRS and developed a scoring system called the Resorlu-Unsal Stone Score to predict the SFR. They reviewed 207 patients who underwent RIRS and showed that stone size, stone composition, stone number, renal malformations, and lower pole infundibulopelvic angle are significant predictors of RIRS outcome. The authors invented the scoring system based on the significant predictors. Similarly, Jung et al. [51] developed another scoring system for RIRS called the Modified S-ReSC or S-ReSC-R [52]. This scoring system is based on the number of sites of renal stones involved. The anatomical sites were 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 calyx (#8–9). If the stone is located in the inferior caliceal area (#3, #8–9), one additional point per site is added to the original score. The advantage of this scoring system is that it was externally validated for the first time [52] and its predictive accuracy was shown to be better than that of the Resorlu-Unsal Stone Score. Both scoring systems have been helpful for separating patients into outcome groups and for determining plans of treatment.

2. Efficacy and safety of RIRS

Previous studies showed that the SFR of RIRS ranges from 73.6% to 94.1% [53]. Compared with the SFR of PCNL, the SFR of RIRS was lower (odds ratio [OR], 2.19; 95% confidence interval [CI], 1.53–3.13; $p<0.00001$). The operative time of RIRS ranged from 43.1 to 67.5 minutes, which was longer than that of PCNL (OR, –4.81, 95% CI: –14.05 to 4.43, $p=0.03$). Complication rates ranged from 0% to 25%, which was lower than for PCNL (OR, 1.61; 95% CI, 1.11–2.35; $p<0.01$). Hospital stay was shorter for RIRS than for PCNL (OR, 1.28; 95% CI, 0.79–1.77; $p<0.00001$). Common complications of RIRS were fever (2%–28%), prolonged antibiotic use (4%–5%), and sepsis (3%–5%) and less common complications were bleeding (<5%), steinstrasse, and ureteral injuries.

3. Renal function

Previous investigations addressed whether stone treatment results in renal functional change [54,55]. Data on renal morphology and function are usually based on radiological examinations, combined with blood tests and urinalysis. Although Giusti et al. [55] showed that RIRS is safe in the treatment of renal stones without worsening renal function, these data did not provide information on separate renal function. Separate renal function can be estimated by diethylenetriamine pentaacetic acid (99mTc-DTPA) or technetium-99m dimercaptosuccinic acid (99mTc-DMSA). Recently, the author of the present review reported perioperative data for separate renal function [56]. In that study, separate renal function was deteriorated in one-third of patients (53 of 148, 35.8%) with renal stones >10 mm who underwent RIRS or miniaturized PCNL. The abnormal separate renal function showed postoperative recovery in 31 patients (58.5%). The study included 148 patients (117 RIRS and 31 miniaturized PCNL) and there were no statistically significant differences between the two patient groups in the deterioration of separate renal function or in postoperative recovery.

4. How to improve surgical techniques

A variety of surgical techniques can be utilized to perform RIRS. Many investigators understand that RIRS has a steep learning curve if they do not have an assistant to help. There has been a single investigation to show the learning curve of RIRS [28]. Cho et al. [28] retrospectively investigated 100 patients who underwent single-session RIRS to treat mid-sized stones and analyzed the learning curve by using CUSUM (cumulative sum) analysis for monitoring change in fragmentation efficacy. The CUSUM curve showed that the 56th case was the change point at which a plateau was reached. The acceptable level of fragmentation efficacy was 25 mL/min. Stone multiplicity and sites involved were significant predictors of the SFR for RIRS.

5. Basic principles of surgical technique

Surgical technique will continue to change in the future with new developments in instruments. Essentially, the use of various instruments should be based on increased surgical efficiency, decreased complications, and improved cost-benefit ratio. The commonly used equipment and devices for RIRS are as follows:

- Flexible and (semi) rigid ureteroscopes
- Fluoroscopy (C-arm) with radiation protectors
- Guidewires
- 5-Fr ureteral catheter or dual-lumen catheter
- Contrast medium and balloon catheter if needed
- Ureteral access sheath (10/12, 12/14, 14/16 Fr, 28/35/45/55 cm)
- Holmium:YAG laser with laser fiber (200/365 μm)
- Stone basket (<2 Fr)
- Irrigation pump

The patient is positioned in a dorsal lithotomy position. The first step is securing access to the ureter. Either cystoscopic or ureteroscopic access to the ureter is appropriate. A hydrophilic guidewire is placed in the renal pelvis under fluoroscopy. This catheter is often changed into a stiff guidewire using an open-ended 5-Fr ureteral catheter. The ureteral lumen or ureterovesical junction can be dilated by use of a balloon dilatation catheter or by ureteroscopy.

1) Preoperative double J catheter insertion

When there is a narrowing or stricture in the ureter, a ureteral double J (DJ) stent can be inserted preoperatively. The stent is then retracted several weeks later and a stiff guidewire is inserted into the DJ stent. Previous investigations showed that preoperative ureteral stenting was associated with a high SFR and decreased operative time and cost for larger stones [57-59]. However, this topic is still controversial, because patients may undergo an additional preoperative stenting procedure and may suffer from a longer duration of discomfort related to preoperative DJ stenting [60].

2) Ureteral access sheath

After ureteral cannulation, a ureteral access sheath is usually placed on the guidewire to the level of the ureteropelvic junction. There have been no absolute indications for the use of ureteral access sheaths. Ureteral access sheaths allow repeated ureteroscopic access to the renal pelvis and facilitate removal of multiple stone fragments. Although it is controversial whether the placement of ureteral access sheaths helps to increase the SFR [61,62], the sheaths seem to be helpful for maintaining a continuous flow of irrigation fluid and an intra-renal low-pressure system [63,64]. Ureteral access sheaths may induce ureter injury in certain situations [65]. However, there is little evidence for whether preoperative stenting reduces ureter injury [57,59]. Ureteral access sheaths would not be necessary when a single passage of a stone is necessary after most of the stones are fully fragmented. However, bladder distention may induce narrowing of the ureterovesical junction, which may disturb drainage of irrigation fluid and a clear field of vision.

Several companies have developed a variety of new ureteral access sheaths [66]. The sizes of the most commonly used ureteral access sheaths range from 10/12 to 14/16 Fr in diameter and from 28 to 55 cm in length. Larger ureteral access sheaths are expected to be more beneficial for continuous irrigation of fluid but may be more hazardous to the ureter than smaller sheaths. However, little evidence has yet been reported [63,67].

Almost all fiberoptic and digital ureteroscopes can fit through a 12/14 ureteral access sheath. The new standard 10/12 Fr sheaths and the minimization of flexible ureteroscope size will influence surgical trends in RIRS in the future.

3) Stone removal using a holmium laser: dust versus fragments

A flexible ureteroscope is then inserted through the access sheath or on a guidewire. The holmium:YAG laser has become the gold standard lithotrite for RIRS [14]. The holmium laser consists of optical elements of fiber and plastic coating and has dual actions of producing stone dust or fragments mainly by the photothermal reaction [68,69]. Acoustic shock waves by cavitation bubbles are less important. However, bubbles would improve photonic energy transmission into a renal stone. The fragmented stones can be removed by a stone basket and stone dust is small enough to pass through the urine. The author of the present

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review has performed about 500 cases of RIRS and favors the fragmentation technique over dust formation, especially for patients with large stones >10 mm, because the dust may hinder visualization of the clear operative field and it may be difficult to differentiate a small fragmented stone in the midst of dust. Stones from other calices can be repositioned into a single upper or middle calyx to increase the surgical efficiency and the durability of flexible ureteroscopy during the dust technique. The holmium laser power is usually set to 10 to 15 W with 0.5–1.2 J and 5–15 Hz. However, the setting may differ according to the method of lithotripsy [70] and surgeons usually increase the frequency (Hz) and maintain the power (W) when they perform the dust technique to increase the chance of laser lithotripsy.

Laser fibers sized 200 or 365 μm are usually used for treatment of stones. Small fibers (200–270 μm) are expected to be superior to larger ones (365 μm) because of similar fragmentation efficacy, increased efficiency of fluid irrigation, and increased flexibility [71]. However, the power (W) and energy (J) are important to maintain the fragmentation efficacy, and 365-μm laser fibers are more widely used than 200-μm fibers [72]. In flexible ureteroscopy, 200-μm laser fibers should be used to break lower pole stones.

Although the working channels of flexible ureteroscopy are >3 Fr, stone retrieval baskets <2 Fr are usually used to acquire maximal deflection of flexible ureteroscopy and constant irrigation of fluid [73]. The tipless design of stone retrieval baskets permits the capture of small stones even at the base of the renal pelvis and calices.

6. Combined procedures

The combination of RIRS with other techniques is promising [74-76]. Endoscopic combined intrarenal surgery using flexible ureteroscopy and miniature PCNL (endoscopic combined intrarenal surgery) or extracorporeal lithotripsy (lithotripsy endoscopically controlled by ureterorenoscopy) increase positive surgical outcomes, especially in complex renal stone cases. However, previous investigations have not yet shown increased SFRs [74-76]. This approach would decrease the necessity of multiple percutaneous tracts, which would be helpful to decrease bleeding risk and radiation exposure. Furthermore, combined procedures deserve consideration for removal of stones associated with infundibular stenosis and caliceal diverticulum [77].

NEW APPROACHES TO FLEXIBLE URETEROSCOPY

Some investigators have reported a newly developed robotic RIRS system [78,79]. It is not clear whether this technique improves surgical outcomes or not. The potential advantages of robotic RIRS are improved ergonomics and instrument stability. An early clinical result showed data for 81 patients with renal calculi with a mean stone volume of 1,296 mm^3 and a safe platform with significant improvement of ergonomics [79].

CONCLUSIONS

RIRS is an effective and safe treatment method for active removal of renal stones and detection of urothelial malignancy. RIRS will continue to evolve through technical improvements to the instrumentation. Urologists must make the best choice for their patients depending on surgical efficiency with this developing armamentarium, considering safety during the surgical procedure, the cost-benefit ratio, their area of expertise, and various patient characteristics.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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