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Retrograde Flexible Ureteroscopy: Reshaping the Upper Urinary Tract Endourology

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Summary.- Introduction of retrograde flexible ureteroscopy represented a leap forward in upper urinary tract endourology. Nowadays, areas of the pyelocaliceal system accessible otherwise only by percutaneous or open surgery, can be approached in a retrograde fashion, using the anatomical pathways. The flexible ureteroscopes evolved from the limited deflectable first generation ones to the digital very maneuverable models. The ancillary instruments and the energy sources underwent a similar evolution. Flexible ureteroscopy is a very useful investigative method, especially in patients with equivocal data provided by the imaging. Introduction of this procedure decreased significantly the number of cases with so called “essential” hematuria. The conservatively treated upper urinary tract tumors can be also followed-up more efficiently, the recurrence being identified before becoming radiological obvious. Initially reserved only for diagnostic purposes, flexible uretero-pyeloscopy may be used also in the treatment of various pathological conditions of the upper urinary tract such as lithiasis, stenosis, tumors, pyelocaliceal abnormalities etc. However, technical limitations regarding the visibility and access are still influencing the outcome of the method. The characteristics of the available flexible endoscope, and how they are influenced by the used energy sources and ancillary instruments is crucial for achieving the best performances. Also the particularities of the lesion and upper urinary tract anatomy have a significant impact over the flexible ureteroscopic approach. Despite the already achieved efficacy, the technological progress may still allow various improvements of the method, including robotic flexible ureteroscopy.


Resumen.- La introducción de la ureteroscopia retrógrada flexible representó un salto adelante en la endourología del tracto urinario superior. Hoy en día se puede acceder por vía retrógrada, utilizando las vías anatómicas, a áreas del sistema pielocalicial que de otra manera solo eran accesibles por vía percutánea o cirugía abierta. Los ureterorrenoscopios flexibles han evolucionado desde la primera generación con un grado de deflexión limitado hasta los modelos digitales de alta maniobrabilidad. Los instrumentos auxiliares y las fuentes de energía han seguido una evolución similar. La ureteroscopia flexible es un método diagnóstico muy útil, especialmente en pacientes con datos radiológicos.
INTRODUCTION

The first retrograde flexible ureteroscopy was performed by Marshall in 1964, using a 9F endoscope produced by American Cystoscopes Makers Inc. However, without a working channel and with no possibilities of active deflection, this procedure only had a diagnostic role. Later on in the 80’s, Bagley, Huffman and Lyon started to develop the modern flexible ureteroscope by adding three essential technical features: a working channel, an irrigation system and active deflection capabilities.

The development of these endoscopes altered the performances of the first generation flexible ureteroscopes. This decreased maneuverability and visibility also reduced, making the visibility even worse.

Having a working channel of 3.6F, smaller than the one of semirigid endoscopes, the irrigation flow is also reduced, making the visibility even worse.

This decreased maneuverability and visibility altered the performances of the first generation flexible ureteroscopes.

A second generation endoscope, ACMI DUR-8 Elite (ACMI Corporation, Southborough, MA, USA) offered improved accessibility to the pyelocaliceal system by adding a second active deflection site at the distal end. With this new capability, the endoscope received a supplementary 130º down deflection to the 170º/180º initial one.

Other companies adopted a different approach in solving the maneuverability issue. Third generation models such as Storz Flex-X and Storz Flex-X2 (Karl Storz Endoscopy, Tuttlingen, Germany) had a single active deflection of 270º, a working channel of 3.6F and a tip diameter of 7.5F. The optical system, consisting in a coherent bundle of optical fibers, had the disadvantages of small endoscopic field and reduced resolution by comparison to the semirigid ureteroscopes. Each optical fiber is transmitting a small part of the field, the final image being a composite one. However, the outer cladding of the fibers is not permeable for light, thus generating the “moiré” effect, specific for the fiberoptic flexible ureteroscopes.

Initially reserved only for diagnostic purposes, flexible uretero-pyeloscopy may be used in the treatment of various pathological conditions of the upper urinary tract such as lithiasis, stenosis, tumors, pyelocaliceal abnormalities etc.

The flexible ureteroscopes

The flexible ureteroscopes have specific design and technical characteristics. The main components of such endoscopes are represented by the working channel, the optical system, the light system and the deflection mechanism.

The first generation flexible ureteroscopes such as Storz 11274AA (Karl Storz Endoscopy, Tuttlingen, Germany) had a single active deflection of only 170º/120º, a working channel of 3.6F and a tip diameter of 7.5F. The optical system, consisting in a coherent bundle of optical fibers, had the disadvantages of small endoscopic field and reduced resolution by comparison to the semirigid ureteroscopes. Each optical fiber is transmitting a small part of the field, the final image being a composite one. However, the outer cladding of the fibers is not permeable for light, thus generating the “moiré” effect, specific for the fiberoptic flexible ureteroscopes.

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Other companies adopted a different approach in solving the maneuverability issue. Third generation models such as Storz Flex-X and Storz Flex-X2 (Karl Storz Endoscopy, Tuttlingen, Germany) had a single site active deflection of 270º in both directions (the so-called “exaggerated deflection”).

However, the poor visibility still remained an issue in these fiberoptic flexible endoscopes. The fourth generation ureteroscopes tried to solve this problem by using a different type of optical system. In the DUR-D model (ACMI Corporation, Southborough,
the fiberoptic bundle was replaced by a CMOS chip placed at the tip. It offered a larger endoscopic field with improved resolution, thus increasing the performances of the method. Similarly, Olympus developed the URF-Vo model (Olympus, Melville, NY, USA), with a CCD chip at the tip and a new technology added (narrow band imaging – NBI). Some innovations also occurred regarding the light system. In the ACMI DUR-D model, the optical fiber bundles responsible for the light transmission were replaced with LED lamps at the distal end of the ureteroscope.

Unfortunately, these new digital flexible ureteroscopes have a larger tip by comparison to the conventional ones (situation imposed by the dimensions of the chip). Due to this fact, despite their improved visibility, the access in various areas of the pyelocaliceal system such as calices with a narrow infundibulum may be impeded.

Energy sources

In order to maintain the maneuverability of flexible endoscopes, only sources capable to deliver the energy through small caliber flexible probes or fibers should be used.

Electro-hydraulic lithotripsy devices and Ho:YAG may be used in the treatment of upper urinary tract lithiasis. For tumor ablation or incisions, various lasers (such as Ho:YAG and Nd:YAG) and electrosurgical devices may be applied.

The development of Ho:YAG represented a milestone, offering the means to efficiently treat a wide range of pathologies: larger stones, tumors, stenosis etc.

Access sheaths

The access sheath was developed in its modern form by Newman in 1985 [3]. However, the first models presented some insertion difficulties. Nowadays, the access sheaths manufactured from new materials became resistant and flexible, however displaying axial rigidity and a thin profile. This accessory instrument allows facile insertion of the flexible ureteroscope, especially when multiple ureteral passages are required. It also assures straight alignment of the endoscope in the upper urinary tract thus prolonging its lifespan and efflux of the irrigation fluid from the pyelocaliceal system, resulting in reduced pressure [4].

Ancillary instruments

Similar with the probes and fibers associated with the energy sources, ancillary instruments (graspers, baskets etc.) should have a small caliber and improved flexibility in order to be used during these procedures.

Inserting a larger or stiffer instrument through the working channel will decrease the maximal deflection as well as the irrigation flow of the flexible ureteroscope, with a negative effect on both maneuverability and visibility.

The discovery of new alloys like Nitinol allowed the development of thinner and flexible but in the same time resistant and durable ancillary instruments, thus increasing the performances of retrograde flexible ureteroscopic approach [5].

Diagnostic flexible uretero-pyeloscopy

Using flexible ureteroscopes made theoretically possible the inspection of the entire pyelocaliceal system in a retrograde fashion, despite its complex anatomy. With the development of this technology, the endoscopic diagnosis took a dramatic leap forward.

However, being invasive, the method is usually reserved for cases in which imaging modalities provide equivocal data.

The main indications for this investigative method are:

- filling defects on the upper urinary tract
- unilateral hematuria
- abnormal cytology with normal cystoscopic aspects
- follow-up of patients with upper urinary tract transitional cell carcinoma treated conservatively
- upper urinary tract obstruction

One of the main goals of the method is to establish the benign or malignant nature of the lesions.

Accessing the entire pyelocaliceal system is of the utmost importance in establishing the correct diagnosis. The complete evaluation may be achieved in 66-95.7% of the cases, the success rate
being influenced by the pyelocaliceal anatomy, the performances of the used flexible ureteroscope, the ancillary instruments deployed when biopsy is needed etc. In many cases, the access problems occur while trying to approach the inferior calyx.

In our experience, the pyelocaliceal system was thoroughly approached in 95.7% of the patients (6).

In cases with unilateral hematuria, the diagnosis may be accurately provided in 78-96% of the cases (7, 8, 9, 10) (Figure 1). So, the incidence of so-called „essential“ hematuria decreased, many patients being able to receive the appropriate treatment.

The new Olympus URF-Vo offers the new NBI technology, which describes more accurately the vascular pattern of various areas of the urothelium, thus improving the detection of possibly malignant lesions.

Being able to inspect the entire pyelocaliceal system and to perform biopsies, the flexible ureteroscopic evaluation offers a sensitivity of 93% by comparison to imaging which has a sensitivity of only 73% (11).

A key issue in using this method as a diagnostic tool in urothelial malignancies is its ability to provide the correct characterization of the tumors. Guarnizo et al., performing multiple cold-cup biopsies during 40 ureteroscopies, identified the accurate grade in 78% of the cases (12).

Surveillance of patients with conservatively treated upper urinary tract urothelial carcinoma should be very strictly performed, including periodical endoscopic evaluation. Retrograde flexible ureteroscopy is considered the most important follow-up method in these cases (13).

Treatment of pyelocaliceal lithiasis

The development of flexible ureteroscopes extended the indications of retrograde approach to the pyelocaliceal lithiasis (Figure 2). This was especially useful in cases of failed SWL or percutaneous procedures, in which semirigid ureteroscopy was not possible (such as patients with urinary diversions).

SWL is less invasive than flexible ureteroscopy and quite efficient for calculi smaller than 20 mm, in which the stone-free rate reaches 92%. However, this rate may be 53.7-63% for calculi larger than 2 cm and only 41% for those located in the inferior calyx (14, 15, 16). In cases of extracorporeal lithotripsy failure, another therapeutic method is required. Despite the good success rates of percutaneous procedures, they are still associated with a significant potential morbidity. In this regard, the flexible retrograde approach is a quite appealing method, applicable in the treatment of pyelocaliceal lithiasis.

FIGURE 1. Upper urinary tract TCC in a patient with unilateral hematuria.

FIGURE 2. Retrograde flexible ureteroscopic approach of an upper caliceal calculus.
Moreover, calculi located in the inferior calyx are associated with a poor clearance of the fragments after SWL, so they may benefit from retrograde flexible ureteroscopy as first therapeutic alternative (Figure 3). The same indications should be provided for patients who require rapid and complete removal of the entire stone burden (pilots, seamen etc.). Being less traumatic than the semirigid ones, flexible ureteroscopes may be used even in pregnant patients.

The stone-free rate in pyelocaliceal lithiasis treatment varies between 62 and 98%, the mean number of procedures ranging between 1 and 2.4 (17-19).

These results are influenced by the way in which success is defined, case selection criteria, the equipments used, stones’ characteristics and position.

The standard definition for a successful intervention differs among authors. According to some studies, it is represented by the achievement of a stone-free pyelocaliceal system, while in others, the persistence of a 2-4 mm stone fragment (considered clinically insignificant) is acceptable.

Case selection also seems to influence the results. In the studies which only included patients with SWL-resistant calculi, the success rates were reduced between 62-69.7% (15, 18, 20). One explanation for this fact is that anatomical particularities associated with a poor clearance rate following extracorporeal lithotripsy may also prevent an efficient retrograde flexible ureteroscopic approach (15, 21). Also, the energy source influences the method’s efficacy. The use of Ho:YAG laser is associated with a superior success rate, independent from calculi’s chemical composition (22, 23).

Calculi location is another parameter influencing the method’s outcome. The inferior calyx approach may be an issue, especially when using older generation endoscopes. The reported success rate for this location varies between 79-91%, multiple interventions being sometimes required (21, 24, 25, 26) (Figure 4). Relocating the calculus from the lower pole and performing lithotripsy in more accessible areas improved the success rates. Schuster et al. reported an increase of the stone-free rates from 77 to 89% for inferior calyx calculi smaller than 10 mm and from 29 to 100% for those between 10 and 20 mm (26). Similarly, Kourambas increased the success of the procedure by relocating the lower pole calculi from 83 to 90% (25).

Stone size may also influence the stone-free rate. After a single procedure, Grasso and Ficazzola reported a success rate of 94% for calculi smaller than 10 mm, of 95% for those between 11 and 20 mm and of only 45% for those larger than 20 mm (24). However, the development of the endoscopes...
and energy sources (and especially the use of Ho: YAG laser) improved the efficacy even in patients with a large stone burden (22, 23, 27).

Treatment of pyelocaliceal diverticulae

Retrograde flexible ureteroscopic approach is indicated in the treatment of symptomatic pyelocaliceal diverticulae smaller than 1.5 cm, with or without intradiverticular lithiasis (28) and especially of those located in the anterior calyx, difficult to be approached percutaneously (29).

Variable data regarding the performances of retrograde flexible ureteroscopic approach of pyelocaliceal diverticulae are published in the literature due to different standards in defining the success of this procedure (a stable absence of the symptoms, stone-free patient or disappearance of the diverticular cavity).

The flexible ureteroscopic approach of the diverticulae is dependant on their position. The upper and mid-caliceal ones are more successfully treated by comparison to the inferior caliceal ones: 84% vs. 29% (19, 30) (Figure 5). Once the access to the diverticular neck is achieved (Figure 6), it should be recalibrated by balloon dilation or, preferably, by electric/laser incision. The intra-diverticular stones may be removed in 83-100% of the cases (28, 31). The ablation of the intradiverticular cavity by firing the defocused laser inside it was advocated by some authors.

In our experience, the persistence of the diverticular cavity is acceptable if there is a large communication between it and the pyelocaliceal system, if no symptoms persist and if the patient is stone-free (19).

Treatment of upper urinary tract TCC

With the advent of flexible ureteroscopes and the introduction of lasers, the method started to be successfully applied in the treatment of upper urinary tract TCC. The imperative indications are the presence of solitary kidney, bilateral tumors, chronic renal failure and significant co-morbidities impeding the open surgery. This approach has optimal results in small tumors (< 1.5 cm) located in the upper ureter or the pyelocaliceal system. For the larger ones or for those in patients with characteristics predicting a difficult retrograde approach (complex anatomy, lower pole location etc.) another approach (such as percutaneous surgery) must be taken into consideration (32).

The features influencing the outcome are tumor grade, size and multiplicity. The tumor-free rate in patients with low and high grade tumors conservatively treated was 76% and 40%, respectively. Tumor size influences both the immediate and long-term success. Tumors smaller than 1.5 cm are more often completely resected (91% vs. 36%) and less often present recurrences (25% vs. 50%) by comparison to the larger ones (33). Regarding multifocality, Keeley et al. reported that 50% of patients with multiple...
lesions had residual tumoral tissue while this occurred only in 19% of the cases with solitary malignancies (34). Tumor location doesn’t seem to influence the oncological outcome, the recurrence rate being similar for lesions located in the ureter or in the renal pelvis (31.2% vs. 33%) (35).

Optimizing retrograde flexible ureteroscopy

As previously described, there are some technical limitations associated with retrograde flexible ureteroscopy which directly influence the efficacy of the method. The optical system of the conventional fiberoptic flexible ureteroscopes offers a small area and low resolution images with superimposed moiré effect. The new digital endoscopes partially solved this problem, the chip-in-the-tip transmitting a high resolution image and a three times larger endoscopic field (Figure 7).

In order to optimize the procedure, all factors reducing the visibility or maneuverability of the ureteroscopes should be minimized.

For that purpose, the irrigation flow should be kept as high as possible and the alteration of the pyelocaliceal medium clarity (e.g. hematuria, pyuria) should be avoided. The insertion of various ancillary instruments may decrease the flow even more, proportionally with their diameter. Applying pressure irrigation may partially compensate this influence. However, the use of 3F accessories decreases the irrigation almost to 0, regardless of its pressure (36, 37). Despite the fact that almost all models have a 3.6F working channel, the flow seems to be more influenced by the ancillary instruments’ insertion in older models by comparison to the new digital ones. The insertion of these instruments impedes not only on the visibility but also reduces the maneuverability. The graspers, baskets, probes and fibers increase the stiffness of the flexible ureteroscope and consequently, the access to some pyelocaliceal areas (especially to the lower pole) becomes difficult if not impossible. However, this influence is reduced in the new generation flexible ureteroscopes by comparison to older models. For the Storz 11274AA endoscope, the insertion of various accessories (1.6F electrohydraulic probe, 3F extraction or triradiate graspers, 2F Nitinol baskets) reduces the maximal deflection angle by 8 to 50.6% while in the Olympus URF-Vo, with the same instruments, this parameter decreased only by 0 to 21.1% (38) (Figure 8).

In order to improve access as well as visibility, especially when difficult areas such as the lower pole are targeted, the thinner and more flexible accessories should be used (Figure 9) and the baskets may be unsheathed (thus increasing their flexibility and decreasing their caliber). Also, calculi from the inferior calyx can be relocated in the renal pelvis in order to be fragmented there by using larger instruments.
The relation between various anatomical features and the success of retrograde flexible ureteroscopy (and especially the lower pole access) were studied. Elbahnasy et al. considered the concomitant presence of an infundibulo-pelvic angle under 90º, an inferior infundibulum longer than 3 cm and an infundibular width smaller than 5 mm as a negative predictor of the flexible ureteroscopic access to the lower pole. However, these parameters influence in a reduced manner the outcomes of endoscopic treatment of inferior calyx lithiasis by comparison to their impact on the results of extracorporeal lithotripsy (39).

For Grasso and Ficazzola, only the infundibular length and width correlated in a statistically significant manner with the success of the retrograde flexible endoscopic approach (24).

In our experience, for the 7.5F Storz 11274AA fiberoptic flexible ureteroscope, the presence of an infundibulo-pelvic angle lower than 30º, or the association of an infundibulo-pelvic angle between 30º and 90º and an infundibular length longer than 3 cm is significantly correlated with a poor lower pole access (40). These features did not influence the performances of the more maneuverable Olympus URF-Vo. However, the larger tip of the digital ureteroscope (8.5F) impeded its access to calices with the infundibular width smaller than 4 mm (38).

Also, the flexible ureteroscopes are fragile and costly instruments. In order to maximize their lifespan, these endoscopes should be carefully operated, sterilized and stored. Even under these circumstances, there was described a phenomenon of maximal deflection angle reduction which occurs.
over time, especially after prolonged inferior calyx approach.

Older models required major repairs after 3-13 hours or 6-15 procedures (41). Pietrow et al. studied 4 models of 7.5F flexible ureteroscopes, reporting a mean number of 50.3 passages into the upper urinary tract until 25° were lost from the maximal deflection angle (42).

Despite the technological progress, this phenomenon continued to occur (however within a longer period of time) in third generation endoscopes. Regarding the Storz Flex-X model, after 50 procedures (17 hours and 15 minutes) the ventral maximal deflection decreased from 270° to 208°, the dorsal one from 270° to 133° and the irrigation flow (at 100 cm H2O) from 50 ml/min to 40 ml/min (43).

In a prospective randomized study, Monga et al. evaluated the durability of 7 flexible ureteroscopes: Storz 11274AA and Flex-X, ACMI DUR-8 and DUR-8 Elite, Wolf 7330.170 and 7325.172, Olympus URF-P3. ACMI DUR-8 Elite and Olympus URF-P3 seem to be the most durable devices: the first one had the longest period in use without major repairs (494 minutes), while the second model reached the longest interval of lower pole approach. Both ureteroscopes were models with the longest operative time involving ancillary instruments inserted through the working channel (44).

In order to minimize this effect, some authors advocated the reduction of inferior calyx approach time by relocating calculi from the lower pole into the renal pelvis (37).

Another major repair reason consists in the breakage of the optical system’s fibers due to excessive torque or deflection, thus generating black dots on the endoscopic field and impairing the visibility. The development of digital endoscopes solved this issue by replacing the optical fibers bundle with a chip mounted at the tip of the endoscope.

According to our experience, the new digital flexible ureteroscope Olympus URF-Vo presented a significantly improved durability by comparison to the fiberoptic ones. However, further studies aiming to assess this parameter are required (38).

Robotic flexible ureteroscopy was recently proposed by Desai et al. In an experimental study on swine, the robotically manipulated endoscope succeeded to access 98% of the targeted calices with a reduction of the infundibular approach time from 15 minutes to 49 seconds. Robotic flexible ureteroscopy offers potentially improved maneuverability and ergonomics (45). However, further development of the method is required before it may be applied on a wide scale on humans.

**CONCLUSIONS**

Despite the technical limitations, retrograde flexible ureteroscopy is already an efficient method which significantly improved and diversified the endoscopic approach in many upper urinary tract pathologies.

The parameters influencing the success rate of the retrograde flexible ureteroscopy with the available endoscope, energy sources and ancillary instruments applied to the lesion’s characteristics should be known and taken into consideration when this approach is taken into consideration.

However, there are still numerous alternatives concerning future developments: new materials to be used for the construction of endoscopes or ancillary instruments, energy sources’ improvement, robotics, further miniaturization of the CCD and CMOS chips translating into a consecutive decrease of the endoscopes’ caliber etc. All of the aspects mentioned above create unlimited possibilities for the development of retrograde flexible ureteroscopy.

**REFERENCES AND RECOMMENDED READINGS**

(*of special interest, **of outstanding interest)


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