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**TITOLO TESI**

**International Cooperation in Endourology:  
Percutaneous and Flexible Ureteroscopic Treatment  
of Lower Pole Kidney Stones**

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## **ABSTRACT**

### **Introduction**

Lower pole kidney stones represent at time a challenge for the urologist. The gold standard treatment for intrarenal stones  $<2$  cm is Extracorporeal Shock Wave Lithotripsy (ESWL) while for those  $>2$  cm is Percutaneous Nephrolithotomy (PCNL). The success rate of ESWL, however, decreases when it is employed for lower pole stones, and this is particularly true in the presence of narrow calices or acute infundibular angles. Studies have proved that ureteroscopy (URS) is an efficacious alternative to ESWL for lower pole stones  $<2$  cm, but this is not reflected by either the European or the American guidelines. The aim of this study is to present the results of a large series of flexible ureteroscopies and PCNLs for lower pole kidney stones from high-volume centers, in order to provide more evidences on the potential indications of the flexible ureteroscopy for the treatment of kidney stones.

### **Materials and Methods**

A database was created and the participating centres retrospectively entered their data relating to the percutaneous and flexible ureteroscopic management of lower pole kidney stones. Patients included were treated between January 2005 and January 2010. Variables analyzed included case load number, preoperative and postoperative imaging, stone burden, anaesthesia (general vs. spinal), type of lithotripter, access location and size, access dilation type, ureteral access sheath use, visual clarity, operative time, stone-free rate, complication rate, hospital stay, analgesic requirement and follow-up time. Stone-free rate was defined as absence of residual fragments or presence of a single fragment  $<2$  mm in size at follow-up imaging.

Primary end-point was to test the efficacy and safety of flexible URS for the treatment of lower pole stones; the same descriptive analysis was conducted for the PCNL

approach, as considered the gold standard for the treatment of lower pole kidney stones. In this setting, no statistical analysis was conducted owing to the different selection criteria of the patients.

Secondary end-point consisted in matching the results of stone-free rates, operative time and complications rate of flexible URS and PCNL in the subgroup of patients harbouring lower pole kidney stones between 1 and 2 cm in the higher diameter.

Statistical analysis has been performed using the SPSS software™ (16<sup>th</sup> version); the  $\chi^2$ -test and 1-way ANOVA test have been used when comparing groups for categorical and continuous variables, respectively: a two-sided *p* value <0.05 was considered statistically significant.

## **Results**

A total 246 patients met the criteria for inclusion. There were 117 PCNLs (group 1) and 129 flexible URS (group 2). Ninety-six percent of cases were diagnosed by CT KUB scan. Mean stone burden was  $175\pm 160$  and  $50\pm 62$  mm<sup>2</sup> for groups 1 and 2, respectively. General anaesthesia was induced in 100 % and 80% of groups 1 and 2, respectively. Pneumo-ultrasonic energy was used in 84% of cases in the PCNL group, and holmium laser in 95% of the cases in the flexible URS group. The mean operative time was  $76.9\pm 44$  and  $63\pm 37$  minutes for groups 1 and 2 respectively. There were 12 major complications (11%) in group 1 (mainly Grade II complications according to Clavien classification) and no major complications in group 2. Mean hospital stay was 5.7 and 2.6 days for groups 1 and 2, respectively. Ninety-five percent of group 1 and 52% of group 2 required analgesia for a period longer than 24 hours. Intraoperative stone-free rate after a single treatment was 88.9% for group 1 and 79.1% for group 2. Overall, 6% of group 1 and 14.7% of group 2 required a second look procedure. At 3 months, stone-free rates were 90.6% and 92.2% for groups 1 and 2, respectively, as documented by

follow-up CT KUB (22%) or combination of intra-venous pyelogram, regular KUB and/or kidney ultrasound (78%).

In the subanalysis conducted comparing 82 vs 65 patients who underwent PCNL and flexible URS for lower pole stones between 1 and 2 cm, intraoperative stone-free rates were 88% vs 68% ( $p= 0.03$ ), respectively; anyway, after an auxiliary procedure which was necessary in 6% of the cases in group 1 and 23% in group 2 ( $p=0.03$ ), stone-free rates at 3 months were not statistically significant (91.5% vs 89.2%;  $p=0.6$ ).

Conversely, the patients undergoing PCNL maintained a higher risk of complications during the procedure, with 9 cases observed in this group versus 0 in the group of patients treated with URS ( $p=0.01$ )

### **Conclusions**

These data highlight the value of flexible URS as a very effective and safe option for the treatment of kidney stones; thanks to the latest generation of flexible devices, this new technical approach seems to be a valid alternative in particular for the treatment of lower pole kidney stones less than 2 cm. In high-volume centres and in the hands of skilled surgeons, this technique can approach the stone-free rates achievable through PCNL in lower pole stones between 1 and 2 cm, with a very low risk of complications.

These findings can constitute the basis for a revision of the international guidelines with respect to the indications for the treatment of lower pole kidney stones; anyway, a randomized clinical trial is needed to confirm this statement.

Furthermore, the results confirm the high success rate and relatively low morbidity of modern PCNL for lower pole stones, with no difference detectable between the prone and supine position.

## INTRODUCTION

### Prevalence and incidence of kidney stones

Urolithiasis, or urinary stone disease, represents an enormous clinical and financial burden for the Western countries' health care systems. It has been reported that in the U.S. urolithiasis accounts for more than 2 million office visits and nearly 200,000 hospital admissions each year, with an estimated annual cost of more than \$2 billion [1]. According to the data recorded from a survey undertaken by ISTAT (Italian Institute of Statistical Analysis) in 2003, urolithiasis was ranked the 18th most important disease that required ordinary admission in the hospitals of the Italian National Health System (102.222 admissions per year), with an average duration of hospitalization of 4.2 days [2]. In 1998, the estimated cost to the Italian National Health System of hospitalization due to urolithiasis was ca. 500 billion of Lira (ca. 230 million Euros at the current exchange rates). Furthermore, recent decades have witnessed an upward trend in the epidemiological indexes for urolithiasis in Italy (Table 1); consequently the aforementioned figures are probably now underestimated [2], [3].

	1983	1993	2003
Prevalence (%)	1.17	1.7	2.20
Incidence (%)		0.17	
Hospitalization (n)		80.000	102.222

**Table 1** Trends in epidemiological indexes in respect of urolithiasis in Italy

The Italian data reflect the changes in prevalence and incidence that have been recorded all over the world in recent decades. A recent review collected and compared the prevalence and incidence of nephrolithiasis from countries where data for more than a single time period were available (Table 2).

In countries reporting prevalence rates in the 1980s and 1990s, the non-weighted, average global prevalence was 3.25% in the 1980s and 5.64% in the 1990s [4].

Reported Kidney Stone Prevalence by Country and Year			
Country	Year	Population	Prevalence
United States	1964-1972	All	2.62%
	1976-1980	All	3.8%
	1982	All	5.4%
	1988-1994	All	5.2%
Italy	1983	All	1.17%
	1993-1994	All	1.72%
Scotland	1977	All	3.83%
	1987	All	3.5%
Spain	1977	All	0.1%
	1979	All	3.0%
	1984	All	4.16%
	1987	All	2.0%
	1991	All	10.0%
Turkey	1989	All	14.8%

**Table 2** Reported kidney stone prevalence by country ad year (from Romero V. et al [4])

Other findings confirm that in Spain an increase in the prevalence of urolithiasis has been observed in recent decades: in 1986, a national epidemiologic study supported by the Spanish Urological Association (AEU) estimated a prevalence of 4.16%, while more recently this figure has risen to 5.06% [5].

In the US, the reported annual incidence of urolithiasis was 164/100.000 inhabitants [6] but in the '90s Curhan et al. [7] reported an incidence of 0.273-0.326% of total annual incidence of urolithiasis in a population of 45.000 males aged >40 years.

In Japan, the incidence of nephrolithiasis has doubled over a 40-year time period in both men and women and the increase has been most prominent in the last 10-20 years [4].



The causes of the increases in the prevalence and incidence of urolithiasis are still unclear.

Various factors have been suggested to be responsible, but the most widely accredited hypothesis concerns environmental factors. Particular emphasis is placed on the roles played by dietary and climate changes: the increased consumption of starchy and fatty foods, the higher dietary intake of meat and sodium, the low daily intake of fluids and the global warming are all closely related to obesity and dehydration, which are listed among the most important risk factors for the development of kidney stones.

However, another factor must also be taken into consideration: since the widespread use of ESWL from the 80's, onward as a first-line therapy for all kidney stones, most patients have harboured residual fragments after the treatments. Politis et al. [8], demonstrated that although correct fragmentation is obtained in up to 98% of cases after ESWL, the fragments are eliminated in only 75%.

### **Changes in the natural history of kidney stones**

Usually most residual fragments have been considered clinically insignificant and in different series they have been variously defined as less than 2,3,4 or 5 mm in maximum diameter when calculating the stone-free rates.

That has had a twofold consequence:

- 1) a higher risk of recurrences;
- 2) a significant change in renal stone location.

To support point number 1,) the data published in 1996 by Carr et al. [9] showed a trend toward higher stone recurrence rates in ESWL-treated patients; after 1 year of follow-up there was a significantly higher rate of stone recurrence among patients treated with ESWL than among patients who underwent PCNL (22% vs 4%,  $p=0.004$ ).

In support of point number 2), the same Authors also found that more new stones recurred in the lower calices compared with the baseline location in the ESWL group, unlike in the PCNL group. They concluded that this may have been due to microscopic sand particles migrating to dependent calices and acting as a nidus for new stone formation.

Lingeman et al. [10] reported similar data: in a meta-analysis published in 1994, they used a combined data set from the AUA Nephrolithiasis Guidelines Panel review (1965 to 1991) and observed an increase in the percentage of shock wave lithotripsy treatments for renal calculi in the lower pole (2% in 1984 to 48% in 1991). The change in stone distribution may be explained by the tendency for small fragments to accumulate in the lower pole owing to gravitational forces, as a results of incomplete stone clearance after ESWL.

In the current clinical practise, calculi in the lower pole represent 34-66% of all calculi requiring treatment [11] [12].

The correct management depends on many factors, specifically on patient (age, BMI, comorbidities), anatomical (calyx geometries) and stone (burden, hardness) characteristics. The potential impact of so many factors makes the treatment of lower pole stones one of the more controversial topics in endourology today.

## **BACKGROUND OF LOWER POLE CALCULI**

### **Efficacy of ESWL and PCNL based on lower pole anatomic characteristics of the lower pole collecting system**

ESWL is widely considered the first-line therapy for most of renal stones and specifically for those less than 2 cm in maximum diameter.

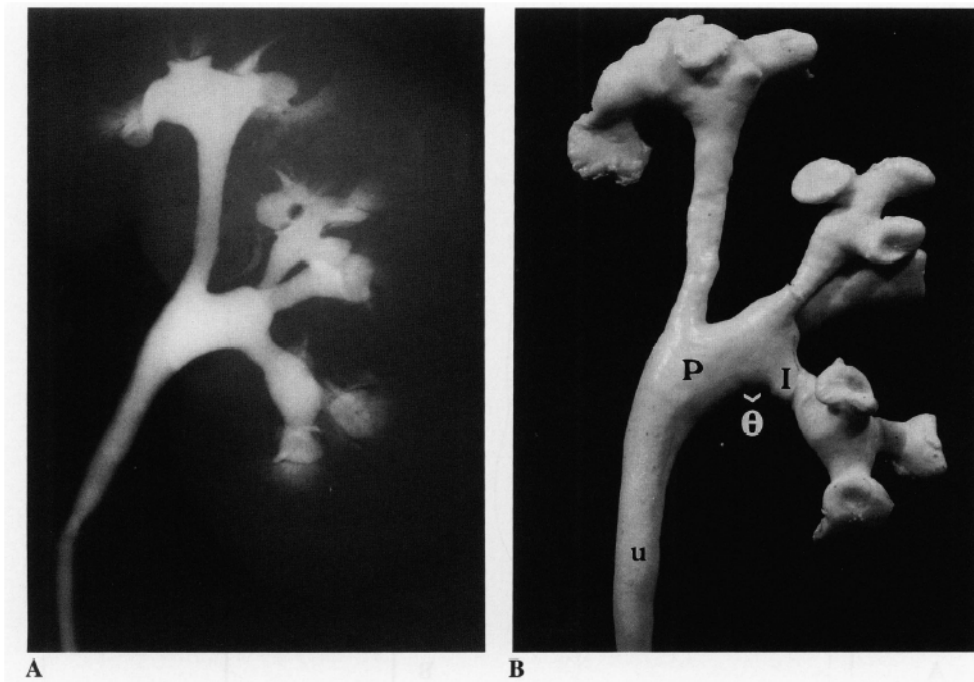
After the first series reporting overall stone-free rates approaching 90% [13], [14], several further reports questioned the real efficacy of ESWL. The first published data from the United States ESWL study, collecting the first 2501 treatments conducted in USA, reported a 34% rate of fragments retention at 3 months of follow-up [15]. Similar findings were reported by other Authors, whose data were summarized by Renner & Rassweiler [16]: in their review they highlighted that expected stone-free rates ranged from 70% to 90% for upper and middle calyceal calculi, but from 50% to 70% for lower pole calculi.

Lingeman et al. [10], in their aforementioned meta-analysis, showed an overall stone-free rate for ESWL of 60% when considering lower pole stones. When stratification was performed for stone size, the group of patients who underwent ESWL showed stone-free rates of 74%, 56%, and 33% for stones less than 10, 11 to 20, and greater than 20 mm, respectively.

Similar results were published more recently by Obek et al. [12] who obtained stone-free rates of 70%, 57%, and 53% for stones of <10, 11 to 20, and >20 mm in maximum diameter, respectively.

In an attempt to explain the poor results of ESWL in lower pole stones, Sampaio and Aragao [17] first argued that different geometric calyceal parameters may influence the clearance of fragments after treatment. They analyzed the inferior-pole collecting

system anatomy in 146 three-dimensional polyester endocasts of the pelvicalyceal system and supported the role of an acute infundibular-renal pelvic angle (Fig. 1), an infundibula smaller than 4 mm in diameter, and the presence of multiple calyces as adverse prognostic factors for clearance of the stone fragments after ESWL.



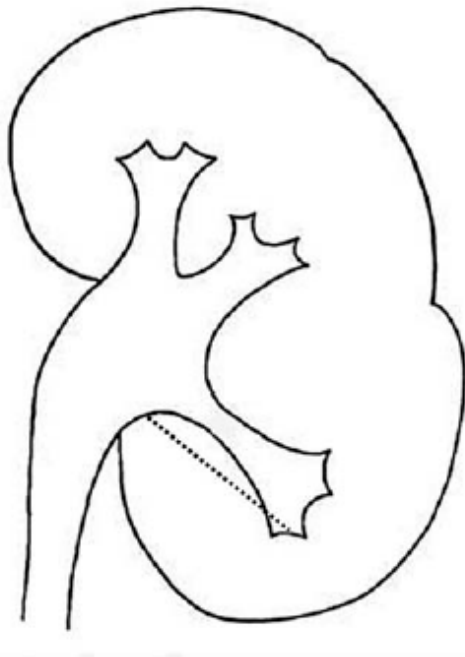
**Fig.1.** Example of an acute infundibular-renal pelvic angle. **A** Retrograde pyelogram of the left kidney, showing an angle of less than  $90^\circ$  between the lower infundibulum and the renal pelvis. **B** Three-dimensional pelvicalyceal endocast from the same kidney. P= pelvis; I= infundibulum;  $\Theta = 60^\circ$  angle. (From Sampaio and Aragao [17]).

Subsequently the same group started a prospective trial in which they found that 72% of patients who underwent ESWL for lower pole stones became stone-free when the infundibulopelvic angle was greater than  $90^\circ$ , whereas only 23% were rendered stone-free when this angle was  $<90^\circ$  [18].

Similarly, Elbahnasy et al. [19] investigated retrospectively the relationship between (a) lower pole infundibular length and width and infundibulopelvic angle, measured at IVP, and (b) clearance of solitary lower pole stones less than 1.5 cm treated with ESWL or

flexible ureteroscopy: they found that an infundibulopelvic angle  $<90^\circ$ , an infundibular length  $>5$  cm, and an infundibular width  $>3$ mm each had a statistically significant influence on stone clearance after ESWL. The unfavourable effects of these factors was less pronounced when ureteroscopy was performed.

Other Authors have studied other parameters, finding that the height of the infundibulum can significantly influence the stone-free rates of ESWL for lower pole stones if less than either 22 [20] or 15 mm [21], (Fig 2).



**Fig. 2.** *Infundibular length (mm), measured as the distance between the most distal point of the calyx containing the calculus and the midpoint of the lower lip of the renal pelvis (From Arzoz-Fabregas et al. [20])*

In view of the poor results of ESWL for lower pole stones, Lingeman et al. [10] retrospectively compared outcomes from studies of solitary lower pole stones treated with ESWL (13 reports) and PCNL (4 reports). Patients treated with ESWL had significantly lower stone-free rates (59.2% vs 90%,  $p<0.0001$ ). When patients were grouped according to stone size ( $<10$  mm, 11 to 20 mm,  $>20$  mm) stone-free rates were 74% vs 100%, 56% vs 89%, and 33% vs 94% for patients treated with ESWL and

PCNL, respectively. On the basis of these findings, the Authors suggested that patients with lower pole stones <1 cm could be treated with ESWL, but recommended PCNL when stones >1 cm are present.

These retrospective studies formed the basis for a multi-centre lower pole study group, better known as the Lower Pole Study Group. This group set up the first (and to date the only realized) prospective randomized trial study to compare PCNL and ESWL in patients with symptomatic lower pole calculi. The 3-month postoperative stone-free rates were 95% for the PCNL group vs 37% for the ESWL group ( $p<0.001$ ). Stone-free rates stratified by stone size were consistent with a prior study demonstrating for ESWL stone-free rates of 68% for stones <10 mm, 55% for stones 10-20 mm, and 29% for stones 20-30 mm; corresponding stone-free rates for the PCNL group were 100%, 93% and 86% [22].

Gerber [23] reported the data of a postal survey conducted in the U.S., where the 65% and 21% of the 205 urologists who answered the questionnaires preferred ESWL for stones sized 1-2 cm and >2 cm, respectively. Despite the poor outcomes of ESWL for lower pole stones >1 cm, ESWL was (and still is) widely accepted as a less invasive and ambulatory procedure that could be offered as a first-line therapy for any renal stone.

Moreover, some Authors argued the clinical impact of the stones in the lower pole calices and therefore some works have been focused on the natural history of this class of stones.

### **Observation vs active treatment for lower pole small stones**

First retrospective experiences regarding patients with asymptomatic calyceal stones showed a cumulative risk of need for intervention from 48.5% up to 83% within the first 5 years of follow up [24] [25] [26].

Subsequently, Keeley et al. [27] developed a randomized trial in which 228 patients with asymptomatic calyceal stones <15 mm in diameter were randomly selected to undergo observation or ESWL; it is noteworthy that the lower pole stones in both groups accounted for a 72% and 73% of stones, respectively. At a mean follow-up of 2.2 years, there was no significant difference in stone-free rate between the two groups, the rate being 17% in the observation group vs 28% in the ESWL group (OR 0.66, 95% CI 0.32-1.37;  $p=0.27$ ). Moreover, there was no evidence of differences in terms of symptoms, quality of life, or renal function. The Authors concluded that prophylactic ESWL for small asymptomatic lower pole stones does not offer any clinical advantage compared with an observational attitude, even though the latter is associated with a greater risk of further treatment, including analgesics, antibiotics, or a procedure (21% vs 15%; OR 0.57, 95%CI 0.21-1.53;  $p=0.27$ ).

More recently some prospective studies on the natural history of asymptomatic lower pole stones have been published. Inci et al. [28] evaluated prospectively the natural history of 24 patients with asymptomatic lower calyceal stones, regardless of their size and the number, who were followed up for a mean of 52.3 months. An increase in stone size was observed in 33.3% of the cases at the end of the follow-up, with a mean in size of 135% compared with the baseline value; 11.1% of the patients required intervention, even though none of these patients were among those who experienced an increase in stone size.

Yuruk et al. [29] followed prospectively 99 patients with asymptomatic lower pole stones <2cm, who were randomly selected for PCNL, ESWL, or observation, and evaluated with CT scan and renal scintigraphy for stone-free rates and renal parenchymal functionality.

At 3 months of follow-up, stone-free rates were 96.7%, 54.8%, and 0% for PCNL, ESWL, and observation group, respectively ( $p<0.0001$ ); in the latter group 8 patients (21.8%) required intervention (medical treatment or procedure), becoming stone-free at the end of the follow-up. Surprisingly, renal scars were detected more often in the ESWL group ( $n=5$ , 16.1%) than in the PCNL ( $n=1$ , 3.2%), and observation groups ( $n=0$ ), respectively. The Authors concluded that giving the pros and cons of the three treatment modalities, further results must be evaluated comparing using new digital flexible ureterorenoscopy devices.

### **First experiences of flexible ureteroscopy for the treatment of lower pole stones**

Several studies of use of flexible ureteroscopy for the treatment of patients with lower pole stones were published from the second half of '90s, after the advent of small (6.7 to 8.5 Fr), active, deflectable ureterorenoscopes and flexible lithotripter devices, such as the 1.9Fr flexible electrohydraulic lithotripsy or the 200-360 $\mu$ m holmium laser fibres. In these first series, encouraging stone-free rates were reported, ranging from 82% to 94% [30], [31], [32], [33], [34], [35].

The Grasso and Ficazzola [35] series accounted among the largest experience, with 70 stone burdens available for follow-up results. The overall stone-free rate was 76%, and it rose to 84% when the eight cases with failed access to the calyx were excluded; in the latter cases, a long lower pole infundibulum (greater than 3 cm) or infundibular stricture were noted to be negative factors.. The Authors were able also to satisfactorily treat stones greater than 2 cm, achieving a noteworthy stone-free rate of 81%, though a two-stage procedure was frequently needed in these cases. They concluded that the lower pole calculi can be successfully treated ureteroscopically, taking into consideration preoperatively the anatomic variants that might affect the result.



In order to confirm what was widely postulated, i.e. that flexible ureteroscopy for lower pole stones would improve ESWL outcome without incurring the additional morbidity of PCNL, another prospective randomized trial was set up by the Lower Pole Study Group, comparing ESWL and ureteroscopy for lower pole calyceal calculi  $\leq 1$  cm [36]. However, the results failed to demonstrate a significant better outcome for the flexible URS group, with a stone-free rate of 35% and 50% for ESWL and flexible URS group ( $p=0.92$ ), respectively; moreover, ESWL was associated with greater patient acceptance and shorter convalescence.

Another strategy for flexible URS has been proposed in some works: keeping ESWL as first-line therapy for lower pole calculi, flexible URS was tested in case of failure of the extracorporeal treatment. Stav et al. [37] reported a retrospective series of 81 patients who underwent flexible URS from 1996 to 2002 after they had undergone multiple ESWL. The overall stone-free rates was 64% (43% stone-free immediately and 21% with residual fragments  $< 3$  mm); the majority of patients harboured lower pole stones, with 31 pts (38%) with a solitary lower pole stone and 8 pts (11%) with stones located in the lower pole and in another calyx. Most of the residual larger stones (more than 3mm in diameter) were at the lower pole (11 of 13 patients) and the procedure was considered a failure in 9 of 15 cases owing to inability to place the ureteroscope in the lower pole because of decreased laser fibre deflection. The Authors concluded that flexible ureteroscopy represents an effective approach for renal stones  $< 2$  cm that are resistant to multiple ESWL; the procedure has a higher likelihood of be ineffective in case of lower pole stones.

More recently a Danish group tested the efficacy of flexible ureteroscopy after that ESWL failed to render stone-free 35 patients with renal stones [38]; all the patients at the time of flexible ureteroscopy had a stone burden less than 2 cm in accumulated

diameter. The flexible URS procedure was successfully executed in all the 35 cases, of whom 16 (42.1%) had stones located in the lower pole. The overall stone-free rate (including patients with residual fragments <4 mm) was 68% after a single setting; stratifying for site, stone-free rates were 81% - 75% - 60% and 44% for stones in the lower, middle and upper calyx, and renal pelvis, respectively. After a second setting of flexible URS, the overall stone-free rates reached 76%. The Authors concluded that flexible URS is a safe and effective procedure for ESWL-resistant kidney stones <20 mm in size, even in cases with an abnormal anatomy and an unfavourable stone composition.

## CURRENT APPLICATION OF FLEXIBLE URETEROSCOPY

### Role of flexible ureteroscopy according to international guidelines

The American Urological Association and the European Association of Urology periodically publish their updated versions of their guidelines; with regards to urolithiasis disease, the AUA published the Guidelines on Staghorn Calculi and Ureteral Calculi in 2005 and 2007, and these have been reviewed in 2010 and 2009, respectively. The EAU published the first version of the Guidelines on Urolithiasis in 2001 and from then on an updated version has been published every year [39].

No mention of flexible ureterorenoscopy can be found in the AUA guidelines, while in the EAU guidelines some notes have been reported only in the last 3 versions.

In the EAU Urolithiasis Guidelines of 2010, a section was reserved for the retrograde intrarenal surgery, where the standard steps of the technique were assessed together with the indications for the procedure and the related complications (Table 3).

- |   |
|---|
| <ul style="list-style-type: none"><li>• Fluoroscopic equipment must be available in the operating room</li><li>• Pre-operative imaging of urinary tract confirms location of stone and identifies anatomical abnormalities</li><li>• The use of a safety guidewire (usually an 0.035-inch, non-hydrophylic, floppy tip) is recommended</li><li>• Flexible ureteroscopes are most easily introduced via an additional guidewire or through an ureteral access sheath, although last-generation scopes allow bare passage in experienced hands</li><li>• Endoscopic intracorporeal lithotripsy can be performed by (Ho:YAG) laser lithotripsy, ballistic (= pneumatic) lithotripsy, ultrasonic lithotripsy and with electrohydraulic lithotripsy (EHL) in selected situations. Lithotripsy devices are described in Appendix 1</li><li>• Small stones and fragments are best retrieved with a basket or a forceps (6-9)</li><li>• Stent placement at the end of the procedure is optional and debatable (10-16)</li></ul> |
|---|

**Table 3.** *Standard technique for the basic endoscopy procedure (from EAU Guidelines on Urolithiasis, 2010)*

It is reported that <<Flexible URS has not been recommended as a first-line treatment for renal calculi, and there are no valid data to support such a recommendation. However, because using ESWL for lower pole stones has poor results, flexible URS could become a reliable first-line treatment for lower pole stones  $\leq 1.5$  cm>>.

In fact it is worth underlining that the majority of the series published have used out-of-date devices rather than the most recent commercially available generation of fibrescopes. It must be bore in mind that during the past decade, the main manufacturers marketing flexible ureteroscopes have launched several updated versions of their former products, in an effort to maximize the manoeuvrability, visibility and durability of the instruments of small calibre (<9 Fr), and eventually to improve their efficacy and safety.

### Technological evolution of the ureteroscopic devices

Since 2000, several works have been published comparing the mechanical and optical characteristics of several flexible ureteroscopes produced by the four main manufacturers.

In 2000 Afane J.S. et al. [40] evaluated four flexible ureteroscopes from December 1997 to December 1999: the Storz 11274AA, the Circon-ACMI AUR-/, the Wolf 7325.172, and the Olympus URF/P3. Their characteristics are displayed in Table 4.

	Storz 11274AA	Circon-ACMI AUR-7	Wolf 7325.172	Olympus URF/P3
Length (mm.):				
Total	990	1,000	940	1,010
Working	700	650	700	700
Outer diameter (Fr):				
Shaft tip	7.5	7.2/7.4	7.0	8.1
Shaft	8.7	7.4-9.5	8.0-9.0	8.4
Channel inner diameter (Fr)	3.6	3.6	3.6	3.6
Optical system:				
View field (degrees in air)	90	92	95	90
View direction (degrees)	0	0	0	0
Field depth (mm.)	2-50	2-40	3-50	2-50
Deflection mechanism type	Intuitive	Intuitive	Intuitive	Counterintuitive
Active deflection angulation range (degrees down/up)	170/120	160/120	160/130	180/180
Min. force needed on actively deflected ureteroscope for secondary deflection (lbs.)	0.22	0.10	0.20	0.05

All ureteroscopes had secondary passive deflection.

**Table 4.** Characteristics of four flexible ureteroscopes from major manufacturers (From Afane J.S. et al. [40])

The Authors noted that the luminosity (2 to 6.8 lumens) and irrigant flow (from 57 to 77 ml/min at a pressure of 100 mmHg) of all endoscopes remained relatively unchanged; the major exception was the Olympus device, which, with its undetachable light cord system, provided a two- to threefold greater luminosity in comparison with the other ureteroscopes. Each endoscope required repair after 6 to 15 uses and in 40% of the cases

this was due to poor or complete loss of deflection, mostly as a consequence of the mechanical stress involving in gaining access to the lower pole (this accounted for 29% of the cases).

Just two years later, Parkin J. et al. [41] performed a similar comparison involving the same manufacturers. This study tested two new fibrescopes, the ACMI DUR-8 and the Wolf 9 Fr, together with the fibrescopes from Storz and Olympus that were tested in the aforementioned reported. Both the newest ureteroscopes had a bevelled tip that was smaller in diameter, and in comparison with the previous models the ACMI DUR-8 had respect the previous model a more exaggerated degree of deflection and the Wolf 9 Fr had a work channel of 4 Fr. Interestingly, in this report the performances of the devices were tested with the auxiliary instruments placed in the work channel (Table 5).

Variable	Manufacturer			
	ACMI	Olympus	Storz	Wolf
<b>Size, F</b>				
Tip	6.75*	6.9*	7.5	6*
Shaft	8.7	8.4	8.7	9
Channel	3.6	3.6	3.6	4
Working length, mm	650	700	700	600
<b>Optics</b>				
Direction, °	9	0	0	0
Field of view, °	80	90	90	60
Image size, cm <sup>2</sup>	22	25	20.4	22
<b>Active tip deflection</b>				
Specification, °	180/170	180/180	170/120	160/130
Channel empty, °	163/153	180/170	154/120	152/121
% Loss with:				
200 µm laser	17	22	25	15
365 µm laser	30	43	35	26
EHL probe	4	4	7	1
3 F graspers	55	62	57	55
<b>Irrigation flow rate, mL/min</b>				
Channel empty	88	72	74	116
200 µm laser	44	53	42	72
365 µm laser	36	32	31	58
EHL probe	34	52	32	56
3 F graspers	N	N	N	6
UK list price, £	15 000	8950	5995	4999

\*bevelled tip; N, negligible; EHL, electrohydraulic lithotripter.

Tip deflection was 87-100% of the manufacturers' specification and decreased by similar percentages with instruments in the working channel. The irrigation flow rate was reported to be much greater for the Wolf 9Fr owing to the 4 Fr working channel.

**Table 5.** Characteristics of the four flexible ureteroscopes tested by Parkin J. et al. [41]

Some years later, during which time new devices had been launched on the market, another comparison was carried out between the ACMI DUR-8 Elite, Storz Flex-X, Wolf 7325.172 and 7330.072, and Olympus URF-P3 flexible ureteroscopes [42]. The ACMI device was characterized by a secondary active deflection command which conferred on the instrument an extra 130-degree deflection. The Storz Flex-X was the first with an exaggerated 270-degree deflection in both upward and downward directions; moreover it was equipped with a bevelled and smaller tip (6.7 Fr) and the length of the working probe was slightly reduced (from 70 to 65 cm). Finally, the Wolf 7330.072 had a further wider 4.5 Fr working channel and an optical quartz bundle to improve optic resolution (Table 6).

*TABLE 1. Angles of deflection with various accessories*

	ACMI DUR-8 Elite			Storz Flex-X	Wolf 7330.072	Wolf 7325.172	Olympus URF-P3
	Down/Up Primary	Active Secondary	Active 1 + 2	Down/Up	Down/Up	Down/Up	Down/Up
Empty	164/152	132	266	246/233	156/128	159/122	160/146
200 μm Laser probe	134/120	102	247	223/204	148/124	150/116	152/138
365 μm Laser probe	88/92	95	197	180/159	104/92	90/79	110/87
1.9Fr EHL probe	149/135	107	248	225/204	126/114	131/117	145/133
2.2Fr basket	156/130	110	250	240/210	135/123	136/124	147/140
3.0Fr basket	144/126	108	245	220/203	133/124	136/129	145/132
2.6Fr grasping forceps	128/121	98	228	207/182	130/110	127/115	138/132

**Table 6.** *Angles of deflection of flexible ureteroscopes with various accessories in the working channel (From Abdelshehid C. et al. [42])*

The researchers highlighted that the greatest amount of tip deflection and the highest light output was found in the Storz and ACMI ureteroscopes, while a superior flow and a better optical performance were registered for the Wolf 7330.072 ureteroscope.

More recently, the last generation of ureteroscopes was compared by Paffen et al. [43] with respect to their physical properties: the main updates were provided in the Storz Flex-X2, which incorporated on the tip a ceramic coat to protect the optical fibres, and in the Wolf 7325.076 (known as “Viper”) with an exaggerated deflection of +/- 270 degrees (Table 7).

		<i>Storz Flex-X<sup>2</sup></i>		<i>ACMI DUR-8 Elite</i>				<i>Olympus XURF-P5</i>		<i>Wolf 7325.076</i>	
		↑	↓	↑	↓	↘	↙	↑	↓	↑	↓
Empty	$\angle$ (°)	256.0	264.3	164.5	157.8	125.4	285.6	182.2	287.6	265.7	258.4
	r (mm)	11.6	10.6	9.7	11.1	8.6	10.2	8.2	9.5	11.0	11.1
200 $\mu$ m laser fiber	$\angle$ (°)	246.1	244.3	151.4	148.4	125.9	274.1	180.4	272.3	252.3	247.6
	r (mm)	12.7	12.2	11.3	11.7	8.6	11.2	8.3	11.3	11.5	11.4
365 $\mu$ m laser fiber	$\angle$ (°)	191.0	199.8	117.0	113.8	121.9	232.8	108.3	207.0	211.8	203.6
	r (mm)	16.6	16.5	14.9	16.8	9.8	12.3	16.1	15.7	16.0	15.9
2.2 F nitinol basket	$\angle$ (°)	250.7	256.5	158.2	153.7	133.1	287.0	181.9	280.6	259.9	259.0
	r (mm)	11.7	11.1	10.6	11.0	8.7	10.3	8.3	11.4	11.0	11.1
3 F nitinol basket	$\angle$ (°)	246.1	260.9	158.0	155.8	137.0	284.7	182.3	275.9	254.3	251.4
	r (mm)	11.9	10.6	10.7	11.0	8.9	10.3	8.3	11.5	11.2	11.1

\*The pictures shown are of the deflection angle closest to the mean value.

**Table 7.** Maximum active tip deflection angle and radius of curvature evaluated for an empty working channel and with instruments inserted (From Paffen M. et al. [43])

The Authors performed different in vitro evaluations, testing also some new properties like the torsion stiffness as well as the optical distortion. They were able to quantify and objectify the differences of the properties among the new generation of ureteroscopes: the ACMI DUR-8 Elite, with its shortest working length, had the highest flow rate; the Olympus XURF-P5 and Wolf Viper recorded the best scores in optical properties; the Storz Flex-X2 and Wolf Viper reached the wider angle of deflection and the lowest torsion stiffness.

Thanks to the improvements in the physical characteristics achieved in the last generation of flexible ureteroscopes, more Authors have now published their experiences with extended indications and complex procedures in the renal collecting system. In these reports, stone-free rates of 60–80% have been obtained for URS treatment of lower pole stones [44], [45], [46], [47].

Despite this progress in techniques and technologies, one problem seems to have remained unsolved: according to a recent report [48], no improvement has been recorded regarding the durability of the devices in comparison with the former models. All of the aforementioned last generation of ureteroscopes appeared comparable with respect to durability, which was found to range from 5.3 to 18 cases on average, with no apparent significant improvement over the previous experiences with older fibrescope models.

On the other hand, however, another study found a significant increase in durability of a new-generation of flexible ureteroscope, the Storz Flex X2 [49]: the Authors reported a need of repair after 50 procedures. By the time of the final 50<sup>th</sup> procedure, however, an important deterioration in deflection (by 23% in the upward and 50% in the downward direction) was noted and the number of broken image fibres accounted for six.

In conclusion, modern digital flexible ureteroscopes (Olympus URF-V0, ACMI DUR-D) do seem to have improved manoeuvrability and visibility compared with the conventional fiberoptic scopes as the light cord has been eliminated and they have improved optical resolution with CMOS (complementary metal oxide semiconductor) technology.



## **MATERIALS AND METHODS**

The lack of strong scientific evidence is reflected in the limited recommendations tailored for flexible URS in the international guidelines.

Furthermore, the paucity of evidence is a logical consequence of the world of today, where improvements in technology outpace the time needed to prove their efficacy, according to the rigid criteria of scientific methodology.

In an effort to provide data of good quality and to take advantage of the technical skills reached in centres of high volume and specialization, a scientific society has recently been set up: the International Cooperation in Endourology.

This society is legally registered in Paris and has 7 official members (A. Breda, M. Brehmer, T. Knoll, E. Liatsikos, P. Osther, C. Scoffone, O. Traxer) and has one associated member (F. Millan). A president is to be appointed every 2 years. The current president is O. Traxer.

The main objective of the group is to develop prospective studies addressing the more controversial aspects of endourology; however, retrospective studies are also needed to assess the background of subsequent projects.

This is the reason why the first step of the new group has been to set up a common database where the data of patients treated for renal and ureteral calculi in the participating institution during the past 5 years have been entered. These data have recently been reviewed and processed with respect to the role of flexible URS in lower pole stones, the impact of high BMI during supine and prone PCNL and the usefulness of the ureteral access sheaths during flexible URS.

A database has been created and the centres have retrospectively entered their data relating to the percutaneous and flexible ureteroscopic management of lower pole kidney stones. Patients included were treated between January 2005 and January 2010.

Variables analyzed included case load number, preoperative and postoperative imaging, stone burden, anesthesia (general vs. spinal), type of lithotripter, access location and size, access dilation type, ureteral access sheath use, visual clarity, operative time, stone-free rate, complication rate, hospital stay, analgesic requirement and follow-up time. Stone-free rate was defined as absence of fragments, or presence of a single fragment < 2mm in size at follow-up imaging at 3 months.

The centres involved have been the Departments of Urology of:

*Fundacion Puigvert, Autonomia University, Barcelona, Spain*

*San Luigi Hospital, Turin, Italy*

*Patras University, Patras, Greece*

*Karolinska University Hospital, Stockholm, Sweden*

*Frederica Hospital, University of Southern Denmark, Fredericia, Denmark*

*Tenon Hospital, University of Paris, Paris, France*

*Klinikum Sindelfingen-Böblingen, Sindelfingen, Germany*

The indication for selecting patients for PCNL or flexible ureteroscopy was based on the international guidelines: generally, PCNL was offered to patients with a high stone burden of lower pole stones, while ureteroscopy was reserved as a therapeutic alternative to ESWL for lower pole stone sized less than 2 cm.

The stone surface was calculated with the conventional ellipsoid formula: higher diameter \* lower diameter \* 0.25 \*  $\pi$ . In the case of multiple stones, the value of the higher diameter entered in the database corresponded to the sum of the higher diameters of each stone.

Primary end-point was to test the efficacy and safety of flexible URS for the treatment of lower pole stones; the same descriptive analysis was conducted for the PCNL approach, as considered the gold standard for the treatment of lower pole kidney stones.

In this setting, no statistical analysis was conducted owing to the different selection criteria of the patients.

Secondary end-point consisted in matching the results of stone-free rates, operative time and complications rate of flexible URS and PCNL in the subgroup of patients harbouring lower pole kidney stones between 1 and 2 cm in the higher diameter.

Statistical analysis has been performed using the SPSS software™ (16<sup>th</sup> version); the  $\chi^2$ -test and 1-way ANOVA test have been used when comparing groups for categorical and continuous variables, respectively: a two-sided  $p$  value  $<0.05$  was considered statistically significant.

## RESULTS

### Global results

#### *Patient demographics*

The main demographic characteristics of the patients entered in the database are summarized on Table 8.

A total of 246 patients met the criteria for inclusion. There were 117 (47.6%) PCNLs (group 1) and 129 (52.4%) flexible URSs (group 2).

<b>No. of patients</b>	246
<b>Age (range)</b>	53 (19-84)
<b>Gender</b>	
<b>Male</b>	143
<b>Female</b>	103
<b>ASA score</b>	
<b>1</b>	68 (27.6%)
<b>2</b>	124 (50.4%)
<b>3</b>	37 (15%)
<b>4</b>	7 (2.8%)
<b>BMI (range)</b>	25.8 (14.8-50)
<b>Stone side</b>	
<b>Right</b>	109 (44.3)
<b>Left</b>	137 (55.7)
<b>N. of stones</b>	
<b>Single</b>	128 (52%)
<b>Multiple</b>	118 (48%)

**Table 8.** *Main demographic characteristics of the patients entered in the database*

The mean stone burden was 175 mm<sup>2</sup> (SD: ±160), and 59 mm<sup>2</sup> (SD: ±62.7) for groups 1 and 2, respectively ( $p=0.0001$ ). Mean stone size (higher diameter) was 19.5 and 9.9 mm, respectively ( $p=0.0001$ ) (Table 9).

General anaesthesia was induced in 100 % and 80% of groups 1 and 2, respectively; regional anaesthesia was induced in the remaining 20% of group 2.

Overall, the mean operative time was 76.96 (SD:  $\pm$  44.3) and 63.69 (SD:  $\pm$ 37) minutes for groups 1 and 2, respectively. The mean hospital stay was 5.7 (SD:  $\pm$ 3.3) and 2.6 (SD:  $\pm$ 1.7) days for groups 1 and 2, respectively.

Ninety-five percent of the patients in group 1 and 52% of those in group 2 required analgesia for a period longer than 24 hours.

	<b>PCNL</b>	<b>URS</b>
<b>No. of patients</b>	117	129
<b>Stone size: surface (mm<sup>2</sup>)</b>	175	59
<b>Stone size: higher diam. (mm)</b>	19.5	9.9
<b>OR time (min)</b>	76.9	63.69
<b>Analgesic requirement</b>	95%	52%
<b>Hospital stay (days)</b>	5.7	2.6

**Table 9.** Findings in group 1 (PCNL) and group 2 (flexible URS) patients

#### *Characteristics of PCNL procedures*

In the case of percutaneous access, the procedure was performed according to the surgeon's preferred position and to the patient's anatomical characteristics. Prone access was performed in 52 patients (44.4%), while the supine position was preferred in 65 patients (55.6%) (Table 10).

The number of accesses to the kidney was always single except in one case where a double access was needed. In most of the cases, prone PCNL was performed with an access to the lower pole: in only 3 cases of the 35 cases for which complete data were available, the access was performed through the middle or the upper pole calyx; all of the supine PCNLs were performed with lower pole access.

The access was mostly performed by the surgeons themselves, since the support of the radiologist was required only sporadically and mostly in cases of prone PCNL.

The calibre of the Amplatz sheath placed in the access tract was mostly the standard 30 Fr; in almost a third of the cases a mini-PCNL approach was performed with an access tract of 24 Fr or less in calibre.

	<b>Prone PCNL</b>	<b>Supine PCNL</b>
<b>No. of patients</b>	52	65
<b>Access performed by (%):</b>		
<b>Urologist</b>	82.7	98.4
<b>Radiologist</b>	17.3	1.6
<b>Site of access (%):</b>		
<b>Lower pole</b>	91.4	100
<b>Middle pole</b>	5.7	0
<b>Upper pole</b>	2.9	0
<b>Method of dilation (%):</b>		
<b>Balloon</b>	66.7	41.5
<b>Telescoping</b>	33.3	58.5
<b>Calibre of the access tract (%):</b>		
<b>30 Fr</b>	76.9	66.2
<b>28 Fr</b>	1.9	1.5
<b>26 Fr</b>	0	1.5
<b>24 Fr</b>	17.9	29.2
<b>22 Fr</b>	1.9	0
<b>18 Fr</b>	1.9	1.5

**Table 10.** *Details of prone and supine PCNLs*

#### *Characteristics of flexible-URS procedures*

In the case of a ureteroscopic approach to the calculi, the ureteral access sheath was used in 66 pts (50.4%) (Table 11).

In case of its placement, the inner calibre of the ureteral access sheath (UAS) was of 9.5, 11, 12 and 13 Fr in 50.8%, 3.1%, 7.7%, and 38.5% of the cases, respectively. Ureteral access sheath length was 35 cm, 45 cm and 55 cm in 55%, 40% and 5% of the cases, respectively. The mean operative time was 65.03±38 and 65.24±40 minutes for UAS and no UAS groups, respectively ( $p=0.2$ ). Subjective visual clarity was defined as good in 84% and 72% of the UAS and no UAS groups, respectively ( $p=0.09$ ). None ureteral stricture was reported in the postoperative period with a mean follow-up of 25 months.

	<b>URS with UAS</b>	<b>URS without UAS</b>
<b>No. of patients</b>	65	62
<b>Length of UAS (%):</b>		
<b>55</b>	5	-
<b>45</b>	40	-
<b>35</b>	55	-
<b>Inner calibre of the UAS (%):</b>		
<b>13 Fr</b>	38.5	-
<b>12 Fr</b>	7.7	-
<b>11 Fr</b>	3.1	-
<b>9.5 Fr</b>	50.8	-
<b>Good visual clarity (%)</b>	84	72
<b>Mean operative time (min)</b>	65	65
<b>Ureteral stricture</b>	0	0

**Table 11.** *Details of flexible URS with or without the use of ureteral access sheath.*

### *Lithotripter devices*

With respect to the lithotripter devices employed during the procedures, pneumatic-ultrasonic lithotripsy was the most common modality of disintegration used in the PCNL group (84% of cases), while holmium laser was the most common lithotripter in the flexible URS group (95% of cases).

### *Complications*

In one case of PCNL the procedure was aborted, while this happened in three cases of flexible URS.

There were 12 major postoperative complications (11%) in group 1 and no major complications in group 2 (Table 12). Basically, the majority of the complications were recorded as Grade II according to the Clavien-Dindo classification of surgical complication: blood loss requiring transfusion occurred in 5% and urinoma was observed in 3% of the PCNL cases.

Grade III complications occurred in 3% of the cases of PCNL, consisting of pleural perforation and arterio-venous fistula.

No Grade IV or V complications were observed.

	<b>Clavien-Dindo classification</b>	<b>PCNL</b>	<b>URS</b>
<b>Complications</b>		12	0
<b>DVT</b>	Grade II	0 (0%)	0 (0%)
<b>Urinoma</b>	Grade II	3 (3%)	0 (0%)
<b>Blood loss requiring transfusion</b>	Grade II	6 (5%)	0 (0%)
<b>Pleural perforation</b>	Grade III	2 (2%)	0 (0%)
<b>Vascular accident</b>	Grade III	0 (0%)	0 (0%)
<b>Visceral</b>	Grade III	0 (0%)	0 (0%)
<b>AVF</b>	Grade III	1 (1%)	0 (0%)
<b>PE</b>	Grade IV	0 (0%)	0 (0%)

**Table 12.** Complications in the two patient groups. DVT: deep vein thrombosis. PE: pulmonary embolism. AVF: arteriovenous fistula

#### *Stenting and follow-up*

The procedures ended with the placement of a ureteral double J stent and/or a nephrostomy tube in 90.5% of group 1 and 91.4% of group 2 (Table 13).

The removal of the nephrostomy tube was performed on average after 2.5 days (SD±1.4); the double J stent was removed after a mean of 17.7 days (SD±22.06).

Follow-up imaging modalities were reported in only 59 cases, with CT KUB scan and the combination of intra-venous pyelogram, regular KUB, and/or kidney ultrasound being the most common imaging tools employed.

	<b>PCNL</b>	<b>URS</b>
<b>Stenting</b>	Nephrostomy tube: 105/116	Double J: 117/128
<b>Stent removal (days)</b>	2.5±1.4	17.7±22.06
<b>Follow-up</b>	25 months (59 cases)	
<b>None</b>	13%	1%
<b>CT KUB</b>	23%	21%
<b>IVP</b>	7%	23%
<b>US</b>	46%	43%
<b>KUB</b>	11%	11%

**Table 13.** Data on stenting and follow-up imaging in the two patient groups



### *Stone-free rates*

Intraoperative stone clearance (no residual fragments) after a single treatment was 88.9% for group 1 and 79.1% for group 2 (Table 14). Overall, 6% of group 1 and 14.7% of group 2 required a second-look procedure, which was markedly more necessary within the patients who had undergone ureteroscopy. In both groups, URS was the auxiliary procedure most often performed, followed by PCNL and ESWL. At 3 months, stone-free rates (no fragments or fragments <2 mm) were 91% and 89% for groups 1 and 2, respectively, as documented by follow-up CT KUB (22%) or a combination of intravenous pyelogram, regular KUB, and/or KUB ultrasound (78%).

	<b>PCNL</b>	<b>URS</b>
<b>Postoperative stone clearance (%)</b>	88.9	79.1
<b>2<sup>nd</sup> look/auxiliary procedures (%)</b>	7 (6%)	19 (15%)
<b>ESWL</b>	1 (33%)	3(17%)
<b>URS</b>	3 (50%)	10 (51%)
<b>PCNL</b>	1 (17%)	6(32%)
<b>Embolization</b>	1 (16%)	0 (0%)
<b>3-month SFR (%)</b>	90.6	92.2
<b>SFR, single stones (%)</b>	46/48 (96%)	69/75 (92%)
<b>SFR, multiple stones (%)</b>	57/65 (87%)	42/50 (84%)

**Table 14.** *Data on stone clearance and stone-free rates (SFR) in the two patient groups*

A subanalysis conducted within the PCNL group showed that there was no significant difference in the 3-month stone-free rates achieved using the prone and supine positions these being 92.3% and 89.2%, respectively.

A subanalysis conducted within the URS group showed that there was no significant difference in the 3-month stone-free rates achieved using the ureteral access sheath or not these being 85% and 72%, respectively.

### Results for patients with lower pole stone between 1 and 2 cm

A statistical analysis has been performed within the subgroups of patients who harboured lower pole stones between 1 and 2 cm in accumulated diameter.

#### *Patient demographics*

There were more patients treated in the PCNL subgroup (Table 15); interestingly, there were a significantly greater number of patients in the URS subgroup with a poorer ASA classification, suggesting that this procedure has also been chosen for its lower risk of morbidity and complications.

	<b>PCNL</b>	<b>URS</b>	<b><i>p</i></b>
<b>No. of patients</b>	82	65	
<b>Gender</b>			
<b>Male</b>	47	41	
<b>Female</b>	35	24	
<b>ASA score</b>			0.007
<b>1</b>	32 (39%)	13 (21%)	
<b>2</b>	35 (43)	31 (51%)	
<b>3</b>	15 (18%)	11 (18%)	
<b>4</b>	0	6 (10%)	
<b>BMI (range)</b>	26	24	0.12
<b>Stone side</b>			
<b>Right</b>	39	25	
<b>Left</b>	43	40	
<b>No. of stone</b>			0.40
<b>Single</b>	43 (52%)	39 (60%)	
<b>Multiple</b>	39 (48%)	26 (40%)	

**Table 15.** Main demographic characteristics of the patients with lower pole stone between 1 and 2 cm

The mean stone size, in terms of surface and higher diameter, was significantly larger in the PCNL subgroup than in the URS subgroups ( $p<0.0001$ ) (Table 16).

For these subgroups of patients, no significant difference in operative time was recorded ( $p=0.22$ ), but there were significant differences in analgesic requirement and hospital stay ( $p<0.0001$ ).

	<b>PCNL</b>	<b>URS</b>	<b><i>p</i></b>
<b>Stone size: surface (mm<sup>2</sup>)</b>	128	78	0.0001
<b>Stone size: higher diam (mm)</b>	15.5	12.9	0.0001
<b>OR time (min)</b>	79	70	0.22
<b>Analgesic requirement</b>	93%	53%	0.0001
<b>Hospital stay (days)</b>	5.4	3	0.0001

**Table 16.** Findings in group 1 (PCNL) and group 2 (URS) patients with lower pole stone between 1 and 2 cm

#### *Complications*

A statistically difference was observed in the rate of complications in the subgroups, with Grade II complications (urinoma and blood loos requiring transfusion) being the most frequent (Table 17).

	<b>PCNL</b>	<b>URS</b>	<b><i>p</i></b>
<b>Abortion</b>	0	2 (3.1%)	0.19
<b>Complications</b>	9	0	0.01
<b>DVT</b>	0 (0%)	0 (0%)	
<b>Urinoma</b>	3 (0%)	0 (0%)	
<b>Blood loss requiring transfusion</b>	5 (5%)	0 (0%)	
<b>Pleural perforation</b>	0 (%)	0 (0%)	
<b>Vascular accident</b>	0 (%)	0 (0%)	
<b>Visceral perforation</b>	0 (0%)	0 (0%)	
<b>AVF</b>	1 (1%)	0 (0%)	
<b>PE</b>	0 (0%)	0 (0%)	

**Table 17.** Complication in the two patient groups with lower pole stone between 1 and 2 cm. DVT: deep vein thrombosis. PE: pulmonary embolism. AVF: arteriovenous fistula

In almost all patients in the URS subgroup (93%) a double J stent was needed, while in the PCNL subgroup a nephrostomy tube was placed in 90% of cases after the procedure.

The removal of the nephrostomy tube was performed on average after 2.7 days (SD  $\pm 1.7$ ); the double J stent was removed after a mean of 21 days (SD  $\pm 28.7$ ).

### *Stenting and follow-up*

During follow-up, the main imaging modalities, as shown in the general analysis, were CT KUB scan and the combination of intra-venous pyelogram, regular KUB and/or KUB ultrasound, the former being most often used in cases of PCNL and the latter in the URS subgroup.

	<b>PCNL</b>	<b>URS</b>
<b>Stenting</b>	Nephrostomy tube: 73/81	Double J: 61/65
<b>Stent removal (days)</b>	2.7 $\pm$ 1.7	21 $\pm$ 28
<b>Follow-up</b>	18 months (49 cases)	
<b>None</b>	11.4%	0%
<b>CT KUB</b>	34%	17%
<b>IVP</b>	7%	15%
<b>US</b>	38%	47%
<b>KUB</b>	13%	20%

**Table 18.** Data on stenting and follow-up imaging in the two patient groups with lower pole stone between 1 and 2 cm

### *Stone-free rates*

In this subanalysis, intraoperative stone clearance (no residual fragments) after a single treatment was again in favour of group 1, in which 88.9% of patients were rendered stone-free versus the 79.1% in group 2 ( $p=0.03$ ).

In group 2, a higher number of patients required an auxiliary procedure (23%, compared to 6% in group 1;  $p=0.03$ ), which in most cases consisted in a second ureteroscopic setting (54%).

At 3 months, stone-free rates (no fragments or fragments  $<2$ mm) were 91.5% and 89.2% for groups 1 and 2, respectively, as documented by follow-up CT KUB (22%) or combination of intravenous pyelogram, regular KUB, and/or KUB ultrasound (78%).

No significant differences were observed between the groups when the stone-free rate was calculated separately for cases with single and cases with multiple lower pole stones (Table 19).

	<b>PCNL</b>	<b>URS</b>	<b><i>p</i></b>
<b>Postoperative stone clearance (%)</b>	88	68	0.03
<b>2<sup>nd</sup> look/auxiliary procedures (%)</b>	5 (6%)	15 (23%)	0.03
<b>ESWL</b>	1 (33%)	2 (13%)	
<b>URS</b>	2 (50%)	8 (54%)	
<b>PCNL</b>	0 (0%)	4 (27%)	
<b>Embolization</b>	1 (16%)	0 (0%)	
<b>3-month SFR (%)</b>	91.5	89.2	0.6
<b>SFR, single stones (%)</b>	41/43 (95%)	38/39 (97%)	0.6
<b>SFR, multiple stones (%)</b>	34/39 (87%)	20/26 (77%)	0.28

**Table 19.** Data on stone clearance and stone-free rates (SFR) in the two patient group with lower pole stone between 1 and 2 cm

## **DISCUSSION**

The management of lower pole stones is one of today's "hot topics" in endourology. Observation, ESWL, URS and PCNL are all possible options that can be offered to patients depending on patient (BMI, comorbidities, presence of pain), anatomical (calyx geometries), and stone (burden, hardness) characteristics.

ESWL is currently still considered the first-line therapy for lower pole stones, even though it has been demonstrated to have the lower stone-free rates among the active removal modalities: in the most popular literature reports, the stone-free rate at 3 months has ranged from 37% to 70%, with poorer results for stones >1 cm, where the stone-free rate does not overcome the 50% [10], [11], [12], [22], [50].

PCNL has a higher success rate, and it is indicated above all for larger lower pole calculi (> 1cm); however, PCNL is more invasive and has a higher associated morbidity than ESWL [51], [52].

With the advances in endourologic technology, flexible ureteroscopy (or flexible URS, or Retrograde Intra-Renal Surgery) has gained popularity as a treatment option that can combine a high rate of success with a low risk of morbidity.

The first experiences published in the literature reported high success rates: after the advent of small (6.7 to 8.5 Fr), active, deflectable ureterorenoscopes and flexible lithotripter devices, these first series showed stone-free rates ranging from 80% to 94% (Table 20) [30], [31], [32], [33], [34], [35].

It is worth noting that the models of ureteroscope employed in these works had a limited degree of flexibility (less than 150°) and a reduced durability (repair needed after an average of 6 to 15 procedures) [40].

The majority of the lower pole stones treated with flexible URS were less than 1 cm in size.

References	No. of patients	No. of lower pole stones (%)	% lower pole success rate for 1 treatment
Elashry et al. [30]	45	37 (65)	94
Gould [31]	86	30 (35)	83
Menezes et al. [33]	37	14 (35)	80
Tawfik et al. [34]	155	23 (31)	87
Grasso et al. [35]	79	90 (100)	82 (residual <2 mm)

**Table 20** Details from various series regarding flexible URS (Modified from Albala et al. [40])

However, the enthusiastic reactions to these series calmed down after the publication of the results of the sole randomized clinical trial available, that compared ESWL and URS in patients with lower pole stones <1 cm. Despite a 15% difference in stone-free rate between the two groups (35% vs 50%, respectively), no statistically significant difference was observed between the two modalities. Likewise, no differences were noted in complication rates, length of hospital stay, or need for secondary procedures. Recovery time, however, was shorter for ESWL than for URS (8 vs 26 days,  $p=0.0006$ ), mostly done for the placement of a ureteral catheter at the end of the ureteroscopic procedures [36].

From then on, many refinements were made in ureteroscopic instrumentation, with improvements in primary and secondary deflection of the new-generation of flexible ureteroscopes for easier access to the lower pole calyx. Furthermore, the introduction of effective intracorporeal lithotripsy devices such as the holmium: YAG laser has greatly enhanced the ability to successfully treat lower pole stones; in the event that calyceal anatomy precludes in-situ fragmentation, nitinol retrieving devices which minimize loss

of deflection of the ureteroscope, can be used to reposition the stone from the lower pole calyx to a less dependent, more readily accessible calyx [53]. Schuster et al. [54] found significantly superior stone-free rates for displaced lower pole stones larger than 1 cm compared with stones treated *in situ*.

Similarly, the use of a ureteral access sheath has been shown to improve stone-free rates, by maintaining low intrarenal pressure, increasing visual clarity, and facilitating stone-fragments extraction [55], [56].

According to the last international guidelines, flexible ureteroscopy is a second-line treatment for kidney stones except for lower pole stones, where it can be considered a reliable alternative to ESWL for stones  $\leq 1.5$  cm.

All of the technological and technical improvements, however, have extended the indication for flexible ureteroscopy in some series: Mariani et al. [47] published their successful experience with 13 patients with 20 to 40 mm kidney stones; in 11 of the 13 cases the stones were harboured partially or totally in the lower pole. Their stone-free rate after 3 months was 92%, with no residual fragments, and reached a 100% when ignoring residual fragments  $< 4$  mm; supplementary settings were needed in 3 cases.

A multi-institutional study has recently reported on the use of flexible ureteroscopy for the management of renal stone burdens from 2 to 3 cm: the Authors retrospectively reviewed the data of 120 patients who underwent flexible ureteroscopy, where 36% of the cases harboured lower pole stones. At 3 months, 63% of patients had a residual stone burden of 0 to 2 mm, and 83% had a residual burden of less than 4 mm [46].

A comparison between flexible ureteroscopy and percutaneous nephrolithotomy was carried out for medium-size (1-2 cm) renal calculi, in a single-institution, retrospective study; among the 15 patients treated with the percutaneous approach and the 12 treated with the ureteroscopic one, there were 7 (46.7%) and 4 (33.3%) patients with lower pole



stones, respectively. The Authors found that stone-free (87% vs 76%;  $p=0.36$ ) and complication (2 vs 0;  $p=0.49$ ) rates were higher for PCNL, but the differences were not statistically significant [57].

Supported by all these and further experiences, it is commonly believed that flexible ureteroscopy could be the treatment of choice above all for lower pole stones  $>1$  cm and  $<2$  cm.

Similar findings are reflected in our results: in our experience URS is a safe and efficacious modality for the treatment of lower pole calculi, that must be considered a valid alternative to PCNL in selected cases.

Even though the two whole populations cannot be directly compared, above all owing to the different stone burdens, some important considerations can be emphasized. The data highlight the possible value of latest generation of flexible URS as an alternative treatment to ESWL for lower pole kidney stones less than 2 cm: in our series, with a stone burden of 1 cm in maximum diameter on average for patients who underwent URS, the postoperative stone clearance rate (no residual fragments) was 79.1% and the stone free rate at 3 months reached 92.2%. These results are substantially better than the poor results achieved with ESWL in this setting, which, as already mentioned, yields stone-free rates ranging from 37% to 70% at 3 months with residual fragments  $<4$  mm.

A comparison between ESWL and flexible URS was not conducted for the difficulty to collect the data of ESWL and for the heterogeneity of the ESWL procedures among the institutions.

The results also confirm the high success rate and relatively low morbidity of modern PCNL for lower pole stones  $> 2$ cm: the postoperative stone clearance rate differs only slightly from the 3-month stone-free rate (with residual fragments  $<2$  mm), at 88.9% and 90.6%, respectively, highlighting the immediate and very high rates achieved

through this approach. Moreover, our results have demonstrated once again that the prone and the supine PCNL positions are equally effective, with 92.3% and 89.2% of stone-free rates at 3 months.

Further interesting data emerge from the subanalysis conducted in patients with lower pole stones between 1 and 2 cm. Even though the two subpopulations differed with regard to stone size, which was still significantly larger in the PCNL group (15.5 vs 12.9 mm on average;  $p=0.0001$ ), a statistical analysis was conducted the same, assuming that this subsetting of patients might be comparable for the restricted range of stone size selected.

Interestingly, patients treated with URS had a significantly higher rate of comorbidities: according to the ASA classification, there were a significantly more higher risk patients in the URS group, in which some patients also scored as ASA 4. These data suggest that in clinical practise, surgeons could consider flexible ureteroscopy as first-line therapy in cases of high surgical risk for comorbidities, among patients with lower pole stones >1 cm.

Another important consideration can be done by comparing the stone-free rates: at 3 months, there was no significant difference between the two groups (91.5% vs 89.2%;  $p=0.6$ ) even though the result for the URS group was achieved after a significantly higher rate of auxiliary procedures (6% vs 23%;  $p=0.03$ ). In particular, a second setting of URS was necessary in more than half of the patients (8 out of 15) requiring a second treatment.

Finally, it is worth remarking on the advantages observed in the URS group compared with the PCNL group in terms of lower rate of analgesic requirement (53% vs 93%;  $p=0.0001$ ), length of hospital stay (3 vs 5.4 days;  $p=0.0001$ ), and reduced complication rate (0 vs 9;  $p=0.01$ ).

To our knowledge, up to now there has been only one other direct comparison of PCNL and flexible ureteroscopy for lower pole stones >1cm. That study was presented at the AUA annual meeting of 2003 and was never published: Kuo et al. [58] from the Lower Pole Study Group presented a poster where 28 patients were prospectively randomized to undergo PCNL or URS for treatment of lower pole calculi sized 11 to 25 mm. Fifteen PCNLs and 13 URSs were compared. The complication rate (2 vs 0;  $p$ = not significant) and operative time were similar (111 vs 125 min;  $p$ =not significant), while hospital stay (2.8 vs 0 days;  $p$ <0.001) and recovery time (23.5 vs 10 days;  $p$ <0.05) were significantly shorter in the URS group. A higher percentage of the URS group required secondary treatment (9.1% vs 25%;  $p$ = 0.59). Finally, no significant difference was recorded for stone-free rate at 3-month postoperatively (66.7% vs 45.6%;  $p$ =0.40).

Most of these findings overlapped our current results, which makes our study important in its field. Even though it was retrospectively conducted with all the multitude of bias that can entail, this is a multi-centre study in which a huge amount of data for a particular group of patients have been collected and analysed.

To date this is the largest published series of patients with lower pole stones treated by percutaneous nephrolithotomy and flexible ureteroscopy.

## **CONCLUSIONS**

These data highlight the value of flexible URS as a very effective and safe option for the treatment of kidney stones; thanks to the latest generation of flexible devices, this new technical approach seems to be a valid alternative in particular for the treatment of lower pole kidney stones less than 2 cm.

In high-volume centres and in the hands of skilled surgeons, this technique can approach the stone-free rates achievable through PCNL in lower pole stones between 1 and 2 cm, with a very low risk of complications.

These findings can constitute the basis for a revision of the international guidelines with respect to the indications for the treatment of lower pole kidney stones; anyway, a randomized clinical trial is needed to confirm this statement.

Furthermore, the results confirm the high success rate and relatively low morbidity of modern PCNL for lower pole stones, with no difference detectable between the prone and supine position.

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