



Guidelines

2007 Guideline for the Management of Ureteral Calculi[☆]

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Introduction

The American Urological Association Nephrolithiasis Clinical Guideline Panel was established in 1991. Since that time, the Panel has developed three guidelines on the management of nephrolithiasis, the most recent being a 2005 update of the original 1994 *Report on the Management of Staghorn Calculi* [1]. The European Association of Urology began their nephrolithiasis guideline project in 2000, yielding the publication of *Guidelines on Urolithiasis*, with updates in 2001 and 2006 [2]. While both documents provide useful recommendations on the management of ureteral calculi, changes in shock-wave lithotripsy technology, endoscope design, intracorporeal lithotripsy techniques, and laparoscopic expertise have burgeoned over the past five to ten years.

Under the sage leadership of the late Dr. Joseph W. Segura, the AUA Practice Guidelines Committee suggested to both the AUA and the EAU that they join efforts in developing the first set of internationally endorsed guidelines focusing on the changes introduced in ureteral stone management over the

last decade. We therefore dedicate this report to the memory of Dr. Joseph W. Segura whose vision, integrity, and perseverance led to the establishment of the first international guideline project.

This joint EAU/AUA Nephrolithiasis Guideline Panel (hereinafter the Panel) performed a systematic review of the English language literature published since 1997 and a comprehensively analyzed outcomes data from the identified studies.

Based on their findings, the Panel concluded that when removal becomes necessary, SWL and ureteroscopy remain the two primary treatment modalities for the management of symptomatic ureteral calculi. Other treatments were reviewed, including medical expulsive therapy to facilitate spontaneous stone passage, percutaneous antegrade ureteroscopy, and laparoscopic and open surgical ureterolithotomy. In concurrence with the previously published guidelines of both organizations, open stone surgery is still considered a secondary treatment option. Blind basketing of ureteral calculi is not recommended. In addition, the Panel was able to provide some guidance

regarding the management of pediatric patients with ureteral calculi. The Panel recognizes that some of the treatment modalities or procedures recommended in this document require access to modern equipment or presupposes a level of training and expertise not available to practitioners in many clinical centers. Those situations may require physicians and patients to resort to treatment alternatives.

This article will be published simultaneously in *European Urology* and *The Journal of Urology*[®]. The Panel believes that future collaboration between the EAU and the AUA will serve to establish other internationally approved guidelines, offering physician and patient guidance worldwide.

Methodology

The Panel initially discussed the scope of the guideline and the methodology, which would be similar to that used in developing the previous AUA guideline. All treatments commonly employed in the United States and/or Europe were included in this report except for those that were explicitly excluded in the previous guideline or newer treatments for which insufficient literature existed. In the analysis, patient data were stratified by age (adult versus child), stone size, stone location, and stone composition. Later, however, the data were found to be insufficient to allow analysis by composition. The outcomes deemed by the Panel to be of particular interest to the patient included the following: stone-free rate, number of procedures performed, stone-passage rate or probability of spontaneous passage, and complications of treatment. The Panel did not examine economic effects, including treatment costs.

Outcomes were stratified by stone location (proximal, mid, and distal ureter) and by stone size (dichotomized as ≤ 10 mm and > 10 mm for surgical interventions, and ≤ 5 mm and > 5 mm for medical interventions and observation where possible; exceptions were made when data were reported, for example as < 10 mm and ≥ 10 mm). The mid ureter is the part of the ureter that overlies the bony pelvis, i.e., the position of the ureter that corresponds to the sacroiliac joint; the proximal ureter is above and the distal ureter is below. Treatments were divided into three broad groups:

1. Observation and medical therapy
2. Shock-wave lithotripsy and ureteroscopy
3. Open surgery, laparoscopic stone removal, or percutaneous antegrade ureteroscopy.

The review of the evidence began with a literature search and data extraction. Articles were selected from a database of papers derived from MEDLINE[®] searches dealing with all forms of urinary tract stones. This database was maintained by a Panel chair. The abstract of each paper was independently reviewed by an American and a European Panel member, and articles were selected for data extraction if any panel member felt it might have useful data. Additional articles were suggested by Panel members or found as references in review articles. In total, 348 citations entered the extraction process. An American and a European Panel member each independently extracted data from each article onto a standardized form. The team members reconciled the extractions, and the data were entered into a Microsoft Access[®] (Microsoft, Redmond, WA) database. The Panel scrutinized the entries, reconciled the inconsistencies in recording, corrected the extraction errors, and excluded some articles from further analysis for the following reasons:

1. The article was included in the previous guideline.
2. The article did not provide usable data on the outcomes of interest.
3. Results for patients with ureteral stones could not be separated from results for those with renal stones.
4. The treatments used were not current or were not the focus of the analysis.
5. The article was a review article of data reported elsewhere.
6. The article dealt only with salvage therapy.

A total of 244 of the 348 articles initially selected had extractable data. Articles excluded from evidence combination remained candidates for discussion in the text of the guideline.

The goal was to generate outcomes tables comparing estimates of outcomes across treatment modalities. To generate an outcomes table, estimates of the probabilities and/or magnitudes of the outcomes are required for each intervention. Ideally, these are derived from a synthesis or combination of the evidence. Such a combination can be performed in a variety of ways depending on the nature and quality of the evidence. For this report, the Panel elected to use the Confidence Profile Method [3], which provides methods for analyzing data from studies that are not randomized controlled trials. The Fast*Pro computer software [4] was used in the analysis. This program provides posterior distributions from meta-analyses from which the median

can be used as a best estimate, and the central 95% of the distribution serves as a confidence interval. Statistical significance at the $p < 0.05$ level (two-tailed) was inferred when zero was not included in the CI.

Because of the paucity of controlled trials found on literature review, however, the outcome for each intervention was estimated by combining single arms from various clinical series. These clinical series frequently had very different outcomes, likely due to a combination of site-to-site variations in patient populations, in the performance of the intervention, in the skill of those performing the intervention, and different methods of determining stone-free status. Given these differences, a random-effects, or hierarchical, model was used to combine the studies.

Evidence from the studies meeting the inclusion criteria and reporting a given outcome was combined within each treatment modality. Graphs showing the results for each modality were developed to demonstrate similarities and differences between treatments.

The available data for procedures per patient would not permit a statistical analysis using these techniques. Unlike the binary outcome of stone-free status (the patient either is or is not stone free), the number of procedures per patient is a discrete rate. In some cases discrete rates can be approximated with a continuous rate, but in order to meta-analyze continuous rates, a measure of variance (e.g., standard deviation, standard error) is needed in addition to the mean. Unfortunately, measures of variance were rarely reported in the studies reviewed. As a result, numbers of procedures per patient were evaluated by calculating the average across studies weighted by the number of patients in each study. Procedures per patient were counted in three totals: primary procedures, secondary procedures, and adjunctive procedures. Primary procedures were all consecutive procedures of the same type aimed at removing the stone. Secondary procedures were all other procedures used to remove the stone. Adjunctive procedures were defined as additional procedures that do not involve active stone removal. One difficulty in estimating the total number of procedures per patient is that secondary and adjunctive procedures were not reported consistently. Since the Panel had decided to analyze primary, secondary, and adjunctive procedures separately, only studies that specifically reported data on a type of procedure were included in estimates for that procedure type. This approach may have overestimated numbers of secondary and adjunctive procedures because some articles

may not have reported that procedures were not performed.

It is important to note that, for certain outcomes, more data were reported for one or another treatment modality. While resulting CIs reflect available data, the probabilities for certain outcomes can vary widely within one treatment modality. In addition, the fact that data from only a few RCTs could be evaluated may have somewhat biased results. For example, differences in patient selection may have had more weight in analyses than differing treatment effects. Nevertheless, the results obtained reflect the best outcome estimates presently available.

Studies that reported numbers of patients who were stone free after primary procedures were included in the stone-free analysis. Studies that reported only the combined number of patients who either were stone free or had "clinically insignificant fragments" were excluded. Many studies did not indicate how or when stone-free status was determined. The stone-free rate was considered at three time points: after the first procedure, after all consecutive procedures using the primary treatment, and after the total treatments.

Initially, the Panel divided complications into three broad categories: acute, long-term, and medical; however, after examining the available evidence, the Panel determined that this breakdown was not useful. Several factors caused inaccuracy in the estimates, but did so in opposite directions, thereby reducing the magnitude of inaccuracy. For example, including studies that did not specifically mention that there were no occurrences of a specific complication may have led to overestimates of complication rates when meta-analyzed. By combining similar complications, the Panel also potentially mitigated the overestimate by making it more likely that a complication in the class was reported. The probability that a patient will have a complication may still be overstated slightly because some patients experienced multiple complications. Since the grouping of complications varies by study, the result of the meta-analysis is best interpreted as the mean number of complications that a patient may experience rather than as the probability of having a complication. Moreover, since reporting of complications is not consistent, the estimated rates given here are probably less accurate than the CIs would indicate. There were insufficient data to permit meaningful meta-analyses of patient deaths.

Data analyses were conducted for two age groups. One analysis included studies of patients ages 18 or

younger (or identified as pediatric patients in the article without specifying age ranges). The adult analysis included all other studies even if children were included.

After the evidence was combined and outcome tables were produced, the Panel met to review the results and identify anomalies. From the evidence in the outcome tables and expert opinion, the Panel drafted the treatment guidelines.

In this guideline the standard, recommendations, and options given were rated according to the levels of evidence published from the U.S. Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research [5]:

- Ia. Evidence obtained from meta-analysis of randomized trials
- Ib. Evidence obtained from at least one randomized trial
- IIa. Evidence obtained from at least one well-designed controlled study without randomization
- IIb. Evidence obtained from at least one other type of well-designed quasi-experimental study
- III. Evidence obtained from well-designed nonexperimental studies, such as comparative studies, correlation studies, and case reports
- IV. Evidence obtained from expert committee reports, or opinions, or clinical experience of respected authorities

As in the previous AUA guideline, the present statements are graded with respect to the degree of flexibility in application. Although the terminology has changed slightly, from the original AUA reports, the current three levels are essentially the same. A “standard” is the most rigid treatment policy. A “recommendation” has significantly less rigidity, and an “option” has the largest amount of flexibility. These terms are defined as follows:

1. **Standard:** A guideline statement is a standard if: (1) the health outcomes of the alternative interventions are sufficiently well known to permit meaningful decisions, and (2) there is virtual unanimity about which intervention is preferred.
2. **Recommendation:** A guideline statement is a recommendation if: (1) the health outcomes of the alternative interventions are sufficiently well known to permit meaningful decisions, and (2) an appreciable, but not unanimous majority agrees on which intervention is preferred.
3. **Option:** A guideline statement is an option if: (1) the health outcomes of the interventions are not

sufficiently well known to permit meaningful decisions, or (2) preferences are unknown or equivocal.

The draft was sent to 81 peer reviewers of whom 26 provided comments; the Panel revised the document based on the comments received. The guideline was submitted first for approval to the Practice Guidelines Committee of the AUA and the Guidelines Office of the EAU and then forwarded to the AUA Board of Directors and the EAU Executive Board for final approval.

The guideline is posted on the American Urological Association website, www.auanet.org, and on the European Association of Urology website, www.uroweb.org. Chapter 1 will be published in *The Journal of Urology* and in *European Urology*.

Results of the Outcomes Analysis

The results of the analysis described in this chapter provide most of the evidentiary basis for the guideline statements. Further details and tables corresponding to the figures in this section are found in Chapter 3 and the Appendixes.

The panel’s attempt to differentiate results for pediatric patients from those for adults was not completely successful as most studies included both adults and children. Where possible, the panel performed two analyses, one including all studies regardless of patient age, and a second including only those studies or groups of patients that were comprised entirely of pediatric patients.

Observation and Medical Therapies

Stone-passage rates

Only limited data were found on the topic of spontaneous passage by stone size. For stones ≤ 5 mm, meta-analysis of five patient groups (224 patients) yielded an estimate that 68% would pass spontaneously (95% CI: 46% to 85%). For stones > 5 mm and ≤ 10 mm, analysis of three groups (104 patients) yielded an estimate that 47% would pass spontaneously (95% CI: 36% to 59%). Details of the meta-analysis are presented in Appendixes 8 and 9.

Two medical therapies had sufficient analyzable data: the calcium channel blocker nifedipine and alpha-receptor antagonists. Analyses of stone-passage rates were done in three ways. The first combined all single arms evaluating the therapies. Using this approach, meta-analysis of four studies of nifedipine (160 patients) yielded an estimate of a 75% passage rate (95% CI: 63% to 84%). Six studies

examined alpha blockers (280 patients); the meta-analysis yielded a stone-passage rate of 81% (95% CI: 72% to 88%).

The second method was a standard Bayesian hierarchical meta-analysis of the available RCTs that compared either nifedipine or alpha blockers to control therapies. The results for nifedipine showed an absolute increase of 9% in stone-passage rates (95% CI: -7% to 25%), which was not statistically significant. Meta-analysis of alpha blockers versus control showed an absolute increase of 29% in the stone-passage rate (95% CI: 20% to 37%), which was statistically significant.

The Panel also attempted to determine whether alpha blockers provide superior stone passage when compared to nifedipine. Two randomized controlled trials were identified. When hierarchical meta-analysis was performed on these two studies, tamsulosin provided an absolute increase in stone-passage rate of 14% (95% CI: -4% to 32%) which was not statistically significant. When nonhierarchical methods were used, the stone-passage improvement increased to 16% (95% CI: 7% to 26%) which was statistically significant. Finally, the Panel used the results of the meta-analyses versus controls (second method above) to determine the difference between alpha blockers and calcium channel blockers. This method allows the use of more data but is risky since it depends on the control groups having comparable results. The analysis yielded a 20% improvement in stone-passage rates with alpha blockers, and the 95% CI of 1% to 37% just reached statistical significance.

Shock-wave Lithotripsy and Ureteroscopy

Stone-free rates were analyzed for a number of variant methods of performing SWL and URS. The Panel attempted to differentiate between bypass, pushback, and in situ SWL as well as differences between lithotripters. Most differences were minimal and did not reach statistical significance. For that reason, the data presented in this Chapter compare the meta-analysis of all forms of SWL to the meta-analysis of all forms of URS. The Panel also attempted to differentiate between flexible and rigid ureteroscopes. Details of the breakdowns by type of SWL and URS are given in Chapter 3. Data were analyzed for both efficacy and complications. Two efficacy outcomes were analyzed: stone-free rate and procedure counts. Complications were grouped into classes. The most important classes are reported herein. The full complication results are in Appendix 10.

Analyses were performed for the following patient groups where data were available.

1. Proximal stones ≤ 10 mm
2. Proximal stones > 10 mm
3. Proximal stones regardless of size
4. Mid-ureteral stones ≤ 10 mm
5. Mid-ureteral stones > 10 mm
6. Mid-ureteral stones regardless of size
7. Distal stones ≤ 10 mm
8. Distal stones > 10 mm
9. Distal stones regardless of size

Analyses of pediatric groups were attempted for the same nine groups, although data were lacking for many groups.

Efficacy Outcomes

Stone-free rates

The Panel decided to analyze a single stone-free rate. If the study reported the stone-free rate after all primary procedures, that number was used. If not and the study reported the stone-free rate after the first procedure, then that number was used. The intention of the Panel was to provide an estimate of the number of primary procedures and the stone-free rate after those procedures. There is a lack of uniformity in the literature in reporting the time to stone-free status, thereby limiting the ability to comment on the timing of this parameter.

The results of the meta-analysis of stone-free data are presented for the overall group in [Table 1](#) and [Fig. 1](#). The results are presented as medians of the posterior distribution (best central estimate) with 95% credible intervals (Bayesian confidence intervals).

This analysis shows that overall, for stones in the proximal ureter ($n = 8,670$), there was no difference in stone-free rates between SWL and URS. However, for proximal ureteral stones < 10 mm ($n = 1,129$), SWL had a higher stone-free rate than URS, and for stones > 10 mm ($n = 523$), URS had superior stone-free rates. This difference arises because the stone-free rate for proximal ureteral stones treated with URS did not vary significantly with size, whereas the stone-free rate following SWL negatively correlated with stone size. For all distal stones, URS yields better stone-free rates overall and in both size categories. For all mid-ureteral stones, URS appears superior, but the small number of patients may have prevented results from reaching statistical significance.

Unfortunately, RCTs comparing these treatments were generally lacking, making an accurate assess-

Table 1 – Stone-Free Rates for SWL and URS in the Overall Population

Overall Population	AUA/EAU Ureteral Stones Guideline Panel			
	Stone Free Rate - Primary Treatments or First Treatment			
	SWL		URS	
	G/P	Med/95% CI	G/P	Med/95% CI
Distal Ureter	50 6981	74% (73–75)%	59 5952	94% (93–95)%
Distal ureter < 10 mm	17 1684	86% (80–91)%	13 1622	97% (96–98)%
Distal ureter > 10 mm	10 966	74% (57–87)%	8 412	93% (88–96)%
Mid Ureter	31 1607	73% (66–79)%	30 1024	86% (81–89)%
Mid ureter < 10 mm	5 44	84% (65–95)%	5 80	91% (81–96)%
Mid ureter > 10 mm	2 15	76% (36–97)%	5 73	78% (61–90)%
Proximal Ureter	41 6428	82% (79–85)%	46 2242	81% (77–85)%
Proximal ureter < 10 mm	14 886	90% (85–93)%	9 243	80% (73–85)%
Proximal ureter > 10 mm	11 293	68% (55–79)%	8 230	79% (71–87)%

G = Number of Groups/Treatment arms extracted; P = Number of Patients in those groups.

ment impossible. However, the posterior distributions resulting from the meta-analysis can be subtracted, yielding a distribution for the difference between the treatments. If the CI of this result does not include zero, then the results may be considered

to be statistically significantly different. This operation is mathematically justifiable but operationally risky: if the patients receiving different treatments are different or if outcome measures are different, results may be meaningless. Nonetheless, the Panel

Stone Free Rates after Primary/First Treatment

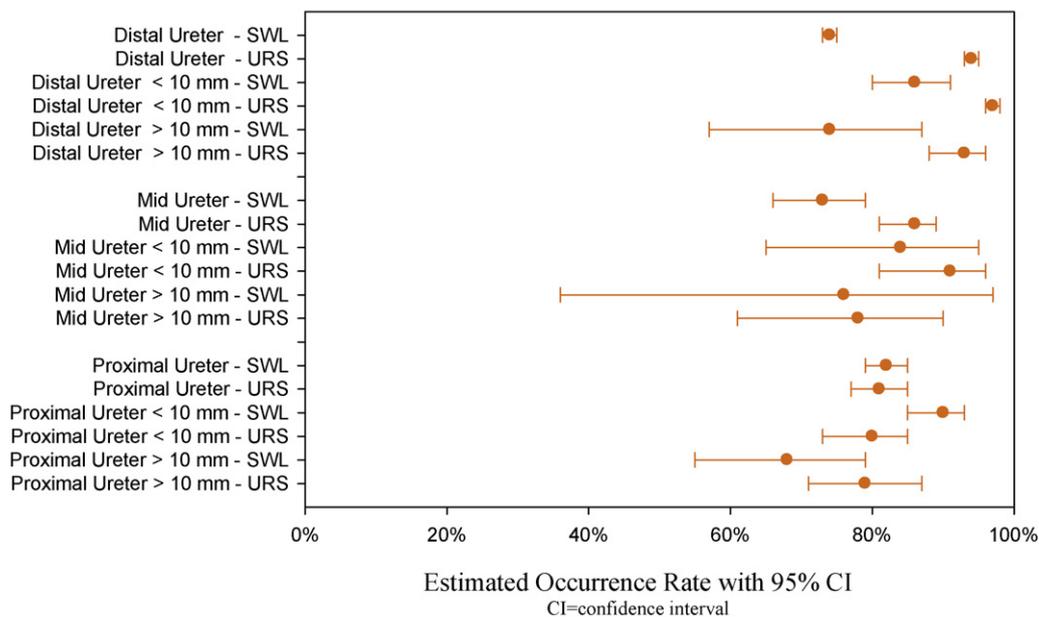


Fig. 1 – Stone-Free Rates for SWL and URS in the Overall Population.

Table 2 – Stone-Free Rates for SWL and URS, Pediatric Population

Pediatric Population	AUA/EAU Ureteral Stones Guideline Panel			
	Stone Free Rate - Primary Treatments or First Treatment			
	SWL		URS	
	G/P	Med/95% CI	G/P	Med/95% CI
Distal Ureter	8	80%	9	92%
	229	(68–90)%	151	(86–96)%
Distal ureter < 10 mm	5	86%	2	86%
	135	(78–92)%	29	(72–98)%
Distal ureter > 10 mm	2	83%		
	26	(58–97)%		
Mid Ureter	6	82%	3	80%
	33	(63–94)%	11	(52–96)%
Mid ureter < 10 mm	4	80%		
	16	(41–98)%		
Mid ureter > 10 mm	1	96%	1	78%
	6	(67–100)%	5	(37–99)%
Proximal Ureter	7	81%	5	57%
	101	(69–90)%	18	(25–85)%
Proximal ureter < 10 mm	5	89%		
	43	(72–98)%		
Proximal ureter > 10 mm	3	63%		
	16	(21–94)%		

G = Number of Groups/Treatment arms extracted; P = Number of Patients in those groups.

performed the comparison and found that URS stone-free rates were significantly better than SWL rates for distal ureteral stones ≤10 mm and >10 mm and for proximal ureteral stones >10 mm. The

stone-free rate for mid-ureteral stones was not statistically significantly different between URS and SWL. The results with URS using a flexible ureteroscope for proximal ureteral stones appear better

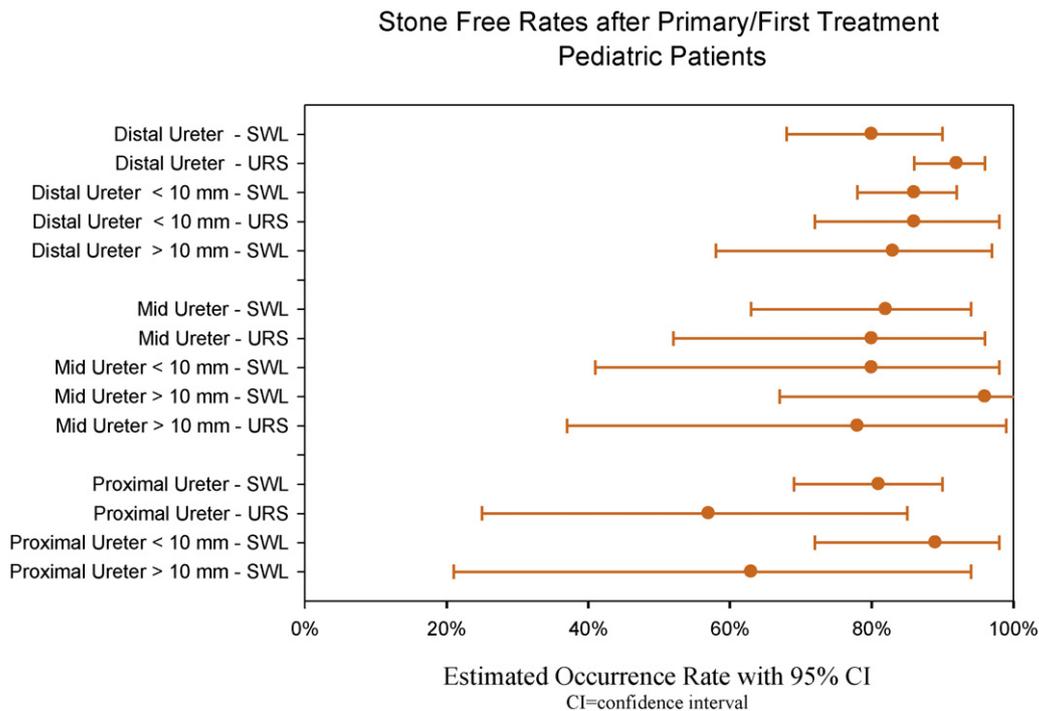


Fig. 2 – Stone-Free Rates for SWL and URS, Pediatric Population.

Table 3 – Procedure Counts for SWL and URS in the Overall Population

Overall Population	Procedure Counts											
	Grps/Pts	#Procs	Grps/Pts	#Procs	Grps/Pts	#Procs	Grps/Pts	#Procs	Grps/Pts	#Procs	Grps/Pts	#Procs
	SWL						URS					
	Primary		Secondary		Adjunctive		Primary		Secondary		Adjunctive	
Distal Ureter	48/7117	1.22	30/5069	0.12	15/3875	0.03	56/5308	1.04	25/5124	0.03	24/2848	0.36
Distal ureter < 10 mm	16/1618	1.34	5/170	0.12			12/1117	1.01	6/492	0.05	4/305	0.88
Distal ureter > 10 mm	11/951	1.44	3/1026	0.10			5/231	1.02	1/69	0.14	1/110	1.00
Mid Ureter	10/291	1.11	9/316	0.18	4/241	0.23	25/686	1.04	15/934	0.07	8/357	0.09
Mid ureter < 10 mm	2/31	1.29					4/32	1.00	2/34	0.34	1/7	1.14
Mid ureter > 10 mm	3/53	1.76					2/18	1.00	1/35	0.31	1/5	0.20
Proximal Ureter	37/5902	1.31	20/2131	0.07	13/1329	0.24	42/1634	1.02	27/1831	0.26	14/1159	0.17
Proximal ureter < 10 mm	16/1243	1.26	5/150	0.14	3/114	0.77	6/68	1.00	4/62	0.39	3/27	0.52
Proximal ureter > 10 mm	10/409	1.49	5/83	0.21	4/45	0.56	5/137	1.07	4/130	0.13	1/14	0.21

than those achieved with a rigid device, but not at a statistically significant level.

Stone-free results for pediatric patients are shown in Table 2 and Fig. 2. The very small number of patients in most groups, particularly for URS, makes comparisons among treatments difficult. However, it does appear that SWL may be more effective in the pediatric subset than in the overall population, particularly in the mid and lower ureter.

Procedure Counts

Procedure counts were captured as three types:

1. Primary procedures – the number of times the intended procedure was performed.
2. Secondary procedures – the number of times an alternative stone removal procedure(s) was performed.

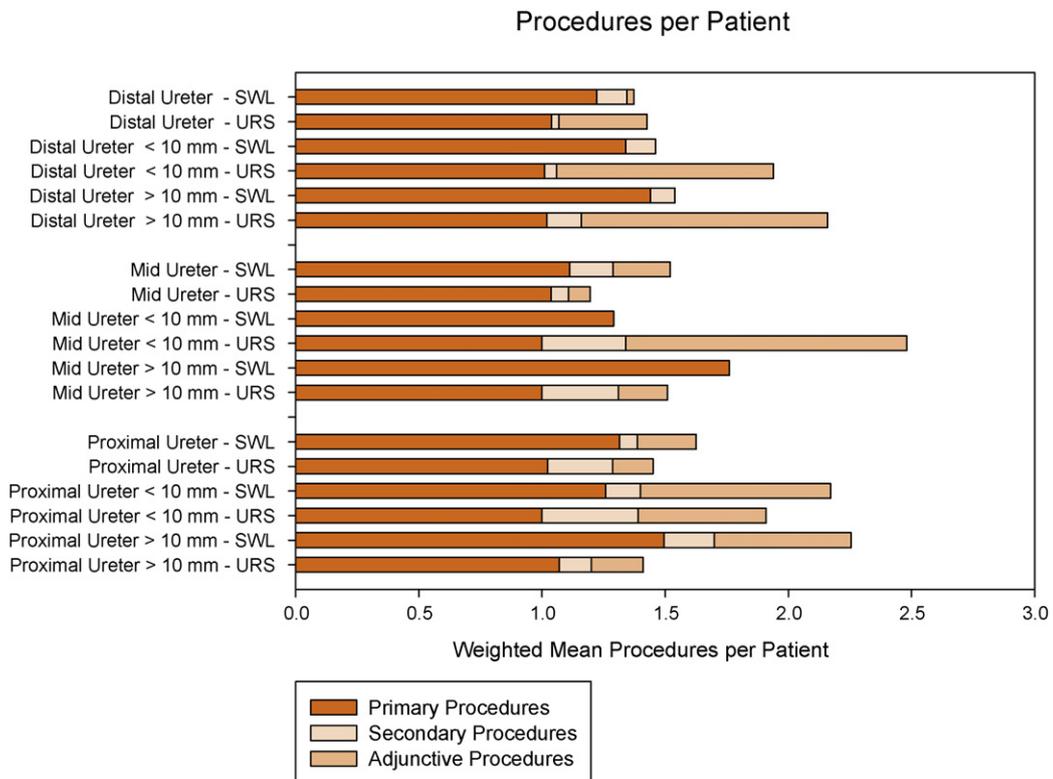


Fig. 3 – Procedure Counts for SWL and URS in the Overall Population.

3. Adjunctive procedures – additional procedures performed at a time other than when the primary or secondary procedures were performed; these could include procedures related to the primary/secondary procedures such as stent removals as well as procedures performed to deal with complications; most adjunctive procedures in the data presented represent stent removals. It is likely that many stent-related adjunctive procedures were underreported, and thus the adjunctive procedure count may be underestimated.

As mentioned in Chapter 2, it was not possible to perform a meta-analysis or to test for statistically significant differences between treatments due to the lack of variance data, and only weighted averages could be computed. The procedure count results for the overall population are shown in Table 3 and Fig. 3. Fig. 3 results are presented as stacked bars.

Procedure count results for pediatric patients are shown in Table 4 and Fig. 4. Again, the numbers of patients with available data were small and did not support meaningful comparisons among treatments.

Complications

The articles were extracted for various complications; however, the Panel believes the following are the most relevant:

1. Sepsis
2. Steinstrasse
3. Stricture
4. Ureteral injury
5. Urinary tract infection

Serious complications, including death and loss of kidney, were sufficiently rare that data were not available to estimate their rates of occurrence. Other complications are listed in Chapter 3.

The complication rates for the overall population by treatment, size, and location are shown in Table 5.

Table 6 summarizes complications for all pediatric groups. Since there are few groups and patients, it was not possible to stratify data by stone size or location. The reported frequencies of pain may be inaccurate because of inconsistent reporting.

Other Surgical Interventions

Small numbers of studies reported on open surgery, laparoscopic stone removal, and percutaneous antegrade ureteroscopy. Because these procedures are usually reserved for special cases, the reported data should not be used to compare procedures with each other or with SWL or URS. As expected, these more invasive procedures yielded high stone-free rates when used.

A single pediatric report provided procedure counts for two patients who had one open procedure each. Two studies reported stone-free rates for children with open procedures ($n = 5$ patients); the computed stone-free rate was 82% (95% CI: 43% to 99%).

The Index Patient

In constructing these guidelines, an “index patient” was defined to reflect the typical individual with a ureteral stone whom a urologist treats. The following definition was created.

Table 4 – Procedure Counts for SWL and URS in the Pediatric Population, All Locations

Pediatric Population	Procedure Counts											
	Grps/ Pts	#Procs	Grps/ Pts	Procs	Grps/ Pts	#Procs	Grps/ Pts	#Procs	Grps/ Pts	#Procs	Grps/ Pts	#Procs
	SWL						URS					
	Primary		Secondary		Adjunctive		Primary		Secondary		Adjunctive	
Distal Ureter	7/212	1.38	4/98	0.08	2/43	0.07	10/185	1.05	7/190	0.09	5/96	0.72
Distal ureter < 10 mm	5/135	1.42	1/14	0.36			2/63	1.00	4/131	0.11	1/51	0.78
Distal ureter > 10 mm	4/26	1.42										
Mid Ureter	4/32	1.44	1/9	0.11			4/18	1.00	2/12	0.17	2/12	0.75
Mid ureter < 10 mm	3/16	1.50					1/7	1.00	1/7	0.14	1/7	0.71
Mid ureter > 10 mm	1/6	1.33					1/5	1.00	1/5	0.20	1/5	0.20
Proximal Ureter	5/83	1.28	3/38	0.05	1/5	0.00	6/27	1.00	7/38	0.34	1/9	1.00
Proximal ureter < 10 mm	5/43	1.19	1/3	0.00	1/3	0.00	1/9	1.00	2/18	0.33	1/9	1.00
Proximal ureter > 10 mm	4/16	1.38	2/2	0.00	2/2	0.00						

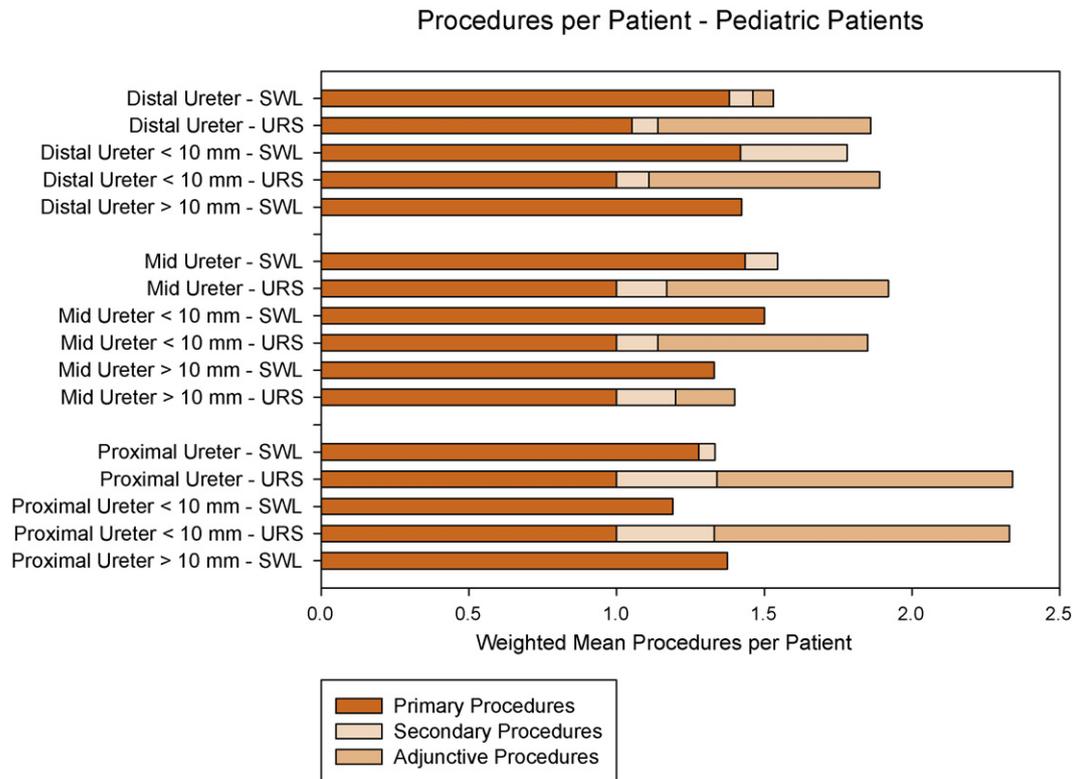


Fig. 4 – Procedure Counts for SWL and URS in the Pediatric Population, All Locations.

The index patient is a nonpregnant adult with a unilateral noncystine/nonuric acid radiopaque ureteral stone without renal calculi requiring therapy whose contralateral kidney functions normally and whose medical condition, body habitus, and anatomy allow any one of the treatment options to be undertaken.

Treatment Guidelines for the Index Patient

For All Index Patients

Standard: Patients with bacteriuria should be treated with appropriate antibiotics.

[Based on Panel consensus/Level IV]

Untreated bacteriuria can lead to infectious complications and possible urosepsis if combined with urinary tract obstruction, endourologic manipulation, or SWL. Urine culture prior to intervention is recommended; screening with dipsticks might be sufficient in uncomplicated cases [2]. In case of suspected or proven infection, appropriate antibiotic therapy should be administered before intervention [6].

Standard: Stone extraction with a basket without endoscopic visualization of the stone (blind basketing) should not be performed.

[Based on Panel consensus/Level IV]

Before the availability of modern ureteroscopes, extraction of distal ureteral stones with a basket with or without fluoroscopy was common. This procedure is, however, associated with an obvious risk of injury to the ureter. It is the expert opinion of the Panel that blind stone extraction with a basket should not be performed, and that intraureteral manipulations with a stone basket should always be performed under direct ureteroscopic vision. Fluoroscopic imaging of the stone alone is not sufficient.

For Ureteral Stones <10 mm

Option: In a patient who has a newly diagnosed ureteral stone <10 mm and whose symptoms are controlled, observation with periodic evaluation is an option for initial treatment. Such patients may be offered an appropriate medical therapy to facilitate stone passage during the observation period.

[Based on review of the data and panel opinion/Level 1A]

Table 5 – Complications Occurrence Rates with SWL and URS, Overall Population

	SWL		URS	
	Groups/Patients	Med/95% CI	Groups/Patients	Med/95% CI
Distal Ureter				
Sepsis	6 2019	3% (2–5)%	7 1954	2% (1–4)%
Steinstrasse	1 26	4% (0–17)%		
Stricture	2 609	0% (0–1)%	16 1911	1% (1–2)%
Ureteral Injury	1 45	1% (0–5)%	23 4529	3% (3–4)%
UTI	3 87	4% (1–12)%	3 458	4% (2–7)%
Mid Ureter				
Sepsis	2 398	5% (0–20)%	4 199	4% (1–11)%
Steinstrasse	1 37	8% (2–20)%		
Stricture	1 43	1% (0–6)%	7 326	4% (2–7)%
Ureteral Injury			10 514	6% (3–8)%
UTI	1 37	6% (1–16)%	1 63	2% (0–7)%
Proximal Ureter				
Sepsis	5 704	3% (2–4)%	8 360	4% (2–6)%
Steinstrasse	3 235	5% (2–10)%	1 109	0% (0–2)%
Stricture	2 124	2% (0–8)%	8 987	2% (1–5)%
Ureteral Injury	2 124	2% (0–8)%	10 1005	6% (3–9)%
UTI	5 360	4% (2–7)%	2 224	4% (1–8)%

The Panel performed a meta-analysis of studies in which spontaneous ureteral stone passage was assessed. The median probability of stone passage was 68% for stones ≤ 5 mm ($n = 224$) and 47% for those > 5 and ≤ 10 mm ($n = 104$) in size (details previously discussed and provided in the appendixes). The Panel recognized that these studies had certain limitations including nonstandardization of the stone size measurement methods and lack of analysis of stone position, stone-passage history, and time to stone passage in some. A meta-analysis of MET was also performed which demonstrated that alpha blockers facilitate stone passage and that the positive impact of nifedipine is marginal. This analysis also indicates that alpha blockers are superior to nifedipine and, hence, may be the preferred agents for MET (details provided in the Appendixes). A similar benefit of MET was demonstrated in a recently published meta-analytic study [7]. The methods of analysis used in this study were somewhat different as the absolute improvement in stone passage was calculated in our study and the

relative improvement in the latter. The vast majority of the trials analyzed in this and our analysis were limited to patients with distal ureteral stones. The majority of stones pass spontaneously within four to six weeks. This was demonstrated by Miller and Kane [8], who reported that of stones ≤ 2 mm, 2 to 4 mm and 4 to 6 mm in size, 95% of those which passed did so by 31, 40, and 39 days, respectively. In a choice between active stone removal and conservative treatment with MET, it is important to take into account all individual circumstances that may affect treatment decisions. A prerequisite for MET is that the patient is reasonably comfortable with that therapeutic approach and that there is no obvious advantage of immediate active stone removal.

Standard: Patients should be counseled on the attendant risks of MET including associated drug side effects and should be informed that it is administered for an “off label” use.

[Based on Panel consensus/Level IV]

Table 6 – Complication Occurrence Rates–Overall, Pediatric Population

Complications of Treatment - PEDIATRIC	SWL		URS	
	Groups/Patients	Med/95% CI	Groups/Patients	Med/95% CI
Bleeding	2	5%	1	17%
Overall Significant complications	206	(0-24)%	66	(9-27)%
Pain	1	1%	5	5%
Retention	38	(0-6)%	65	(1-14)%
Sepsis	3	18%	3	5%
Skin	106	(9-30)%	98	(1-13)%
Stricture	1	2%	1	4%
Ureteral Obstruction	63	(0-7)%	26	(0-17)%
UT1	2	4%	3	3%
Infection	101	(1-12)%	73	(0-9)%
Stent Migration	1	0%		
Ureteral Injury	168	(0-1)%		
Ureteral Obstruction	1	1%		
UT1	25	(0-9)%		
Stricture	4	2%		
Other Long Term CX	283	(1-6)%		
	2	2%		
	63	(0-9)%		
			2	6%
			91	(2-13)%
			1	5%
			25	(0-17)%
			6	6%
			216	(3-10)%
			1	1%
			26	(0-9)%
			1	2%
			12	(0-19)%
			5	5%
			106	(2-11)%
			1	12%
			43	(5-24)%

G = number of groups/treatment arms extracted; P = number of patients in those groups.

Standard: Patients who elect for an attempt at spontaneous passage or MET should have well-controlled pain, no clinical evidence of sepsis, and adequate renal functional reserve.

[Based on Panel consensus/Level IV]

Standard: Patients should be followed with periodic imaging studies to monitor stone position and to assess for hydronephrosis.

[Based on Panel consensus/Level IV]

Standard: Stone removal is indicated in the presence of persistent obstruction, failure of stone progression, or in the presence of increasing or unremitting colic.

[Based on Panel consensus/Level IV]

For Ureteral Stones >10 mm

Although patients with ureteral stones >10 mm could be observed or treated with MET, in most cases

such stones will require surgical treatment. No recommendation can be made for spontaneous passage (with or without medical therapy) for patients with large stones.

For Patients Requiring Stone Removal

Standard: A patient must be informed about the existing active treatment modalities, including the relative benefits and risks associated with each modality.

[Based on Panel consensus/Level IV]

Specifically, both SWL and URS should be discussed as initial treatment options for the majority of cases. Regardless of the availability of this equipment and physician experience, this discussion should include stone-free rates, anesthesia requirements, need for additional procedures, and associated complications. Patients should be informed that URS is associated with a better chance

of becoming stone free with a single procedure, but has higher complication rates.

Recommendation: For patients requiring stone removal, both SWL and URS are acceptable first-line treatments.

[Based on review of the data and Panel consensus/Level 1A-IV (details provided in Chapter 3)]

The meta-analysis demonstrated that URS yields significantly greater stone-free rates for the majority of stone stratifications.

Recommendation: Routine stenting is not recommended as part of SWL.

[Based on Panel consensus/Level III]

The 1997 AUA guideline, *Report on the Management of Ureteral Calculi*, stated that "Routine stenting is not recommended as part of SWL [9]." The 1997 guideline Panel noted that it had become common practice to place a ureteral stent for more efficient fragmentation of ureteral stones when using SWL. However, the data analyzed showed no improved fragmentation with stenting [9]. The current analysis demonstrates similar findings. In addition, studies assessing the efficacy of SWL treatment with or without internal stent placement have consistently noted frequent symptoms related to stents [10-13].

Option: Stenting following uncomplicated URS is optional.

[Based on Panel consensus/Level 1A]

Several randomized prospective studies published since the 1997 AUA guideline document have demonstrated that routine stenting after uncomplicated URS may not be necessary [10,14-19]. It is well documented that ureteral stenting is associated with bothersome lower urinary tract symptoms and pain that can, albeit temporarily, alter quality of life [15-17,20-26]. In addition, there are complications associated with ureteral stenting, including stent migration, urinary tract infection, breakage, encrustation, and obstruction. Moreover, ureteral stents add some expense to the overall ureteroscopic procedure and unless a pull string is attached to the distal end of the stent, secondary cystoscopy is required for stent removal [27].

There are clear indications for stenting after the completion of URS. These include ureteral injury, stricture, solitary kidney, renal insufficiency, or a large residual stone burden.

Option: Percutaneous antegrade ureteroscopy is an acceptable first-line treatment in select cases.

[Based on Panel consensus/Level III]

Instead of a retrograde endoscopic approach to the ureteral stone, percutaneous antegrade access can be substituted [28]. This treatment option is indicated:

- in select cases with large impacted stones in the upper ureter
- in combination with renal stone removal
- in cases of ureteral stones after urinary diversion [29]
- in select cases resulting from failure of retrograde ureteral access to large, impacted upper ureteral stones [30].

Option: Laparoscopic or open surgical stone removal may be considered in rare cases where SWL, URS, and percutaneous URS fail or are unlikely to be successful.

[Based on Panel consensus/Level III]

The 1997 AUA guideline stated that "Open surgery should not be the first-line treatment [9]." The invasiveness and morbidity of open surgery can be avoided. In very difficult situations, however, such as with very large, impacted stones and/or multiple ureteral stones, or in cases of concurrent conditions requiring surgery, an alternative procedure might be desired as primary or salvage therapy. Laparoscopic ureterolithotomy is a less invasive alternative to open surgery in this setting. Comparative series indicate that open surgical ureterolithotomy can be replaced by laparoscopic ureterolithotomy in most situations [31,32]. From the 15 case series of laparoscopic ureterolithotomy included in the Panel's literature review, the median stone-free rate was 88% for the primary treatment. It is notable that this success was achieved when virtually all of the procedures were for large and/or impacted calculi.

Recommendations for the Pediatric Patient

Option: Both SWL and URS are effective in this population. Treatment choices should be based on the child's size and urinary tract anatomy. The small size of the pediatric ureter and urethra favors the less invasive approach of SWL.

[Based on review of data and Panel consensus/Level III]

Recommendations for the Nonindex Patient

Standard: For septic patients with obstructing stones, urgent decompression of the collecting system with either percutaneous drainage or ureteral stenting is indicated. Definitive treatment of the stone should be delayed until sepsis is resolved.

[Based on Panel consensus/Level III]

The compromised delivery of antibiotics into the obstructed kidney mandates that the collecting system be drained to promote resolution of the infection. The choice of drainage modality, whether percutaneous nephrostomy or ureteral stent, is left to the discretion of the urologist, as both have been shown in a randomized trial to be equally effective in the setting of presumed obstructive pyelonephritis/pyonephrosis [33]. Definitive treatment of the stone should be delayed until sepsis has resolved and the infection is cleared following a complete course of appropriate antimicrobial therapy.

Discussion

There are two significant changes in treatment approach that distinguish the present document from the guideline published by the AUA in 1997. The most significant change is the use of retrograde URS as first-line treatment for middle and upper ureteral stones with a low probability of spontaneous passage. This change reflects both the vast technological improvements that have been made during the last decade and the experience and facility that surgeons now have with the procedure. The other change is the establishment of effective MET to facilitate spontaneous stone passage. These advances, the current status of other technologies and procedures, issues related to nonindex patients, and future directions and research germane to this condition will be subsequently discussed.

Medical Expulsive Therapy

There is growing evidence that MET, the administration of drugs to facilitate stone passage, can be efficacious. Studies have demonstrated that this approach may facilitate and accelerate the spontaneous passage of ureteral stones as well as stone fragments generated with SWL [34–38]. Our meta-analysis demonstrated the effectiveness of MET. Nine percent (CI: –7% to 25%) more patients receiving nifedipine passed their stones than did controls in our meta-analysis, a difference that was not

statistically significant. In contrast, a statistically significant 29% (CI: 20% to 37%) more patients passed their stones with alpha blocker therapy than did control patients. These findings indicate that alpha blockers facilitate ureteral stone passage while nifedipine may provide a marginal benefit. Therefore, the Panel feels that alpha blockers are the preferred agents for MET at this time. Similar findings have been reported by Hollingsworth and associates⁷, who recently performed a meta-analysis of studies involving alpha blockers or nifedipine in patients with ureteral stones. The differences in methodology from our study have been previously mentioned. Patients given either one of these agents had a greater likelihood of stone passage than those not receiving such therapy. The pooled-risk ratios and 95% CIs for alpha blockers and calcium channel blockers were 1.54 (1.29 to 1.85) and 1.90 (1.51 to 2.40) [7]. The benefit of adding corticosteroids was reported to be small [7,37]. Tamsulosin has been the most common alpha blocker utilized in these studies. However, one small study demonstrated tamsulosin, terazosin, and doxazosin as equally effective in this setting [39]. These studies also demonstrated that MET reduces the stone-passage time and limits pain. The beneficial effects of these drugs are likely attributed to ureteral smooth muscle relaxation mediated through either inhibition of calcium channel pumps or alpha-1 receptor blockade. Further prospective and randomized studies are warranted to determine the patients who best respond to MET. A large, multicenter, randomized, placebo-controlled study has recently been funded in the United States for this purpose. Patients with ureteral stones in all segments of the ureter will be randomized to tamsulosin or placebo.

Shock-wave Lithotripsy

Shock-wave lithotripsy was introduced to clinical practice as a treatment for ureteral stones in the early 1980s. Today, even with the refinement of endourologic methods for stone removal such as URS and PNL, SWL remains the primary treatment for most uncomplicated upper urinary tract calculi. The meta-analysis published by the AUA Nephrolithiasis Guideline Panel in 1997 documented that the stone-free rate for SWL for proximal ureteral stones overall was 83% (78 studies, 17,742 patients). To achieve this result, 1.40 procedures were necessary per patient. The results were very similar in the distal ureter, with a stone-free rate of 85% (66 studies, 9,422 patients) necessitating 1.29 primary and secondary procedures per patient. There was no significant difference between various SWL

techniques (SWL with pushback, SWL with stent or catheter bypass, or SWL in situ). Consequently, the Panel suggested that the use of a ureteral stent to improve stone-free rates was not warranted. This observation is also confirmed by the present analysis. However, there may be circumstances such as when the stone is small or of low radiographic density where a stent or ureteral catheter (sometimes using a contrast agent) may help facilitate localization during SWL. The Panel considered complications of SWL for ureteral stones to be infrequent.

The current meta-analysis analyzed SWL stone-free results for three locations in the ureter (proximal, mid, distal). The SWL stone-free results are 82% in the proximal ureter (41 studies, 6,428 patients), 73% in the mid ureter (31 studies, 1,607 patients), and 74% in the distal ureter (50 studies, 6,981 patients). The results in the 1997 guideline, which divided the ureter into proximal and distal only, reported SWL stone-free results of 83% and 85%, respectively. The CIs for the distal ureter do not overlap and indicate a statistically significant worsening of results in the distal ureter from the earlier results. No change is shown for the proximal ureter. The cause of this difference is not clear. Additional procedures also were infrequently necessary (0.62 procedures per patient for proximal ureteral stones, 0.52 for mid-ureteral stones, and 0.37 for distal ureteral stones). Serious complications were again infrequent. As expected, stone-free rates were lower and the number of procedures necessary were higher for ureteral stones >10 mm in diameter managed with SWL.

The outcomes for SWL for ureteral calculi in pediatric patients were similar to those for adults, making this a useful option, particularly in patients where the size of the patient (and ureter/urethra) may make URS a less attractive option.

The newer generation lithotriptors with higher peak pressures and smaller focal zones should, in theory, be ideal for the treatment of stones in the ureter but instead have not been associated with an improvement in stone-free rates or a reduction in the number of procedures needed when this treatment approach is chosen. In fact, the SWL stone-free rates for stones in the distal ureter have declined significantly when compared with the 1997 AUA analysis. The explanation for the lack of improvement in SWL outcomes is unknown.

Although ureteroscopic stone removal is possible with intravenous sedation, one clear advantage of SWL over URS is that the procedure is more easily and routinely performed with intravenous sedation or other minimal anesthetic techniques. Therefore,

for the patient who desires treatment with minimal anesthesia, SWL is an attractive approach.

Shock-wave lithotripsy can be performed with the aid of either fluoroscopy or ultrasound. While some stones in the proximal and distal ureter can be imaged with US, this imaging modality clearly limits SWL application in the ureter when compared to fluoroscopy. However, a combination of both fluoroscopy and US can facilitate stone location and minimize radiation exposure.

As documented in the 1997 AUA report, there appears to be little, if any, advantage to routine stenting when performing SWL for ureteral stones.

Concerns have been raised, too, regarding the use of SWL to treat distal ureteral calculi in women of childbearing age because of the theoretical possibility that unfertilized eggs and/or ovaries may be damaged. To date, no objective evidence has been discovered to support such concerns, but many centers require that women age 40 or younger be fully informed of the possibility and give their consent before treatment with SWL [40-44].

Ureteroscopy

Ureteroscopy has traditionally constituted the favored approach for the surgical treatment of mid and distal ureteral stones while SWL has been preferred for the less accessible proximal ureteral stones. With the development of smaller caliber semirigid and flexible ureteroscopes and the introduction of improved instrumentation, including the holmium:YAG laser, URS has evolved into a safer and more efficacious modality for treatment of stones in all locations in the ureter with increasing experience world-wide [45,46]. Complication rates, most notably ureteral perforation rates, have been reduced to less than 5%, and long-term complications such as stricture formation occur with an incidence of 2% or less [47]. Overall stone-free rates are remarkably high at 81% to 94% depending on stone location, with the vast majority of patients rendered stone free in a single procedure (Fig. 1 and Chapter 3).

In 1997, the AUA Nephrolithiasis Clinical Guideline Panel recommended SWL for <1 cm stones in the proximal ureter and either SWL or URS for >1 cm proximal ureteral stones [9]. With improved efficacy and reduced morbidity currently associated with ureteroscopic management of proximal ureteral stones, this modality is now deemed appropriate for stones of any size in the proximal ureter. Indeed, the current analysis revealed a stone-free rate of 81% for ureteroscopic treatment of proximal ureteral stones, with surprisingly little difference in

stone-free rates according to stone size (93% for stones <10 mm and 87% for stones >10 mm). The flexible ureteroscope is largely responsible for improved access to the proximal ureter; superior stone-free rates are achieved using flexible URS (87%) compared with rigid or semirigid URS (77%). These stone-free rates are comparable to those achieved with SWL.

The middle ureter poses challenges for all surgical stone treatments; the location over the iliac vessels may hinder access with a semirigid ureteroscope, and identification and targeting of mid-ureteral stones for SWL has proved problematic due to the underlying bone. Despite the limitations, ureteroscopic management is still highly successful; a stone-free rate of 86% was demonstrated in the current analysis, although success rates declined substantially when treating larger stones (>10 mm) compared with smaller stones (78% versus 91%, respectively).

Ureteroscopic treatment of distal ureteral stones is uniformly associated with high success rates and low complication rates. An overall stone-free rate of 94% was achieved with either a rigid or semirigid ureteroscope, with little drop off in stone-free rates when treating larger stones. On the other hand, flexible URS was less successful than rigid or semirigid URS for distal ureteral stones, particularly those >10 mm, likely due to difficulty maintaining access within the distal ureter with a flexible ureteroscope.

A number of adjunctive measures have contributed to the enhanced success of ureteroscopic management of ureteral calculi. Historically, stones in the proximal ureter have been associated with lower success rates than those in the mid and distal ureter, in part because the proximal ureter is more difficult to access and stone fragments often become displaced into the kidney where they may be difficult to treat. Improved flexible ureteroscopes and greater technical skill, along with the introduction of devices to prevent stone migration [48,49] have improved the success of treating proximal ureteral stones.

Although the efficacy of URS for the treatment of ureteral calculi has been amply shown, the need for a ureteral stent with its attendant morbidity has biased opinion towards SWL in some cases. Clearly, SWL is associated with fewer postoperative symptoms and better patient acceptance than URS. However, a number of recent prospective, randomized trials have shown that for uncomplicated URS, the ureter may be left unstented without undue risk of obstruction or colic requiring emergent medical attention [10,14–19].

Ureteroscopy can also be applied when SWL might be contraindicated or ill-advised. Ureteroscopy can be performed safely in select patients in whom cessation of anticoagulants is considered unsafe [50]. In addition, URS has been shown to be effective regardless of patient body habitus. Several studies have shown that morbidly obese patients can be treated with success rates and complication rates comparable to the general population [51,52]. Finally, URS can be used to safely simultaneously treat bilateral ureteral stones in select cases [53–55].

Percutaneous Antegrade Ureteroscopy

Percutaneous antegrade removal of ureteral stones is a consideration in selected cases, for example, for the treatment of very large (>15 mm diameter) impacted stones in the proximal ureter between the ureteropelvic junction and the lower border of the fourth lumbar vertebra [30,56]. In these cases with stone-free rates between 85% and 100%, its superiority to standard techniques has been evaluated in one prospective randomized [57] and in two prospective studies [28,30]. In a total number of 204 patients, the complication rate was low, acceptable, and not specifically different from any other percutaneous procedure.

Percutaneous antegrade removal of ureteral stones is an alternative when SWL is not indicated or has failed [58] and when the upper urinary tract is not amenable to retrograde URS; for example, in those with urinary diversion [29] or renal transplants [59].

Laparoscopic and Open Stone Surgery

Shock-wave lithotripsy, URS, and percutaneous antegrade URS can achieve success for the vast majority of stone cases. In extreme situations or in cases of simultaneous open surgery for another purpose, open surgical ureterolithotomy might rarely be considered [60,61]. For most cases with very large, impacted, and/or multiple ureteral stones in which SWL and URS have either failed or are unlikely to succeed, laparoscopic ureterolithotomy is a better alternative than open surgery if expertise in laparoscopic techniques is available. Both retroperitoneal and transperitoneal laparoscopic access to all portions of the ureter have been reported. Laparoscopic ureterolithotomy in the distal ureter is somewhat less successful than in the middle and proximal ureter, but the size of the stone does not appear to influence outcome.

Although highly effective, laparoscopic ureterolithotomy is not a first-line therapy in most cases

because of its invasiveness, attendant longer recovery time, and the greater risk of associated complications compared to SWL and URS.

Special Considerations

Pregnancy

Renal colic is the most common nonobstetric cause of abdominal pain in pregnant patients requiring hospitalization. The evaluation of pregnant patients suspected of having renal colic begins with ultrasonography, as ionizing radiation should be limited in this setting. If the US examination is unrevealing and the patient remains severely symptomatic, a limited intravenous pyelogram may be considered. A typical regimen includes a preliminary plain radiograph and two films, 15 minutes and 60 minutes following contrast administration. Noncontrast computed tomography is uncommonly performed in this setting because of the higher dose of radiation exposure. Magnetic resonance imaging can define the level of obstruction, and a stone may be seen as a filling defect. However, these findings are nonspecific. In addition, there is a paucity of experience with using this imaging modality during pregnancy [62].

Once the diagnosis has been established, these patients have traditionally been managed with temporizing therapies (ureteral stenting, percutaneous nephrostomy), an approach often associated with poor patient tolerance. Further, the temporizing approach typically requires multiple exchanges of stents or nephrostomy tubes during the remainder of the patient's pregnancy due to the potential for rapid encrustation of these devices.

A number of groups have now reported successful outcomes with URS in pregnant patients harboring ureteral stones. The first substantial report was by Ulvik, et al [63] who reported on the performance of URS in 24 pregnant women. Most patients had stones or edema, and there were no adverse sequelae associated with ureteroscopic stone removal. Similar results have been reported by Lifshitz and Lingeman [64] and Watterson et al [65] who found that the ureteroscopic approach was both diagnostic and therapeutic in pregnant patients with very low morbidity and the need for only short-term ureteral stenting, if at all, afterwards. When intracorporeal lithotripsy is necessary during ureteroscopic treatment of calculi in pregnant patients, the holmium laser has the advantage of minimal tissue penetration, thereby theoretically limiting risk of fetal injury.

Pediatrics

Both SWL and URS are effective treatment alternatives for stone removal in children. Selection of the most appropriate treatment has to be based on the individual stone problem, the available equipment and the urologist's expertise in treating children. Children appear to pass stone fragments after SWL more readily than adults [66-71].

Ureteroscopy may be used as a primary treatment or as a secondary treatment after SWL in case of poor stone disintegration. Less efficient SWL disintegration might be seen in children with stones composed of cystine, brushite and calcium oxalate monohydrate or when anatomic abnormalities result in difficulties in fluoroscopic or ultrasonographic visualization of the stone [72-74].

One of the main problems with pediatric URS is the size of the ureteroscope relative to the narrow intramural ureter and the urethral diameter. This problem has lately been circumvented by the use of smaller ureteroscopes, for example, mini or needle instruments as well as small flexible semirigid or rigid ureteroscopes and pediatric (6.9 Fr) cystoscopes. With the availability of 4.5 and 6.0 Fr semirigid ureteroscopes, a 5.3 Fr flexible ureteroscope and a holmium:YAG laser energy source, instrument-related complications have become uncommon [73-75]. However, the utilization of proper technique remains the most important factor for generating successful outcomes in this population. Percutaneous stone removal is also possible in pediatric patients with comparable indications to those in adults. Such an approach might be considered for stone removal in children with a malformation of the lower urinary tract.

Cystine stones

Individuals with cystinuria are considered nonindex patients by the Panel for a variety of reasons. There are limited data regarding treatment outcomes in this group [76-83]. In vitro studies also show that these stones are commonly resistant to SWL, although the degree of resistance may be variable [77,78]. The structural characteristics of these stones are thought to contribute to their decreased SWL fragility. In addition, some of these stones may be barely opaque on standard imaging or fluoroscopy, potentially compromising shock-wave focusing. In contrast to SWL, technology currently utilized for intracorporeal lithotripsy during URS, including the holmium laser, ultrasonic and pneumatic devices, can readily fragment cystine stones [81].

Certain imaging characteristics may predict SWL outcomes for this patient group. Bhatta and colleagues reported that cystine stones having a rough-

appearing external surface on plain film imaging were more apt to be fragmented with shock-wave energy than those with a smooth contour [82]. Kim and associates reported that the computed tomography attenuation coefficients of the latter were significantly higher than the rough-type stones [83]. Other types of stones with higher attenuation values have also been demonstrated to be resistant to shock-wave fragmentation [84].

Patients with this rare genetic disorder typically have their first stone event early in life, are prone to recurrent stones, and are consequently subject to repetitive removal procedures. In addition, patients with cystinuria are at risk for developing renal insufficiency over time [85,86]. Prophylactic medical therapy and close follow-up can limit recurrence.

Uric acid stones

Uric acid calculi are typically radiolucent, thus limiting the ability to treat such patients using in situ SWL. However, this approach may be possible with devices that use US if the stone can indeed be localized. When properly targeted, these stones fragment readily with SWL. Uric acid stones have lower computed tomography attenuation values, and can usually be distinguished from calcium, cystine, and struvite calculi [87]. The presence of a low attenuation or a radiolucent stone, particularly in a patient with a low urinary pH, should lead the clinician to suspect this diagnosis. Manipulation of the urinary pH with oral potassium citrate, sodium citrate, or sodium bicarbonate to a level ranging from 6.0 to 7.0 may obviate the need for surgical intervention. Moreover, this medical treatment may allow stone dissolution in patients whose symptoms are controllable, should prevent the development of future uric acid stones, and has also been shown to enhance stone clearance with SWL [88]. Medical expulsive therapy may be administered concomitantly. Ureteroscopy is a very effective method of treating patients who are not candidates for observation [89].

Research and Future Directions

Ten years have elapsed since the last publication of the AUA guidelines, and one year since the EAU recommendations on ureteral stones. Extensive cooperation between AUA and EAU Panel members has produced this unique collaborative report. This venture should provide the foundation for future collaborative efforts in guideline development.

The Panel encountered a number of deficits in the literature. While the management of ureteral

stones remains commonly needed, few RCTs were available for data extraction. The data were inconsistent, starting from the definition of stone sizes and ending with variable definitions of a stone-free state. These limitations hinder the development of evidence-based recommendations.

To improve the quality of research, the Panel strongly recommends the following:

- conducting RCTs comparing interventional techniques like URS and SWL
- conducting pharmacological studies of stone-expulsion therapies as double-blinded RCTs
- reporting stone-free data without inclusion of residual fragments
- using consistent nomenclature to report stone size, stone location, stone-free rates, time point when stone-free rate is determined, or method of imaging to determine stone-free rate
- reporting data stratified by patient/stone characteristics, such as patient age, stone size, stone location, stone composition, gender, body mass index, and treatment modality
- reporting all associated treatments including placement of ureteral stents or nephrostomies
- using standardized methods to report acute and long-term outcomes
- developing methods to predict outcomes for SWL, URS, and MET
- providing measures of variability such as standard deviation, standard error, CI, or variance with corresponding average patient numbers
- reporting raw data to facilitate meta-analyses

The Panel suggests focusing on the following issues in future investigations:

- investigating the proposed current efficacy problems of second and third generation shock-wave machines and developing approaches to improve SWL
- determining the safety of each technique with respect to acute and long-term effects
- investigating the promising medical stone expulsion in basic research studies and in clinical trials to unravel the underlying mechanisms and to optimize the treatment regimens
- addressing issues such as patient preferences, quality of life, and time until the patient completed therapy when evaluating treatment strategies. To date, only a few studies have addressed patient preference [90–92].
- although largely dependent on different health systems, addressing cost-effectiveness

Conflicts of interest

G.M. Preminger has a financial interest and/or other relationship with Boston Scientific and Mission Pharmacal.

D.G. Assimos has a financial interest and/or other relationship with Medical Review in Urology and Altus.

J.E. Lingeman has a financial interest and/or other relationship with Boston Scientific, Lumenis, Olympus, Storz Medical and Cook Urological.

S.Y. Nakada has a financial interest and/or other relationship with Cook Urological.

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J.S. Wolf Jr. has a financial interest and/or other relationship with Omeros Corporation.

Acknowledgements and Disclaimers

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The mission of the Panel was to develop either analysis- or consensus-based recommendations, depending on the type of evidence available and Panel processes to support optimal clinical practices in the management of ureteral calculi. This document was submitted to 81 urologists and other health care professionals for peer review. After revision of the document based upon the peer review comments, the guideline was submitted for approval to the Practice Guidelines Committee of the AUA and the Guidelines Office of the EAU. Then it was forwarded to the AUA Board of Directors and the EAU Executive Board for final approval. Funding of the Panel and of the PGC was provided by the AUA and the EAU, although Panel members received no remuneration for their work. Each member of the PGC and of the Panel furnished a current conflict of interest disclosure to the AUA.

The final report is intended to provide medical practitioners with a current understanding of the principles and strategies for the management of ureteral calculi. The report is based on an extensive review of available professional literature as well as clinical experience and expert opinion. Some of the medical therapies currently employed in the management of ureteral calculi have not been approved

by the US Food and Drug Administration for this specific indication. Thus, doses and dosing regimens may deviate from that employed for the Food and Drug Administration-approved indications, and this difference should be considered in the risk-versus-benefit assessment.

This document provides guidance only, and does not establish a fixed set of rules or define the legal standard of care. As medical knowledge expands and technology advances, this guideline will change. Today it represents not absolute mandates but provisional proposals or recommendations for treatment under the specific conditions described. For all these reasons, the guideline does not preempt physician judgment in individual cases. Also, treating physicians must take into account variations in resources, and in patient tolerances, needs and preferences. Conformance with the guideline reflected in this document cannot guarantee a successful outcome.

Abbreviations and Acronyms

AUA	=	American Urological Association
CI	=	confidence interval
CIs	=	credible intervals
EAU	=	European Association of Urology
Gps/Pts	=	groups/patients
Med	=	medium
MET	=	medical expulsive therapy
#Procs	=	No. procedures
RCTs	=	randomized controlled trials
SWL	=	shock-wave lithotripsy
URS	=	ureteroscopy
US	=	ultrasound
UTI	=	urinary tract infection

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