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Qualitative Review of Clinical Guidelines for Medical and Surgical Management of Urolithiasis: Consensus and Controversy 2020

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Purpose: Many major guidelines across the globe address the medical and surgical management of urolithiasis. We elected to compare and contrast the recommendations among the 5 most highly cited guidelines on stone disease to offer insights on where evidence has created a consensus and where there remains ongoing controversy and hence a need for the pursuit of studies that will provide a higher level of evidence.

Materials and Methods: We reviewed the American Urological Association 2019 medical and 2016 surgical guidelines, the 2016 Canadian Urological Association guidelines, the 2020 European Association of Urology guidelines, the 2019 National Institute for Health and Care Excellence and the 2019 Urological Association of Asia guidelines. Tables correlating guideline statements by topic were created, and a comparative analysis was conducted to ascertain consensus and discordance.

Results: Comparative analysis of recommendations from the American Urological Association guidelines to the Canadian Urological Association, European Association of Urology, National Institute for Health and Care Excellence guidelines and Urological Association of Asia revealed a high consensus surrounding the medical management of stones. In terms of the surgical management of stones, there is high consensus regarding the treatment of ureteral stones including medical expulsive therapy using alpha blockers, not prestenting for uncomplicated ureteroscopy and employment of either ureteroscopy or shockwave lithotripsy as first line treatment. There is high consensus among the American Urological Association, European Association of Urology, National Institute for Health and Care Excellence and Urological Association of Asia guidelines regarding renal stone treatment. The Canadian Urological Association does not have guidelines on the management of renal stones. Unlike the American Urological Association and National Institute for Health and Care Excellence, the Canadian Urological Association and European Association of Urology make specific recommendations regarding selection of patients for shockwave lithotripsy procedures, including stone density, skin-to-stone distance, treatment rate, acoustic coupling and postshockwave lithotripsy use of medical expulsive therapy.

Conclusions: There are many areas of consensus and only minor areas of conflict among the most up-to-date American Urological Association, Canadian Urological Association, European Association of Urology, National Institute for Health and Care Excellence and Urological Association of Asia guidelines on the medical and surgical management of stone disease. Conflicts among guidelines and areas of low evidence, such as followup imaging strategies and stone

Abbreviations and Acronyms

AUA = American Urological Association
CP = clinical principle
CT = computerized tomography
CUA = Canadian Urological Association
EAU = European Association of Urology
EO = expert opinion
NICE = National Institute for Health and Care Excellence
PCNL = percutaneous nephrolithotomy
RCT = randomized control trial
SWL = shockwave lithotripsy
UAA = Urological Association of Asia
UAS = ureteral access sheath
URS = ureteroscopy

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surveillance, the use of a ureteral access sheath in ureteroscopy and guidance on the use of miniaturized percutaneous nephrolithotomy, are opportunities for novel, impactful high grade clinical studies.

Key Words: kidney calculi, ureteral calculi, urolithiasis, consensus, evidence-based practice

THE medical and surgical treatment of urolithiasis is complex. Though certain aspects of management are universal as a result of high quality research and evidence-based practice, there still exists divergence in areas of care due to the lack of high level evidence and a preponderance of expert opinion. Worldwide, urologists have compiled guidelines on how to properly manage patients with urolithiasis both medically and surgically.

However, the methodologies upon which evidence are classified differ among the guideline. For example, the American Urological Association includes well-conducted randomized control trials and "strong observational studies," such as cohort studies and case-control studies, in its highest level of evidence (ie Grade A). In contradistinction, the European Association of Urology,[1] Canadian Urological Association[2,3] and Urological Association of Asia[4] assign the highest grade only to meta-analyses of RCTs or well-designed individual RCTs. Well-designed observational studies are graded second tier levels of evidence at best. Even when guidelines converge, the strength of recommendation may differ based on what the experts of the respective associations designate as high level evidence.

In the absence of high level evidence, the guidelines diverge greatly as they become dependent on expert opinions (ie "eminence-based medicine").[5] The areas in which expert opinions predominate are fields for studies that would yield higher levels of evidence. Accordingly, we elected to review the consensus and conflicts in recommendations among the 5 most highly cited guidelines on stone disease: the AUA,[6–8] EAU,[1] CUA[2,3] National Institute of Health and Care Excellence[9] and Urological Association of Asia.[4]

METHODS

A web search was performed for urolithiasis guidelines using keywords: "kidney stone", "urolithiasis", "guidelines". Each national and international urology society webpage was reviewed. In addition, a PubMed® search was performed with search terms: "kidney stone", "urolithiasis", "guidelines". Guidelines were included in the analysis if they were in the English language and published after 2015.

All guideline recommendations and the cited supportive evidence grades were independently assessed (LX, RA). Guideline statements were then correlated by topic and a comparative analysis was conducted to ascertain consensus and conflict (PJ). Consensus was defined as complete agreement among all guidelines for a given topic.

RESULTS

Review of websites based on inclusion and exclusion criteria revealed 5 published guidelines: the AUA 2016 Surgical Management and 2019 update to the 2014 Medical Management guidelines,[6–8] 2016 CUA guidelines,[2,3] 2019 NICE guidelines,[9] 2020 EAU guidelines, and 2019 UAA guidelines.[4] The results are further divided into medical management and surgical management; however, the CUA guidelines do not address the surgical management of renal stones.[2,3] The EAU and UAA guidelines are the most comprehensive.[1,4] The NICE guidelines only highlight key points that have moderate or high level evidence and thus omit multiple topics.[9]

Grades of Evidence

Comparative analysis of the 5 guidelines for grading evidence revealed several striking differences, which resulted in myriad recommendations (Appendix 1). There is agreement between the CUA and EAU guidelines that Level 1, the highest level of evidence, is reserved for meta-analyses of RCTs.[1–3] The UAA may also imply that its highest grade of Level 1 evidence must come from "multiple large-scale RCTs."[4] However, the CUA states that a "good quality RCT" could, in and of itself, also provide Level 1 evidence, whereas the EAU deems this "Level 1b" evidence and the UAA deems this Level 2 evidence.[1–4] However, the AUA states its highest level of evidence "Grade A" as well-conducted RCTs and "exceptionally strong observational studies." Its lowest quality evidence "Grade C" includes "observational studies that provide conflicting information or design problems (eg, small sample size)."[6–8] However, the CUA and EAU eschew these observational studies; their lowest, nonexpert opinion Level 3 evidence is defined as "good-quality retrospective case-control studies" or "well-designed nonexperimental studies…and case reports" (Appendix 1).[1–3]

Per the AUA, any level of evidence can engender a "Strong" recommendation, while only Grade C evidence engenders "Weak" or "Conditional" recommendations.[6–8] Likewise, per the EAU, all levels of evidence (Level 1-4) can engender "Strong" recommendations while only Level 3-4 evidence or no evidence engender "Weak" recommendations

(Appendix 2).[1] Similarly, per the UAA, multiple levels of evidence (Level 1-4) can engender Grade A recommendations whereas Levels 2 to 5 evidence can engender Grade B or "Grade C1" evidence (Appendix 2). Unique to UAA is its readiness to recommend against certain practices, with "Grade C2" defined as a "not recommend" and Grade D defined as "recommended not to do" (Appendix 2).[4]

NICE Guidelines, in contrast to the other 4 guidelines, employed a completely different set of evidence quality assessment and recommendation grading system. They predominantly considered RCTs, with a few observational studies, for recommendation establishment and graded evidence based upon systematic review principles for risk of bias assessment (Appendix 1). Furthermore, recommendations from NICE are descriptive (ie high, moderate, low and very low) rather than numbered.[9]

Medical Management

Comparative analysis of the AUA medical management of urolithiasis guidelines to the respective CUA, EAU, NICE and UAA guidelines revealed high consensus with few areas of discordance (fig. 1). For the initial evaluation, 4 of the guidelines recommend obtaining detailed medical and dietary history, serum chemistries, and urinalysis +/- urine culture (AUA: CP; CUA: Grade C; EAU: Strong; NICE: omitted; UAA: Grade B). Additional metabolic testing is recommended by the AUA, CUA, EAU and UAA (omitted in NICE) with regards to the utilization of 24-hour urine collections. However, they differed regarding which patient populations should undergo a metabolic evaluation. All guidelines recommend high risk or recurrent stone formers to undergo metabolic evaluation, while the AUA and CUA also recommend optional workup for interested first-time stone formers. In addition, the AUA recommends either 1 or 2, 24-hour urine collections; however, the CUA, EAU and UAA recommend 2 collections (AUA: Grade B; CUA: Grade C; EAU: not specified; UAA: Grade B). If stones are captured, all guidelines recommend stone analysis by infrared spectroscopy or x-ray diffraction (AUA: CP; CUA: Grade C; EAU: not specified; NICE: No Evidence).[1,3,4,8,9]

Lifestyle and dietary modifications play a significant role in the medical management of urolithiasis. All guidelines recommend fluid intake to achieve urine output greater than 2.5 liters per day (AUA: Grade B; CUA: Grade B; EAU: Strong; NICE: Low to Very Low; UAA: Grade A). For general stone prevention, guidelines recommend diets high in fruits and vegetables (AUA: EO; CUA: Grade C; EAU: not specified; NICE: omitted; UAA: Grade B).[1,3,4,8,9]

For calcium stone formers, guidelines recommend dietary calcium intake of 1,000 to 1,200 mg daily (AUA: Grade B; CUA: Grade C; EAU: not specified; NICE: omitted; UAA: Grade C1). While there was no distinction based upon different calcium stone compositions, all followup discussions stated that the evidence was based on calcium oxalate stone formers albeit without any separation for monohydrate or dihydrate composition. All guidelines recommend restriction of sodium intake for stone prevention; however, each guideline varies in their upper limit. The AUA and CUA recommend less than 2,300 mg of sodium daily, while the EAU and UAA recommend less than 3,000 to 5,000 mg of sodium daily (AUA: Grade B; CUA: Grade B; EAU: Strong; UAA: Grade C1). The NICE guidelines recommend less than 6,000 mg of sodium daily (NICE: High to Moderate).[1,3,4,8,9]

For patients with recurrent calcium stones, the treatment of hypercalciuria is with a thiazide diuretic among all of the guidelines (AUA: Grade B; CUA: Grade A–B; EAU: Strong; NICE: Moderate to Very Low; UAA: Grade B). None of the guidelines recommend a specific thiazide. Potassium citrate is recommended as adjunctive therapy to thiazides in recurrent calcium stone formers (AUA: Grade B; CUA: Grade A–B; EAU: Strong; NICE: Moderate to Very Low; UAA: Grade B).[1,3,4,8,9]

All guidelines recommend that calcium stone formers who also have hypocitraturia be prescribed alkali citrate therapy (AUA: Grade B; CUA: Grade A–B; EAU: Strong; NICE: Moderate to Very Low; UAA: Grade C1). In addition to alkali citrate, the EAU and UAA also specifically highlight sodium bicarbonate as a viable first line therapy (EAU: Strong); there is no additional discussion regarding the hypothetical possible risk of an increase in urinary calcium.[1,3,4,8,9]

Only the EAU further provides specific pharmacological recommendations for calcium phosphate stone formers: hypercalciuric patients should be given thiazide diuretic (EAU: Strong) and acidify urine (L-Methionine) if urinary pH is high (EAU: Weak).[1]

For patients with calcium stones and hyperuricosuria, allopurinol is recommended by the AUA, CUA and EAU (AUA: Grade B; CUA: Grade B; EAU: Strong; UAA: not specified). The EAU also recommends Febuxostat as a second line agent (EAU: Strong). In this regard, it should be noted that in 2019 the U.S. Food and Drug Administration issued a safety alert because clinical trial data revealed an increased risk of cardiac death compared to allopurinol. Finally, the AUA is the only guideline to recommend empiric therapy with thiazide and/or citrate in recurrent calcium stone formers in the absence of any discernible metabolic abnormalities (AUA: Grade B).[1,2,8]

For uric acid stone formers, guidelines recommend limiting animal protein intake (AUA: EO; CUA:

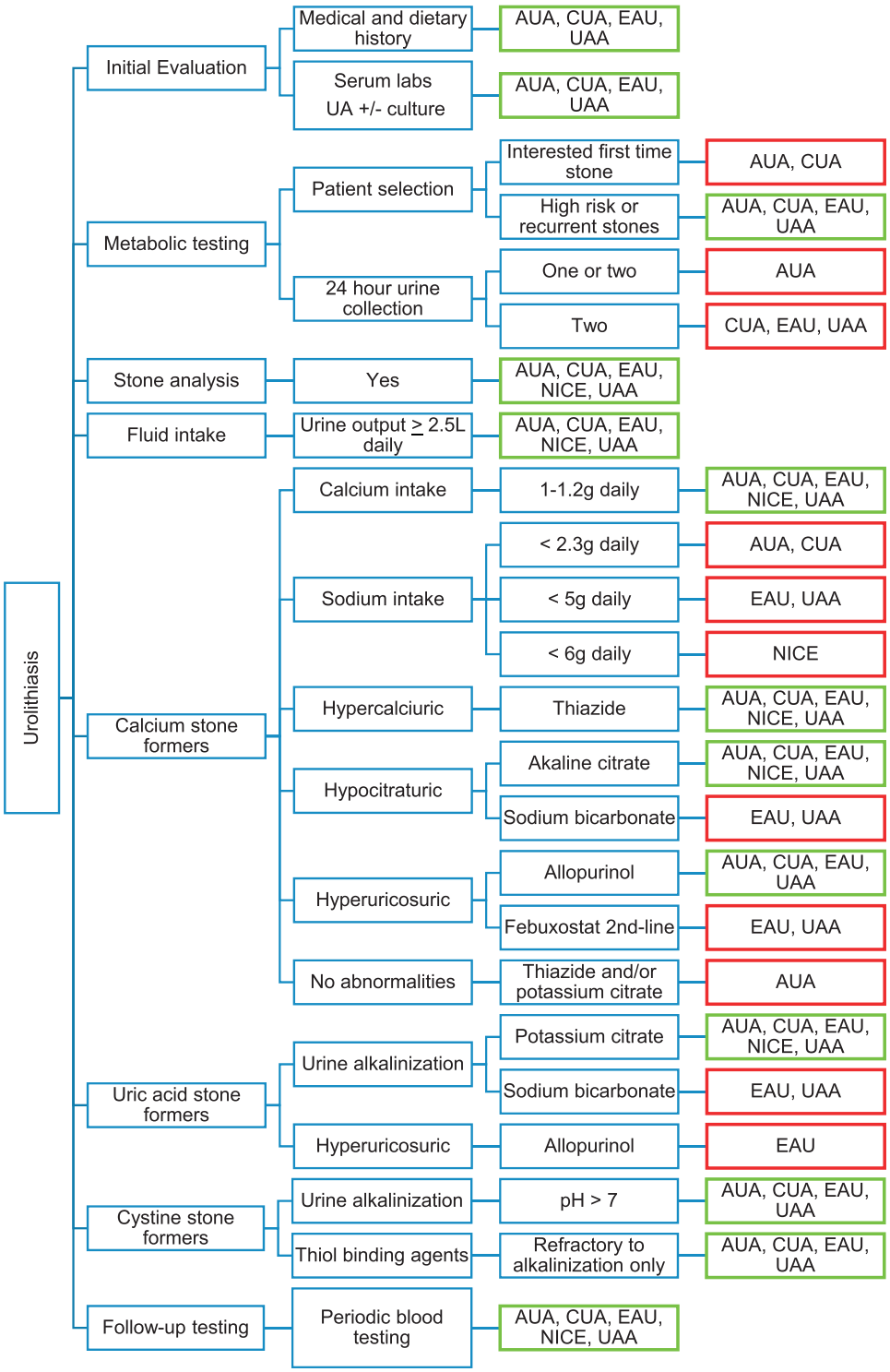


Figure 1. Consensus tree diagram for medical management of urolithiasis

Grade C; EAU: Strong; UAA: omitted). Urine alkalization with alkaline citrates is recommended almost universally (AUA: EO; CUA: Grade B; EAU: Strong; UAA: Grade A). The AUA specifically recommends against routine use of allopurinol as first line therapy for uric acid stone formers (AUA: EO), while in contradistinction, the EAU supports allopurinol as first line treatment in the presence of hyperuricosuria in uric acid stone formers (EAU: Strong).[1,2,8]

For cystine stone formers, the CUA, EAU and UAA recommend increased fluid intake to achieve urine output of at least 3L (CUA: not specified; EAU: Strong; UAA: not specified). The AUA guidelines do not discuss increased fluid intake specific to cystine

stone formers. All guidelines recommend urinary alkalization to achieve a urine pH 7-7.5 (AUA: EO; CUA: Grade C; EAU: Strong; UAA: Grade B). If refractory to alkalization, then thiol binding agents may be initiated (AUA: EO; CUA: Grade C; EAU: Strong; UAA: Grade B). The NICE guidelines do not address cystine stone management.[1,2,4,8]

After initiation of dietary and/or medical therapy, all guidelines recommend followup 24-hour urine collections to assess the response to therapy. The AUA and CUA recommend a followup 24-hour urine collection within 6 months while the EAU and UAA recommend followup within 8 to 12 weeks to assess the response to therapy (AUA: EO; CUA: not specified; EAU: not specified; NICE: omitted; UAA: Grade B). Periodic blood tests are recommended to monitor for any adverse effects of pharmacological therapy (AUA: Grade A; CUA: not specified; EAU: not specified; NICE: not specified; UAA: not specified). All guidelines include a recommendation for periodic followup imaging studies to assess for stone growth or new stone formation. However, no specific recommendations are made regarding timing or imaging modality (AUA: EO; CUA: not specified; EAU: not specified; UAA: Grade A).[1,2,4,8,9]

Surgical Management

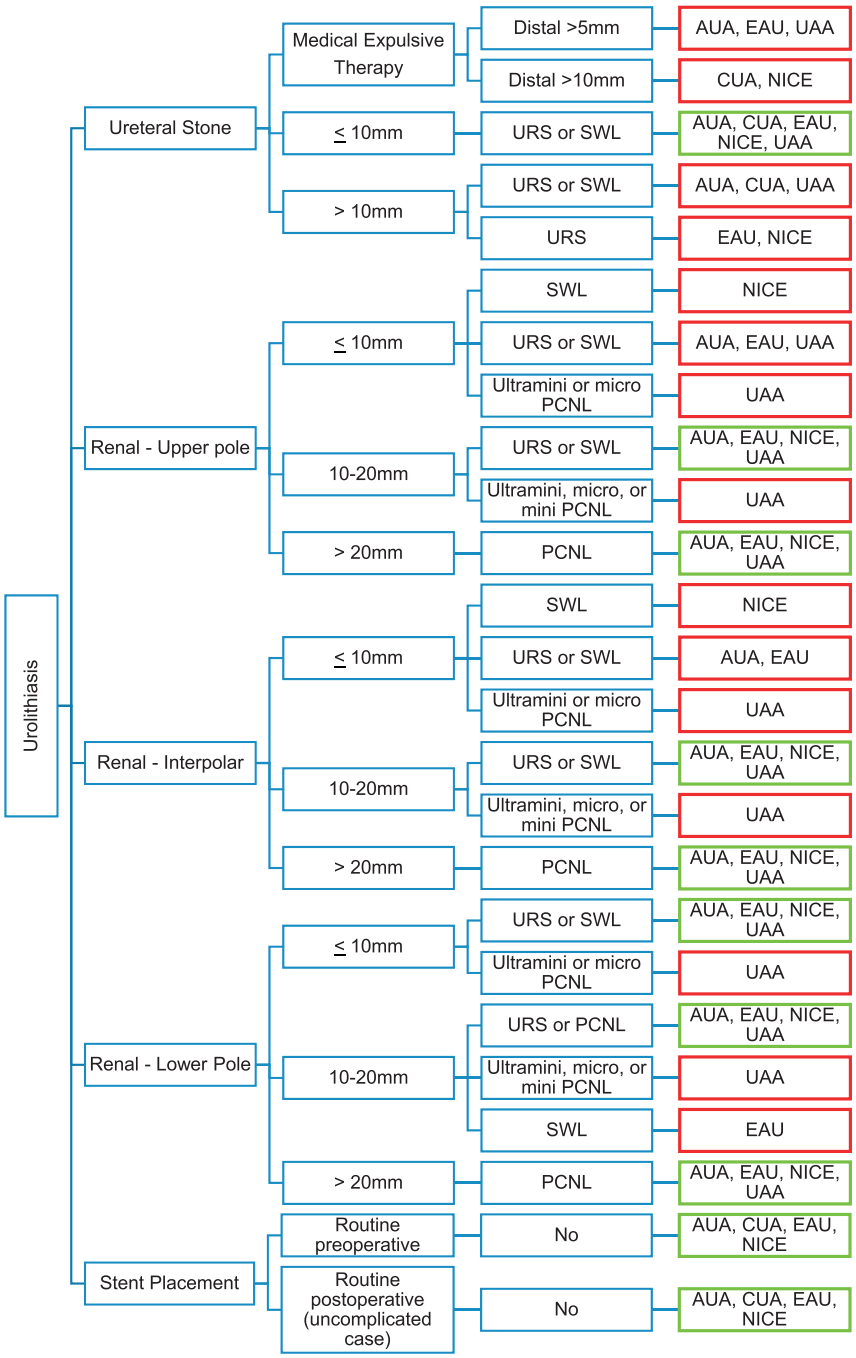
For the surgical management of stones, there is nearly universal consensus regarding the treatment of renal and ureteral stones among all guidelines (fig. 2). The CUA addresses ureteral stone management but omits surgical management of renal stones. Preoperative imaging recommendations vary among the guidelines. The AUA, EAU and UAA suggest that noncontrast computerized tomography is helpful to determine the optimal surgical intervention (AUA: Grade C; EAU: Strong; UAA: Grade B). A noncontrast CT is recommended prior to performing a PCNL (AUA: Grade C; EAU: Strong; UAA: Grade B). In addition, both guidelines recommend use of contrast enhanced studies if in the surgeon's judgment the renal collecting system anatomy needs further assessment (AUA: Grade C; EAU: Strong). Furthermore, the AUA guidelines recommend functional imaging studies (with DTPA [diethylenetriaminepentaacetic acid] or MAG-3 [mercaptuacetyltriglycine]) if there is suspicion of significant renal function loss (AUA: Grade C).[1,2,4,6,7]

The AUA, CUA, EAU and UAA emphasize the importance of obtaining a urinalysis and/or urine culture prior to surgical intervention to rule out a urinary tract infection (AUA: Grade B; CUA: not specified; EAU: Strong). In the setting of an acute ureteral obstruction with infection, the recommendation is for prompt urinary drainage with either a ureteral stent or nephrostomy tube and proceeding with definitive stone treatment at a later date (AUA: Grade C; CUA: Grade B; EAU: Strong; NICE: omitted; UAA: Grade A). Patients undergoing surgical stone intervention should be given appropriate antibiotic prophylaxis (AUA: CP; EAU: Strong).[1,2,4,6,7]

There is high consensus with the use of alpha blockers for medical expulsive therapy for distal ureteral stones. The AUA, EAU and UAA recommend use of alpha blockers for distal ureteral stones greater than 5 mm while the CUA and NICE recommend its use for distal ureteral stones less than 10 mm (AUA: Grade B; CUA: Grade A; EAU: Strong; NICE: High to Very Low; UAA: Grade A).[1,2,4,6,7,9]

For the management of a ureteral stone that either fails to pass or is not a candidate for medical expulsive therapy, all guidelines recommend ureteroscopy or SWL if the stone is less than or equal to 10 mm (AUA: Grade B; CUA: Grade B; EAU: Strong; NICE: Moderate to Very Low; UAA: Grade B). For stones >10 mm, the AUA, CUA and UAA recommend use of either URS or SWL, while the EAU and NICE recommend only ureteroscopy as first line therapy (AUA: Grade B, CUA: Grade B, EAU: Strong; NICE: Moderate to Very Low; UAA: Grade B). The EAU guidelines are further stratified by the stone's location in the ureter. However, there was no difference in the recommendations. In contrast, with regard to a ureteral stone's location, the AUA recommends URS as first line therapy for mid and distal ureteral stones (AUA: Grade B). The AUA and CUA guidelines note that SWL has lower stone clearance rates compared to URS for ureteral stones >10 mm. In addition, 4 guidelines specifically counsel that patients need to be informed that while URS provides a higher stone-free rate, it also has a higher complication rate than SWL (AUA: Grade B; CUA: Grade B; EAU: Strong; UAA: Grade B).[1,2,4,6,7,9]

Other factors influencing treatment modality of ureteral stones include suspected stone composition, stone density and skin-to-stone distance. AUA states that URS is preferred over SWL for suspected cystine or uric acid ureteral stones (AUA: EO). CUA recommends patients with known cystine, calcium oxalate monohydrate and brushite stones are likely better treated with URS. In addition, the CUA and UAA state that ureteral stones with a density >1,000 HU or skin-to-stone >10 cm are better served with URS (CUA: Grade B; UAA: not specified). Also, the EAU recommends URS over SWL for obese patients (EAU: Strong). The NICE guidelines do not comment on any of these variables. The CUA specifically recommends the use of holmium laser for lithotripsy of ureteral stones while the EAU states that holmium:YAG is the most effective lithotripsy system for flexible URS (Strong), pneumatic and ultrasound systems can also be used with disintegration efficacy in rigid URS. The



Note – the CUA does not have published guidelines on management of renal stones

Figure 2. Consensus tree diagram for first line treatment of ureteral and renal stones

AUA specifically recommends against the use of the electrohydraulic lithotripter for ureteral stones (AUA: EO; CUA: Grade B; EAU: Strong).[1,2,4,6,7,9]

Guidelines for the surgical treatment of renal stones are more heterogeneous. The AUA, EAU and UAA guidelines divide first line therapy based upon stone location and size. The NICE guidelines delineate management based upon stone size only. There are no CUA guidelines for the management of renal stones. Only the UAA addresses the clinical indications for ultra, micro, and miniPCNL. The NICE guidelines recommend SWL for renal stones <10 mm, URS or SWL for renal stones between 10 and 20 mm, and PCNL for stones >20 mm for first line therapy (NICE: Moderate to Very Low). For stones <10 mm, regardless of location, the AUA, EAU and UAA recommend URS or SWL, while UAA also recommends the use of ultraPCNL and microPCNL. For stones >20 mm, regardless of location, all 4 guidelines recommend PCNL as first line therapy

(AUA: Grade C; EAU: Strong; NICE: Very Low; UAA: Grade B). For lower pole stones between 10 and 20 mm, the AUA and EAU guidelines recommend URS or PCNL (AUA: Grade B; EAU: Strong). The EAU also states the use of SWL is acceptable in these cases provided favorable conditions (eg broad infundibulopelvic angle, short infundibulum, short skin-to-stone distance, wide infundibulum, or shockwave favorable stone composition; EAU: not specified). UAA also recommends the use of ultraPCNL, microPCNL and miniPCNL.[1,4,6,7,9]

All guidelines recommend against the routine placement of stents prior to surgical intervention; however, prior stenting facilitates ureteroscopic access and URS outcomes. (AUA: Grade B; CUA: Grade B; EAU: Strong; NICE: Moderate to Very Low; UAA: Omitted).[1,2,6,7,9]

After uncomplicated ureteroscopy, all guidelines recommend against the use of routine stent placement (AUA: Grade A; CUA: Grade B; EAU: Strong; NICE: Moderate to Very Low; UAA: Omitted). The CUA specifically recommends against the routine use of stents with SWL, which can impede stone fragment passage and lower stone-free rates. Furthermore, they do not decrease the risk of steinstrasse or infection after SWL (CUA: Grade A). The EAU, on the other hand, mentions that while routine use of internal stents before SWL does not improve stone-free rates nor lower the number of auxiliary treatments, it may reduce formation of steinstrasse. After uncomplicated PCNL, nephrostomy tube placement is optional per the AUA, while the EAU recommends either tubeless (without nephrostomy tube) or totally tubeless (without nephrostomy tube or ureteral stent; AUA: Grade C; EAU: Strong). The NICE committee and UAA did not recommend one approach over the other.[1,2,4,6,7,9]

Unlike the AUA and NICE, the CUA, EAU and UAA make recommendations regarding selection of patients for SWL procedures, including stone density, skin-to-stone distance, treatment rate, acoustic coupling, and postSWL use of medical expulsion therapy. There is universal consensus between the CUA and EAU guidelines with regard to these specific parameters (fig. 3). Both guidelines recommend proper use of a coupling agent and other technical considerations for high efficiency of SWL (CUA: Grade C; EAU: Strong).[1,2,4]

Additional surgical principles are highlighted in each of the guidelines. In particular, the AUA guidelines recommend a safety wire should be used for "most endoscopic procedures" (AUA: EO). The AUA guidelines also specifically state that clinicians must use normal saline irrigation for PCNL and URS (AUA: Grade B). Only the CUA guidelines provide recommendation on the use of ureteral access sheaths for flexible ureteroscopy. The CUA

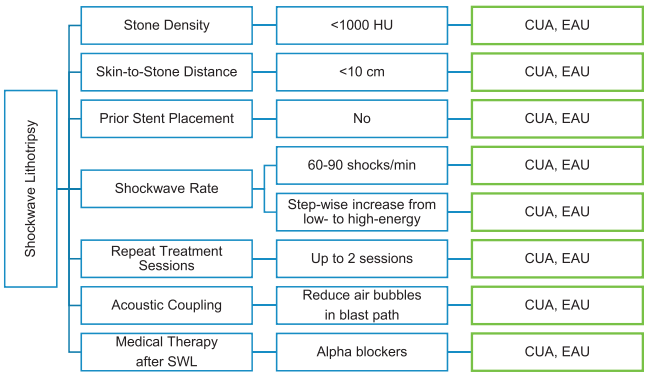


Figure 3. Consensus tree diagram for use of shockwave lithotripsy.

states that a UAS remains a "highly useful tool in the armamentarium of the urologist during flexible ureteroscopy." However, more studies are needed "to determine safety, define cost-effectiveness, and determine clinical impact of the reduction of ureteral and intrarenal pressures" (CUA: Grade C). The AUA and EAU discuss the benefits and disadvantages of UAS but provide no specific recommendations regarding its use. UAA does not comment on use of UAS.[1,2,4,6,7]

All the guidelines except for NICE highlight recommendations on treatment of pregnant patients. The CUA and EAU provide further recommendations on patients with urinary diversions. The AUA, EAU and UAA also provide recommendations regarding management of pediatric urolithiasis.[1,2,4,6,7,9]

DISCUSSION

Urolithiasis affects 1 in 11 individuals in the United States.[10] At least half of the individuals who have had a stone will experience another.[11] As such, the management of urolithiasis spans beyond the acute management of the initial stone, calling for medical measures to prevent recurrence and effective surgical therapy.

Guidelines are established based on peer-reviewed published evidence-based medicine. They are designed to facilitate clinicians in the management of a given disease. However, in the absence of high grade levels of evidence, there is often discordance among guidelines published by different urology organizations due to a default to local eminence-based experience. Fortunately, our review of the 5 major guidelines found high levels of consensus. This concordance likely reflects contemporary guidelines incorporating the same recently published data. Areas of controversy were not surprisingly generated from lower levels of evidence.

The areas of controversy highlight topics with a paucity of high level evidence in need of future research. To wit, the AUA recommends utilizing any imaging modality (plain film, ultrasound or CT) for followup without any recommendations of timing. This is similarly omitted or poorly discussed in the other guidelines. The absence of strong recommendations has led to widespread disparity of reported therapeutic success rates since imaging modalities other than fine-cut CT scans have a high degree of false negatives, thereby inflating the "stone-free" rate. In addition, none of the guidelines suggested how "stone-free" status should be defined, further adding to the wide range of reported postoperative rates of success.

We also note that none of the guidelines make strong recommendations on the type of imaging modality that should be used when assessing patients' stone burden. Noncontrast CT is generally held as the gold standard for imaging as it has higher sensitivity and specificity when compared to x-ray and ultrasound.[12,13] However, with noncontrast CT there is an understandable concern for radiation exposure.[13] Recent RCTs demonstrate that low dose CT and now ultralow dose CT may mitigate these concerns, although these prospective study cohorts remain relatively small.[14–16]

Another area of controversy is the use of allopurinol in uric acid stone formers. AUA recommends against it as first line therapy while the EAU makes a strong recommendation for use of allopurinol in conjunction with urine alkalization for treatment of hyperuricosuria (>4.0 mmol/day) and/or hyperuricemia (>380 μmol). Upon closer analysis, the AUA omits articles cited by the EAU, which may explain this discrepancy. The EAU references Marchini et al's matched case comparative study examining stone composition distribution among gout and nongout patients.[17] They found that allopurinol changes the stone composition distribution in patients with gout, similar to that in stone formers without gout, by reducing fewer pure uric acid stones.

Another area of low evidence include the use of UAS during flexible URS. Only the CUA recognizes the use of UAS. However, no specific recommendations are made. The AUA and EAU briefly discuss the potential advantages and disadvantages of UAS but do not make any recommendations. While there is controversy in the published literature regarding UAS, there is a growing body of evidence to suggest its potential benefits. A systematic review by Breda et al in 2016 noted several advantages of UAS: facilitation of repeated retrograde intrarenal access, lower intrarenal pressure, less harm to the ureter and ureteroscope and improved stone extraction.[18] Traxer et al, 2015, in a prospective cohort study found no difference in stone-free rate when UAS was used compared to no UAS.[19] However, the UAS group had higher American Society of Anesthesiologists® scores and larger stones. They also note that use of UAS did not increase the risk of ureteral damage or bleeding, and reduced postoperative infectious complications.[19] Absence of attention to UAS may reflect the fact that guidelines will always trail the current literature.

Currently, only UAA guidelines distinguish between the indications for traditional PCNL vs miniPCNL, microPCNL or ultraminiPCNL. There is a paucity of high quality evidence regarding the use of smaller tract sizes, as the EAU explicitly acknowledges,[1] and more research on this area is recommended. As additional studies are published regarding the efficacy of miniPCNL vs conventional PCNL tracts, this approach will need to be addressed in future guidelines. Further research is warranted to provide the guideline panels with higher levels of evidence and stronger recommendations.

Lastly, cyber connectivity has contributed immensely to globalization and circulation of information. Today, all urological societies have urolithiasis working groups. We propose that these various groups come together to develop a single universal urolithiasis guideline. Pradere et al has also highlighted the need for universal collaborative effort to reduce confusion of management.[20] To be sure, there may be regional discrepancies in terms of stone disease incidence. Worldwide, stone disease may still be most common in Caucasian males.[21] Although its prevalence is lower, urolithiasis is still one of the most common urological complaints in Asian countries.[22] Any patient afflicted with urolithiasis would benefit from a single guideline vetted by the world's experts and updated on a biennial basis.

CONCLUSIONS

There are many areas of consensus with some minor areas of controversy among the most up-to-date AUA (2019 − medical/2016 − surgical), CUA (2016), EAU (2020), NICE (2019), and UAA (2019) guidelines on the management of stone disease. Areas of controversy stem from topics with a paucity of high level evidence such as postoperative imaging for stone surveillance, the use of UAS during URS and the indications for miniPCNL. These are all important areas for further research. Lastly, given the amount of effort necessary to create a guideline and the need for frequent review and update, the time may be ripe for a structured biennial global effort.

Appendix 1. *Methodology of evidence level determination*

AUA

Grade	Description
A	high quality evidence; high certainty: well-conducted randomized clinical trials (RCTs); exceptionally strong observational studies
B	moderate quality evidence; moderate certainty: RCTs with some weaknesses; generally strong observational studies
C	low quality evidence; low certainty: observational studies that provide conflicting information or design problems (such as very small sample size)

CUA

Level	Description
1	meta-analysis of RCTs or good quality RCT
2	low-quality RCT or meta-analysis of good-quality prospective cohort studies
3	good-quality retrospective case-control studies or case series
4	expert opinion based on "first principles" or bench research, not on evidence

EAU

Level	Description
1a	Meta-analysis of randomized trials
1b	at least one randomized trial
2a	one well-designed controlled study without randomization
2b	one other type of well-designed quasi-experimental study
3	well-designed nonexperimental studies, such as comparative studies, correlations studies and case reports
4	expert committee reports or opinions or clinical experience of respected authorities

NICE

Level	Description
Very Low	Nonrandomized trial OR Randomized trial with more than one very serious (1) risk of bias, (2) inconsistency, (3) indirectness, or (4) imprecision, or downgraded from higher levels because of reasons listed below*
Low	Randomized trial with no more than ONE very serious concern (either (1) risk of bias, (2) inconsistency, (3) indirectness, or (4) imprecision), or downgraded from higher levels because of reasons listed below*
Moderate	Randomized trial with no more than ONE serious concern (either (1) risk of bias, (2) inconsistency, (3) indirectness, or (4) imprecision), or downgraded from higher levels because of reasons listed below*
High	Randomized trial with no serious (1) risk of bias, (2) inconsistency, (3) indirectness, and (4) imprecision

(continued)

Appendix 1. (*continued*)

UAA

Level	Description
1	Evidence obtained from multiple large-scale RCTs
2	Evidence obtained from single RCT or low-quality RCT
3	Evidence obtained from nonrandomized controlled studies
4	Evidence obtained from observational studies
5	Evidence obtained from case studies or expert opinions

* Evidence can be downgraded because of: high risk of bias (1 increment), very high risk of bias (2 increments), heterogeneity (1 or 2 increments), unclear subgroup analysis (1 or 2 increments), confidence interval crossing one MID (1 increment), and confidence interval crossing both MIDs (2 increments).

Appendix 2. *Evidence level and recommendation strength correlation among guidelines*

Guideline	Evidence	Recommendation
AUA	Grade A—C	Strong
	Grade C	Moderate or conditional
	No evidence	Expert Opinion (EO)
	No evidence	Clinical Principle (CP)
CUA	Level 1	Grade A
	Level 2	Grade B
	Level 4	Grade C
	Level 5	Grade D
EAU	Level 1—4	Strong
	Level 3—4	Weak
	No evidence	Weak
NICE	No correlation provided	
UAA	Level 1—4	Grade A
	Level 2—4	Grade B
	Level 2—5	Grade C1: may consider
	Level 2—5	Grade C2: not recommended
	Level 4—5	Grade D: recommended not to do

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