DEVELOPMENT OF A GUIDELINE FOR SURGICAL STONE MANAGEMENT

WHY?

Common problem
Effective established treatment regimens
Lack of uniformity of treatment
Previous guidelines – 2005 & 2007

AUA Nephrolithiasis Guidelines Panel, 2016
CHAPTER 1: AUA GUIDELINE ON MANAGEMENT OF STAGHORN CALCULI: DIAGNOSIS AND TREATMENT RECOMMENDATIONS

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BACKGROUND STAGHORN CALCULI

Staghorn calculi are branched stones that occupy a large portion of the collecting system. Typically, they fill the renal pelvis and branch in several or all of the calyces. The term "partial staghorn" calculus designates a branched stone that occupies part but not all of the collecting system while "complete staghorn" calculus refers to a stone that occupies virtually the entire collecting system. Unfortunately, there is no consensus regarding the precise definition of staghorn calculi, as the term is applied as a statement of the technique required for a staghorn designation; consequently, the term "staghorn" is often used to refer to any branched stone occupying more than two-thirds of the collecting system, or pelvis, with one or more calyceal extensions. Furthermore, the designation of "partial" or "complete" staghorn calculi does not imply any specific volume criteria.

Staghorn calculi are most frequently composed of mixtures of magnesium ammonium phosphate (struvite) and/or calcium carbonate apatite. Stones composed of cystine or uric acid, either in pure form or mixed with other components, can also be associated with staghorn calculi but calcium oxalate or phosphate stones only rarely grow in this configuration. Struvite/calcium carbonate apatite stones also are referred to as "infection stones" because of their strong association with urinary tract infection caused by specific organisms that produce the urease that promotes the generation of ammonia and hydroxide from urea.

The resultant alkaline urinary environment and high ammonia concentrations, along with abundant phosphate and magnesium in urine, promote crystallization of magnesium ammonium phosphate (struvite), leading to formation of large, branched calculi. Other stones may result from the formation of an exoporphyrin-IX calcium biofilm and the incorporation of mucoproteins and other organic compounds into this matrix. Calcium ammonium phosphate (bacillus) calculi are also formed from both the surface and inside of the stone have demonstrated that bacteria reside within the stone thereby causing the stone to maintain its calcium and other substances while the stones remain sterile inside. Repeated urinary tract infections with urea-splitting organisms may develop.

METHODS USED TO DEVELOP THE 2004 GUIDELINES

The American Urological Association Guidelines Task Force 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.

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. The guideline documents provide recommendations on the management of ureteral calculi, changes in shock-wave lithotripsy technology, endoscopic design, intracorporeal lithotripsy techniques, and laparoscopic expertise have been published.

Under the auspices of the European Association of Urology, a joint task force of the American Urological Association and the European Association of Urology was formed. 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. These situations may require physicians and patients to resort to treatment alternatives.

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 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 (less than 18, 18 to 40, and greater than 40 years of age), stone location, and stone composition. Later, however, the data were found to be insufficient to allow analysis by composition. The recommendations deemed by the Panel to be of particular interest to the reader are 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 consider economic effects, including treatment costs.

Outcomes were stratified by stone location (proximal, mid, and distal ureter) and by stone size (dichotomized at 10 mm and 20 mm and 10 mm and 15 mm). Survival analysis was performed using the Kaplan-Meier method as noted.
Purpose: This Guideline is intended to provide a clinical framework for the surgical management of patients with kidney and/or ureteral stones. The summary presented herein represents Part I of the two-part series dedicated to Surgical Management of Stones: American Urological Association/Endourological Society Guideline. Please refer to Part II for an in-depth discussion of patients presenting with ureteral or renal stones.

Materials and Methods: A systematic review of the literature (search dates 1/1/1985 to 3/31/2015) was conducted to identify peer-reviewed studies relevant to the surgical management of stones. The review yielded an evidence base of 1,911 articles after application of inclusion/exclusion criteria. These publications were used to create the Guideline statements. Evidence-based statements of Strong, Moderate, or Conditional Recommendation were developed based on benefits and risks/burdens to patients. Additional directives are provided as Clinical Principles and Expert Opinions when insufficient evidence existed.

Results: The Panel identified 12 adult Index Patients to represent the most common cases seen in clinical practice. Three additional Index Patients were also created to describe pediatric and pregnant patients with such stones. With these patients in mind, Guideline statements were developed to aid the clinician in identifying optimal management.

Conclusions: Proper treatment selection, which is directed by patient- and stone-specific factors, remains the greatest predictor of successful treatment outcomes. This Guideline is intended for use in conjunction with the individual patient's treatment goals. In all cases, patient preferences and personal goals should be considered when choosing a management strategy.

Key Words: nephrolithiasis; ureteroscopy; nephrostomy, percutaneous

BACKGROUND
Kidney stones are a common and costly disease; it has been reported that over 8.8% of the United States population will be affected by this malady, and direct and indirect treatment costs are estimated to be several billion dollars per year in this country.1–3 The surgical treatment of kidney stones is complex, as there are multiple competitive treatment modalities, and in certain cases more than one modality may be appropriate.

The surgical management of patients with various stones described...
Net benefit (or net harm) is substantial
Benefits > Risks/Burdens (or vice versa)
Applies to most patients in most circumstances and future research is unlikely to change confidence

AUA Nephrolithiasis Guidelines Panel, 2016
Benefits > Risks/Burdens (or vice versa)
Net benefit (or net harm) is moderate
Applies to most patients in most circumstances and future research is unlikely to change confidence

MODERATE RECOMMENDATION

AUA Nephrolithiasis Guidelines Panel, 2016
GUIDELINES STATEMENTS

CONDITIONAL RECOMMENDATION

Benefits = Risks/Burdens
Best action depends on individual patient circumstances
Future research unlikely to change confidence

AUA Nephrolithiasis Guidelines Panel, 2016
CLINICAL PRINCIPLE
A component of clinical care that is very widely agreed upon by urologists for which there may or may not be evidence in the medical literature

EXPERT OPINION
A statement, achieved by consensus of the Panel, based on members’ clinical training, experience, knowledge, and judgment

AUA Nephrolithiasis Guidelines Panel, 2016
PTS WITH UNCOMPPLICATED URETERAL STONES ≤10 MM SHOULD BE OFFERED OBSERVATION - THOSE WITH DISTAL STONES SHOULD BE OFFERED MET WITH $\alpha$-BLOCKERS

Because of the low side effect profile and demonstrated efficacy, the Panel feels that a trial of $\alpha$-blockers in patients with <10 mm stones in any location of the ureter, despite a small benefit, can be considered until larger scale trials are available.

Patients should be informed that medications for MET are prescribed for an off label indication.

Strong Recommendation; Evidence Level Grade B
In a patient with a newly diagnosed ureteral stone < 10 mm whose symptoms are controlled, appropriate medical therapy with periodic evaluation is recommended as initial treatment.

Evidence: IA

EAU - AUA Nephrolithiasis Panel, 2007
Medical expulsive therapy in adults with ureteric colic: a multicentre, randomised, placebo-controlled trial

Robert Pickard, Kathryn Starr, Graeme MacLennan, Thomas Lam, Ruth Thomas, Jennifer Burr, Gladys McPherson, Alison McDonald, Kenneth Anson, James N'Dow, Neil Burgess, Terry Clark, Mary Kilonzo, Katie Gillies, Kirsty Shearer, Charles Boachie, Sarah Cameron, John Norrie, Samuel McClinton

Summary

Background Meta-analyses of previous randomised controlled trials concluded that the smooth muscle relaxant drugs tamsulosin and nifedipine assisted stone passage for people managed expectantly for ureteric colic, but emphasised the need for high-quality trials with wide inclusion criteria. We aimed to fulfil this need by testing effectiveness of these drugs in a standard clinical care setting.

Methods For this multicentre, randomised, placebo-controlled trial, we recruited adults (aged 18–65 years) undergoing expectant management for a single ureteric stone identified by CT at 24 UK hospitals. Participants were randomly assigned by a remote randomisation system to tamsulosin 400 μg, nifedipine 30 mg, or placebo taken daily for up to 4 weeks, using an algorithm with centre, stone size (≤5 mm or >5 mm), and stone location (upper, mid, or lower ureter) as minimisation covariates. Participants, clinicians, and trial personnel were masked to treatment assignment. The primary outcome was the proportion of participants who did not need further intervention for stone clearance within 4 weeks of randomisation, analysed in a modified intention-to-treat population defined as all eligible patients for whom we had primary outcome data. This trial is registered with the European Clinical Trials Database, EudraCT number 2010-019469-26, and as an International Standard Randomised Controlled Trial, number 69423238.

Findings Between Jan 11, 2011, and Dec 20, 2013, we randomly assigned 1167 participants, 1136 (97%) of whom were included in the primary analysis (17 were excluded because of eligibility and 14 participants were lost to follow-up). 303 (80%) of 379 participants in the placebo group did not need further intervention by 4 weeks, compared with 307 (81%) of 378 in the tamsulosin group (adjusted risk difference 1.3% [95% CI −5.7 to 8.3]; p=0.73) and 304 (80%) of 379 in the nifedipine group (0.5% [−5.6 to 6.5]; p=0.88). No difference was noted between active treatment and placebo (p=0.78), or between tamsulosin and nifedipine (p=0.77). Serious adverse events were reported in three participants in the nifedipine group (one had right loin pain, diarrhoea, and vomiting; one had malaise, headache, and chest pain; and one had severe chest pain, difficulty breathing, and left arm pain) and in one participant in the placebo group (headache, dizziness, lightheadedness, and chronic abdominal pain).

Interpretation Tamsulosin 400 μg and nifedipine 30 mg are not effective at decreasing the need for further treatment to achieve stone clearance in 4 weeks for patients with expectantly managed ureteric colic.

Funding UK National Institute for Health Research Health Technology Assessment Programme.

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1136 patients with stones ≤10mm at any ureteral site randomized to receive tamsulson 0.4mg, nifedipine 30mg or placebo for up to 4 weeks

Need for intervention used as surrogate for stone passage – No difference between groups

Raised questions about the efficacy of MET

Pickard, 2015
URETERAL CALCULI

LANCET RTC

80% background rate of spontaneous passage in the placebo group

Short duration of follow-up

Choice of primary outcome:
Further imaging obtained if “clinically indicated”

Pickard, 2015
“However, because of the low side effect profile of α-blockers and the demonstrated efficacy of α-blockers in patients with <10 mm stones in any location of the ureter, the AUA Nephrolithiasis Guidelines Panel feels that a trial of these agents in this patient population, despite the lack of demonstrable benefit, can be considered an option until larger scale trials are available to provide more definitive direction.

A Systematic Review and Meta-Analysis

URETERAL CALCULI – 2016 MET - Meta Analysis

RCTs involving alpha blockers in adults with ureteral calculi – Through Oct 2015

53 eligible trials
22 different countries
5,611 patients

Those with larger stones treated with an alpha blocker had a 58% higher risk of stone passage.

RRs for upper/mid and lower ureteral stones 1.50 (1.12 – 2.23) and 1.51 (1.39 – 1.66)
Conclusions

Alpha blockers are effective at facilitating ureteral stone passage.

The benefit of alpha blockers appears to be greatest in patients with larger stones.
URETERAL CALCULI

MEDICAL MANAGEMENT
URETERAL STONES
CLINICIANS MAY OFFER A-BLOCKERS AND ANTI-MUSCARINIC THERAPY TO REDUCE STENT DISCOMFORT

α-blockers have been shown in multiple RCTs to reduce stent related discomfort

Several meta-analyses and systematic reviews of the literature have demonstrated significant improvement in urinary symptoms, body pain index score of the Ureteral Stent Symptom Questionnaire, total International Prostate Symptom Score, Visual Analogue Pain Scale and QoL with use of α-blockers compared to placebo or no treatment

Strong Recommendation, Evidence Level Grade B
URETERAL CALCULI

ADJUVANT MEDICAL THERAPY

**Efficacy**
- Facilitated stone passage
- Improved stone free rates

**Morbidity**
- Pain
- Quality of life
All patients underwent flexible URS with a 365µ holmium laser fiber and received codeine.

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Flomax</th>
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<tbody>
<tr>
<td>Mean stone size (mm)</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Renal / ureteral calculi</td>
<td>22 / 16</td>
<td>22 / 18</td>
</tr>
<tr>
<td>Stone free</td>
<td>69%</td>
<td>87%*</td>
</tr>
<tr>
<td>Ureteral colic</td>
<td>22.2%</td>
<td>5.4%*</td>
</tr>
</tbody>
</table>

* = p < 0.01

John & Razdan, 2010
IMPACT OF ALPHA-BLOCKERS ON STENT SYMPTOMS
META-ANALYSIS

Yakoubi & Monga, 2011

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Mean Difference</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Urinary Sx</td>
<td></td>
<td>0.005</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td>0.0004</td>
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<tr>
<td>Gen Health</td>
<td></td>
<td>0.001</td>
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</table>
RENNAL STONES

PTS WITH LOWER POLE STONES >10 MM SHOULD BE INFORMED THAT PNL HAS A HIGHER STONE-FREE RATE BUT GREATER MORBIDITY

PNL should be considered the primary treatment for most cases, but patients should be informed of the nature of the procedure, expected morbidity and potential complications.

PNL with smaller access sheaths (mini-PCNL or micro-PCNL) may allow similar outcomes with lower complication rates.

Strong Recommendation; Evidence Level Grade B
LOWER POLE CALCULI
STONE-FREE RATES BY STONE SIZE

1-10mm: 12/19 (p=0.019)
11-20mm: 6/26 (p=0.0001)
21-30mm: 1/7 (p=0.015)

Lower Pole Study Group, 2001
LOWER POLE CALCULI
STONE-FREE RATES - OVERALL

Lower Pole Study Group, 2001

37%
95%
P < .0001

SWL
PNL

Lower Pole Study Group, 2001
LOWER POLE CALCULI

EFFICIENCY QUOTIENT

Lower Pole Study Group, 2001
LOWER POLE CALCULI

INDICATIONS FOR URETEROSCOPY

- Coexistence of ureteral stones / stricture
- Size less than 1.5 cm
- Bleeding diathesis
- Renal anomalies
- Solitary kidney
- Morbid obesity
URS MANAGEMENT OF LOWER POLE CALCULI

SCOPE DEFLECTION

7.5F Flex scope
2.4F N-basket
200µ fiber
Grasp lower pole stone
Release in upper pole
URS MANAGEMENT OF LOWER POLE CALCULI

RESULTS

Successful access 100%
Fragmentation rate 100%
Complications None
Stone-free rate 84%

Kourambas, et al, 2000
URS FOR LOWER POLE STONES

STONE-FREE RATES

* = p < 0.05


In Situ Stones

25/32

Displaced Stones

14/16

* = p < 0.05

### URS FOR LOWER POLE STONES

#### IN SITU VERSUS DISPLACEMENT

<table>
<thead>
<tr>
<th></th>
<th>In Situ</th>
<th>Displace</th>
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<tbody>
<tr>
<td>Stone diameter (mm)</td>
<td>8.0</td>
<td>10.3*</td>
</tr>
<tr>
<td>Operative time (min)</td>
<td>64</td>
<td>80*</td>
</tr>
<tr>
<td>Stone free – Total</td>
<td>71%</td>
<td>94%</td>
</tr>
<tr>
<td>&lt; 1 cm</td>
<td>77%</td>
<td>89%</td>
</tr>
<tr>
<td>&gt; 1 cm</td>
<td>29%</td>
<td>100%*</td>
</tr>
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* = p < 0.05

Schuster & Wolf, 2002
URS - LOWER POLE
STONE DISPLACEMENT
LOWER POLE CALCULI

SWL vs PNL vs URS

SWL less invasive, but less effective than PNL for lower pole stones, especially for stones greater than 10 mm

SWL stone-free rates dependent on stone burden and renal anatomy

PNL stone-free rates independent of stone burden and renal anatomy

URS should be considered in patients with low volume lower pole stones who are not candidates for SWL or PNL
RENAL STONES

IN PTS UNDERGOING UNCOMPLICATED PNL WHO ARE PRESUMED STONE FREE, N-TUBE IS OPTIONAL

In the appropriately selected patient, tubeless PNL can result in similar stone-free and complication rates as standard PNL.

Patients undergoing tubeless PNL with an indwelling stent should be counseled that cystoscopy and stent removal will be required sometime after the procedure.

Conditional Recommendation; Evidence Level Grade C
POST-PNL DRAINAGE

METHODS TO REDUCE PATIENT MORBIDITY

- Injection of nephrostomy tube site
- Use of smaller nephrostomy tubes
- Tubeless PNL
- Tubeless, stentless, PNL
Etiology of post-PNL pain remains elusive

Size of nephrostomy tract?
Size of nephrostomy tube?

30 consecutive patients undergoing PNL for stone disease

Preoperatively randomized to receive:
- 22F Councill tip catheter
- 10F Cope loop

Percutaneous access tracts dilated to 30F

Pietrow, et. al, 2003
POST-PNL DRAINAGE

POST-OPERATIVE PAIN SCORES

Pain score (0-10)

6hr  POD#1  POD#2  POD#14

10F catheter
22F catheter

* p < .05

Pietrow, et. al, 2003
POST-PNL DRAINAGE

TUBELESS PNL

Leave ureteral stent in place of nephrostomy tube

> 250 studies on tubeless PNL since 1997

No significant ↑ in post-op complications

Large stone burden

Multiple nephrostomy tracts

Supracostal tracts
## FACTORS IMPACTING LOS

### RETROSPECTIVE REVIEW

1669 patients undergoing PNL for renal calculi

Multivariate, regression analysis

<table>
<thead>
<tr>
<th>Factors ↑ LOS</th>
<th>Factors ↓ LOS</th>
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<tbody>
<tr>
<td>Diabetes</td>
<td>Tubeless PNL</td>
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<tr>
<td>Impaired renal function</td>
<td></td>
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<tr>
<td>Stone Size</td>
<td></td>
</tr>
<tr>
<td># access tracts</td>
<td></td>
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<tr>
<td>Intercostal access</td>
<td></td>
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Akman, Binbay, et al, 2011
Tubeless vs standard: 320 cases & 323 controls
Tubeless vs small-bore: 55 cases & 54 controls

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<thead>
<tr>
<th></th>
<th>Tubeless</th>
<th>Standard</th>
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<tbody>
<tr>
<td>Pain score (VAS)</td>
<td>-3.25*</td>
<td></td>
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<tr>
<td>Morphine (mg)</td>
<td>-6.03*</td>
<td></td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>-1.35*</td>
<td></td>
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<tr>
<td>Return normal activity (days)</td>
<td>-4.34*</td>
<td></td>
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No difference in SFR, blood transfusion, complications

Ni, et al, 2011
Tubeless PNL was associated with the least postoperative pain and the nephrostomy tube may be the main source of such discomfort.

Tubeless PNL is associated with less pain and quicker recovery compared with standard or small-bore PNL, in the management of uncomplicated renal calculi.

Ni, et al, 2011
Reduced flank pain, but…

Stent symptoms

Need for stent removal (cysto)

Now just leave external ureteral catheter in place post-op

Ureteral and Foley catheter removed on POD 1
TUBELESS, STENTLESS PNL

External ureteral catheter

Intra-operative KUB
TUBELESS, STENTLESS PNL

Tubeless

Stentless (stone free)
Five RCTs and four CCTs included - 652 patients

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<thead>
<tr>
<th></th>
<th>Tubeless</th>
<th>Standard</th>
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<tr>
<td>Analgesic requirements</td>
<td>-0.59*</td>
<td></td>
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<tr>
<td>Hospital stay (days)</td>
<td>-1.09*</td>
<td></td>
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</table>

No difference in: Op time, SFR, blood transfusion, complications

TUBELESS, STENTLESS PNL

CONTRAINDICATIONS

Significant bleeding (fibrin plug?)

Supra-costal access (use internal stent)

Thin patients with limited peri-renal fat
  (consider fibrin plug)
Consider tubeless, stentless PNL for most patients with renal calculi < 2.5 cm

- Patient stone-free at end of the case
- No stent-related morbidity
- Larger prospective, randomized trials needed to discern role for tubeless versus small N-tube
Most ureteral stones pass spontaneously

2nd and 3rd generation SWL less effective than 1st generation HM3

Endoscopic approaches more efficient for lower pole stone removal

Stenting is still morbid

AUA Nephrolithiasis Guidelines Panel, 2016
URETERAL CALCULI

WHAT’S NEW IN 2018

Medical expulsive therapy still works

Improved stone-free rates with ureteroscopy
  Holmium and pneumatic lithotripsy
  Enhanced fiberoptic imaging

Further reductions in post-PNL patient morbidity

AUA Nephrolithiasis Guidelines Panel, 2016