Obstructive Uropathy

Watid Karnjanawanichkul
Obstructive uropathy

- Functional or anatomic obstruction of urinary flow at any level of the urinary tract
  - The point of obstruction can be as proximal as the calyces and as distal as the urethral meatus
Obstructive nephropathy

- Functional or anatomic renal damage that’s cause from obstruction
Obstruction

- Congenital or acquired
- Benign or malignant
- Baseline condition of the kidneys
- Partial or complete
- Unilateral or bilateral
- Acute or chronic
Pathologic changes of obstruction

- Lymphatic dilation, interstitial edema
- Collecting duct and tubular dilatation
- Widening of Bowman's space, tubular basement membrane thickening, cell flattening, and cytoplasmic hyalinization
- Inflammatory cell response
Pathologic changes

-Interstitial fibrosis and thickening of the tubular basement membranes
- Cortical thinning and development of glomerular crescents were present at the 3- to 4-week interval
Post-obstructive Diuresis

- This occurs mainly after relief of BUO or obstruction of a solitary kidney, it can rarely occur when there is a normal, contralateral kidney.
- Normal physiologic response to the volume expansion and solute accumulation.
Causes of obstructive uropathy

**Anatomic abnormalities**
- PUV, CBN, stricture urethra, polyp of ureter

**Compression from extrinsic masses or processes**
- Reproductive system: pregnancy, uterine prolapse
- GI tract: Crohn’s disease, diverticulitis
- GU tract: BPH, CA prostate
- Blood vessels: aneurysm, retrocaval ureter
- Retroperitoneum: fibrosis, TB, sarcoidosis, lymphoma
Causes of obstructive uropathy

**Functional abnormalities**
- NB, UPJ obstruction, UVJ obstruction

**Mechanical obstruction**
- Crystal – renal tubule
- Blood clot, renal papillae – renal pelvis, ureter
- **Urolithiasis** – renal pelvis, ureter, urethra
Urolithiasis

- Epidemiology
- Classification
- Pathogenesis
- Pathophysiology
- Approach to patients
- Treatment
Epidemiology

- The lifetime prevalence of kidney stone disease is estimated at 1% to 15%.
  - Age, gender, race, and geographic location
• Stone occurrence is relatively uncommon before age 20 but peaks in incidence in the fourth to sixth decades of life
• Women show a bimodal distribution of stone disease, demonstrating a second peak in incidence in the sixth decade of life
Gender

• Stone disease typically affects adult men more commonly than adult women
  – Two to three times more frequently
Race/Ethnicity

- Prevalence of stone disease
  - Whites
  - Hispanics: 70% of whites
  - Asians: 63% of whites
  - African Americans: 44% of whites
Higher prevalence of stone disease is found in hot, arid, or dry climates such as the mountains, desert, or tropical areas.
Geography

- Worldwide: high stone prevalence
  - The United States, British Isles, Scandinavian and Mediterranean countries, northern India and Pakistan, northern Australia, Central Europe, portions of the Malay peninsula, and China
Pathogenesis

Unstable Supersaturation Region
1. Spontaneous nucleation
2. Rapid growth
3. Aggregation

Formation product

Metastable Region
1. Limited aggregation on protein
2. No spontaneous nucleation
3. Secondary nucleation/epitaxial growth

Solubility product

Undersaturation Region
1. No nucleation or growth
2. Crystal dissolution possible
Phenomena

Nucleation will occur
Inhibitors not generally effective

Formation Product

Crystal growth will occur
Crystal aggregation will occur
Inhibitors will impede or prevent crystallization
De novo nucleation is very slow
Heterogeneous nucleation may occur
Matrix may be involved

Concentration Product

Solubility Product

Crystals will not form
Existing stones may dissolve

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Stone varieties

- **Calcium calculi** 80%
- **Non-calcium calculi**
  - Struvite 10%
  - Uric acid 5-10%
  - Cystine 1%
  - Xanthine
  - Indinavir
  - Others : Silicate
Classification

Common Crystalline Components of Calculi

- CaOx/CaP
- CaP
- UA
- Stru
- Cyst
- Other
Calcium Stone

1. Hypercalciuria
2. Hyperoxaluria
3. Hyperuricouria
4. Hypocitraturia
1. Hypercalciuria

- Absorptive Hypercalciuria
- Renal Hypercalciuria
- Resorptive Hypercalciuria
Absorptive hypercalciuria

↓ Serum Pi  → ↑ 1,25 (OH)_2 D_3  

↑ Jejunal calcium absorption

↑ Serum Calcium (high normal)

↑ Filtered calcium

↓ Renal tubular reabsorption

↑ Urinary calcium excretion
Renal Hypercalciuria

Functional tubular defect

↓

Renal calcium leak

↓

Serum calcium

↑ PTH

↑ 1:25 (OH)$_2$ D$_3$

↑ Intestinal calcium absorption
Resorptive Hypercalciuria

- Hyperparathyroidism
- Excessive PTH-dependent bone resorption
- Enhanced intestinal absorption of calcium
2. Hyperoxaluria

- Primary hyperoxaluria
- Enteric hyperoxaluria
- Dietary hyperoxaluria
Primary hyperoxaluria
Enteric Hyperoxaluria

- Most common cause of hyperoxaluria
- Associated with chronic diarrheal states
  - Fat malabsorption results in sponification of fatty acids with divalent cations
Dietary Hyperoxaluria

• Overindulgence in oxalate-rich foods
  – Nuts, chocolate, brewed tea, spinach, broccoli, strawberries, and rhubarb
• *Oxalobacter formigenes*, an oxalate-degrading intestinal bacterium
3. Hyperuricosuria

- Hyperuricosuria increases urinary levels of monosodium urate, which in turn promotes calcium oxalate stone formation
4. Hypocitrauria

- Citrate is an important inhibitor that can reduce calcium stone formation
- Reduces urinary saturation of calcium salts by complexing with calcium
- Directly prevents spontaneous nucleation of calcium oxalate
Citrate

- Acid-base state is the primary determinant of urinary citrate excretion
- Metabolic acidosis reduces urinary citrate levels secondary to enhanced renal tubular reabsorption and decreased synthesis of citrate in peritubular cells
Renal Tubular Acidosis

• RTA is a clinical syndrome characterized by metabolic acidosis resulting from defects in renal tubular hydrogen ion secretion and urinary acidification.
There are three types of RTA (1, 2 and 4)

RTA occurs as a result of impairment of net excretion of acid into the urine (type 1) or of reabsorption of bicarbonate (type 2)
RTA

- The most common type of stone associated with distal RTA is calcium phosphate as a result of hypercalciuria, hypocitraturia, and increased urinary pH.
Uric acid Stone

- All mammals, except *humans and Dalmatians*, synthesize the enzyme uricase, which catalyzes the conversion of uric acid to allantoin, the end product of purine metabolism.

- Because allantoin is 10 to 100 times more soluble in urine than uric acid, humans are prone to uric acid stone formation.
Relationship between undissociated uric acid, total uric acid, and urinary pH
Uric acid Stone

- The three main determinants of uric acid stone formation are low pH, low urine volume, and hyperuricosuria
- The most important pathogenetic factor is \textit{low urine \textit{pH}}
Pathophysiology

Uric acid nephrolithiasis

- Low urine volume
  - Diarrheal states
- Low urinary pH
  - High animal protein diet
- Hyperuricosuria
  - Primary gout

Obesity ↔ Insulin resistance

- Myeloproliferative disorders
- Uricosuric medications
- Congenital disorders

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Cystine Stone

- Cystine stones are rare, occurring in the United States and Europe with an incidence of only 1 in 1,000 to 1 in 17,000
  - In children, cystinuria is the cause of up to 10% of all stones
- Autosomal recessive
  - Two genes involved in the disease have been identified, $SLC_3A_1$ and $SLC_7A_9$
**Infection Stone**

- Magnesium ammonium phosphate hexahydrate (MgNH₄PO₄ • 6H₂O)
- Infection with urease-producing bacteria is a prerequisite for the formation of infection stones
Infection Stone

• The most common urease-producing pathogens are *Proteus*, *Klebsiella*, *Pseudomonas*, and Staphylococcus species with *Proteus mirabilis* the most common organism associated with infection stones.
Struvite Stone

- Infection stone
  - Female > Male (2:1)
  - Radiopaque: Staghorn calculi

- Treatment requires eradication of infection and stone removal
Miscellaneous Stones

- Xanthine and Dihydroxyadenine Stones
- Ammonium Acid Urate Stones
  - Laxative abuse, recurrent urinary tract infection, recurrent uric acid stone formation, and inflammatory bowel disease
- Matrix Stones
Medication-Related Stones

- **Calcium stone**
  - Loop diuretic (furosemide, bumetanide), acetazolamide, topiramate, and zonisamide

- **Ephedrine, Triamterene, Guaifenesin, Silicate, Indinavir, Ciprofloxacin**
Approach to the patients
Evaluation of stone formers

- Patients presented with acute flank pain
  - Loin pain
  - Vomitting
  - Mild fever

- Patients with established nephrolithiasis (metabolic evaluation)
  - Medical management to prevent recurrence after a 1st stone episode is not most effective
Indications for a Metabolic Stone Evaluation

- Recurrent stone formers
- Strong family history of stones
- Intestinal disease (chronic diarrhea)
- Pathologic skeletal fracture
- Osteoporosis
- Hx of UTI with calculi
Indications for a Metabolic Stone Evaluation

- Personal Hx of gout
- Infirm health
- Solitary kidney
- Anatomic abnormalities
- Renal insufficiency
- Stone composed of cystine, uric acid or struvite
Dietary Modification

- High fluid intake
- Decrease intake of animal protein
- Normal calcium intake
- Restrict salt intake
Dietary Modification

- Decrease dietary oxalate
- Cranberry juice
- Ascorbic acid
- Potassium & magnesium
Acute flank pain

• History
  – Family history of nephrolithiasis
  – Previous history of nephrolithiasis
  – Recent dehydration
  – Recurrent UTI
  – Recurrent flank pain with N/V
Acute flank pain

• Physical examination
  – Flank, testicular or labial tenderness
  – No rebound tenderness
  – Normal or mildly decreased bowel sound
  – Fever
Acute flank pain

- **Lab investigation**
  - CBC
  - UA : hematuria, pH, Crystal
  - Imaging :
    - Plain KUB : initial screening
    - IVP : obstruction, anatomical abnormalities
    - USG : non-opaque stone, obstruction
    - CT scan : non-opaque stone, obstruction
Pain Management

• Treatment should be stratified with NSAIDs
  – Inhibition of prostaglandin synthesis
  – Reduce collecting system pressure
  – Reduction in renal blood flow

• Narcotic analgesics
  – Rescue pain is not controlled adequately with NSAIDs or adjunct to NSAIDs therapy
Surgical Management of Urolithasis
Introduction

- PCNL, URS, ESWL has almost eliminate open stone surgery (OSS)
- Goal: Maximal stone clearance with minimal morbidity
Renal calculi

Optional treatment:

1. ESWL
2. PCNL
3. Retrograde ureteroscopic intrarenal surgery (RIRS)
4. Sandwich technique
   - PCNL + ESWL
   - RIRS + ESWL
Simple renal calculi

- 80-85% success by ESWL

ESWL (Extra-corporal shockwave lithotripsy)
(Shockwaves from outside the body are used to break the stone)
ESWL

- Poor result factors
  1. Large renal calculi (>22.2 mm²)
  2. Stone within dependent or obstructed portion of the collecting systems
  3. Stone composition
     - Calcium oxalate monohydrate
     - Brushite
  4. Obesity
Nonstaghorn calculi, ESWL

- **Complication**
  - Steinstrasse
    - Stone > 3 cm (8%)

- **Success rate**
  - < 10 mm  79.9%
  - 10-20 mm  64%
  - > 20 mm  53.7%
Staghorn calculi

- Pelvic stone + 2 extended calyceal groups
- Most: Struvite stone
Staghorn calculi

- Staghorn stone
  - 10 year mortality
    - Untreated stone: 28%
    - Treated stone: 7.2%
  - CRF
    - Untreated stone: 36%
    - Treated stone: 28%
Surgical management

1. Open stone surgery
   - Stone free rate: 85%
   - Stone recurrence: 30% (6yr)

2. PCNL+/- ESWL
   - Stone free rate: 85%

3. ESWL
   - Stone free rate: 51.2%
     - Auxiliary procedure: 30.5%
Surgical management

Guideline

- PCNL +/- ESWL
  - First line management of staghorn calculi
- ESWL, OSS
  - Not to be first line management
Renal stone 1-2 cm

- Lower pole: ESWL or PCNL
- All other sites: ESWL

< 1 cm

> 2 cm

ESWL or PCNL

ESWL

PCNL
Ureteric stone

• Width of stone is the most importance factor of spontaneous passage
  – < 4 mm : 80%
  – 4-6 mm : 59%
  – > 6 mm : 21%
Proximal ureteric stone

- **Stone < 1 cm**
  - ESWL: 84%
  - URS: 56%

- **Stone > 1 cm**
  - ESWL: 72%
  - URS: 44%

- **Complication**
  - ESWL: 4%
  - URS: 11%
Proximal ureteric stone

- Stone < 1cm
  - ESWL

- Stone > 1 cm
  - ESWL
  - URS
  - PCNL
Distal ureteric stone

• Not be used as a primary approach
  – Blind basket
  – OSS
• Acceptable option
  – ESWL
  – URS
Ureteral calculus stone location

Proximal ureter
- Stone size
  - < 1.5 cm: ESWL in situ
  - > 1.5 cm: Ureteroscopic treatment or ESWL in situ

Distal ureter
- Any size
  - ESWL in situ or ureteroscopic treatment
Ureteric stone

- Laparoscopic ureterolithotomy
  - Failed ESWL / URS
  - Stone > 1.5 cm
RANDOMIZED TRIAL OF THE EFFICACY OF TAMSULOSIN, NIFEDIPINE AND PHLOROGLUCINOL IN MEDICAL EXPULSIVE THERAPY FOR DISTAL URETERAL CALCULI

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Method

480 patients with acute renal colic evaluated

244 patients not distal ureteral stones

236 patients with distal ureteral stones

26 patients not eligible

210 patients randomised

Group A phloroglucinol (n=70)

Group B tamsulosin (n=70)

Group C nifedipine (n=70)
### Table 1. Baseline patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD</td>
<td>39.8 ± 12.7</td>
<td>43.8 ± 13.9</td>
<td>41.8 ± 15.4</td>
<td>0.252</td>
</tr>
<tr>
<td>No. men/women</td>
<td>50/20</td>
<td>54/16</td>
<td>51/19</td>
<td>0.726</td>
</tr>
<tr>
<td>No. rt/lit stones</td>
<td>39/31</td>
<td>41/29</td>
<td>40/30</td>
<td>0.943</td>
</tr>
<tr>
<td>Stone size (mm):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>6.2 (1.7)</td>
<td>7.2 (2.4)</td>
<td>6.2 (1.5)</td>
<td>0.002</td>
</tr>
<tr>
<td>Median (range)</td>
<td>6 (4–11.8)</td>
<td>7 (4–18)</td>
<td>6 (4–11)</td>
<td>0.004</td>
</tr>
<tr>
<td>IQR</td>
<td>3.7–5</td>
<td>5.5–8</td>
<td>5–7</td>
<td></td>
</tr>
</tbody>
</table>

Total of 70 patients per group.

### Table 2. Randomization results

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. expulsion (%)</td>
<td>45 (64.3)</td>
<td>68 (97.1)</td>
<td>54 (77.1)</td>
<td>≤0.0001</td>
</tr>
<tr>
<td>Time to expulsion (hrs):</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Median</td>
<td>120</td>
<td>72</td>
<td>120</td>
<td>≤0.0001</td>
</tr>
<tr>
<td>IQR</td>
<td>72–168</td>
<td>24–120</td>
<td>72–192</td>
<td></td>
</tr>
<tr>
<td>No. hospitalization (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urgent</td>
<td>11 (15.7)</td>
<td>0</td>
<td>3 (4.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Delayed</td>
<td>13 (18.6)</td>
<td>1 (1.4)</td>
<td>11 (15.7)</td>
<td>0.004</td>
</tr>
<tr>
<td>Totals</td>
<td>24 (34.2)</td>
<td>1 (1.4)</td>
<td>14 (20)</td>
<td>≤0.0001</td>
</tr>
<tr>
<td>Total No. ureteroscopy (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Analgesic use (No. vials):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>≤0.0001</td>
</tr>
<tr>
<td>IQR</td>
<td>1–5</td>
<td>0–0</td>
<td>0–1</td>
<td></td>
</tr>
<tr>
<td>No. workdays lost:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>≤0.0001</td>
</tr>
<tr>
<td>IQR</td>
<td>2–6.25</td>
<td>1–2</td>
<td>1–5</td>
<td></td>
</tr>
</tbody>
</table>

Total of 70 patients per group.
Efficacy of $\alpha$-Blockers for the Treatment of Ureteral Stones

J. Kellogg Parsons,*,† Lori Ann Hergan, Kyoko Sakamoto and Charles Lakin

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### Table 2. Summary of studies meeting inclusion criteria for analysis

<table>
<thead>
<tr>
<th>References</th>
<th>No. Pts</th>
<th>α-Blocker</th>
<th>Prior SWL</th>
<th>Days Treatment†</th>
<th>Stone Size (mm)</th>
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</thead>
<tbody>
<tr>
<td>Cervenakova et al(^{12})</td>
<td>102</td>
<td>Tamsulosin</td>
<td>No</td>
<td>8</td>
<td>1–10</td>
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<tr>
<td>Dellabella et al(^{10})</td>
<td>60</td>
<td>Tamsulosin</td>
<td>No</td>
<td>28</td>
<td>3.8–13</td>
</tr>
<tr>
<td>Kupeli et al(^{1})</td>
<td>78</td>
<td>Tamsulosin</td>
<td>Yes</td>
<td>15</td>
<td>3–15</td>
</tr>
<tr>
<td>Tekin et al(^{17})</td>
<td>75</td>
<td>Terazosin</td>
<td>No</td>
<td>28</td>
<td>5–15</td>
</tr>
<tr>
<td>Autorino et al(^{14})</td>
<td>64</td>
<td>Tamsulosin</td>
<td>No</td>
<td>14</td>
<td>3–10</td>
</tr>
<tr>
<td>Porpiglia et al(^{9})</td>
<td>55</td>
<td>Tamsulosin</td>
<td>No</td>
<td>28</td>
<td>3–10</td>
</tr>
<tr>
<td>Dellabella et al(^{8})</td>
<td>140</td>
<td>Tamsulosin</td>
<td>No</td>
<td>14</td>
<td>4–18</td>
</tr>
<tr>
<td>Rosim et al(^{10})</td>
<td>60</td>
<td>Tamsulosin</td>
<td>No</td>
<td>42</td>
<td>3–13</td>
</tr>
<tr>
<td>Resim et al(^{12})</td>
<td>67</td>
<td>Tamsulosin</td>
<td>Yes</td>
<td>42</td>
<td>10–30</td>
</tr>
<tr>
<td>Yilmaz et al(^{14})</td>
<td>114</td>
<td>Tamsulosin</td>
<td>No</td>
<td>30</td>
<td>Less than 10</td>
</tr>
<tr>
<td>De Sio et al(^{11})</td>
<td>96</td>
<td>Tamsulosin</td>
<td>No</td>
<td>14</td>
<td>5.1–7.9</td>
</tr>
</tbody>
</table>

\(^a\) Doses include 0.4 mg tamsulosin daily, 5 mg terazosin daily, 4 mg doxazosin daily.

\(^†\) Maximum period of conservative treatment after which intervention was initiated in patients who did not pass stone.
Bladder calculi

• 5% of all urinary calculi
• Risk factors
  – BOO
  – Neurogenic bladder
  – FB
  – Bladder diverticulum
Bladder calculi

• Composition
  – Struvite stone
  – Calcium oxalate
  – Uric acid stones
Treatment

- Cystolitholapaxy
  - Contraindication
    - Small bladder capacity
    - Multiple stones
    - > 2 cm
Treatment

- **Small stones**
  - EHL
  - Pneumatic
  - Holmium

- **Large stones**
  - Cystolithotomy
Knowledge