

## INTRODUCTION:

- Bladder stones are rare in Western world, comprising 5% of all urolithiasis<sup>1</sup>
- Endemic stones, usually in children, are associated with dehydration, diarrhea, infection and dietary deficiencies<sup>2</sup>
- Neurogenic bladder, history of augmentation and foreign bodies (retained sutures, indwelling ureteral or Foley catheters) pose risk for formation of bladder calculi<sup>2</sup>
- Composition of bladder stones which was once predominantly magnesium ammonium phosphate (MAP)<sup>1</sup>, has recently changed--now predominantly calcium oxalate<sup>3</sup>
- Uric acid cystolithiasis is increasing, possibly associated with changing demographics and increased incidence of metabolic syndrome<sup>4</sup>
- Bladder stones postulated to form from 2 separate processes:
  - Upper tract stones retained in bladder and with further crystallization and growth
  - de novo* formation in the bladder secondary to urinary stasis and obstruction<sup>5</sup>
- Bladder outlet obstruction commonly cited as inciting factor for bladder stone formation, but incidence in men requiring surgery for BPE only about 2%<sup>6</sup>
- Formation of bladder stones in men with BPE was absolute indication for prostatic reduction surgery<sup>7</sup>
- Recent studies demonstrate efficacy of removing bladder stones and treating BPE conservatively for symptom management<sup>8,9</sup>
- Other factors:
  - History of upper tract stones and renal colic associated with bladder stones<sup>10</sup>
  - Bladder stone patients presenting with urinary retention more likely to have had recent renal colic compared to those presenting with LUTS<sup>3</sup>
  - In men with BPE, uric acid bladder calculi associated with lower urinary pH and higher urinary uric acid<sup>10</sup>
- Some men refuse or defer therapy for bladder outlet obstruction due to religious reasons and/or concerns regarding retrograde ejaculation
- To our knowledge, no studies have looked at bladder stone recurrence after bladder stone treatment
- We describe the clinical and metabolic differences between patients who do and do not have bladder stone recurrence

## METHODS :

- Database of patients undergoing bladder stone procedures from 2012-2017 at a tertiary referral center retrospectively analyzed
- Patients with bladder stones associated with foreign bodies (e.g., stents, catheters, suprapubic tubes), on clean intermittent catheterization, having neurogenic bladder, having bladder augment, or having urinary diversion excluded
- 66 patients in final analysis divided into those with (n=19) and those without recurrence (n = 47)
- Data analyzed included 24-hour urine results, stone analysis, prostate size, presence of intra-prostatic protrusion (IPP), post-void residual (PVR), flow rate, known prior diagnosis of BPE, compliance with medications, follow-up time and time to recurrence.
- Our usual treatment regimen:
  - Surgical removal of stones (cystolitholapaxy with holmium laser or percutaneous extraction of bladder stones)
  - Those refusing outlet surgery were evaluated in a metabolic stone clinic with 24-hour urine collection (Litholink, Chicago, IL)
  - Chemical stone analysis was done on all extracted stones (Quest Diagnostics, Secaucus, NJ)
  - Stone prevention counseling and placement on diet and/or medications
  - Optimize treatment for BPE with alpha-blockers, 5 alpha reductase inhibitors, and PDE inhibitor as indicated
- Patient non-compliance defined as patients not taking at least 80% of the prescribed dose of medications, averaged monthly, as assessed with post-operative visits.
- Data was analyzed using the IBM SPSS Statistics 24 (Released 2015, Armonk, NY) software.
- Descriptive and univariate statistics run to determine means and empirical relationships between parameters of interest.
- T-test and chi-squared statistics were used to determine statistical significance in several epidemiological and 24-hour urine parameters between groups, including BMI, total stone burden and presence of metabolic abnormalities .

| Table 1:                          | Non-Recurrent<br>(n = 47) | Recurrent<br>(n = 19) | P-value                    |
|-----------------------------------|---------------------------|-----------------------|----------------------------|
| <b>Demographics:</b>              |                           |                       |                            |
| Mean Age (years)                  | 65.2 (±14)                | 67.4 (±9)             | 0.453 <sup>b</sup>         |
| Mean BMI                          | 29.1                      | 27.8                  | 0.358 <sup>b</sup>         |
| <b>Clinical:</b>                  |                           |                       |                            |
| Known History of BPE              | 30                        | 18                    | <b>0.047<sup>a*</sup></b>  |
| Non-Compliance with BPE Rx        | 28% (n=13/47)             | 37% (n=7/19)          | <b>0.038<sup>a*</sup></b>  |
| Non-Compliance with Stone Regimen | 29% (n=2/7)               | 61% (n=8/13)          | <b>0.0001<sup>a*</sup></b> |
| Use of Two or More Medications    | 36% (n=16/44)             | 84% (n=16/19)         | <b>0.008<sup>a*</sup></b>  |
| Mean Follow-Up (months)           | 12                        | 14                    | 0.694 <sup>b</sup>         |
| Mean Stone Burden                 | 2.48 cm                   | 3.25 cm               | 0.404 <sup>b</sup>         |
| Mean Prostate Size (cc)           | 68.13 cc                  | 66.84 cc              | 0.926 <sup>b</sup>         |
| Mean Max Flow Rate                | 7.36 ml/sec               | 9.79 ml/sec           | 0.221 <sup>b</sup>         |
| Mean Post Void Residual           | 112.32 ml                 | 95.28 ml              | 0.682 <sup>b</sup>         |
| Mean Uric Acid                    | 6.1                       | 5.8                   | 0.565 <sup>b</sup>         |

Table 1. Demographics, clinical characteristics and voiding dynamics between patients with and without bladder stone recurrence

| Table 2:                                     | Non-             | Recurrent        | P-value                   |
|--|------------------|------------------|---------------------------|
| <b>24 Hour Urine Parameters<sup>b</sup>:</b> | <b>Recurrent</b> | <b>Recurrent</b> | <b>P-value</b>            |
| Vol24<br>(n= 42/47)                          | 1.99             | 1.50             | <b>0.048<sup>a*</sup></b> |
| Ca24   | 187.17           | 181.23           | 0.875                     |
| Ox24   | 42.33            | 38.08            | 0.371                     |
| Cit24  | 574.5            | 709.00           | 0.177                     |
| pH   | 6.04             | 5.64             | <b>0.050<sup>a*</sup></b> |
| UA24   | 0.652            | 0.531            | 0.70                      |

Table 2: 24 hour urine parameter differences between patients with and without bladder stone recurrence

## RESULTS:

- 66 patients; 19 bladder stone recurrences in mean of 14 mos.
- All patients male
- No differences in age (65.2 vs 67.4) and BMI (29.1 vs 27.8) between the non-recurrent and recurrent groups
- No differences in mean prostate size (68.13 vs 66.84 cc), flow rate (7.36 vs 9.79 mL/sec), PVR (112.32 vs 95.28 cc), stone burden (2.48 vs 3.25 cm) and uric acid levels (6.1 vs 5.8 mg/dL) between non-recurrent and recurrent groups
- No patients had previous prostate surgery and none proceeded to prostatic surgery after bladder stone treatment
- 30 of 47 (64%) in the non-recurrent group had a known history of BPE, compared to 18/19 (95%) (p = 0.048)
- 36% vs 84% of patients required 2 or more medications to control BPE and/or calculus disease in non-recurrent and recurrent groups, respectively (p = 0.008)
- Non-compliance with BPE and stone regimen medications 28% and 29% respectively, in non-recurrent group compared to 37% and 61% in recurrent group (p = 0.038 and p = 0.0001) (See Table 1).
- 47/66 patient (71%) of study participants had completed at least one adequate 24-hour urine study
  - no differences in urinary calcium, citrate, oxalate and uric acid levels
  - Total urine volume lower in recurrent patients (1.5L vs 1.99L, p = 0.048).
  - Urine pH lower in the recurrent group (5.64) vs 6.04, p = 0.05). (See Table 2).

## CONCLUSIONS:

The etiology of bladder stone formation is multifactorial with bladder outlet obstruction and metabolic disturbances as major contributors.

Both must be addressed and treated accordingly.

Patients prescribed multiple medications were found to have a higher rate of recurrence, possibly secondary to compliance.

Medication non-compliance is a major risk factor for formation of recurrent bladder stones in men who do not undergo outlet procedures.

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