Characteristics of patients surgically treated for primary hyperparathyroidism with and without urolithiasis

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Supervisor: Dr. 李苑如
INTRODUCTION

• Urolithiasis is a common disease in the general population.

• Lifetime risk is approximately 3–5% in women and 10–15% in males, with an increased incidence during the past two to three decades\textsuperscript{1,2}
INTRODUCTION

• The etiology of urolithiasis is multifactorial, but hypercalcemia and hypercalciuria are known to be the primary risk factors for stones.\(^3\)

• Patients with primary hyperparathyroidism (PHPT) tend to have elevation of serum calcium level and urine calcium level.

• Primary hyperparathyroidism is a known risk factor for urolithiasis.
2010, Wu et al: Prevalence assessed using imaging techniques (Patients number: 3388)

=> Prevalence rate: 8%

Adopt from “Nephrolithiasis and renal calcifications in Primary Hyperparathyroidism” L. Rejnmark et al, J Clin Endocrinol Metab, 2011 Aug
PREVALENCE RATE – TEMPORAL TREND

y = -0.7657x + 1560.5
R² = 0.0668

Adopt from “Nephrolithiasis and renal calcifications in Primary Hyperparathyroidism” L. Rejnmark et al, J Clin Endocrinol Metab, 2011 Aug
PURPOSE

• We hope to characterize the biochemical and pathological features of patients with primary hyperparathyroidism (PHPT) with and without urolithiasis.
MATERIAL AND METHOD

• Patients:
  - 49 patients with hyperparathyroidism who underwent parathyroidectomy were collected from 2002-2010.
  - 14 patients were ESRD. (Secondary hyperparathyroidism)
  - 35 patients were included (PHPT patient)

• Subgroups:
  I: Patients with urolithiasis and without urolithiasis before parathyroidectomy
  II: Patients with stone recurrence and without stone recurrence after parathyroidectomy (PTX)
• Demographics: Age, Body weight, Gender, Plasma Calcium, Plasma Phosphate, PTH, Plasma Creatinine and Pathology result.

• Operation: Routine bilateral cervical exploration performed. Pre-operative biopsy is not routine.

• Duration of follow-up: 1 year

• Stone recurrence: Patients who underwent parathyroidectomy got urolithiasis within one year. (KUB, Computed tomography, Renal echo)
## RESULT

Table 1: Preoperative biochemistry and pathology in 35 patients with primary hyperparathyroidism

<table>
<thead>
<tr>
<th>Parameter</th>
<th>With urolithiasis</th>
<th>Without urolithiasis</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients</td>
<td>25</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Male/Female</td>
<td>9/16</td>
<td>5/5</td>
<td>p=0.47</td>
</tr>
<tr>
<td>Age</td>
<td>61.60 ± 12.60</td>
<td>57.20 ± 14.20</td>
<td>p=0.17</td>
</tr>
<tr>
<td>BW</td>
<td>60.80 ± 8.94</td>
<td>63.00 ± 11.37</td>
<td>p=0.27</td>
</tr>
<tr>
<td>Serum Cr</td>
<td>1.17 ± 0.51</td>
<td>1.46 ± 1.38</td>
<td>p=0.18</td>
</tr>
<tr>
<td>eGFR</td>
<td>59.73 ± 25.10</td>
<td>70.72 ± 41.29</td>
<td>p=0.17</td>
</tr>
<tr>
<td>Serum Ca</td>
<td>3.21 ± 0.65</td>
<td>3.44 ± 2.10</td>
<td>p=0.30</td>
</tr>
<tr>
<td>Serum P</td>
<td>2.89 ± 1.09</td>
<td>3.01 ± 0.83</td>
<td>p=0.38</td>
</tr>
<tr>
<td>PTH</td>
<td>310.05 ± 347.50</td>
<td>375.17 ± 542.55</td>
<td>p=0.50</td>
</tr>
<tr>
<td>Pathology:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoma/Hyperplasia</td>
<td>17/8</td>
<td>9/1</td>
<td>p=0.23</td>
</tr>
</tbody>
</table>
### TABLE 2: Post-operative biochemistry and pathology in 25 patients with pre-operative stone formation. Comparison between stone recurrence and without stone recurrence.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>With stone recurrence</th>
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<th>p value</th>
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<tbody>
<tr>
<td>No of patients</td>
<td>9</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Male/Female</td>
<td>4/5</td>
<td>8/8</td>
<td>NS *</td>
</tr>
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<td>59.31 ± 11.25</td>
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<td>BW</td>
<td>58.11 ± 6.91</td>
<td>62.75 ± 9.73</td>
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<td>Serum Cr</td>
<td>1.06 ± 0.26</td>
<td>1.60 ± 1.79</td>
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<td>Serum Ca</td>
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<td>P&lt;0.05</td>
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<td>Serum P</td>
<td>2.95 ± 1.62</td>
<td>3.06 ± 1.37</td>
<td>P=0.42</td>
</tr>
<tr>
<td>PTH</td>
<td>429.15 ± 507.99</td>
<td>230.87 ± 190.92</td>
<td>P=0.08</td>
</tr>
<tr>
<td>Pathology:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoma/ Hyperplasia</td>
<td>8/1</td>
<td>9/7</td>
<td>P=0.08</td>
</tr>
</tbody>
</table>
RESULT

• There are no significant differences between parahyperthyroïsm patients with urolithiasis and without urolithiasis before operation in Age, Gender, Body weight, Renal function, Plasma calcium, Plasma phosphatate, PTH and Pathological type.
RESULT

• The overall stone recurrence rate: 36 %

• Patients with stone recurrence after parathyroidectomy have higher plasma calcium level than without stone recurrence (3.55 vs 2.94, p<0.05)

• No significant difference on pre-operative and post-operative group:
  - Age
  - Body weight
  - Plasma PTH, P
  - Creatinine and estimated GFR
  - Pathological type
DISCUSSION AND LITERATURE REVIEW

- Studies on potential predictors for stone formation in patients with PHPT
- Studies on potential predictors for stone recurrence after parathyroidectomy
AGE

- Wu et al. 2010: 3388 patients with PHPT, retrospective study (J Clin Endocrin Metab)
  - Increase risk of nephrolithiasis: younger age
  - Hyperparathyroidism: younger age predominant

- Odvina et al. 2007: 131 patients with PHPT, retrospective study (Uro Res)
  - Increase risk of nephrolithiasis: younger age
  - Stone-former vs. Non-stone former(y/o): 49.8 vs. 53.8(p < 0.05)
AGE

- Mollerup et al. 1999: 297 patients, prospective (World J Surgery)
  - Increased risk of nephrolithiasis: younger age
    (50 y/o vs. 61 y/o, p< 0.00001)

- Soreide et al. 1996: 1038 patients undergoing initial cervical exploration for primary hyperparathyroidism (PHPT), retrospective (Surgery)
  - Patients with renal stones were more often younger male patients
AGE

- **No effect of age on risk of nephrolithiasis:**
  - 2009 Berger et al: (J Urol.)
    patient number: 60 patients with primary hyperparathyroidism
  
  - 2002 Frokjaer: patient number: 91 patients (World J Surgery)
  
  - NTUH: 35 patients with primary hyperparathyroidism
GENDER

• Cooperberg et al. 2007: 339 patients undergoing surgery for PHPT (Int J Urol)
  - Nephrolithiasis was more common among men than women (40% vs 15%, P < 0.001)

• Odvina et al. 2007: 131 patients with PHPT, retrospective study (Uro Res)
  - Nephrolithiasis was more common among men than women (38% vs 23.2%, P < 0.05)

• Seroide et al. 1996: 1038 patients undergoing initial cervical exploration for primary hyperparathyroidism (pHPT), retrospective (Surgery)
  - Nephrolithiasis was more common among men than women (42% vs 21%, P < 0.001)
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PLASMA CALCIUM LEVEL

• Lower in stone former group:

• Mollerup et al. 1999: 297 patients, prospective
  - Stone former vs non-stone former (2.90 vs 3.04, \( p < 0.001 \))
PLASMA CALCIUM LEVEL

- No difference between stone former and non-stone former group:
  - 2009 Berger: patient number: 60 patients with primary hyperparathyroidism (J Urol.)
  - 2007 Odvina: 131 patients with PHPT, retrospective study (Uro Res)
  - 2002 Frokjaer: patient number: 91 patients (World J Surgery)
  - 1996 Seroide: 1038 patients, retrospective (Surgery)
  - NTUH: 35 patients with primary hyperparathyroidism
PLASMA PHOSPHATE LEVEL

• Lower in stone former group:
  - Seroide et al. 1996: 1038 patients, retrospective (Surgery)
    => plasma phosphate was lower in stone former group
    Stone former vs. Non-stone former: 2.7 vs. 2.8 (p < 0.05)

  - Odvina et al. 2007: 131 patients with PHPT, retrospective study (Uro Res)
    => plasma phosphate was lower in stone former group
    Stone former vs. Non-stone former: 2.55 vs. 2.74 (p < 0.05)
PLASMA PHOSPHATE LEVEL

- No difference between stone former and non-stone former group:
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  - 2002 Frokjaer: patient number: 91 patients (World J Surgery)
  - 1999 Mollerup: 297 patients, prospective (World J Surgery)
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PLASMA PTH LEVEL

• No difference between stone former and non-stone former group:
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### SUMMARY: POTENTIAL PREDICTORS

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<th>Potential predictors</th>
<th>Studies reporting increased risk</th>
<th>Studies reporting no effects</th>
</tr>
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<tbody>
<tr>
<td>Age (Increased potential in younger age)</td>
<td>(1) Wu et al. 2010 (2) Odvina et al. 2007 (3) Mollerup et al. 1999 (4) Soreide et al. 1996</td>
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| Plasma phosphate (Lower in stone former group) | (1) Seroide et al. 1996  
(2) Odvina et al. 2007                   | (1) Berger et al. 2009  
(2) Frokjaer et al. 2002  
(3) Mollerup et al. 1999  
(4) Silverberg et al. 1990  
(5) NTUH                        |
| Plasma PTH level                          | None                                                   | (1) Berger et al. 2009  
(2) Odvina et al. 2007  
(3) Frokjaer et al. 2002  
(4) Mollerup et al. 1999  
(5) Seroide et al. 1996  
(6) Silverberg et al. 1990  
(7) NTUH                        |
The potential predictor of stone recurrence after parathyroidectomy

Renal stone and primary hyperparathyroidism: Natural history of renal disease after successful parathyroidectomy.
1999 MOLLERUP ET AL

- 107 patients: Urolithiasis and parathyroidectomy
- Prospective follow up
- 5 years follow up
- Overall stone recurrence rate: 29.9%

<table>
<thead>
<tr>
<th>Parameter</th>
<th>With recurrent stone(s)</th>
<th>Without recurrent stone(s)</th>
<th>( p )</th>
</tr>
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<tbody>
<tr>
<td>No. of patients</td>
<td>32</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Male/female</td>
<td>17/15</td>
<td>30/45</td>
<td>NS**</td>
</tr>
<tr>
<td>Age at operation (years)</td>
<td>47</td>
<td>49</td>
<td>NS*</td>
</tr>
<tr>
<td>(11–69)</td>
<td>(12–78)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum calcium (mmol/L)</td>
<td>2.83</td>
<td>2.90</td>
<td>NS*</td>
</tr>
<tr>
<td>(2.58–3.91)</td>
<td>(2.60–4.00)</td>
<td></td>
<td></td>
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<tr>
<td>Parathyroid hormone ((\mu g/L))</td>
<td>0.78</td>
<td>0.73</td>
<td>NS*</td>
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<td>(0.25–2.60)</td>
<td>(0.36–0.97)</td>
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<td>Adenoma/hyperplasia (mg)</td>
<td>18/14</td>
<td>61/14</td>
<td>&lt; 0.05**</td>
</tr>
<tr>
<td>Weight of adenoma/hyperplasia</td>
<td>350</td>
<td>500</td>
<td>0.0014*</td>
</tr>
<tr>
<td>(47–3500)</td>
<td>(60–12,880)</td>
<td></td>
<td></td>
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Results are medians, with ranges in parentheses.
*Mann-Whitney U-test (level of significance \( p \leq 0.05 \)).
**Fischer’s exact test (level of significance \( p \leq 0.05 \)).
Patients with stone recurrence after parathyroidectomy have higher plasma calcium level than without stone recurrence (3.55 vs 2.94, p<0.05)

Table 2: Post-operative biochemistry and pathology in 25 patients with pre-operative stone formation. Comparison between stone recurrence and no stone recurrence.

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<td></td>
</tr>
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<td>Pathology:</td>
<td>8/1</td>
<td>9/7</td>
<td>P=0.08</td>
<td></td>
</tr>
</tbody>
</table>

- NS: no significant difference
- (a) Fisher’s exact test
- (b) Student t test
PATIENT STATUS POST PTX WITH STONE RECURRENCE

• Clinical studies have indicated that surgical cure does not completely eradicate hypercalciuria and hypophosphatemia, suggesting that these patients have some additional mineral disorder (2009 Park et al. BJU Int. 103: 670-678)

• Associations between BMI and risk of renal stones after PTX: It has been suggested that the increased incidence of nephrolithiasis in the general population during the last two to three decades. This maybe due to an increased excretion of urinary oxalate, uric acid, sodium, and phosphate in obese subjects (2008 Negri AL et al. Urol Res 36:303-307)
LIMITATIONS
• Problem 1: Small population (n=35)
• Problem 2: Retrospective study
  - Variable follow-up interval after parathyroidectomy: 12 months ~ 10+ years
  - Some missing data: KUB image, Lab data
• Problem 3: More important stone predictors are not available
  - 24hr Urine calcium level
  - Urine calcium concentration
  - Plasma Vitamin D3
  - Weight of parathyroid gland
CONCLUSION

• There are no significant differences between PHT patients with urolithiasis and without urolithiasis in age, gender, body weight, renal function, plasma calcium, plasma phosphatate, PTH and pathological type.

• The overall stone recurrence rate: 36 %

• Patients with stone recurrence after parathyroidectomy have higher plasma calcium level than without stone recurrence (3.55 vs 2.94, p<0.05)

• In clinical practice, post-parathyroidectomy patients who receive calcium supplement should closely monitor plasma calcium level because of the association of stone recurrence
THANKS FOR YOUR ATTENTION
REFERENCES


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