Persistent/Recurrent Primary Hyperparathyroidism

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Primary Hyperparathyroidism

Take home
Persistence/recurrence

• Persistence: Low 2 – 4% in experienced hands

• Recurrence: Low < 2% in sporadic PHPT but high in MEN1

• Problems of localization

• If localized: Targeted exploration
Primary Hyperparathyroidism

Bilateral neck exploration

- Localization of at least 4 parathyroid glands
- Remove only enlarged glands
- No biopsy of normal appearing glands, to avoid hypoparathyroidism
- Identification of the recurrent laryngeal nerve


Golden Standard
Primary Hyperparathyroidism

Initial exploration
Bilateral neck exploration (BNE)

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Primary Hyperparathyroidism

Bilateral neck exploration (BNE)
Normocalcemia – Initial surgery

3519/3778 (96.2%) patients [92-99.5%] - 8 authors

Karakas, E, Rothmund, M et al: Reoperations in primary hyperparathyroidism – Review of literature
Chirurg 76 (2005) 207-216
Primary Hyperparathyroidism

Initial exploration
Bilateral neck exploration (BNE)

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Primary Hyperparathyroidism

Persistent PHPT

Persistence of the typical laboratory parameters (symptoms) **within 6 months**
Primary Hyperparathyroidism

Recurrent PHPT

Occurrence of the typical symptoms and laboratory parameters of HPT later than 6 months
Primary Hyperparathyroidism

Causes of failure

Persistence

• Overlooked orthotopic / ectopic solitary adenoma
• Missed double adenoma / missed four gland disease
• Missed (ectopic) supernumerary gland
• Local recurrence of incomplete removed adenoma
Primary Hyperparathyroidism

Causes of failure
Persistence

• Overlooked orthotopic / ectopic solitary adenoma

• Missed double adenoma / missed four gland disease

• Missed (ectopic) supernumerary gland

• Local recurrence of incomplete removed adenoma
Abb. 6.4 Normale Lage und Lagevarianten der oberen Nebenschilddrüsen auf der Grundlage einer umfangreichen Autopsiestudie. Die Zahlen entsprechen Angaben in Prozent (nach Akerström u. Mitarb. [1984]).
Primary Hyperparathyroidism

Cause of failure
Overlooked orthotopic / ectopic solitary adenoma

Orthotopic localisation: 59 – 92 % (7 authors)
Ectopic localisation: 28 – 76 % (7 authors)

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Primary Hyperparathyroidism

Causes of failure
Persistence

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Primary Hyperparathyroidism

Cause of failure
Missed double adenoma / missed four gland disease

8 – 62 % (7 authors)

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Primary Hyperparathyroidism

Causes of failure

Persistence

• Overlooked orthotopic / ectopic solitary adenoma
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• Local recurrence of incomplete removed adenoma
Primary Hyperparathyroidism

How often more than 4 glands? (Anatomical studies)

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gilmour, C. (1937, 1938)</td>
<td>27/428</td>
<td>6.5</td>
</tr>
</tbody>
</table>
How often more than 4 glands?
(Functional studies)

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liechty, R.D.</td>
<td>1992</td>
<td>8/71</td>
<td>11</td>
</tr>
<tr>
<td>Thompson, N.W.</td>
<td>1983</td>
<td>18/238</td>
<td>7.6</td>
</tr>
<tr>
<td>Takagi, H.</td>
<td>1992</td>
<td>10/88</td>
<td>11.4</td>
</tr>
<tr>
<td>Numano, M.</td>
<td>1998</td>
<td>94/570</td>
<td>16.5</td>
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<tr>
<td>Meakins, J.L.</td>
<td>1984</td>
<td>3/12</td>
<td>25</td>
</tr>
<tr>
<td>Pattou, F.N.</td>
<td>2000</td>
<td>95/290</td>
<td>32.8</td>
</tr>
</tbody>
</table>
Primary Hyperparathyroidism

Location of supernumerary glands

- Thymus
- Fatty tissue (retrothyroidal, paraesophageal)
Primary Hyperparathyroidism

Supernumerary gland in the thymus
Primary Hyperparathyroidism

Supernumerary (ectopic) gland
Primary Hyperparathyroidism

Case report (G.W.) – supernumerary gland

MIBI with fusion CT
Primary Hyperparathyroidism

Case report (G.W.) – supernumerary gland
Primary Hyperparathyroidism

Cause of failure
Missed (ectopic) supernumerary gland

2 – 21 % (7 authors)

Primary Hyperparathyroidism

Causes of failure
Persistence

- Overlooked orthotopic / ectopic solitary adenoma
- Missed double adenoma / missed four gland disease
- Missed (ectopic) supernumerary gland
- Local recurrence of incomplete removed adenoma
Primary Hyperparathyroidism

Causes of failure

Recurrence

• Local recurrence of incomplete removed adenoma

• Redevelopment of primary hyperplasia (MEN1)
### Multiple Endocrine Neoplasia (MEN) MEN 1

PHPT - initial operation – results (I)

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Persistent n (%)</th>
<th>Recurrent n (%)</th>
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<tbody>
<tr>
<td>Wells (1980)</td>
<td>T+AT: 9</td>
<td>0</td>
<td>4/9 (44)</td>
</tr>
<tr>
<td>Prinz (1981)</td>
<td>S: 12</td>
<td>2/12 (17)</td>
<td>2/12 (17)</td>
</tr>
<tr>
<td>Van Heerden (1983)</td>
<td>S: 26</td>
<td>1/26 (4)</td>
<td>1/26 (4)</td>
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<tr>
<td>Rizzoli (1985)</td>
<td>S: 11</td>
<td>0</td>
<td>2/11 (18)</td>
</tr>
<tr>
<td>Malmaeus (1986)</td>
<td>S: 6</td>
<td>0</td>
<td>2/6 (33)</td>
</tr>
<tr>
<td></td>
<td>T+AT: 18</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mallette (1987)</td>
<td>T+AT: 3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Samaan (1989)</td>
<td>S: 8</td>
<td>0</td>
<td>1/8 (12)</td>
</tr>
<tr>
<td></td>
<td>T+AT: 5</td>
<td>0</td>
<td>0</td>
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Persistent/recurrent hypercalcemia
### Multiple Endocrine Neoplasia (MEN) MEN 1

PHPT - initial operation – results (II)

**Persistent/recurrent hypercalcemia**

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<td>Kraimps (1992)</td>
<td>S: 14</td>
<td>0</td>
<td>7/14 (50)</td>
</tr>
<tr>
<td>Hellmann (1992)</td>
<td>S: 11</td>
<td>0</td>
<td>3/11 (27)</td>
</tr>
<tr>
<td></td>
<td>T+AT: 12</td>
<td>0</td>
<td>1/12 (8)</td>
</tr>
<tr>
<td>O’Riordain (1993)</td>
<td>S: 54</td>
<td>0</td>
<td>16/54 (28)</td>
</tr>
<tr>
<td>Thompson (1997)</td>
<td>S: 27</td>
<td>1/27 (3.4)</td>
<td>5/27 (18.5)</td>
</tr>
<tr>
<td></td>
<td>E: 13</td>
<td></td>
<td>3/13 (23)</td>
</tr>
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Primary Hyperparathyroidism

Anatomic site of disease at reoperation

- Cervical position
  502/635 (79%) – Normal position 280/635 (44%)
- Mediastinal (ectopic) position
  133/635 (21%) – (Aorto-pulmonary window 5/635 (0.7%))

Primary Hyperparathyroidism

Initial vs. reoperations
Biochemical success

<table>
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<tr>
<th>Results</th>
<th>Initial Operation</th>
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Medical University of Vienna, Department of Surgery, 1988-2000
Primary Hyperparathyroidism

Reoperation

Normocalcemia

Success rate: 92 – 96 % (7 authors)

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Primary Hyperparathyroidism

Bilateral neck exploration

- Localization of at least 4 parathyroid glands
- Remove only enlarged glands
- No biopsy of normal appearing glands, to avoid hypoparathyroidism
- Identification of the recurrent laryngeal nerve


Old Golden Standard?
Primary Hyperparathyroidism

New “Golden Standard“?

- Targeted (limited) exploration by minimally invasive techniques
Primary Hyperparathyroidism

Can „failures“ be prevented in the era minimally invasive procedures?

- Preoperative localisation techniques (MIBI a/o US)
- Intraoperative (quick) PTH monitoring
Primary Hyperparathyroidism

Accuracy of different localizing studies

- **Noninvasive**
  - Ultrasonography (small part/real time) 44 – 76%
  - Technetium 99m sestamibi scanning 58 – 88%
  - CT 11 – 79%
  - MRI 57 – 67%

- **Invasive**
  - Selective venous catheterizations and sampling 44 – 88%
  - Selective angiography 49 – 73%
  - Ultrasonography-guided fine-needle aspiration 73 - 82%

Primary Hyperparathyroidism

Can „failures“ be prevented applying minimally invasive procedures?

- Preoperative localisation techniques (MIBI a/o US)
- Intraoperative (quick) PTH monitoring
Primary Hyperparathyroidism

QPTH - monitoring
Baseline value - interpretation

....... different recommendations in literature!
Primary Hyperparathyroidism

Causes of failure
Guided exploration by preoperative localization and intaoperative QPTH monitoring

• Missinterpretation of the intraoperative PTH decay

• „Sleeping Adenoma“ - Recurrence in a second gland which may develop with time
Primary Hyperparathyroidism

QPTH - monitoring

Pitfalls

1. Wrong measurements
   a) technical assay problems
   b) problems with blood sampling
2. „Biochemical“ Frozen Section (Irvin, 1994)
   (take care what you remove!)
3. Very high/low basal values
4. Wrong basal value („extirpation“ value)
5. Renal insufficiency
6. Manipulation before extirpation
Primary Hyperparathyroidism

Open minimally invasive parathyroidektomy (OMIP)
Bilateral neck exploration (BNE)

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Medical University of Vienna, Department of Surgery, 1999-2000
Primary Hyperparathyroidism

Pitfall 1

The missed double adenoma

![Graph showing PTH levels over time](image)
Primary Hyperparathyroidism

Pitfall 2

The „sleeping adenoma“

![Graph showing PTH levels over time during surgery](image-url)

- PTH (pg/ml)
- Op I
- Op II

„Sleeping Adenoma?“
Primary Hyperparathyroidism

Considerations of successful reoperation

- Confirmation of diagnosis (FHH!?)
- Review of previous surgical reports
- Review of previous pathological reports with reevaluation of the specimens/slides
- Localization procedures
Primary Hyperparathyroidism

Localization studies before reexploration

Algorithm

- Hyperfunctioning parathyroid tissue where?
  - MIBI scintigraphy – ultrasonography
    - If negative or unequally:
      - Regionalisation by selective venous sampling for PTH determination
    - If positive:
      - Computerized tomography (CT) or magnetic resonance imaging (MRI) for localization

- Which surgical approach?
Primary Hyperparathyroidism

Persistent/recurrent HPT
Recommended surgical approach

- Limited (targeted) exploration after positive localization procedures with **TWO** techniques to reduce complications and to increase success

- Possible intraoperative use of QPTH to confirm cure

- Cryopreservation
European Society of Endocrine Surgeons

ESES Workshop Vienna

MAY 17-19, 2007
Endoscopic Surgery in Neuroendocrine Pancreatic Tumors
http://www.meduniwien.ac.at/chir-endokrin

Chirurgische Endokrinologie