Hyperparathyroidism: Operative Considerations

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- Primary
- Secondary
- Tertiary

Hyperparathyroidism

- Primary hyperparathyroidism
  - Parathyroid adenoma
  - Parathyroid hyperplasia
  - Multiple parathyroid adenomas
  - Parathyroid carcinoma
Primary Hyperparathyroidism: Background

- Over past 30 years, shift in clinical presentation of primary hyperparathyroidism (PHPT)
- Once viewed as a rare, symptomatic disorder characterized by kidney stones, bone loss, neuromuscular disorders, and other signs of hypercalcemia
- Today, PHPT recognized to have much higher incidence than previously thought

Primary Hyperparathyroidism: Background

- PHPT today
  - Usually only mildly symptomatic or asymptomatic
- Symptomatic PHPT: Benefits of surgery
  - Improved bone density
  - Better cognitive function
  - Less kidney stones
  - Improved quality of life
  - Reduced risk of premature death

Primary Hyperparathyroidism: Background

- Asymptomatic PHPT
  - Indications for surgery first defined in 1990 NIH Consensus Conference
  - Guidelines for surgery refined twice since, most recently in May 2008, by a Third International Workshop

Asymptomatic PHPT: Indications for surgery

- Third International Workshop on Asymptomatic PHPT (2008)
  - One mg/dL above the upper limit of the reference range for serum calcium
  - GFR < 60 mL/min
  - Bone mineral density T-score below -2.5 at any site and/or previous fracture fragility (For premenopausal women or men <40 years old, Z scores rather than T scores are used)
  - Age younger than 50 years
- Surgery recommended for patients who meet any of these guidelines
Asymptomatic PHPT:
Indications for surgery

• Surgery is always an option, even in patients who do not meet surgical criteria, if medical surveillance not possible or desired
• American Association of Clinical Endocrinologists and the American Association of Endocrine Surgeons.
  – “...operative management should be considered and recommended for all asymptomatic patients with PHPT who have a reasonable life expectancy and suitable operative and anesthesia risk factors.” (Endocr Pract. 2005;11(1):49-54.)

Asymptomatic PHPT:
Guidelines for surgery

• Age < 50
  – Greater risk of complications of PHPT over time
  – Over 15 years, 60% of untreated asymptomatic PHPT patients lose >10% bone density

Asymptomatic PHPT:
Guidelines for surgery

• Threshold for serum calcium: One mg/dL above the upper limit of reference range
• Hypercalciuria no longer an indication for surgery
  – No evidence that hypercalciuria is independent risk factor for kidney stones
• Renal function is important consideration
  – GFR <60mL/min → higher risk of complications

Asymptomatic PHPT:
Guidelines for surgery

• PHPT patients have lower bone density and increased fracture risk
• PHPT patients with normal bone density have higher fracture risk
• Surgery decreases risk of fracture in PHPT patients by 30% over 20 years
Asymptomatic PHPT: Guidelines for surgery

- Not yet any clear consensus
  - PHPT and neuropsychiatric disease
  - PHPT and cardiovascular disease
  - Normocalcemic PHPT

PHPT and Neuropsychiatric disease

- Many patients with asymptomatic PHPT have some neurocognitive findings
- Some studies indicate that these neurocognitive deficits improve modestly after surgery
- Randomized prospective trials needed

PHPT and Cardiovascular disease

- It is recognized that escalated cardiovascular risk occurs with marked hypercalcemia
- Cardiovascular consequences of mild PHPT are subtle and have unknown implications
- Further research may alter future surgical recommendations

Normocalcemic PHPT

- Characterized by consistently normal calcium but persistently elevated PTH levels (in absence of recognizable underlying cause of elevated PTH)
- Frequency, natural history, and optimal management remains uncertain
- No guidelines for surgical or medical management at this time
Parathyroidectomy

• Remains the definitive treatment for PHPT
• A cost-effective option for patients with life expectancy of 5 or more years
• Generally safe and effective, but surgeon experience can impact cure and complication rates

Non-surgical management of PHPT

• Patients who do not meet surgical guidelines can be followed safely without surgery
• Monitoring is critical
  – Serum calcium annually
  – Serum creatinine annually
  – Bone density every 1 to 2 years (3 sites)
• Recommendations for calcium intake same as for patients without PHPT

Non-surgical management of PHPT

• Pharmacologic treatment: May have utility, but insufficient long-term data to make recommendation as alternative to surgery
  – Bisphosphonates
  – Estrogen
  – Selective estrogen receptor modulators
  – Calcimimetics

Non-surgical management of PHPT

• Pharmacologic treatment
  – Bisphosphonates
    • Alendronate: Shown to increase bone density of lumbar spine and hip regions, but does not decrease serum calcium
  – Estrogen
  – Selective estrogen receptor modulators
  – Calcimimetics
Non-surgical management of PHPT

- Pharmacologic treatment
  - Bisphosphonates
  - Estrogen
  - Selective estrogen receptor modulators
  - Calcimimetics
  - Cinacalcet: Approved in many European countries for PHPT, is effective in reducing serum calcium, often to normal, but does not result in major changes in BMD

Secondary hyperparathyroidism

- Definition: Overproduction of PTH secondary to chronic abnormal stimulus
- Typically due to chronic renal failure
- Vitamin D deficiency can also be cause
- Most patients with ESRD have elevated PTH

Secondary hyperparathyroidism

- Etiology: In chronic renal failure, PTH is overproduced in response to hyperphosphatemia, hypocalcemia, and impaired 1,25-dihydroxy vitamin D production
- Pathophysiology: Chronic elevated PTH contributes to spectrum of bone disease, cardiovascular calcification, endocrine disturbances, neurobehavior changes

Secondary hyperparathyroidism

- Treatment: Usually medical management
  - Correct Vit D Deficiency
  - Dietary phosphate restriction
  - Phosphate binders
  - Calcium supplementation (< 2g/day)
Secondary hyperparathyroidism

- **Surgical indications:** Bone pain or fracture, calciphlaxis, extraskeletal nonvascular calcifications despite medical therapy
- Parathyroidectomy should be considered in patients with severe hyperparathyroidism (PTH > 800 pg/mL), associated with hyperphosphatemia refractory to medical therapy

Secondary hyperparathyroidism: Surgery

- 4-gland exploration necessary
- Diffuse hyperplasia usually encountered
- Total parathyroidectomy with autotransplantation or 3.5 gland parathyroidectomy

Tertiary hyperparathyroidism

- Development of autonomous hypersecretion of PTH causing hypercalcemia
- Patients with history of chronic secondary hyperparathyroidism, who have persistent hyperparathyroidism after renal transplantation
- 4-gland involvement usually seen

Tertiary hyperparathyroidism

- **Treatment:** total parathyroidectomy with autotransplantation or subtotal parathyroidectomy
Summary

• Hyperparathyroidism: Operative considerations
  – Surgery indicated for all patients with symptomatic PHPT and most patients with asymptomatic PHPT
  – Surgery indicated for severe secondary hyperparathyroidism refractory to medical therapy

References