

Surgical Management of Primary Hyperparathyroidism in Older Adults

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OBJECTIVES: To compare the feasibility, safety, and outcome of parathyroidectomy in the management of primary hyperparathyroidism (PHPT) in individuals aged 75 and older with that of those younger than 50.

DESIGN: Retrospective chart review.

SETTING: Department of Endocrine Surgery, Hospital Paul Desbief (Marseille, France).

PARTICIPANTS: Individuals who underwent surgery from June 2005 to February 2013 (N = 526) had a clinical examination and laboratory and imaging assessments to diagnose PHPT.

MEASUREMENTS: The clinical and biochemical characteristics and surgery outcomes of individuals younger than 50 (n = 80) were compared with the characteristics and outcomes of those aged 75 and older (n = 89).

RESULTS: Most of the participants did not have any specific signs of PHPT, and the diagnosis of PHPT was established in some participants during routine clinical and laboratory examination. Nephrolithiasis and osteitis fibrosa cystica were observed only in the younger group. Urinary calcium decreased with age. Nine participants aged 75 and older did not undergo surgery (four declined, five had medical contraindications). Conventional surgery through transverse cervicotomy was used in the majority of participants. Cure rate was excellent (158/160), with few and reversible minor complications. The coexistence of thyroid lesions was significantly higher in the older (47.5%) than in the younger group (32.3%). Nodules and multinodular goiters were removed in the majority of participants during the parathyroidectomy procedure.

CONCLUSION: With the exception of a few cases with severe associated comorbidities, parathyroidectomy is safe and curative and should be considered as first-line choice for older adult with PHPT. *J Am Geriatr Soc* 62:1759–1763, 2014.

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Primary hyperparathyroidism (PHPT) causes a hypercalcemic state due to excessive parathyroid hormone (PTH) secretion. In most individuals, a benign solitary adenoma with a loss of the feedback control of extracellular calcium on PTH secretion causes the disease. PHPT is the third most frequent endocrine disorder, with greater incidence with age, women aged 50 and older being most affected.¹ Surgery is the only permanent treatment for the disease, but there is a progressive age-related decline in the rate of parathyroidectomy (PTx) after age 70 that seems to be subsequent to a perceived risk:benefit ratio rather than associated comorbidities.² Surveillance or medical treatment have been proposed for individuals who do not undergo surgery.³ The question of the risks and benefits of surgical treatment in the management of PHPT in older adults is a matter of debate.^{4–6}

The aim of the present investigation was to compare the feasibility, safety, and outcome of PTx in the management of PHPT in individuals aged 75 and older with that of individuals younger than 50 and to compare their clinical and biological status.

PARTICIPANTS AND METHODS

Participants

From June 2005 to February 2013, 526 individuals were admitted to the Department of Endocrine Surgery of the Hospital Paul Desbief (Marseille, France) for treatment of PHPT. The diagnosis of PHPT was based on high serum calcium (>2.55 mmol/L) with high (>75 pg/mL) serum intact PTH or PTH concentrations in serum that were not correlated with circulating calcium values.

Study Protocol

Information was collected on the clinical presentation, biochemical and imaging data, and surgery outcomes

from the medical charts of participants (aged <50, ≥75). The Desbief Hospital review board approved the study design.

Laboratory Methods

Serum calcium and 24-hour urinary calcium excretion were measured using standard methods. Serum 1–84 PTH was measured using immunoradiometric assay and serum 25-hydroxyvitamin D (25(OH) D) using radioimmunoassay.

Statistical Analysis

Results are given as means ± standard deviations. Between-group comparisons were tested for statistical significance using chi-square tests for discontinuous variables. Analysis of biochemical parameters using the D'Agostino and Pearson omnibus minimality test revealed that they did not follow a normal distribution, so they were analyzed using the Mann–Whitney *U*-test. Statistical significance was determined at $P < .05$. Statistical analysis was performed using Statview (Abacus Concepts, Berkeley, CA).

RESULTS

Participant Characteristics

Of the 526 individuals referred to the Department of Endocrine Surgery during the 6.5-year period, 80 were younger than 50 (15.2%) and 89 were aged 75 and older (16.9%). The female:male ratio was 0.79 in the younger group and 0.94 in the older group. Individuals aged 51 to 74 (357/526; 67.9%) were not included in the study.

Influence of Age on Clinical Presentation of PHPT

PHPT was asymptomatic or minimally symptomatic in the majority of participants. Nonspecific complaints, including weakness, easy fatigability, and bone and joint pain, were the most common symptoms (Table 1). After the age of 75, these symptoms may be related to age-associated phys-

iological changes. Hypercalcemia was incidentally identified as a part of routine laboratory evaluation for thyroid surgery in 22 participants (13 younger, 9 older). Significant differences were observed in the presentation of PHPT between the younger and older groups. Conditions classically associated with PHPT (nephrolithiasis (27.5%) and osteitis fibrosa cystica (2 cases)) were found only in individuals aged 50 and younger. In this group, PHPT was also diagnosed in five participants during evaluation of multiple endocrine neoplasia. Gastrointestinal symptoms (nausea, constipation) were significantly more frequent in older participants.

Comorbidities and Polymedication

Markers of physiologic vulnerability that appear specifically in older adults were assessed preoperatively in participants aged 75 and older according to guidelines for elderly adults.⁷ Signs of frailty (mild cognitive impairment or dementia, undernutrition, falls, anemia, activity of daily living difficulties) and comorbidity (Charlson index, medication, Table 2) were assessed according to a previously developed methodology.⁸ Four individuals declined surgery and were not included in this evaluation. At least one sign of frailty was found in 14 of 85 participants, including five not eligible for surgery (two with dementia and chair-ridden and three with severe unstable cardiovascular disease). More participants aged 75 and older were being treated for hypertension (58.2%) than those younger than 50 (10.1%). The prevalence of diabetes mellitus was also higher in older (16.5%) than in younger (3.9%) participants. Only older participants were undergoing atrial fibrillation (6.3%), anticoagulant (10.1%), and antiplatelet treatment (12.7%).

Biochemical Parameters

No differences in mean serum calcium (2.75 ± 0.02 vs 2.76 ± 0.02 mmol/L), PTH (179 ± 24 vs 148 ± 9 pg/mL), and 25(OH) D (21.9 ± 1.9 vs 18.1 ± 1.3 ng/mL) were observed between participants younger than 50 and those aged 75 and older, respectively ($P > .05$). Twenty-four-hour urinary calcium was lower in the older (215 ± 24 mg/d) than in the younger (325 ± 17 mg/d) group ($P < .001$).

Table 1. Circumstances of Diagnosis of Primary Hyperparathyroidism

| Circumstances of Diagnosis | ≤50, n = 80 | ≥75, n = 89 | P-Value |
|--|-------------|-------------|---------|
| Routine calcium measurement | 6 | 16 | .04 |
| Routine calcium measurement before thyroid surgery | 13 | 9 | .24 |
| Nonspecific complaints | 27 | 39 | .18 |
| Nephrolithiasis | 22 | 0 | <.001 |
| Skeletal abnormalities ^a | 2 | 5 | .31 |
| Multiple endocrine neoplasia evaluation | 5 | 0 | .02 |
| Neuropsychiatric symptoms | 1 | 3 | .36 |
| Gastrointestinal symptoms | 4 | 12 | .06 |
| Arthralgia | 0 | 3 | .10 |
| Acute hypercalcemia | 0 | 2 | .18 |

^aOsteitis fibrosa cystica in those younger than 50, osteoporosis in those aged 75 and older.

Table 2. Geriatric Assessment of Individuals Aged 75 and Older with Primary Hyperparathyroidism (n = 85)

| Factor | Value |
|---|-------------|
| Dementia, n | 2 |
| Cognitive impairment, n | 4 |
| Undernutrition, n | 6 |
| Disability, n | 2 |
| Falls, n | 2 |
| Anemia, n | 1 |
| Charlson Comorbidity Index ≥3, n | 9 |
| American Society of Anesthesiologists score ≥3, n | 14 |
| Number of medications, mean (standard error) | 4.25 (0.36) |
| ≥1 signs of frailty, n | 14 |

Imaging

Ultrasound and sestamibi scans were not performed in all participants, and the same operator did not perform each technique. When imaging was performed, solitary parathyroid adenomas were detected using sestamibi scan in 77.9% of cases and ultrasound in 46.5%. Scintigraphy and ultrasound were both positive in 33.3% of the cases.

Influence of Age on Surgery Procedure

As reported above, nine participants aged 75 and older did not undergo PTx; four declined, and five were not eligible. Thereafter, five participants were under surveillance, one underwent cinacalcet treatment, and three were lost to follow-up. Conventional surgery using transverse cervicotomy was used in the majority of participants: 63 of 80 aged 50 and younger and 69 of 80 aged 75 and older. A minimally invasive approach under general anesthesia was used in 16 younger and seven older participants and was performed under local anesthesia in five participants ($1 \leq 50$, $4 \geq 75$). In the 28 participants with minimally invasive surgery, parathyroid adenoma was located preoperatively in 94.7% of the cases using sestamibi scan, in 60.9% of the cases using ultrasound, and in 64.7% of the cases using both. Solitary parathyroid adenomas were found in the majority of participants (77.6% of younger, 81.0% of older). Parathyroid hyperplasia was more common in the younger (17.5%) than in the older (8.8%) group.

Influence of Age on Surgery Outcome

Overall surgery outcome was excellent. PHPT was cured in 158 of 160 participants, as demonstrated by normal serum calcium and PTH. Two participants in the older group were not cured. No parathyroid lesion was found in one case, and the participant was kept under surveillance thereafter. PHPT remained after excision of a parathyroid adenoma in the other case, and the participant was treated with cinacalcet thereafter. One participant aged 50 and younger had a cervical hematoma that complicated PTx, and one participant aged 75 and older had delirium. The latter participant underwent surgery under local anesthesia because she had experienced delirium previously after general anesthesia for colonoscopy. These complications were reversible, like other benign side effects such as arthralgia and hypotension reported in three participants aged 50 and younger and seven aged 75 and older. No complications were observed in eight of nine participants with at least one sign of frailty. Transient hypoparathyroidism occurred in five participants aged 50 and younger and in three aged 75 and older. No permanent hypoparathyroidism or vocal cord palsy was observed (Table 3).

Associated Thyroid Lesions

Overall thyroid pathology was present in 31.2% of participants aged 50 and younger and 43.8% of those aged 75 and older. Solitary nodules were removed using lobectomy in 83.3% of younger and 9.5% of older participants. In older participants nodules were not removed in 28.6% cases, and excision was limited to the nodule in 61.9%.

Table 3. Parathyroidectomy Techniques, Outcomes, and Complications in Individuals with Primary Hyperparathyroidism

| | ≤ 50 , n = 80 | ≥ 75 , n = 89 | |
|---|--------------------|--------------------|---------|
| Techniques, Outcomes, and Complications | n | | P-Value |
| Technique | 80 | 80 | .004 |
| Transverse cervicotomy | 63 | 69 | .29 |
| Minimally invasive | 16 | 7 | .04 |
| Local anesthesia | 1 | 4 | .17 |
| Cured | 80 | 78 | .15 |
| Complication | | | |
| Transient hypoparathyroidism | 5 | 3 | .47 |
| Cervical hematoma | 1 | 0 | .32 |
| Delirium | 0 | 1 | .34 |
| Arthralgia | 2 | 4 | .48 |
| Hypotension | 0 | 2 | .18 |
| Phlebitis | 0 | 1 | .34 |
| Pyelonephritis | 1 | 0 | .29 |

Table 4. Type of Thyroid Lesions and Surgical Technique in Individuals with Primary Hyperparathyroidism

| Type of Thyroid Lesion and Surgical Technique | ≤50, n = 80 | ≥75, n = 89 | P-Value |
|---|----------------|-------------|---------|
| | n | | |
| Surgery | 80 | 80 | .004 |
| Solitary nodule | 12 | 21 | .08 |
| Nodule excision | 1 | 13 | .003 |
| Lobectomy | 10 | 2 | <.001 |
| No excision | 1 ^a | 6 | .17 |
| Multinodular goiter | 13 | 17 | .42 |
| Thyroidectomy | 13 | 16 | .37 |
| Normal thyroid | 55 | 42 | .05 |

^aExcision was not performed because of a significant risk of permanent hypoparathyroidism.

Multinodular goiters were also found and removed, with no significant difference in frequency between groups (Table 4).

DISCUSSION

As expected, PHPT was more common after age 50 (84.8%), with 16.9% of participants with PHPT being aged 75 and older, with a female predominance. PHPT manifested differently in older than in younger participants, with neither nephrolithiasis nor osteitis fibrosis cystica observed in the older group. A comparable difference in PHPT presentation between older and younger individuals has been previously reported.^{9,10} Nonspecific complaints (weakness, easy fatigability, bone and joint pain) were the most frequent symptoms. They have been classified as neuromusculoskeletal symptoms. Their origin and their relationship with PHPT are not well understood. Alterations in neuronal function and in type II muscle fibers have been reported.¹¹ Benefits of surgery over observation on the evolution of asymptomatic or minimally symptomatic PHPT have been evaluated in a few random-

ized controlled trials. A significant improvement in bone mineral density has been reported after PTx. The effects of PTx on quality of life are variable. Symptoms such as fatigue; muscle, bone, and joint pain; functional capacity; hypertension; and quality of life improve after PTx in approximately 60% of cases,^{12,13} although no change in quality of life or neuropsychiatric symptoms was observed in a large study after PTx.¹⁴

There was no difference in serum calcium, PTH, and vitamin D levels between groups. Aging was associated with a reduction in urinary calcium excretion. A physiological decrease in renal calcium excretion has been reported after the seventh decade, possibly because of reduced intestinal calcium absorption,^{15,16} although caution must be taken when interpreting such results because of possible incomplete urine collection.

PTx was curative and safe whatever the age and the surgical technique. With the exception of two cases, participants in both groups were cured with few and reversible complications. Transient hypoparathyroidism was observed in a small number of participants in both groups. Reversible complications unrelated to PTx occurred in three younger and eight older participants. Excellent results have been reported in older adults, even in nonagenarians.^{4,17-19} The safety of PTx in older adults was demonstrated in a retrospective study of 1,275 participants aged 65 and older, including 217 aged 80 and older.²⁰ Moderately longer hospital and recovery room stays have been reported in older adults. Rate, timing, and types of complications were similar in younger and older participants.⁶ There is a trend in parathyroid surgery for moving from bilateral neck cervicotomy to minimally invasive surgery. Such an approach is especially interesting in older adults because solitary adenoma is found more frequently in older adults, whereas parathyroid hyperplasia is found more often in younger adults.²¹ Minimally invasive surgery under local anesthesia may also be used in individuals in whom general anesthesia is contraindicated.^{22,23} Along with a careful preoperative geriatric assessment by the medical team, minimally invasive surgery gives excellent results, especially with previous imaging location.^{24,25}

It is important to emphasize the benefits of surgery in older adults and to evaluate whether surgery should be performed. PTx is underused in the management of PHPT in individuals aged 75 and older. The likelihood of PTx decreases linearly in individuals aged 60 and older from those aged 50 to 59 (aged 70–75, odds ratio (OR) = 0.41, aged ≥80, OR = 0.11).² The indication for PTx was defined in the 2008 National Institutes of Health Consensus Conference,²⁶ although medical surveillance may be proposed in asymptomatic or paucisymptomatic older adults with serum calcium levels lower than 2.75 mmol/L, urinary calcium lower than 400 mg/d or 10 mmol/L, normal creatinine clearance and an osteodensitometric T score above –2.5 SD. In the current study, 27 participants aged 75 and older who underwent PTx did not meet the above-mentioned criteria for PTx and could have been simply observed or received pharmacologic therapy. During a mean 4.7-year follow-up of 904 participants, approximately 15% showed progression of the disease, this percentage increasing with age and high PTH levels.²⁷ Few reports are available on the follow-up of individuals with

PHPT under medical surveillance. Bisphosphonates and cinacalcet have been proposed, although they have limited effects on clinical and biological signs of disease. Bisphosphonates could be considered in individuals with low bone mineral density, whereas cinacalcet is more efficient in decreasing calcium levels and improving neuropsychological alterations, but cinacalcet is expensive and may have adverse effects in older adults with comorbidities and polypharmacy.²⁸

Thyroid lesions were associated with PHPT in 31.3% of participants aged 50 and younger and 47.5% aged 75 and older. Such an association was recently reported in 24.7% to 51% of participants.²⁹⁻³¹ The higher prevalence of thyroid lesions in the older group is consistent with the observation that the frequency of thyroid nodules increases throughout life.³² Surgical cure of thyroid lesions was performed in the majority of participants to prevent additional surgery and detect malignancy, but in individuals aged 75 and older, surgery for thyroid lesions may be more limited than in younger individuals because it requires a more-extensive neck dissection than PTx. Routine use of ultrasound in individuals with PHPT is suitable for choosing between bilateral neck exploration and a minimally invasive approach. The coexistence of thyroid nodules may influence the surgical approach for PTx; the minimally invasive method may be reserved for resection of ipsilateral nodules.²⁸ Routine serum calcium measurement before thyroid surgery has been associated with the detection of PHPT in 10.1% of older and 16.3% of younger individuals.³³

PTx is as efficient and safe in older as in younger individuals, so it can be safely proposed to individuals with PHPT whatever their age, avoiding progressive decrease in bone mineral density, long-term surveillance, risk of evolution toward acute hypercalcemia, and possible adverse events of medical treatment for hypercalcemia, but a careful preoperative geriatric assessment should be performed to evaluate the benefits and risks of PTx and to determine eligibility for surgery. Thyroid lesions frequently coexist with PHPT and may be treated during the same surgical procedure.

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Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

Author Contributions: Denizot, Oliver: concept and design. Denizot, Oliver: collection of data. Grino: statistical analysis, intellectual contribution, critical review of the manuscript.

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