Asymptomatic Primary Hyperparathyroidism

Diagnostic Pitfalls and Surgical Intervention

James X. Wu, MD*, Michael W. Yeh, MD

KEYWORDS

• Asymptomatic primary hyperparathyroidism • Parathyroid hormone
• Parathyroidectomy • Hypercalcemia • Nonclassic primary hyperparathyroidism

KEY POINTS

- In most cases, primary hyperparathyroidism can be diagnosed by measuring serum calcium and parathyroid hormone.
- Nearly half of cases of primary hyperparathyroidism have a "nonclassic" presentation, with hypercalcemia and inappropriately normal parathyroid hormone levels.
- Parathyroidectomy has become a more commonplace and safe procedure, but many patients, especially elderly patients, are not appropriately referred for surgical consultation.

INTRODUCTION

Primary hyperparathyroidism (PHPT) is a disease caused by the excess production of parathyroid hormone (PTH), resulting in the dysregulation of calcium metabolism. The current estimated prevalence of PHPT is as high as 1 in every 400 women, and 1 in 1000 men.[1] Symptoms caused by hypercalcemia and elevated PTH levels manifest insidiously over an extended period of time; most patients with PHPT are asymptomatic, with only a small fraction exhibiting classic signs and symptoms. Patients with asymptomatic disease were largely undiagnosed until the advent of the multichannel autoanalyzer in the 1970s, which subsequently led to the adoption of routine serum calcium measurements. Detection of hypercalcemia on routine serum calcium screening has greatly facilitated the diagnosis of PHPT: from 1995 to 2010, the

The authors have nothing to disclose.
Section of Endocrine Surgery, UCLA David Geffen School of Medicine, 10833 Le Conte Avenue, Los Angeles, CA 90095, USA
* Corresponding author. UCLA David Geffen School of Medicine, 10833 Le Conte Avenue, 72-228 CHS, Los Angeles, CA 90095.
E-mail address: JamesWu@mednet.ucla.edu

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incidence of PHPT tripled.[1] This article addresses the diagnosis and surgical management of asymptomatic PHPT.

BIOCHEMICAL DIAGNOSIS OF PRIMARY HYPERPARATHYROIDISM

Our standard biochemical panel for the initial workup of suspected PHPT is shown in **Box 1**. Most ambulatory patients have normal serum phosphorus, creatinine, and albumin. Hence, the diagnosis can be determined by serum calcium and serum PTH in most cases. We routinely measure the serum 25-hydroxy (25-OH) vitamin D level to clarify the diagnosis in borderline cases, and to help differentiate between primary and secondary hyperparathyroidism.

Calcium

Suspicion of asymptomatic hyperparathyroidism typically begins with incidental detection of elevated serum calcium. A single elevation of the serum calcium is frequently spurious. Therefore, repeat testing of the serum calcium is recommended before proceeding further in the diagnostic workup of PHPT. Because 40% to 45% of serum calcium is protein-bound, total serum calcium should be corrected for serum albumin. Corrected serum calcium is calculated by the following: measured total serum calcium (mg/dL) + 0.8 (4.0 – measured serum albumin [g/dL]). Per the recent 2013 guidelines established by the Fourth International Workshop on the Management of Asymptomatic Primary Hyperparathyroidism, total serum calcium should be used to establish the diagnosis and not ionized calcium, because ionized calcium testing is not widely available.[2]

Ionized calcium directly measures the bioactive (free) fraction of serum calcium, which more accurately reflects patients' true calcium status than albumin-corrected total calcium, particularly for patients with hyperparathyroidism.[3] Among patients with histologically confirmed PHPT, up to 24% have elevated ionized calcium levels despite normal total calcium levels.[4,5] Additionally, ionized calcium may be informative in hypoalbuminemic patients (ie, patients with cirrhosis or nephrotic syndrome) with suspected PHPT. However, we have noted greater intra-assay variability when

Box 1
Initial diagnostic workup of hyperparathyroidism

Routine tests

Serum calcium

Parathyroid hormone

Serum phosphorus

Serum creatinine

Serum albumin

Optional tests

Ionized calcium (hypoalbuminemic patients, borderline diagnoses)

25-OH vitamin D (nonclassic presentation or suspected vitamin D deficiency)

Urinary calcium excretion (suggestive family history for FHH)

Abbreviation: FHH, familial hypocalciuric hypercalcemia.

measuring ionized calcium compared with total calcium, which may be attributed to the pH-dependence of ionized calcium.

Parathyroid Hormone

Excess production of PTH can be easily determined by measuring serum PTH. Serum PTH should be interpreted in the context of serum calcium. In patients with hypercalcemia or calcium levels near the upper limit of the reference range, an elevated serum PTH is diagnostic of PHPT. However, a normal PTH level does not rule out PHPT; up to half of patients with PHPT have hypercalcemia with inappropriately normal levels of PTH.[1,6]

PTH assay has undergone evolution over the past 53 years.[7] First-generation PTH assays are obsolete, now replaced by second-generation and third-generation assays. The second-generation PTH assays cross-react with large degradation products of PTH, whereas third-generation assays are more specific for biologically active PTH. Nonetheless, the diagnostic sensitivity of second-generation and third-generation PTH assays are similar for PHPT.[8] In patients with chronic kidney disease, impaired clearance of degradation products of PTH will result in much higher readings with second-generation assays compared with third-generation assays. Third-generation PTH assays also have greater utility as intraoperative PTH assays.[9] Today, most commercial PTH assays are second-generation assays, but also include third-generation assays. Significant variability has been demonstrated between commercially available assays, even between tests of the same generation, so it is important to remain consistent and to interpret results using test-specific reference ranges.[10,11]

Hypercalcemia with Inappropriately Normal Parathyroid Hormone: Nonclassic Primary Hyperparathyroidism

In some patients with PHPT, serum PTH is not elevated above the 95% reference range. An inappropriately normal (nonsuppressed) PTH level despite hypercalcemia is still indicative of disrupted negative feedback, and confirms the diagnosis of nonclassic PHPT. Nonclassic PHPT simply refers to PHPT that presents with elevated serum calcium but inappropriately normal PTH (PTH 21–65 pg/mL). In a study of 3.5 million patients within a vertically integrated health care organization, we found that the number of patients with nonclassic PHPT nearly equaled the number with classic PHPT (**Fig. 1**).[1] Patients with nonclassic PHPT were not regularly monitored, infrequently underwent bone densitometry measurement, and were rarely referred for surgery, reflecting missed or delayed recognition of the diagnosis. In our practice, we

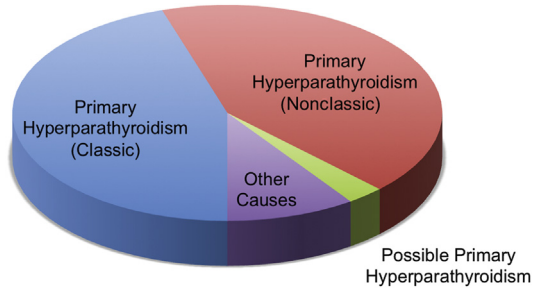

Fig. 1. Causes of hypercalcemia. Classic primary hyperparathyroidism: hypercalcemia and PTH; Nonclassic primary hyperparathyroidism: hypercalcemia with inappropriately normal (nonsuppressed) parathyroid hormone.

have noted considerable confusion on the part of general practitioners and even endocrinologists with regard to establishing the diagnosis nonclassic PHPT.

Vitamin D

Although vitamin D levels are not required to establish the diagnosis of PHPT in patients with "classic" PHPT, serum 25-OH vitamin D levels can clarify the diagnosis in challenging or borderline cases. Because adequate levels of vitamin D can suppress PTH secretion, the Endocrine Society and Institute of Medicine both agree that the reference range of PTH values for vitamin D–replete patients should be lower than for patients who are vitamin D deficient. The strict definition of "vitamin D replete" is controversial, as the Institute of Medicine and 2013 International Workshop both recommend a threshold of 50 nmol/L to be considered "vitamin D replete," whereas the Endocrine Society has recommended a more stringent threshold of 75 nmol/L.[12] Reference ranges for PTH for vitamin D replete versus vitamin D deficient have not been well characterized, and remain an area for future research. Nonetheless, clinicians should have a higher degree of suspicion for PHPT in hypercalcemic patients with inappropriately normal serum PTH who are vitamin D replete.

Vitamin D measurements are also important in patients who have elevated serum PTH but normal or high-normal serum calcium to rule out secondary hyperparathyroidism due to vitamin D deficiency. Vitamin D deficiency is quite commonplace, and may account for normal or high-normal PTH values in patients with PHPT. The estimated prevalence of vitamin D deficiency in adults is as high as 41.6%, and more common among individuals with pigmented skin, obesity, or poor milk intake.[13] Among internal medicine housestaff, 51.4% of residents were found to be vitamin D deficient at some point over the course of a year, more so during winter months.[14] Significant vitamin D deficiency can cause a physiologic increase in PTH secretion, mimicking incipient (normocalcemic) PHPT. PHPT and secondary hyperparathyroidism due to vitamin D deficiency can be distinguished by measuring serum 25-OH vitamin D.

Patients who have undergone malabsorptive bariatric surgery (ie, Roux-en-Y gastric bypass, biliopancreatic diversion with duodenal switch) frequently experience postoperative fat-soluble vitamin deficiencies, including vitamin D deficiency.[15] This does not include purely restrictive bariatric procedures, such as vertical banded gastroplasty or sleeve gastrectomy. Vitamin D deficiency and elevated PTH following malabsorptive bariatric surgery are not only long-term, but may also worsen over time.[16–18] Furthermore, patients who have undergone bariatric surgery have been shown to have impaired calcium absorption despite normal 25-OH vitamin D levels.[19] In our practice, patients who have undergone malabsorptive bariatric surgery are assumed to have secondary hyperparathyroidism due to vitamin D deficiency unless hypercalcemia has been confirmed with laboratory testing.

Urinary Calcium Excretion

Urinary calcium excretion can help distinguish PHPT from familial hypocalciuric hypercalcemia, where patients also experience hypercalcemia and have elevated levels of serum PTH. However, familial hypocalciuric hypercalcemia (FHH) is rare, with an estimated prevalence of 1 in 78,000 in the general population.[20,21] Thus, we only obtain urinary calcium excretion in patients with a suggestive family history. Patients with familial hypocalciuric hypercalcemia will have 24-hour urine calcium excretion less than 100 mg. Of note, patients with vitamin D deficiency superimposed on PHPT can have low 24-hour urinary calcium excretion, although generally closer to low-normal levels of approximately 200 mg.

CONSIDERATIONS FOR DIFFERENTIAL DIAGNOSIS

Familial Hypocalciuric Hypercalcemia

FHH is a disorder caused by a mutation in the calcium-sensing receptor (CaSR) found in a number of organs, including the parathyroid glands and kidneys. The parathyroid glands are unable to sense changes in serum calcium, and do not inhibit secretion of PTH in response to elevated serum calcium. More importantly, CaSR regulates renal excretion of calcium; the CaSR mutation in patients with FHH inhibits renal calcium excretion, leading to hypercalcemia. Patients with familial hypocalciuric hypercalcemia have elevated serum calcium, and up to 20% also have mild elevations in serum PTH, mimicking PHPT. As stated previously, the main distinguishing feature of FHH is low urinary calcium excretion, whereas urinary calcium excretion is normal or high in PHPT. Patients with FHH also typically exhibit hypercalcemia in childhood, and do not show signs and symptoms of hypercalcemia.

Malignancy

Malignancy is the second most common cause of hypercalcemia after PHPT, and the most common cause of hypercalcemia among inpatients. Hypercalcemia of malignancy can occur via a number of different mechanisms: humoral hypercalcemia of malignancy caused by secretion of PTH-related protein (PTHrP), osteoclast-mediated osteolysis typically caused by bony metastatic disease, or, in rare cases, ectopic secretion of 1,25-OH vitamin D or PTH (**Fig. 2**).[22] In most cases, hypercalcemia of malignancy occurs after malignancy is clinically evident. Hypercalcemia of malignancy should lead to suppression of endogenous PTH, so it can easily be distinguished from PHPT by measuring serum PTH and/or serum PTHrP. In rare cases, there can be concomitant hyperparathyroidism where PTH will be elevated as well as parathyroid-related peptide.

Thiazides

Thiazide diuretics act on the distal convoluted tubule of the kidney, reducing calcium excretion, and can cause a mild hypercalcemia. Patients with mild hypercalcemia with normal or high-normal PTH should discontinue thiazide medications and have calcium and PTH reassessed after 3 months. Elevated serum calcium despite withdrawal of thiazides supports the diagnosis of PHPT.

Lithium

The exact mechanism of action of lithium on calcium metabolism is unknown, although it is hypothesized to act downstream of the calcium-sensing receptor.

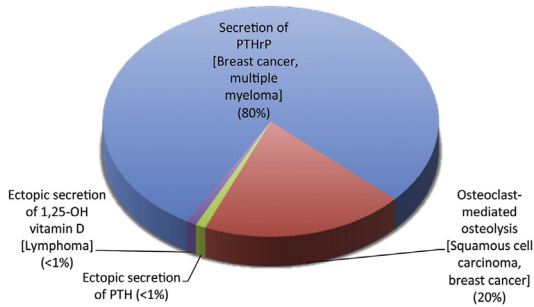

Fig. 2. Mechanisms of hypercalcemia of malignancy.

Lithium appears to interfere with CaSR activity in the parathyroid gland and kidneys, leading to elevated PTH levels, hypercalcemia, and hypocalciuria. If possible, patients with hypercalcemia should be switched to an alternative medication and have their calcium retested.

INDICATIONS, RISKS, AND BENEFITS OF PARATHYROIDECTOMY FOR PRIMARY HYPERPARATHYROIDISM

Surgery is the only curative therapy for PHPT, and is clearly indicated in all symptomatic patients. Even for asymptomatic patients, parathyroidectomy halts, or even reverses, the classic negative effects of this disease: parathyroidectomy decreases the risk of nephrolithiasis and improves bone mineral density (BMD).[23–27] There is also additional evidence that parathyroidectomy may also improve quality of life in "asymptomatic" patients, possibly by alleviating nonspecific or atypical symptoms.[26–29] Finally, there may still be unrecognized effects of asymptomatic PHPT: a large population-based study examining 2299 patients with untreated asymptomatic PHPT found an increased risk of nonfatal and fatal cardiovascular disease and all-cause mortality.[30]

In the past decade, the safety of parathyroidectomy has improved: the overall complication rate following 17,082 patients who underwent parathyroidectomy fell from 8.7% to 3.8% from 1999 to 2008.[31] The most common surgical complication was hypocalcemia, and vocal cord paresis accounts for only 3.7% of all complications.[31]

The indications for surgery in asymptomatic hyperparathyroidism have been an area of intense research and debate. The first official guidelines for surgery for asymptomatic hyperparathyroidism were established in 1990, at a consensus conference sponsored by the National Institutes of Health.[32] These guidelines have undergone several revisions by conferences convened in 2002 and 2008, and most recently during the 2013 Fourth International Workshop on the Management of Asymptomatic Primary Hyperparathyroidism.[2,33–35] The surgical criteria for parathyroidectomy are listed, by year of consensus statement, in **Table 1**. Analyses of the individual components of surgical criteria for PHPT are as follows.

SURGICAL CRITERIA FOR ASYMPTOMATIC PRIMARY HYPERPARATHYROIDISM

Serum Calcium

The most recent 2013 guidelines maintained that surgery is recommended for patients with serum calcium 1.0 mg/dL above the upper limit of the reference range. No recommendations based on ionized serum calcium were made, because the test is not yet widely available. The current recommendation has been in place since 2002, and is based on the consensus that hypercalcemia above this threshold increases the risk of disease progression to symptomatic PHPT. Patients below this threshold who are managed nonoperatively should undergo annual serum calcium testing. Tests for initial evaluation and observation of patients with asymptomatic PHPT are listed in **Table 2**.

Skeletal Criteria

The 2013 Workshop recommends surgery for patients with a T-score less than −2.5 at the lumbar spine, femoral neck, total hip, or distal one-third of the radius on dual-energy X-ray densitometry (DXA). Measurement of bone density at the distal forearm is the most important, but often omitted, part of DXA for patients with PHPT. Bone loss in PHPT occurs more rapidly in cortical bone than trabecular bone; thus, bone loss will

Table 1
Surgical criteria for parathyroidectomy in asymptomatic primary hyperparathyroidism, by year of consensus guidelines

	1990	2002	2009	2013
Serum calcium	1–1.6 mg/dL above reference range	1.0 mg/dL above reference range	1.0 mg/dL above reference range	1.0 mg/dL above reference range
Skeletal criteria	DXA: Z-score <−2	DXA: T-score <−2.5 at any site	DXA: T-score <−2.5 at any site	DXA: T-score <−2.5 at lumbar spine, total hip, femoral neck, or distal one-third radius Vertebral fracture by spinal imaging or vertebral fracture assessment
Renal criteria	eGFR reduction >30% from expected 24-h urine calcium excretion >400 mg	eGFR reduction >30% from expected 24-h urine calcium excretion >400 mg	eGFR <60 mL/min	Creatinine clearance <60 mL/min 24-h urine calcium excretion >400 mg AND High-risk urinary biochemical stone risk analysis Nephrocalcinosis or nephrolithiasis
Age	Age <50	Age <50	Age <50	Age <50

Abbreviations: DXA, dual-energy X-ray absorptiometry; eGFR, estimated glomerular filtration rate.
Adapted from Bilezikian JP, Brandi ML, Eastell R, et al. Guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the Fourth International Workshop. J Clin Endocrinol Metab 2014;99(10):3562.

likely first be evident at the distal forearm, which is mostly composed of cortical bone.[36] Despite this, only 45% of patients with PHPT who receive DXA testing undergo testing of the distal radius.[37] DXA testing reports 2 scores: a Z-score, which reports BMD compared with patients of the same age, gender, and race, as well as a T-score, which is BMD compared with a healthy 30-year-old. Starting in 2002, the consensus conferences have recommended exclusively using the T-score, which is more reflective of absolute changes in BMD over time in the same individual.

This focus on preserving BMD is meant to identify patients who have an elevated fracture risk, and to reduce that risk through surgery. It is clear that patients with asymptomatic PHPT experience progressive bone loss that can be prevented with surgical intervention.[23–27,38] It is currently unknown whether this loss of BMD in asymptomatic PHPT also increases fracture risk. Retrospective studies of patients with PHPT of varying severity have an increased fracture risk compared with age-matched and sex-matched controls, which normalizes after parathyroidectomy.[39,40] Further studies are needed to determine whether parathyroidectomy reduces fracture risk in asymptomatic PHPT.

A new recommendation is to evaluate patients with asymptomatic PHPT for vertebral fractures using radiographs, computed tomography (CT), MRI, or vertebral fracture assessment (VFA). Compared with 4% in age-matched controls, patients with asymptomatic PHPT who meet surgical criteria have a 28% risk of vertebral fracture,

Table 2
Tests for initial evaluation and observation of asymptomatic primary hyperparathyroidism

Initial Evaluation of Asymptomatic Primary Hyperparathyroidism	Observation of Asymptomatic Primary Hyperparathyroidism
Laboratory testing (serum calcium, phosphate, creatinine, albumin, 25-OH vitamin D)	Annual serum calcium
DXA	DXA every 1–2 y
Vertebral spine assessment (radiograph, CT, MRI, or VFA)	Radiograph, CT, MRI, or VFA if patients develop back pain or height loss
24-h urine stone risk profile	Annual estimated glomerular filtration rate, serum creatinine
Renal imaging (radiograph, ultrasound, CT)	24-h biochemical stone profile, renal imaging (radiograph, ultrasound, CT) if suspected nephrolithiasis

Abbreviations: CT, computed tomography; DXA, dual-energy X-ray absorptiometry; VFA, vertebral fracture assessment.

and those who do not meet surgical criteria have an 11% risk.[41] A recent study of 140 patients with PHPT diagnosed in 2009 to 2013 found that 34.7% of patients with asymptomatic PHPT had evidence of vertebral fracture on spinal radiograph.[42] VFA is a particular radiographic methodology using DXA to detect vertebral fractures, but has been found to be less predictive than trabecular bone score in nonosteoporotic patients.[43] Trabecular bone score (TBS) is an emerging technology that better detects and predicts vertebral fracture than BMD determined by DXA. TBS is generated by using computer software to apply a gray-level textural analysis to existing DXA images and should be easily available to institutions able to perform DXA scans.[44] A TBS score of less than 1.2 has an area-under-the-curve of 0.716 for detecting vertebral fractures within in a population that otherwise had similar BMD.[45] Last, TBS has been shown to improve after parathyroidectomy.[45]

Patients with asymptomatic PHPT are recommended to undergo DXA every 1 to 2 years, which must include measurement of 3 different sites, including the distal radius, and imaging or VFA of the spine if they are experiencing height loss or back pain.

Renal Criteria

The 2013 Workshop identified 3 renal criteria for parathyroidectomy: (1) Creatinine clearance less than 60 mL/min, (2) 24-hour urine calcium greater than 400 mg AND increased risk by urinary biochemical stone risk analysis, and (3) nephrolithiasis or nephrocalcinosis seen on radiograph, ultrasound, or CT.

The first criterion, creatinine clearance less than 60 mL/min, represents the onset of stage 3 or greater chronic kidney disease (CKD).[46] This recommendation was made, in part, based on the assumption that serum calcium and PTH levels rise with progressive kidney disease, which may lead to worse disease sequelae of PHPT. However, recent studies have shown that serum calcium is not significantly elevated in stage 3 or 4 CKD, and PTH is only significantly elevated in patients with creatinine clearance less than 30 mL/min.[47,48] Nonetheless, creatinine clearance less than 60 mL/min is associated with altered bone remodeling, suggesting that impaired renal function may negatively impact bone health in a manner unrelated to PTH and calcium in patients with PHPT.[47,48]

Second, surgery is recommended for patients with urinary calcium excretion of greater than 400 mg, and if the patient is determined to be at high risk by urinary biochemical stone risk analysis. Urinary biochemical kidney stone risk panels are widely available through commercial laboratories, and involve testing of calcium, creatinine, uric acid, citric acid, and oxalate levels in urine collected over 24 hours. Although the 1990 Panel had initially recommended surgery for high urinary calcium excretion alone, the 2008 Committee determined that there was no evidence that high urine calcium excretion alone predicts formation of kidney stones.

Finally, the 2013 guidelines recommend patients diagnosed with asymptomatic PHPT should undergo renal imaging to detect subclinical nephrolithiasis or nephrocalcinosis. Renal ultrasound performed on 141 patients with PHPT without a history of nephrolithiasis found silent nephrolithiasis in 11% of patients, compared with 2% in controls.[49] Another recent study found that 35.5% of patients with asymptomatic PHPT were found to have kidney stones on renal ultrasound.[42] Any abnormal findings on renal imaging would be an indication for parathyroidectomy.

Patients who do not undergo surgery should be encouraged to maintain adequate hydration at all times, possibly with above-average fluid intake. These patients should receive annual laboratory testing of estimated glomerular filtration rate and creatinine. If patients have signs and symptoms of possible kidney stones, repeat urine biochemical stone risk profile and/or renal imaging should be obtained.

Age

The 2013 guidelines continue to support age younger than 50 as a criterion for surgery. The rationale is that younger patients have sufficient life expectancy to derive benefit from surgical resection, regardless of disease severity. Among patients younger than 50 who do not meet surgical criteria (aside from age), 27% to 62% will progress to meet surgical criteria in 9 to 10 years.[50,51] None of these patients developed fractures or renal stones during the study period. Moreover, the percentage of disease progression was overestimated: these studies included the development of urinary calcium excretion greater than 400 mg per day as a surgical indication, which was the sole reason nearly half of the patients defined as having progression of disease. Urinary calcium excretion alone was eliminated as a criterion in 2009, and the 2013 Workshop now recommends surgery for urinary calcium excretion of 400 mg per day and high-risk urinary biochemical stone risk profile.

The focus on younger patients should not deter clinicians from recommending surgery in elderly patients who meet surgical criteria. Most patients with PHPT are older than 60, but many older patients who meet surgical criteria are not offered parathyroidectomy.[52] Only 24% of patients older than 70 who meet surgical criteria undergo parathyroidectomy.[52] Even for patients with PHPT who are older than 70 or 80, parathyroidectomy is associated with minimal morbidity, no mortality, high cure rate, and improvement in quality of life.[53,54] In our practice, we assess each patient according to their perioperative risk and "physiologic age" regardless of their chronologic age. Surgery should be offered to all patients with minimal perioperative risk and sufficient life expectancy.

Atypical Symptoms

Cardiovascular

No clear relationship has been established between asymptomatic PHPT and adverse cardiovascular outcomes. A study of 2097 patients with nonoperatively managed PHPT found that mild PHPT is associated with increased cardiovascular mortality, and that baseline PTH levels correlated with all-cause mortality as well as fatal and

nonfatal cardiovascular disease.[55] Although these findings have yet to be confirmed with prospective studies, mild PHPT has been linked to elevated systolic blood pressure, lower 25-OH vitamin D levels, increased carotid artery stiffness, and increased carotid-intima thickness.[56,57] Conversely, a randomized controlled trial of surgery versus observation found no difference in blood pressure, biomarkers of endothelial function, or C-reactive protein 2 years after parathyroidectomy.[58] Several studies also have shown that parathyroidectomy has minimal or no effect on cardiac structure or function at 2 years.[59–61] Currently, there are insufficient data to include cardiovascular factors as criteria for parathyroidectomy. Prospective studies are needed to better characterize the effect of asymptomatic PHPT on cardiovascular outcomes.

Neuropsychiatric and cognitive

Despite being referred to as "asymptomatic" PHPT, many patients who do not exhibit typical signs and symptoms of PHPT do experience nonspecific neuropsychiatric symptoms. Following parathyroidectomy, patients with asymptomatic PHPT have reported improvements in overall quality of life, sleep disturbances, fatigue, aches and pains, weakness, constipation, and memory loss.[26–29] A prospective study of 24 patients with asymptomatic PHPT demonstrated improvement in the Hospital Depression and Mood Rating Scales after parathyroidectomy, using patients undergoing thyroid lobectomy for benign nodules as controls.[62–64] Despite these findings, the 2013 Workshop concluded that improvements in neuropsychiatric symptoms are not consistent between studies, and that there was no reliable method to predict which patients would benefit from surgery; therefore, neuropsychiatric dysfunction should not yet be considered in the decision to perform parathyroidectomy.[2]

SUMMARY

PHPT is a common disease, and the vast majority of patients with PHPT are asymptomatic. Classic PHPT can be easily diagnosed by elevated total calcium and PTH. However, one-half of cases of PHPT are nonclassic, and exhibit hypercalcemia with inappropriately normal (nonsuppressed) levels of PTH. For patients with asymptomatic PHPT, parathyroidectomy has been shown to increase BMD and improve quality of life, and may even decrease risk of fracture and adverse cardiovascular outcomes. It is our belief that surgery should be considered in all patients with asymptomatic PHPT who have minimal perioperative risk and sufficient life expectancy, regardless of chronologic age.

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