

Hyperparathyroidism (primary) NICE guideline: diagnosis, assessment, and initial management

INTRODUCTION

Parathyroid hormone (PTH) is secreted from four parathyroid glands situated behind the thyroid gland. PTH regulates calcium and phosphate levels by its promotion of phosphate excretion and calcium reabsorption in the kidneys; stimulation of osteoclastic activity in the bone resulting in raised serum calcium; and increased intestinal absorption of calcium. Hyperparathyroidism is excessive secretion of PTH and can be primary, secondary, or tertiary:

- primary hyperparathyroidism occurs when ≥ 1 parathyroid glands produce too much PTH (the most common cause is an adenoma);
- secondary occurs when the increased PTH secretion is due to an organic cause (such as kidney, liver, or bowel disease causing hypocalcaemia and a subsequent increase in PTH secretion); and,
- tertiary is a consequence of persistent parathyroid stimulation (such as long-standing secondary hyperparathyroidism), which results in autonomous (unregulated) PTH function.¹

This article summarises the new National Institute for Health and Care Excellence (NICE) guideline for the diagnosis, assessment, and initial management of primary hyperparathyroidism (PHPT).² This article highlights areas of particular importance for primary care. The causes and management of hypercalcaemia outside of the diagnosis and management of PHPT are beyond the scope of this article.

PRESENTATION

The signs and symptoms of PHPT are predominantly brought about by hypercalcaemia and include thirst, increased urine output, and gastrointestinal

symptoms such as constipation. Long-term effects include kidney stones, bone-related complications such as osteoporosis and fractures, and cardiovascular disease. PHPT can also be associated with what the guideline refers to as chronic undifferentiated symptoms such as fatigue, mild confusion, anxiety, depression, irritability, low mood, apathy, insomnia, and bone, muscle, or joint pain.

DIAGNOSIS

Initial diagnostic testing for suspected PHPT within primary care requires the measurement of albumin-adjusted serum calcium and PTH levels.

Patients should have their albumin-adjusted serum calcium measured if they have any of the following features: symptoms of hypercalcaemia such as thirst, frequent or excessive urination, or constipation; osteoporosis or previous fragility fracture; a renal stone; or an incidental finding of elevated albumin-adjusted serum calcium (≥ 2.6 mmol/L). It may also be sensible to consider measuring albumin-adjusted serum calcium for patients with chronic non-differentiated symptoms. The measurement of ionised calcium is not required when testing for suspected PHPT.

The albumin-adjusted serum calcium measurement should be repeated in primary care at least once if the first measurement is either ≥ 2.6 mmol/L; or ≥ 2.5 mmol/L and features of PHPT are present.

PTH should be measured in patients whose albumin-adjusted serum calcium level is either ≥ 2.6 mmol/L on at least two separate occasions; or ≥ 2.5 mmol/L on at least two separate occasions and PHPT is suspected. When measuring PTH, a random sample and a concurrent measurement of the albumin-adjusted serum calcium are required. Repeat PTH measurements are not routinely required in primary care.

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REFERRAL

The guideline advises referral to a specialist with expertise in PHPT if a patient's PTH measurement is:

- above the midpoint of the reference range and PHPT is suspected; or
- below the midpoint of the reference range with a concurrent albumin-adjusted serum calcium level of ≥ 2.6 mmol/L.

Vitamin D deficiency and PHPT can coexist but referral should not be delayed in order to treat an abnormal vitamin D level. Further investigations for PHPT are not needed if the patient's PTH measurement is below the midpoint of the reference range and their concurrent albumin-adjusted serum calcium level is < 2.6 mmol/L. Alternative diagnoses, including malignancy, should be sought if the patient's PTH is below the lower limit of the reference range.

MANAGEMENT

The diagnosis of PHPT will be confirmed by secondary care specialists who at diagnosis should:

- assess symptoms and comorbidities including cardiovascular risk;
- measure estimated glomerular filtration rate (eGFR) or serum creatinine;
- do a dual-energy X-ray absorptiometry (DXA) scan of the lumbar spine, distal radius, and hip; and,
- do an ultrasound scan of the renal tract.

Surgical management is the primary treatment option. If surgery is unsuitable, declined, or unsuccessful, secondary care specialists may consider non-surgical management with calcimimetics depending on the albumin-adjusted serum calcium levels and whether the patient has symptoms of hypercalcaemia. Secondary care may consider a bisphosphonate to reduce fracture risk in patients with PHPT and increased fracture risk.

Further monitoring may be required in primary care. Patients who have had successful parathyroid surgery require their albumin-adjusted serum calcium to be measured once a year, and if abnormal then the diagnostic pathway detailed above should be followed. A specialist opinion should be sought for the monitoring of patients who have osteoporosis or renal stones, and a specialist endocrine opinion should be sought for the monitoring of patients who have had parathyroid surgery for multi-gland disease or have disease

that recurs after successful surgery.

Patients who have not had parathyroid surgery or whose surgery has been unsuccessful require additional monitoring. Their albumin-adjusted serum calcium and eGFR or serum creatinine should be measured once a year, unless the patient is taking cinacalcet. If the results are abnormal then the diagnostic pathway detailed above needs to be followed. Further monitoring of a patient taking cinacalcet should follow the guidance set out in the summary of the product characteristics. A DXA scan should be considered every 2 to 3 years. If a patient presents with a suspected or confirmed renal stone after the diagnosis of PHPT then a repeat ultrasound of the renal tract should be offered, and the patient should be referred back to secondary care.

Pregnant women with PHPT should be managed by a specialist multidisciplinary team and are at an increased risk of hypertensive disease in pregnancy.

COMMENT

NICE recommendations are based on systematic reviews of the best available evidence and explicit consideration of cost-effectiveness. There was a lack of high-quality evidence for most areas and the committee considered factors such as current practice and clinical experience when making the recommendations. This guideline should increase GP awareness of PHPT and clarify the diagnostic, referral, and management processes. It is anticipated that the recommendations could lead to an increased demand for primary care services (for example, appointments or blood tests). However, although the number of albumin-adjusted serum calcium measurements may increase, the number of PTH tests may be reduced.

Provenance

Freely submitted; externally peer reviewed.

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1. NHS. Hyperparathyroidism. 2020. <https://www.nhs.uk/conditions/hyperparathyroidism> [accessed 9 Jun 2020].
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