Update in Parathyroid Imaging

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KEYWORDS

• Parathyroid • Primary hyperparathyroidism • 4D-CT • Sestamibi • Parathyroid ultrasound
• Parathyroid MR imaging

KEY POINTS

- Primary hyperparathyroidism is a clinical diagnosis based on biochemical evaluation; imaging is reserved for patients who have the established diagnosis for parathyroid localization to facilitate focused exploration or exclude ectopic disease.
- Ultrasound imaging has multiple advantages as a first-line modality; however, it performs poorly at visualizing parathyroid pathology within the mediastinum or in retroesophageal or retropharyngeal locations.
- Nuclear scintigraphy is a first-line imaging modality sensitive for both ectopic and eutopic glands, and is often used with ultrasound imaging for preoperative localization.
- Multiphase computed tomography is becoming a viable first-line imaging option, as it has analogous to superior sensitivity for parathyroid localization when compared with scintigraphy and ultrasound imaging.
- Currently, the choice of imaging algorithm is largely based on local expertise and institutional norms.

INTRODUCTION

Primary hyperparathyroidism (PHPT) is characterized by excessive, dysregulated production of parathyroid hormone (PTH) that results in the disruption of normal calcium homeostasis. Overproduction of PTH can be due to an adenomatous, hyperplastic, or carcinomatous parathyroid gland(s) and can be surgically cured. In the last decade, the development of focused surgical techniques using a small incision and limited dissection for removal of a single pathologic parathyroid gland has created the need for more precise localization of the parathyroid lesion(s) by imaging. A variety of imaging protocols and techniques have been used for this purpose. Nuclear medicine scintigraphy and ultrasound are established modalities. Recently, multiphase or 4-dimensional computed tomography (4D-CT) has emerged as modality with several advantages and has become the first-line study in several institutions. MR imaging is used less commonly, although it can be used as a second- or third-line option.

This review provides a background of PHPT and key anatomy, and discusses the parathyroid imaging modalities with updates.

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CLINICAL CONCEPTS FOR PRIMARY HYPERPARATHYROIDISM

PHPT is 2 to 4 times more common in women than men, more common in Caucasians, and usually presents in the fifth through seventh decades of life. A solitary parathyroid adenoma is the most common cause of primary hyperparathyroidism (89%), followed by 4-gland hyperplasia (6%), double adenoma (4%), and parathyroid carcinoma (1%).[1] Most cases are sporadic, although hereditary causes exist, including multiple endocrine neoplasia types 1 and 2A, and familial isolated hyperparathyroidism.[2] A history of prior neck radiation as a child or adolescent is also a risk factor for PHPT.

According to 1 study, 85% of PHPT patients are asymptomatic at presentation,[3] with some estimates being even higher. Although asymptomatic, these patients are at risk for osteoporosis and pathologic fractures, nephrolithiasis, pancreatitis, peptic ulcer disease, renal dysfunction, and cardiovascular disease. For those with clinical manifestations, the classic mnemonic *bones, stones, groans, moans, and psychic overtones*[4] illustrates some of the more common potential symptoms. These include arthralgias, myalgias, constipation, gastrointestinal upset, weakness, and psychiatric and neurocognitive disability, including problems with memory, mood, and concentration.

The diagnosis of primary hyperparathyroidism is established based on biochemical evaluation and criteria rather than imaging; typically, increased serum calcium levels are encountered in the setting of elevated or inappropriately high normal intact PTH levels and normal renal function (**Box 1**). Normocalcemic primary hyperparathyroidism is a subtype of PHPT where PTH levels are increased despite normal serum albumin-adjusted and ionized calcium concentrations, which is confirmed on at least 2 additional occasions over a course of 3 to 6 months.[5,6] Secondary and hereditary causes of hyperparathyroidism should be excluded, including chronic renal failure or insufficiency, vitamin D deficiency, various medications such as lithium and thiazide diuretics, and benign familial hypocalciuric hypercalcemia.

Tertiary hyperparathyroidism is a unique circumstance for which imaging localization may be required. Like secondary hyperparathyroidism, tertiary hyperparathyroidism is associated with chronic renal disease. In these patients, however, persistent parathyroid stimulation related to renal disease is accompanied by autonomously functioning parathyroid tissue that is unresponsive to medical therapy. In this subset of patients, preoperative localization may be necessary to assess for a single adenoma, or in the setting of recurrent or residual disease.

Definitive treatment for primary hyperparathyroidism is surgery, although medical management and surveillance strategies can be used for many asymptomatic patients. The Fourth International Workshop released guidelines for the management of asymptomatic primary hyperparathyroidism to aid in decision making with regard to surgery versus medical management and surveillance (**Box 2**).[7] Recommendations are for all symptomatic patients with PHPT to proceed to surgery, as well as selected asymptomatic patients who meet the criteria outlined in **Box 2**. Note that some opt for surgery over medical surveillance regardless, because parathyroidectomy has a high cure rate.[1]

Broadly speaking, the 2 surgical options to consider are the traditional 4-gland exploration or

Box 1
What the referring clinician needs to know

- The diagnosis of primary hyperparathyroidism is based on clinical and laboratory analysis.
- Imaging is reserved for those for whom surgery is considered.
- Approximately 85% of patients with primary hyperparathyroidism have a single parathyroid adenoma that is amenable to minimally invasive parathyroidectomy. The remainder might require more extensive neck dissection.
- The choice of imaging modality is largely site specific and should be based on the experience and comfort level of the surgeons and radiologists. There is no universally accepted imaging algorithm.
- Patients undergoing reoperation run a higher risk of having an adverse outcome, generally recurrent laryngeal nerve injury. Often surgeons will require 2 concordant imaging studies before performing a repeat parathyroidectomy.
- The sensitivity for detecting smaller glands, multigland disease, and localizing patients who have had previous parathyroid surgery is lower for all available modalities, although multiphase computed tomography seems to be superior in these situations.