The Investigative Evolution of Primary Hyperparathyroidism: an Update

Abstract

Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcaemia encountered in the general population. Traditional investigation of PHPT consisted of Sestamibi and ultrasound (US) scanning followed by a bilateral neck exploration (BNE), which remains the gold standard surgical approach. Newer imaging modalities have however facilitated the movement toward minimally invasive parathyroidectomy and these are discussed.

Abbreviations: PHPT: Primary Hyperparathyroidism; US: Ultrasound; BNE: Bilateral Neck Exploration; MIP: Minimally Invasive Parathyroidectomy; PPV: Positive Predictive Value

Introduction

Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcaemia encountered in the general population [1]. Whilst these patients traditionally presented with symptoms including bone pain, fatigue, nephrolithiasis and depression, the majority of patients are now recognized during routine biochemical screening and are asymptomatic on presentation [1,2]. Traditional investigation of PHPT consisted of Sestamibi and ultrasound (US) scanning followed by a bilateral neck exploration (BNE), which remains the gold standard surgical approach [3]. More recently however there has been a shift toward less invasive more focused surgery in the form of minimally invasive parathyroidectomy (MIP). The utilization of this technique is dependent upon accurate pre-operative localization of the lesion.

Discussion

Primary hyperparathyroidism affects 1% of the population with the vast majority (85-96%) of cases secondary to a single adenoma and the remainder due to double adenomas or multigland hyperplasia [1,4]. Parathyroidectomy is the treatment of choice for symptomatic patients and there is a growing body of evidence to support surgical intervention in asymptomatic patients with mildly elevated serum calcium levels, as a significant improvement in both post-operative bone density and quality of life has been demonstrated in this patient group [5].

In experienced hands, MIP performed in conjunction with intra-operative PTH monitoring offers success rates comparable to those observed in bilateral [6] gland exploration [1.5]. Compared to traditional BNE, MIP is associated with a reduction in cost, less post-operative pain, decreased morbidity and improved cosmesis due to smaller incision size [1,3]. MIP is however entirely dependent upon accurate pre-operative localization of the lesion.

Sestamibi scanning utilizes technetium (Tc99m), which becomes concentrated within intracellular mitochondria following injection. Two hours after injection thyroid cells demonstrate a significant decrease in Tc99m uptake whilst abnormal parathyroid oxyphil cells retain the marker in high mitochondrial concentrations, which is the basis of localization with this technique [1]. A gamma camera is used to obtain planar two dimensional images. Limitations of this technique include the presence of multi-nodular thyroid disease [6], gland hyperplasia, patients with mildly elevated serum calcium (<2.8mmol/L), small adenomas (< 500mg) and obese patients [1,3,5-8]. SPECT scanning is a variation of Sestamibi scanning and utilizes the same radio-active tracer (Tc99m) however is able to provide 3D reconstruction of multiple 2D images obtained during the scan. The addition of CT scanning (SPECT/CT) adds anatomical localization to the functional information obtained during SPECT scanning [1].

Four dimensional CT scanning of the parathyroid’s was first introduced in 2006. It is a contrast CT scan which depends on the perfusion characteristics of parathyroid adenomas as these typically demonstrate a rapid uptake and washout of contrast, which accounts for the fourth dimension [7]. Four separate CT scans are obtained, the first without contrast (pre contrast), the second scan (immediate post contrast) 25 seconds after injection of contrast, the third (early delayed) is performed 30 seconds after the second and the fourth (late delayed) 45 seconds after completion of the early delayed phase scan. The pre contrast scan clearly outlines the iodine rich thyroid gland, whilst the
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Now discussed following routine biochemical screening and is often asymptomatic. This is in stark contrast to the traditional presenting features of nephrolithiasis, osteoporosis, peptic ulcer disease and even pancreatitis. This has coincided with a movement toward focused minimally invasive surgery which is dependent upon accurate localization. Traditional localization strategies often prove inconclusive in those patients that are asymptomatic on presentation with mildly elevated serum calcium, which has resulted in the development of newer imaging modalities. Based on the serum calcium on presentation, a 4D-CT scan should be considered as the initial investigative modality in those patients that present with a mildly elevated serum calcium (<2.8 mmol/l) as sestamibi and SPECT imaging often is not accurate in these patients. In the remainder of patients SPECT scanning should remain the investigation of choice, reserving 4D-CT scanning as an adjunct in inconclusive cases.

References
