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Diagnostic performance of computed tomography for parathyroid adenoma localization; a systematic review and meta-analysis

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ABSTRACT

Abstract purpose: To perform a systematic review and meta-analysis of the sensitivity and positive predictive value (PPV) of CT for preoperative parathyroid localization in patients with primary hyperparathyroidism (pHPT), and subsequently compare the different protocols and their performance in different patient groups.

Materials and methods: We performed a search of the Embase, Pubmed and Cochrane Library databases to identify studies published between January 1, 2000 and March 31, 2016 investigating the diagnostic value of CT for parathyroid localization in patients with biochemical diagnosis of pHPT. Performance of CT was expressed in sensitivity and PPV with pooled proportion using a random-effects model. Factors that could have affected the diagnostic performance were investigated by subgroup analysis.

Results: Thirty-four studies evaluating a total of 2563 patients with non-familial pHPT who underwent CT localization and surgical resection were included. Overall pooled sensitivity of CT for localization of the pathological parathyroid(s) to the correct quadrant was 73% (95% CI: 69–78%), which increased to 81% (95% CI: 75–87%) for lateralization to the correct side. Subgroup analysis based on the number of contrast phases showed that adding a second contrast phase raises sensitivity from 71% (95% CI: 61–80%) to 76% (95% CI: 71–87%), and that adding a third phase resulted in a more modest additional increase in performance with a sensitivity of 80% (95% CI: 74–86%).

Conclusion: CT performs well in localizing pathological glands in patients with pHPT. A protocol with two contrast phases seems to offer a good balance of acceptable performance with limitation of radiation exposure.

1. Introduction

In patients with primary hyperparathyroidism (pHPT), identification of a solitary parathyroid adenoma on preoperative imaging studies may allow for minimally invasive parathyroidectomy (MIP). However, localization remains a challenge in a significant proportion of patients. Although the most commonly used imaging modalities, ultrasound (US) and ^{99m}Tc-sestamibi scintigraphy, perform well in many cases, there remains a substantial number of patients with non-localizing studies [1]. This problem is most frequently encountered in patients with multiple adenomas, four gland hyperplasia or recurrent disease [2,3]. In this situation, surgeons can either perform a more extensive bilateral neck exploration, with its attendant higher risk of complications, or attempt other imaging modalities such as magnetic resonance imaging (MRI) or positron emission tomography (PET) [4]. There are no clear recommendations about which alternate modality is best and

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therefore subsequent choice of imaging varies between hospitals depending upon institutional preference and availability [5].

Computed tomography (CT) is one of the most widely available modalities and its utility in parathyroid localization has been shown in several recently published studies [6–8]. It provides high quality anatomic detail for localization of parathyroid glands in the neck as well as in ectopic locations. In 2006, four-dimensional CT (4D-CT) was introduced by Rodgers et al., and has since been studied extensively [9]. The initial protocol consisted of four phases: pre-contrast, arterial, venous, and delayed phases. The principle behind 4D-CT is that the hypervascularity of parathyroid lesions results in rapid enhancement (detectable in the arterial phase) and washout of contrast (detectable on venous and delayed phases) compared with lymph nodes, which tend to enhance to a lesser degree and retain contrast throughout the venous and delayed phases [10,11].

The multiple contrast phases enable clinicians to differentiate adenomas from other structures based on contrast enhancement over time [11], and its use as part of standard preoperative evaluation has been shown to be cost effective [12,13]. However, there is still debate over the true added value of the additional phases amid concerns about the extra radiation administered [14]. Several studies on 4D-CT have shown similar enhancement of lymph nodes and parathyroid adenomas in the delayed phase [15]. Findings such as these have prompted several institutions to remove the delayed phase and adjust their scanning protocol to three phases, with no apparent reduction in the sensitivity for localizing adenomas [16–18].

Many studies have investigated the use of CT scan in patients with pHPT. However, since inclusion criteria and CT protocols vary greatly among the studies, it is difficult to make recommendations based on any one of them. In 2012, a review examining the performance of 4D-CT in patients with pHPT was published, however, the amount of data was insufficient to perform a meta-analysis [19]. Also, this review did not include patients who had undergone previous parathyroid exploration and did not investigate the performance of standard two-phase CT. Therefore, the purpose of this study was to answer the following question using a systematic review and meta-analysis: What are the sensitivity and positive predictive value (PPV) of CT for preoperative parathyroid adenoma localization in patients with pHPT? We subsequently evaluated the different protocols and their efficacy in various patient groups.

2. Materials and methods

2.1. Search strategy

This systematic review and meta-analysis was conducted using the PRISMA statement [20]. Information with regards to this meta-analysis can be found in the PROSPERO registry under the number CRD42016037048 (http://www.crd.york.ac.uk/PROSPERO). We performed a search of the Embase, Pubmed and Cochrane Library databases to identify studies published between January 1, 2000 and March 31, 2016 investigating the diagnostic value of CT for parathyroid localization in patients with biochemical diagnosis of pHPT. We designed an extensive search filter by using all relevant synonyms and Mesh/Emtree terms (Table 1). We completed our search by cross referencing Web of Science, as well as examining references of selected articles, related reviews, meta-analyses, and guidelines.

Table 1
Search strategy.

Strategy Component and Step No.	Query
Pubmed and Cochrane database	
Patient	
1	Hyperparathyroidism OR parathyroid OR HPT OR PHPT [All Fields]
2	MeSH descriptor hyperparathyroidism explode all trees
Intervention	
3	CT OR CAT OR "Computed Tomography" OR "Computerized Tomography" [All Fields]
4	MeSH descriptor Tomography, X-Ray Computed explode all trees
Performance	
5	Sensitivity OR accuracy OR "positive predictive value" OR PPV [All Fields]
6	MeSH descriptor Predictive value of tests explode all trees
7	MeSH descriptor Sensitivity and Specificity explode of all trees
Embase	
Patient	
1	Hyperparathyroidism OR parathyroid OR HPT OR PHPT
2	EMTREE hyperparathyroidism explosion
Intervention	
3	CT OR CAT OR 'Computed Tomography' OR 'Computerized Tomography'
4	EMTREE computed tomography scanner explosion
Performance	
5	Sensitivity OR accuracy OR 'positive predictive value' OR PPV
6	EMTREE Predictive value explosion
7	EMTREE Sensitivity and Specificity explosion
Merge	
8	1 OR 2
9	3 OR 4
10	5 OR 6 OR 7
11	8 AND 9 AND 10
12	8 AND 9 AND 10 from 2000

2.2. Eligibility criteria for study selection

After completion of the search, all duplicate studies were first removed. All papers published before 2000 were excluded due to technological advances in imaging since that time. The remaining unique publications were screened based on title and abstract for eligibility. A study was considered eligible when the following criteria were met: 1) adults of ≥18 years of age with biochemical non-familial pHPT who underwent CT imaging for localization, and 2) surgical treatment and pathological examination as the gold standard for confirmation of localization. If an article presented data for multiple study groups of which some were eligible for inclusion, the eligible study groups were included if the pertinent data could be extracted.

Case reports, systematic reviews, and meta-analyses were excluded, as were papers that were not focused on pHPT. All titles and abstracts were screened independently by two authors. Any disagreements in selection were discussed with a third author and after consensus the selected papers were screened for full text review.

Studies were ultimately included in the meta-analysis if the following inclusion criteria were met: 1) at least 20 patients investigated with CT scan; 2) extractable and unique data available for the calculation of sensitivity of CT; and 3) histological examination of the resected parathyroid gland(s). To give full insight in our search, we registered the reason for exclusion of every study that was screened full text (Appendix 1 in Supplementary material). Several studies were excluded because only conference abstracts were available and authors did not respond to our request for additional data. To prevent publication bias, we extracted all available data