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Original research

# Retrospective evaluation of the pre- and postoperative factors influencing the sensitivity of localization studies in primary hyperparathyroidism

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# HIGHLIGHTS

• Preoperative localization of a suspected adenoma is essential to perform mini invasive surgery in primary hyperparathyroidism.

- The main factors predicting a low reliability of preoperative localization studies are concomitant thyroid disease and discordant studies.
- In such cases a mini invasive approach is possible but intraoperative PTH monitoring is mandatory.

#### ARTICLE INFO

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# ABSTRACT

*Introduction:* Over the last decades, mini-invasive surgery has become increasingly common for treatment of primary hyperparathyroidism; such approach requires preoperative localization of a suspected parathyroid adenoma. Neck ultrasound (US) and technetium-99 m sestamibi (MIBI) scan are the main imaging studies used for this purpose. The aim of the present study is to evaluate what pre- and postoperative factors may alter the reliability of localization studies.

*Methods:* A retrospective analysis on 212 patients with preoperative diagnosis of primary hyperparathyroidism was conducted. Data collected included demographic data, preoperative workup, operative findings and follow-up. Univariate logistic regression was performed on pre- and postoperative variables. *Results:* US sensitivity was 62.4% and MIBI sensitivity 78.9%. Cure rate after parathyroidectomy was 98.1%. Univariate logistic regression demonstrated that US sensitivity was impaired by lower levels of serum calcium (p < 0.0001), multi-gland disease (p = 0.011) and co-existence of thyroid disease (p = 0.001); MIBI sensitivity was impaired by lower levels of serum calcium (p < 0.001) and multi-gland disease (p < 0.0001).

*Conclusions:* Mild hypercalcaemia, multi-gland disease and co-existing thyroid disease are the main factors affecting sensitivity of preoperative imaging studies. In such patients a mini-invasive approach is possible but the use of intraoperative PTH monitoring is mandatory to reduce the risk of unsuccessful surgery.

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# 1. Introduction

Primary hyperparathyroidism (PHP) is the third most frequent

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endocrine disorder, with a prevalence estimated to be 1% in the over-65 population. Its incidence has increased consistently over recent decades due to the diffusion of screening blood calcium test. Surgery provides the only curative treatment for PHP, reducing both short and long term complications linked to hypercalcaemia. For many years, bilateral neck exploration has been considered the gold standard procedure because it permits the identification and concurrent treatment of multiglandular disease (MGD), thought to be the main cause of persistent PHP [1-3]. Over the last two decades, the use of mini-invasive parathyroidectomy (MIP) has







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become increasingly common, with equivalent cure and lower complication rates compared with traditional exploration [4–7]. The main requirement for MIP is the preoperative localization of a suspected parathyroid adenoma ascertained from imaging studies. The literature reports preoperative ultrasound (US) scan to have an average sensitivity of 76% (range 48–89%), while that of technetium-99 m sestamibi (MIBI) scans is 79% (range 61–100%). This wide range of sensitivity rates raises questions about the reliability of these tests, with some authors suggesting a surgical bilateral approach in all patients with PHP. The aim of this retrospective study was to assess the accuracy of US and MIBI scans and to analyse pre- and postoperative factors that may alter the success of localization studies in patients with PHP.

#### 2. Patients and methods

Having gained ethics approval from our Institutional Board Review we performed a retrospective review of 264 patients who had undergone parathyroidectomy to treat PHP between January 2002 and December 2012 within the Unit of General Surgery at the University of Cagliari, Italy. Only patients with preoperative diagnosis of PHP were included in the study: 21 patients were excluded due to intraoperative suspicion of adenoma caused by morphological alteration of the parathyroid glands during neck surgery for other pathologies; 9 patients with persistent or recurrent PHP were excluded. The data analysed included: age, sex, coexisting thyroid pathology, serum calcium and parathyroid hormone (PTH) levels, the results of preoperative localization studies, surgical procedure, histopathological features and follow up.

Neck US and MIBI scans were performed preoperatively. All patients underwent MIP or bilateral exploration; a bilateral approach was preferred in cases of associated thyroidectomy or discordant preoperative localization studies. Intraoperative PTH determination at 10' and 20' after gland excision is routinely used in our Unit for both bilateral and mini invasive approaches. In cases of negative intraoperative PTH test during MIP, bilateral exploration was performed.

During patient follow-up, serum calcium and PTH levels were tested once a day during hospitalization, once a week for the first month following hospital discharge and then every 6 months. Persistent or recurrent hyperparathyroidism was defined for high levels of PTH detected within or after 6 months post-surgery, respectively.

#### 2.1. Preoperative localization studies

The results of US and MIBI studies were retrospectively assessed. Patient outcome were categorized based on the results of localizing studies and operative findings as follows:

- True positive (TP) result: a single pathological gland found during surgical exploration on the same side where a single abnormality was identified by a scan, and the patient was cured. In cases of MGD a TP result was considered if two or more abnormalities on one or both sides were identified by a scan and subsequently confirmed by neck exploration.
- False positive (FP) result: the absence of any pathology as revealed by surgical exploration of the side of the neck were a scan had indicated a single abnormality or only one enlarged gland revealed by neck exploration where a scan had indicated two or more abnormalities and the patient cured by the excision of just a single gland.
- False negative (FN) result: one or more pathological gland found despite the lack of any such indication from imaging studies; results in which surgical exploration found a second enlarged

gland when only a single abnormality had been identified by a scan; results in which a single gland was identified by both imaging studies and neck exploration, but the patient was not cured, implying the presence of an unrecognized pathological gland.

Due to the varying localization of the parathyroid glands, no distinction between superior and inferior glands was considered for this assessment.

Definitions:

Sensitivity : TP Result / (TP Result + FN Result)

Positive Predictive Value : TP Result/(TP Result + FP Result)

# 2.2. Statistical analysis

Univariate logistic regression analysis was performed to assess the influence of pre- and post-operative variables (age, gender, calcium and PTH serum level, concomitant thyroid disease, histopathological features) on localization study outcome. Continuous data are expressed as mean  $\pm$  standard error of the mean (SEM).

### 3. Results

Two-hundred and twelve patients with preoperative diagnosis of PHP were included in the study; 34 (16%) were male and 178 (84%) female; the mean age was of  $58.8 \pm 12.7$  years. Associated thyroid disease was present in 95 (44.8%) cases. Full demographic data and preoperative data are reported in Table 1.

All patients had undergone preoperative US scan; 180 (84.9%) patients underwent a MIBI scan. Overall, US scans had a sensitivity of 62.4% and a positive predictive value (PPV) of 92.6%; MIBI demonstrated a sensitivity of 78.9% and a PPV of 89.9% (Table 2).

Surgical treatment entailed bilateral exploration in 96 (45.3%) patients (in 89 of these parathyroidectomy was associated with a thyroid resection) and a MIP in 116 (54.7%). The mean operative time was  $96 \pm 39.1$  min and the mean postoperative length of stay was  $2.4 \pm 0.8$  days.

Cure rate after parathyroidectomy was 98.1%. Surgical failure was the outcome in 4 patients: 3 patients presented persistent hyperparathyroidism and 1 recurrent hyperparathyroidism (Table 3).

Histopathological examination demonstrated single-gland disease in 194 (91.5%) cases and multi-gland disease in 17 (8%) patients. In one case (0.5%), no pathological glands were found in the specimen; the patient presented a persistent hyperparathyroidism but refused to undergo any further surgical procedure, thus it was not possible to categorize the patient as having either single or

Table 1	
Demographic and	preoperative data.

Variable	Patients ( $n = 212$ )
Sex	
Male	34 (16%)
Female	178 (84%)
Age (years)	58.8 ± 12.7 (19-86)
Familial HP	4 (1.9%)
Pre-op Calcemia (mg/dl)	$11.4 \pm 1.3 (9.4 - 17.4)$
Pre-op PTH (pg/mL)	315.9 ± 322.3 (26-2500)
Associated thyroid disease	95 (44.8%)
Follow up (months)	74.7 ± 23.2 (3–125)

HP: hyperparathyroidism; PTH: parathyroid hormone.

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