

Noninvasive localization procedures in ectopic hyperfunctioning parathyroid tumors

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Abstract

In primary hyperparathyroidism (pHPT), parathyroidectomy is the treatment of choice, but anatomic variations of ectopic glands may cause surgical failure. Reliable preoperative noninvasive localization procedures would have a positive impact on the operative time and increase recovery rate.

We retrospectively evaluated 186 patients with pHPT who were studied before successful parathyroidectomy by double tracer scintigraphy (^{99m}Tc-pertechnetate+²⁰¹Tl chloride or ^{99m}Tc-pertechnetate +^{99m}Tc-sestamibi, 160 patients), ultrasonography (148 patients) and computerized tomography (CT) scan (92 patients). During bilateral neck exploration, 159 (85.5%) single adenomas, 6 (3.2%) parathyroid carcinomas, and 3 (1.6%) double adenomas were found. Moreover, 18 (9.7%) patients had diffuse chief cells parathyroid hyperplasia. Removed parathyroid glands were in ectopic sites in 41 (22.0%) cases, mainly localized in the upper mediastinum or behind the esophagus. The overall sensitivity was 83.5 and 85.2% for ^{99m}Tc-pertechnetate+²⁰¹Tl chloride and ^{99m}Tc-pertechnetate+^{99m}Tc-sestamibi scintigraphy respectively, 80.4% for CT scan and 81.1% for ultrasonography. In patients with ectopic glands, sensitivity was 81.2, 79.5, 73.3 and 81.6% respectively. In 36 out of 41 patients with ectopic glands in whom the removed parathyroids were correctly localized, mean operative time was 95 min, and in 5 patients without preoperative localization it was 260 min.

In conclusion, in pHPT, preoperative localization of an enlarged parathyroid is helpful, especially in ectopic adenomas and in anatomic variations in location, and it has been proved to reduce operative time and morbidity rate.

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Introduction

Primary hyperparathyroidism (pHPT) is a rare disease characterized by increased production of parathyroid hormone (PTH) and subsequent hypercalcemia, with metabolic alterations mainly in the bones and kidney. In about 80% of cases pHPT is due to a solitary parathyroid adenoma, and in the remaining to diffuse hyperplasia involving all glands; parathyroid carcinoma usually occurs in 1-2% of patients. It is already known that in 20-25% of cases parathyroid glands are in ectopic sites,

variously positioned in the neck or superior mediastinum, and in about 5% of patients it is possible to find a supranumerary gland that sometimes can be pathologic.

In patients with pHPT a reliable preoperative localization of abnormal parathyroid tissue has not yet been established, and the best procedure seems to be to rely upon experienced surgeons. Nevertheless, knowing the presumed site of the pathologic glands would have a positive impact on the operative time. We undertook a retrospective study to determine the efficacy of non-invasive localization procedures in patients with pHPT.

Table 1 Main pre- and postoperative (1 month after surgery) laboratory data (mean \pm s.d.)

Parameters	Normal values	Preoperative	Postoperative
Intact PTH levels (pg/ml)	10-55	206 \pm 115.1	18 \pm 7.8
Total calcium levels (mmol/l)	1.90-2.60	3.06 \pm 0.51	2.11 \pm 0.12

Patients and methods

We studied 186 consecutive patients, 49 (26.3%) men and 137 (73.7%) women, with a mean age of 52 years (range 23-84 years), who underwent two or three different noninvasive localization procedures before neck exploration and successful parathyroidectomy for pHPT, histologically confirmed after surgery. Table 1 shows pre- and postoperative main laboratory data.

One hundred and forty-eight (79.6%) patients were examined by real-time high-resolution ultrasonography (US) with a 7.5 and 10 MHz linear transducer, and 160 (86.0%) by ^{99m}Tc -pertechnetate+ ^{201}Tl chloride or ^{99m}Tc -pertechnetate+ ^{99m}Tc -methoxyisobutylisonitrile (sestamibi) (TMSS) subtraction radionuclide scanning. Positive scan imaging was defined as an increased focal uptake area which persisted over time. In 92 (49.5%) patients a computerized tomography (CT) scan of the neck and upper mediastinum was performed. In most cases two or three different procedures were used in the same patient.

All patients underwent bilateral neck exploration and intraoperative findings were compared with preoperative ones. At surgery 159 (85.5%) patients were found to have a single parathyroid adenoma and 6 (3.2%) a parathyroid carcinoma. In 21 (11.3%) patients multiglandular disease (double adenoma in 3 patients and chief cells diffuse hyperplasia in 18) was found. No biopsies were obtained from glands appearing normal intraoperatively. An associated thyroid disease (26 benign nodules and 3 papillary thyroid carcinomas) was found in 29 (15.6%) patients.

Results

The removed glands ranged from 8 \times 8 \times 5 mm to 60 \times 25 \times 10 mm in size and in 41 (22.0%) patients had an ectopic position, mainly in the upper mediastinum (23 patients) and behind the esophagus (12 patients). Both in patients

with four hyperplastic glands and in patients with double adenomas, each imaging modality was considered positive only when two (or more) enlarged parathyroid glands were correctly localized.

Overall, and for ectopic glands, the sensitivity of localization by the different procedures is shown in Table 2. In the same patients specificity was respectively 100, 66.6, 80.0 and 100% and accuracy was 95.5% (US) and 84.4% (CT scan).

In 36 (87.8%) out of 41 patients with ectopic parathyroid glands who had accurate preoperative localization of enlarged glands, the median operative time was 95 min, compared with an average of 260 min for 5 patients in whom parathyroid adenoma was not detected and localized before operation. In patients with parathyroid hyperplasia, a subtotal parathyroidectomy was performed.

Discussion

In pHPT, successful parathyroidectomy is dependent on the surgeon's experience, which allows localization of 90-95% of abnormal parathyroid glands. Failure to identify the parathyroid tumor or a hyperplastic gland results in increased morbidity. In all patients with pHPT, neck exploration must be bilateral and complete, starting from the bifurcation of the inferior thyroid artery, back to the thyroid lobe, in retropharyngeal and thyro-carotid spaces, into the thymus and upper mediastinum and behind the trachea and esophagus.

Rodriguez *et al.* (1994) reported that preoperative investigation in patients with pHPT is useless because a correct exploration enables the surgeon to find the enlarged gland(s) in more than 90% of cases, and the use of localization procedures should be reserved for patients with persistent or recurrent hyperparathyroidism. In fact preoperative localization of abnormal parathyroid glands is an important aid before re-exploration is performed

Table 2 Overall sensitivity in localizing enlarged parathyroid glands

Sensitivity	$^{99m}\text{Tc}/^{99m}\text{Tc}$ -sestamibi	$^{99m}\text{Tc}/^{201}\text{Tl}$	CT scan	US
Overall	85.2%	83.5%	80.4%	81.1%
True positive results	(69/81)	(66/79)	(74/92)	(120/148)
Ectopic glands	81.2%	79.5%	73.3%	81.6%
True positive results	(13/16)	(31/39)	(11/15)	(31/38)

Table 3 Sensitivity of localizing procedures in primary hyperparathyroidism (number of patients in parentheses)

Technique	Arkles <i>et al.</i> (1996)	Chapuis <i>et al.</i> (1996)	Geatti <i>et al.</i> (1994)	Thompson <i>et al.</i> (1994)	Shaha <i>et al.</i> (1993)
US	76% (100)	76% (447)	81% (42)	—	—
TTSS	81% (100)	—	86% (42)	79% (44)	81% (100)
TMSS	—	80% (70)	95% (42)	—	—
CT scan	—	—	83% (42)	—	—

TTSS, ^{99m}Tc-pertechnetate + ²⁰¹Tl chloride subtraction scintigraphy; TMSS, ^{99m}Tc-sestamibi + ^{99m}Tc pertechnetate subtraction scintigraphy.

Table 4 Dosimetry of parathyroid imaging (O'Doherty *et al.* 1992)

Radiopharmaceutical	Activity (MBq)	Effective dose equivalent (mSv)
^{99m} Tc-pertechnetate	75	1.0
^{99m} Tc-sestamibi	200	2.4 (males) / 3.0 (females)
²⁰¹ Tl-chloride	75	25.0
¹²³ I	20	3.0

(Wei *et al.* 1992). Nevertheless, it has been proved to reduce operative time and morbidity rate also after primary neck exploration.

Table 3 shows that the sensitivity of each technique in localizing single parathyroid tumors ranged from 76 to 81% for US, 79 to 95% for scintigraphy and 57 to 83% for CT scan, and a combination of two or more different imaging techniques may increase sensitivity to 95-98% (Lumachi *et al.* 1989). In our series, TMSS showed respectively 85.2 and 81.2% sensitivity in all patients and in those with ectopic glands, with 100% specificity, while US showed 80.4 and 81.6% sensitivity, 80% specificity and 95.5% accuracy.

A further consideration is radiation dosimetry (effective dose equivalent) in patients who underwent scintigraphy. This seems to be moderate for ¹²³I, ^{99m}Tc-pertechnetate and ^{99m}Tc-sestamibi (Table 4).

In our experience the overall mean operative time was 120 min. In patients having abnormal parathyroid glands localized in ectopic sites, neck exploration required a different median operative time: 95 vs 260 min respectively in 36 patients with positive preoperative localization procedures and in 5 patients without parathyroid adenoma localization before surgery.

In conclusion, preoperative parathyroid localization is helpful in surgical treatment of pHPT, especially if parathyroid glands are in an ectopic site, because it reduces operative time and surgery-related morbidity, and therefore should be performed in all patients with pHPT.

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