
Is Intraoperative Parathyroid Hormone Assay Mandatory for the Success of Targeted Parathyroidectomy?

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- BACKGROUND:** Minimally invasive parathyroidectomy has become the first surgical option for patients with primary hyperparathyroidism (HPT) in many places. Preoperative localization studies are mandatory, and the use of a quick parathyroid hormone (PTH) assay is highly recommended. The aim of this study was to analyze our initial series of targeted parathyroidectomies.
- STUDY DESIGN:** In a 2-year period, 50 patients underwent unilateral neck exploration for HPT under local anesthesia and light sedation. After biochemical diagnosis, a technetium 99m sestamibi scan was performed on all patients, and cervical ultrasonography was obtained in some patients. Frozen section analysis was used to confirm parathyroid tissue in all patients. There was no biochemical intraoperative evaluation of PTH. Demographics, surgical details, results, and complications were analyzed.
- RESULTS:** There were 35 women and 15 men, with a mean age of 56 years (range 23 to 85 years). Mean preoperative calcium was 11.4 mg/dL (range 10.0 to 14.8 mg/dL), and PTH was 342 pg/mL (range 105 to 2,231 pg/mL). Mean surgical time was 52 minutes (range 30 to 100 minutes), and mean hospital stay was 2 days (range 1 to 7 days). Mean parathyroid weight was 1,000 mg (range 117 to 17,000 mg). Sestamibi scan correctly localized the abnormal gland in 47 patients (94%). There was one postoperative complication (bleeding); two patients required contralateral exploration, and persistent hypercalcemia developed in one that required surgical reintervention. After a mean followup of 12 months (range 3 to 25 months), all patients were normocalcemic.
- CONCLUSIONS:** Targeted parathyroidectomy is safe and effective. Despite the fact that quick intraoperative PTH assay was not used, the cure rate was 98%. (J Am Coll Surg 2007;204:286–290. © 2007 by the American College of Surgeons)
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Primary hyperparathyroidism (HPT) is a common disease that is successfully treated by operation. The underlying pathology is a solitary adenoma in 85% to 90% of patients.¹

In 1975, Roth and colleagues² proposed unilateral neck exploration as a less invasive surgical alternative than the classic standard bilateral cervical exploration for treatment of the disease; this technique was subsequently developed by Tibblin³ and associates in Malmo,

Sweden. The improvement of localizing imaging studies and the development of intraoperative parathyroid hormone (IOPTH) measurement made unilateral neck exploration widely accepted by many endocrine surgeons around the world. Several variations of minimally invasive parathyroidectomy have evolved, including video-scopic, videoassisted, radioguided, and focused or targeted parathyroidectomy.

In 2003, we planned to evaluate targeted parathyroidectomy in 50 patients with uniglandular disease diagnosed by localizing studies. The aim of this study was to analyze our experience in this initial series of 50 patients.

METHODS

From January 2003 to June 2005, 74 patients were referred to our service for surgical treatment of primary

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Abbreviations and Acronyms

HPT	= hyperparathyroidism
IOPTH	= intraoperative parathyroid hormone
PTH	= parathyroid hormone

HPT. Biochemical diagnosis was based on calcium, phosphorus, and parathyroid hormone (PTH) measurements. Once the diagnosis was confirmed, a Tc99m sestamibi scan was performed on all patients.

In addition to a strongly positive sestamibi scan for uniglandular disease, inclusion criteria included the absence of multiple endocrine neoplasms, a lack of characteristics possibly suggestive of malignancy, and the absence of concurrent thyroid pathology requiring surgery. Fifty patients met the inclusion criteria for unilateral neck exploration under local anesthesia and light sedation. In 14 of these 50 patients (28%), ultrasonography was performed. Demographics, presentation, surgical details, results, and early and late complications were recorded and analyzed.

Surgical technique

Patients were positioned in a dorsal decubitus position with a pillow behind the back to facilitate head hyperextension. A spinal cervical block was performed using a mixture of Xylocaine (AstraZeneca) and Marcaine (Sanofi). Through a 2-cm transverse lateral incision on the anterior border of the sternocleidomastoid muscle, the platysma muscle was divided and planes were dissected to reach the space between the carotid sheath and the thyroid gland. Once the abnormal gland was identified, it was resected and sent for intraoperative confirmation by histology. Intraoperative biochemical confirmation was not used. When a clearly enlarged gland was not identified, the ipsilateral gland was also identified to have a comparative assessment. Calcium levels were routinely obtained 24 hours after operation and at 1 month.

RESULTS

There were 35 women and 15 men with a mean age of 56 years (range 3 to 85 years). All patients had a biochemical diagnosis of HPT. Mean preoperative calcium was 11.4 mg/dL (range 10.0 to 14.8 mg/dL; normal 8.6 to 10 mg/dL), phosphorus was 2.48 mg/dL (range 1.6 to 4.26 mg/dL; normal 2.5 to 4.5 mg/dL), and PTH was 342 pg/mL (range 105 to 2,231 pg/mL; normal 10 to 55

Table 1. Clinical Presentation

Symptoms	n	%
Musculoskeletal pain	23	46
Hypertension	22	44
Nephrolithiasis	12	24
Peptic disease	10	20
Polyuria/polydipsia	6	12
Depression	3	6
Asymptomatic	3	6
Pancreatitis	2	4
Constipation	1	2

pg/mL). The most common manifestation was musculoskeletal pain (46%), followed by arterial hypertension (44%) and nephrolithiasis (24%). Three patients (6%) were asymptomatic. Clinical presentations are shown in Table 1.

Sestamibi scans were performed in all patients. They were able to localize both the side and the position of the abnormal gland (superior versus inferior) in 35 patients (70%) and only the side in 12 patients (24%). In two patients (4%), it missed the side of the abnormal gland, and in one patient (2%), it localized an abnormal gland, but failed to identify three other enlarged glands. At operation, the inferior thyroid artery was used as a landmark to determine if the gland was superior or inferior. In addition to sestamibi, ultrasonography was performed in 14 patients, with a sensitivity of 49%. For the group of patients in whom both localizing studies were performed, there was good correlation in nine patients (64%). In five patients (35%), ultrasound was negative and sestamibi was positive.

Unilateral exploration was successfully completed in 48 patients (96%). Two patients (4%) required contralateral exploration in the absence of an abnormal gland; one required general anesthesia and in the other, the exploration could be completed under cervical block. A small incision can provoke fracture of the parathyroid capsule, but this was not a complication seen in our series of patients. Average surgical time was 52 minutes (range 30 to 100 minutes), and average hospital stay was 2 days (range 1 to 7 days). In all patients, intraoperative frozen section analysis confirmed hypercellular parathyroid tissue. There were no intraoperative complications. Postoperative bleeding developed in one patient that required reexploration under general anesthesia. Bleeding was controlled with no additional complications.

The right inferior parathyroid gland was the most frequent abnormal gland (19 patients). The left inferior gland was abnormal in 16 patients, the right superior gland in 9, and the left superior gland in 6. Unequal distribution of abnormal glands may be explained by the small number of patients in our series.

Mean parathyroid weight was 1,000 mg (range 117 to 17,000 mg), and mean size was 2.1 cm (range 0.4 to 7.6 cm). Frozen pathology was consistent with adenoma in 49 patients (98%) and hyperplasia in 1.

Postoperative calcium levels 24 hours after operation were normal in all but one patient. Despite resection of an abnormal gland, and an apparently normal ipsilateral gland, persistent hypercalcemia was documented in this patient (12.1 mg/dL); he was reexplored 3 days after the initial procedure and contralateral enlargement of both glands was documented. He became normocalcemic after subtotal parathyroidectomy.

Patients have been followed in the endocrine surgery outpatient clinic for an average of 12 months (range 3 to 25 months). All patients were normocalcemic at the latest followup, with a mean calcium level of 9.08 mg/dL (range 8.4 to 9.8 mg/dL). PTH levels were measured within the first postoperative year in 15 patients, and all measurements were normal. Symptoms and signs related to HPT improved in 46 patients (92%). One patient still had high blood pressure, and three patients experienced musculoskeletal pain (Table 2).

DISCUSSION

Previous studies have shown that parathyroidectomy offers the only definite treatment for patients with HPT. The success of parathyroidectomy depends on the skill and judgment of the surgeon, and bilateral neck exploration has been accepted for decades as the gold standard treatment for primary HPT, with few complications and cure rates > 95%.⁴

Surgical treatment for primary HPT has changed dramatically in the last few years. Several minimally invasive techniques have been developed and are currently under investigation. The best surgical approach should give the highest cure rate with the lowest rate of complications and excellent tolerance.

Since Coakley and colleagues⁵ described the use of sestamibi as a marker for identifying abnormal parathyroid glands, many improvements in the technique have made it the localizing method of choice for primary HPT in most places.⁶ Considering that > 85% of pa-

Table 2. Symptoms and Signs Related to Hyperparathyroidism 1 Year after Operation

Symptoms	n	%
Musculoskeletal pain	3	6
Hypertension	1	2
Asymptomatic	46	92

tients with primary HPT have uniglandular disease, unilateral neck exploration can be performed in patients in whom unilateral disease is demonstrated by imaging techniques.⁷ Sestamibi has sensitivity and specificity of 90% and 98%, respectively.⁸ When used in combination with ultrasonography, sensitivity rises to 98%.⁹ In our study, sestamibi localized the side of the abnormal gland in 94% of patients.

The incidence of multiglandular disease in patients with primary HPT ranges from 10% to 20%.¹⁰ In a period of 14 years, 254 patients with primary HPT underwent surgical treatment in our institution, with a frequency of multiglandular disease of 18%. The low frequency of multiglandular disease in this study can be explained by the exclusion of patients with renal HPT and multiple endocrine neoplasia and the fact that only patients with clear demonstration of uniglandular disease by sestamibi scan were included.

Intraoperative measurement of intraoperative IOPTH during parathyroidectomy was first described by Nussbaum and associates.¹⁰ PTH has a short half-life, and removal of a parathyroid adenoma leads to a sharp decrease in PTH levels.¹¹ A fall in PTH levels of $\geq 50\%$ 10 to 15 minutes after removal of the hyperfunctioning parathyroid gland has been suggested as diagnostic of a cure.¹² When PTH levels decrease < 50%, parathyroid hyperplasia or double adenoma should be suspected and a bilateral neck exploration performed.¹³ Several studies favored the use of IOPTH, stating that it allows intraoperative recognition and resection of additional hyperfunctioning parathyroids missed by preoperative imaging studies.^{14,15} But other studies have reported positive cure rates without IOPTH. Sebag and colleagues¹⁵ showed that IOPTH testing did not improve the outcomes of patients undergoing parathyroidectomy at their institution. Hacıyanlı and associates¹⁶ have also found IOPTH does not reliably predict double adenomas.

We believe that in highly selected populations of HPT patients with clear demonstration of uniglandular disease by sestamibi scan, targeted parathyroidectomy can

Table 3. Characteristics of Hyperparathyroidism in Different Series

Variables	First author		Current series
	Silverberg ¹⁷	Grant ⁶	
Patients, n	61	601	50
Preoperative Ca, mg/dL	10.8	10.9	11.4
Preoperative PTH, pg/mL	126	97	342
Mean parathyroid weight, mg	—	480	1,000
Asymptomatic HPT, %	83	—	6

Ca, calcium; HPT, hyperparathyroidism; PTH, parathyroid hormone.

be safely performed without the need for intraoperative biochemical confirmation.

We adopted the miniincision technique for primary HPT, using local anesthesia, and for this particular study, no IOPTH levels were measured. Patients were candidates for this procedure if they had a clearly positive sestamibi scan alone or in combination with ultrasonography. Two patients required bilateral exploration and only persistent hypercalcemia developed in one. We believe that when a preoperative study clearly demonstrates uniglandular disease, IOPTH measurements are not strictly necessary, giving similar rates of cure as the bilateral neck exploration.¹⁷

Diagnosis of HPT at an early stage is infrequently made in our country (Mexico), and this leads to a more advanced disease at the time of operation. Preoperative calcium and PTH levels, parathyroid size, and weight are higher than are usually reported as is shown in Table 3.^{6,17} In addition, the number of patients with asymptomatic disease is very low. The advanced nature of the disease in our population may explain the high sensitivity of sestamibi scan to identify uniglandular disease and the high cure rate after removal of the diseased gland despite the lack of biochemical confirmation. A study by Grady and coworkers,¹⁸ concluded that as the volume of the gland increases, so does the likelihood of a positive sestamibi scan and a successful minimally invasive surgical approach; a negative scan is consistent with a smaller gland and the patient would benefit from the conventional bilateral method.

The 98% cure rate observed in our study compares favorably with cure rates in other studies describing unilateral or bilateral neck exploration.^{6,14,19-23} Cohen and colleagues²⁴ reported similar results of 98.6% cure rates for patients undergoing minimally invasive parathyroidectomy using local or regional anesthesia.

The patient in whom the initial operation failed in our series would have benefited from IOPTH. It is hard

to determine the percentage of failures that we are willing to accept by using this approach. In the era of bilateral exploration without preoperative localization, a cure rate of $\geq 95\%$ was widely accepted as success.⁴ We believe that a similar percentage could be acceptable for both patients and surgeons with this minimally invasive approach performed under local anesthesia, provided that a subsequent bilateral exploration under general anesthesia would cure the remaining 5%.

With our results, we can suggest that miniincision parathyroidectomy without IOPTH, in our setting, is safe and leads to high cure rates. We believe that this technique can be applied in other countries and settings where there is a combination of a clearly positive sestamibi scan that demonstrates uniglandular disease with symptomatic HPT with advanced disease. We recognize that IOPTH may be of great help in populations in which a higher frequency of multiglandular disease is expected. Targeted parathyroidectomy can be applied when patients present with symptomatic HPT associated with a clearly positive sestamibi scan and advanced disease.

Author Contributions

Study conception and design: Gil-Cárdenas, Reza, Pantoja, Herrera

Acquisition of data: Gil-Cárdenas, Gamino, Pantoja, Herrera

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Drafting of manuscript: Gil-Cárdenas, Pantoja, Herrera

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