Minimally Invasive Parathyroidectomy

Use of Intraoperative Parathyroid Hormone Assays After 2 Preoperative Localization Studies

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Objectives: To review minimally invasive parathyroidectomy (MIP) in patients undergoing initial surgical management of primary hyperparathyroidism (HPT) with preoperative, localizing sestamibi scanning (MIBI), and concordant ultrasonography (US) to determine if intraoperative parathyroid hormone (iPTH) is necessary in these cases. Minimally invasive parathyroidectomy has become an acceptable therapeutic option in treating primary HPT. Preoperative MIBI scanning, high-resolution US with color Doppler flow, and iPTH monitoring have refined this technique.

Design: Retrospective review.

Patients: The medical records of 738 consecutive patients who had undergone surgery for HPT. After excluding revision surgical procedures, secondary and tertiary HPT, unavailable intraoperative parathyroid (PTH) data, concomitant thyroid disease requiring thyroidectomy, and patients without preoperative MIBI or US, 428 patients (58%) were included in the study.

Results: The mean decrease in PTH level was 85%. Of the 428 patients with primary HPT included in the study, 209 patients (49%) had localizing, concordant preoperative MIBI and US. A decline of more than 50% in iPTH levels was observed in 202 patients (97%) after removal of parathyroid tissue localized by MIBI and US. The procedures for 4 patients were converted to bilateral neck explorations after the postexcision PTH level failed to drop less than 50%.

Conclusions: Our results show that iPTH monitoring may be eliminated in MIP surgery in a carefully selected group of patients who have preoperative, localizing MIBI with concordant US. This potentially allows an increase in operating room efficiency and a decrease in costs while performing MIP.


No longer an uncommon disease, primary hyperparathyroidism (HPT) is the most common cause of hypercalcemia in nonhospitalized patients. It affects nearly 1 in 500 women and 1 in 2000 men per year, most often in their fifth, sixth, and seventh decades of life. Recently, more asymptomatic healthy adults have been diagnosed as a result of more routine screening laboratory blood work drawn on yearly checkups.

Parathyroidectomy for primary HPT has experienced a shift from a bilateral neck exploration to less invasive techniques utilizing smaller incisions and unilateral explorations. Improved preoperative localization imaging and the advent of intraoperative parathyroid hormone (iPTH) assays have had considerable influence on the way parathyroid surgery is performed. Minimally invasive parathyroidectomy (MIP) was first introduced in 1995 and has risen in popularity as a result of its smaller incision, decreased operative time, less associated morbidity, and more satisfactory results when compared with traditional parathyroidectomy.

Sestamibi (MIBI) scans and ultrasonography (US) are now commonly used for the preoperative localization of hyperfunctioning parathyroid glands. Although the 1991 National Institutes of Health Consensus Statement declared that no imaging study was necessary prior to initial parathyroidectomy, the use of MIBI scans and US has allowed for expanded application of minimally invasive surgery. Both studies have been shown to be highly specific in localizing disease with variable sensitivity.

Rapid iPTH assays, introduced in 1988, have been useful in recent years serving as “biological frozen sections” to confirm removal of all hyperfunctioning parathyroid tissue. The PTH molecule has a short half-life (2-5 minutes), allowing it to serve as a practical intraoperative marker. A pre-
vious study suggested that a 50% drop in venous PTH levels by 20 minutes after adenoma excision is an accepted criterion for curative surgery.

We reviewed our experience with MIP in patients undergoing initial surgical management for primary HPT who demonstrated preoperative localization by MIBI scanning and US. We sought to determine if iPTH is necessary in this subset of patients and if there is potential to reduce operative time and costs by omitting them.

METHODS

After institutional review board approval was obtained, the medical records of 738 consecutive patients over a 8-year period undergoing surgery by the senior author (G.E.P.) for HPT were retrospectively reviewed. After excluding revision procedures, secondary and tertiary HPT, unavailable iPTH data, concomitant thyroid disease requiring thyroidectomy, and patients without preoperative MIBI scans or US, 428 patients (58%) were included in the study. Information collected included the patients’ age, sex, preoperative imaging results, operative findings, and baseline and 20-minute postexcision iPTH levels.

All patients underwent dual-phase MIBI scanning. The technique is based on the delayed washout of the technetium Tc 99m sulfur colloid (Tc 99m)–MIBI tracer from parathyroid tissue compared with other tissues in the neck, particularly the thyroid. Patients were injected with 20 to 25 mCi (740 MBq) of Tc 99m-MIBI. Early images were taken 10 to 15 minutes after injection, and then delayed images were taken after 2 and/or 4 hours. The MIBI scan results used for this study were established as the preoperative readings of the scans by the attending radiologist as recorded in the medical record. A positive MIBI scan was defined as one that localized and identified hyperfunctioning abnormal parathyroid tissue to 1 side of the neck by retaining the Tc 99m after the delayed washout in the thyroid at 2 and/or 4 hours. This was presumed to be a single adenoma by definition (Figure 1). A nonlocalizing MIBI scan was defined as one that did not localize to a single gland or identified bilateral, hyperfunctioning parathyroid glands.

All patients underwent high-resolution US with color Doppler flow interpretation by attending radiologists. Gray-scale imaging extended from the carotid arteries laterally to the midline and from the hyoid bone superiorly to the thoracic inlet. Parathyroid adenomas were characteristically oval-shaped, with Doppler flow showing an extrathyroidal feeding vessel entering the gland at one of the poles. Internal vascularity was usually in a peripheral distribution.

The results of preoperative MIBI and US studies were defined as concordant or discordant. Concordant, localizing studies agreed on the tracheal side of the hyperfunctioning parathyroid tissue (ie, right or left). Concordant, nonlocalizing studies concurred that there was no specified site of hyperfunctioning parathyroid tissue. Last, discordant studies showed different tracheal sides of localization. Discordant studies also occurred when one study localized and one did not.

Intraoperative PTH assays were conducted using the Immulite immunoassay system (Diagnostics Product Corp, Los Angeles, California). Blood specimens for PTH assay were drawn after induction of anesthesia prior to making the cervical incision (baseline level) and 20 minutes following removal of the abnormal gland or glands (postexcision).

In patients with concordant, localizing, and discordant preoperative studies, MIP was initially attempted. In discordant studies when 1 study was nonlocalizing, an MIP was attempted based on the localizing study. If both studies localized to opposite sides of the neck, unilateral exploration was started on the side specified by the MIBI scan. Using a skin crease, a small curvilinear transverse cervical incision (2-2.5 cm) was made in the low anterior aspect of the neck. A unilateral neck exploration was performed, and the enlarged parathyroid gland was excised. Successful excision of hyperfunctioning parathyroid tissue was defined as a decrease of 50% or more from the baseline iPTH level at 20 minutes after excision. Failure to drop the baseline iPTH level by more than 50% resulted in expansion of the operation to a bilateral neck exploration with identification of all parathyroid glands. After excision of all abnormal parathyroid tissue, baseline PTH levels were compared with 20-minute postexcision PTH levels, and a drop of more than 50% was considered curative.

When considering the entire group (n=428), the mean baseline PTH level was 263.92 pg/mL (263.92 ng/L). The mean 20-minute postexcision PTH level was 38.82 pg/mL (38.82 ng/L). The mean percentage of decrease in PTH level from baseline among all patients was 85%. The mean age of the patients who were included in the study was 58 years; 77% of the patients were female. The sensitivity of MIBI and US was 75% and 71%, respectively, while the specificity was 81% and 71%, respectively. The positive predictive value for MIBI was 97% vs 94% for US.

In 284 patients, findings from preoperative MIBI and US agreed in pinpointing the disease to the same side (concordant, localizing) or not specifying the location (concordant, nonlocalizing). Concordant, localizing imaging was seen in 209 patients while concordant, nonlocalizing imaging was found in 75 patients. Discordant study findings were seen in 143 patients.
In the 209 patients with concordant, localizing studies, an MIP was attempted. In 202 patients (97%), the iPTH fell more than 50% within 20 minutes of excision. The procedures of 4 patients (3%) were converted to bilateral neck explorations after the postexcision PTH levels failed to drop more than 50% following excision of an enlarged parathyroid gland in the anatomic location corresponding to the preoperative MIBI and US. In all 4 cases, bilateral neck exploration revealed double adenomas (in 1 of these cases the adenoma was retroesophageal), and all patients demonstrated a drop of more than 50% in baseline PTH levels after resection of all hyperfunctioning parathyroid tissue. Three other patients had reductions of baseline PTH levels of 44%, 48%, and 48%, and their operations were concluded. These patients were asymptomatic at postoperative follow-up.

A total of 143 patients had discordant preoperative studies; of these, 67 patients (47%) had localizing MIBI scans with nonlocalizing US. Only 58 of these 67 patients (87%) had successful MIP. Sixty-eight patients (48%) had localizing US with nonlocalizing MIBI. In 53 of 68 of these patients (78%), MIP was successfully performed. Eight patients had MIBI and US studies that localized to opposite sides of the neck. Successful MIP was performed in 3 of these patients (38%) (Figure 2). Combining these groups, 115 of 143 patients (80%) had successful MIP (P < .01 vs concomitant, localizing studies) (Table). After expansion to bilateral exploration, 138 of 143 patients (97%) had successful excision based on iPTH criteria.

Seventy-six patients had discordant, nonlocalizing studies. Successful MIP was performed in 31 of these patients (41%). Interestingly, in these 76 patients, 43 (57%) were found to have an adenoma involving 1 parathyroid gland despite preoperative imaging results.

**Table. Surgical Results in Concordant vs Discordant Preoperative Studies**

<table>
<thead>
<tr>
<th>Imaging Findings</th>
<th>Total Number of Patients in Each Group</th>
<th>Patients With Successful MIP, No.</th>
<th>Patients With Unsuccessful MIP, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concordant, localizing MIBI and US</td>
<td>209</td>
<td>202 (97)</td>
<td>7</td>
</tr>
<tr>
<td>Discordant MIBI and US</td>
<td>143</td>
<td>114 (80)</td>
<td>29</td>
</tr>
<tr>
<td>Concordant, nonlocalizing MIBI and US</td>
<td>76</td>
<td>31 (41)</td>
<td>45</td>
</tr>
</tbody>
</table>

Abbreviations: MIBI, sestamibi scanning; MIP, minimally invasive parathyroidectomy; US, ultrasonography.

*P < .01 when comparing the MIP success rate in the concordant, localizing MIBI and US group with the discordant MIBI and US group.

In patients undergoing initial surgical treatment for primary HPT to determine if efforts to further reduce cost and increase efficiency are attainable. Our current protocol for iPTH involves drawing a baseline PTH level and repeating the PTH level 20 minutes after removal of the hyperfunctioning gland. Using the iPTH assay has greatly enhanced our ability to achieve successful removal of parathyroid adenomas through small incisions. However, recent publications by Gawande et al.9,10 have not demonstrated improved results using iPTH monitoring during parathyroidectomy in patients with discordant preoperative MIBI scanning and US. Haber et al.11 found that discordant localization by MIBI scanning and US had a positive predictive value of 100% in 47 patients. Agarwal et al.12 have shown increased cost associated with using iPTH assays. This review adds more data for surgeons performing parathyroidectomy and agrees with previous findings reported by Gawande et al.10 and Haber et al.11 First, obtaining 2 preoperative localization studies that are concordant resulted in a 97% rate of successfully performed MIP vs an 80% success rate with only 1 study. This compares well with the 97% success rate quoted in previous large studies by Irvin et al.13 and Lew et al.14 involving 421 and 225 patients, respectively. Second, adding iPTH measurement in patients with discordant, preoperative studies provided only a minor benefit. Over an 8-year period, only 7 of 209 patients with discordant, preoperative localization had surgical failure after removal of the specified gland and would have needed revision surgery.

Another question that came about during our efforts was the comparison of MIP to minimally invasive radio-guided parathyroidectomy (MIP), which involves the patient receiving an MIBI scan on the day of surgery with initial images immediately after injection and delayed images available after 60 to 150 minutes depending on the
If this scan is localizing, the patient undergoes MIRP approximately 3 hours after initial injection, allowing the surgeon to be guided to the parathyroid adenoma with a handheld gamma probe.\textsuperscript{16,17} A recent study evaluating MIP use without iPTH showed a cure rate of 98% in 112 patients at 4 years’ follow-up.\textsuperscript{15} Our results with MIP in a similar patient population were comparable (97%). The difference in the procedures lies in the amount of management needed on the operative day. Patients undergoing MIRP require coordination between the operating room, the nuclear medicine department, the surgeon, and the nuclear medicine radiologist to time everything correctly so that the operating room moves efficiently. In our MIP protocol, patients receive all testing (preoperative MIBI and US) prior to the surgery date, allowing for a well-organized, outpatient operative day. Minimally invasive parathyroidectomy eliminates the need for any extra-intraoperative equipment, namely, MIBI with gamma probes and/or US.\textsuperscript{15,17}

In conclusion, MIP has become the standard way of dealing with primary HPT. With the advent of improved preoperative localization studies, there are data showing a decreased need for iPTH sampling in patients undergoing initial surgery for primary HPT with preoperative, localizing MIBI scans and concordant US. There is potential to substantially reduce costs associated with laboratory fees, operating room time, and anesthesia time by eliminating the use of iPTH in these patients.

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Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Smith, Magnuson, Vidrine, Kulberson, and Peters. Acquisition of data: Smith, Vidrine, Kulberson, and Peters. Analysis and interpretation of data: Smith, Kulberson, and Peters. Drafting of the manuscript: Smith, Vidrine, and Kulberson. Critical revision of the manuscript for important intellectual content: Smith, Magnuson, Kulberson, and Peters. Statistical analysis: Smith, Vidrine, and Kulberson. Administrative, technical, and material support: Smith and Peters. Study supervision: Magnuson and Peters.

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REFERENCES