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# Minimally Invasive/Focused Parathyroidectomy in Patients With Negative Sestamibi Scan Results

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**Objective:** To examine the feasibility of minimally invasive/focused parathyroidectomy in patients with primary hyperparathyroidism and negative results on preoperative sestamibi scanning.

**Design:** Retrospective review.

**Setting:** Hospital.

**Patients:** A total of 452 patients with primary hyperparathyroidism underwent parathyroidectomy between January 2005 and December 2009.

**Main Outcome Measures:** Preoperative sestamibi scans were reviewed, and their influence on the surgical outcome was examined. Records of the intraoperative and postoperative findings were also reviewed.

**Results:** Seventy-seven patients (17.0%) were found to have negative results on preoperative sestamibi scans, and these patients formed our cohort study group. In this

group, neck ultrasonography performed as an adjunct was able to preoperatively localize an area that was suggestive of a single adenoma in 61 patients (79.2%), 53 of whom were confirmed to have a single adenoma intraoperatively (sensitivity, 80.3%; specificity, 27.3%; positive predictive value, 86.9%; and negative predictive value, 18.8%). In total, 66 of 77 patients (85.7%) were confirmed to have a single adenoma at the time of surgery.

**Conclusions:** Negative results on sestamibi scans should not be used as exclusion criteria for minimally invasive/focused parathyroidectomy in patients with primary hyperparathyroidism. In our study, 66 patients with negative results on preoperative scans were found to have a single adenoma and were surgically cured by minimally invasive/focused parathyroidectomy.

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**P**RIMARY HYPERPARATHYROIDISM (PHPT) is the most common cause of hypercalcemia in the outpatient setting. Preoperative localization and the intraoperative parathyroid hormone (PTH) assay have revolutionized the surgical management of these cases. Over the years, minimally invasive/focused parathyroidectomy (MIFP) has rapidly gained popularity as the procedure of choice for patients with PHPT.<sup>1,2</sup> It has been shown to have many advantages over traditional bilateral 4-gland parathyroid exploration, including decreased pain, small incisions, lower morbidity, and decreased length of hospital stay.<sup>1,3-5</sup> This procedure, however, relies on perioperative imaging techniques to identify the affected parathyroid gland. Before surgery, technetium 99 sestamibi scanning is most commonly used to determine whether the patient has a single adenoma and, if so, to

identify its location. When the results of the scans are negative, surgeons often recommend bilateral 4-gland parathyroid exploration to identify affected glands. Therefore, false-negative results on sestamibi scans may preclude patients from targeted minimally invasive parathyroidectomy, although a single-gland adenoma may still be discovered at the time of bilateral neck exploration. The objective of this study was to examine the feasibility of intraoperative PTH monitoring-guided MIFP in patients with PHPT and negative results on preoperative sestamibi scanning. Intraoperative PTH monitoring was used to evaluate the intraoperative success of the procedure. The intraoperative criterion for successful parathyroidectomy was defined as follows: intact PTH levels should decrease by more than 50% and fall into the normal range from the highest preincisional or preexcisional hormone levels in a peripheral

blood sample obtained 10 minutes after removal of abnormal parathyroid tissue.<sup>6,7</sup> We have also used this criterion to treat double adenomas in PHPT.<sup>8</sup>

## METHODS

A total of 452 consecutive patients with PHPT underwent parathyroidectomy at Johns Hopkins Hospital, Baltimore, Maryland, between January 2005 and December 2009. All patients underwent preoperative technetium 99 sestamibi scintigraphy at our institution using single-photon emission computed tomography. Images were performed at 15 minutes and 2 hours after injection, as described previously.<sup>9</sup>

All patients also underwent concomitant cervical ultrasonography as an additional localization study. Patients with a positive results on ultrasonography of the neck underwent MIFP with intraoperative PTH testing. None of the patients in our study had previously undergone thyroid or parathyroid surgery. All patients underwent PTH testing in the operating room to confirm removal of all affected glands. A failure of PTH levels to decrease by 50% and fall into the normal range 10 minutes after resection of the image-identified adenoma was an indication for bilateral neck exploration.

## RESULTS

We identified 77 patients (17.0%) in our database with PHPT and negative results on sestamibi scanning. The mean age of the patients was 54 years; 25.9% were male; the average preoperative calcium level was 11.1 mg/dL (to convert to millimoles per liter, multiply by 0.25); and the average preoperative PTH level was 113.4 mg/dL (to convert to nanograms per liter, multiply by 1.0). To investigate further localization, all patients underwent cervical ultrasonography in the Department of Radiology at Johns Hopkins Hospital. Sixty-one of them (79.2%) had results that suggested an adenoma, and 53 of the 61 patients were confirmed to have a single adenoma at the time of surgery (sensitivity, 80.3%; specificity, 27.3%; positive predictive value, 86.9%; and negative predictive value, 18.8%). The sensitivity, specificity, positive predictive value, and negative predictive value of sestamibi scanning in localizing a single adenoma in our study were 83.5%, 23.4%, 90.2%, and 14.3%, respectively.

Of the 77 patients with negative results on sestamibi scans, 66 (85.7%) were found to have a single adenoma at the time of surgery. Of the remaining patients, 8 (10.4%) had a double adenoma, and 3 (3.9%) had 4-gland hyperplasia. Fifty-three patients who were found to have a single adenoma underwent MIFP alone, and the remaining 13 patients underwent 4-gland exploration that confirmed the evidence of single-gland disease.

## COMMENT

Primary hyperparathyroidism has been recognized as a disease process since the 1920s, when it was discovered in both Europe and the United States.<sup>1,10</sup> Since that time, the recognition, diagnosis, and treatment of PHPT have evolved because of improved laboratory testing, accurate preoperative localization, and less invasive surgical procedures. Once a diagnosis of PHPT is made and the

patient is deemed an appropriate surgical candidate, preoperative localization of the involved gland(s) aids in the choice of operation (MIFP vs bilateral 4-gland exploration). Preoperative localization of the abnormal gland(s) has become even more important in the era of minimally invasive parathyroid surgery. The 2 most common imaging modalities are ultrasonography and technetium 99m sestamibi scintigraphy. The sensitivity of sestamibi–single-photon computed tomographic scanning in the present study was similar to that reported in the literature (range, 71% to 88%).<sup>11–13</sup>

Ultrasonography is particularly beneficial because it is inexpensive, can be performed by the surgeon in office settings, can be repeated easily, and does not involve ionizing radiation. A point of concern with preoperative imaging is the case involving PHPT and a negative sestamibi scan result. Such cases represent an important subset in which traditional 4-gland operative exploratory surgery is widely advocated at the expense of MIFP. However, MIFP is rapidly gaining popularity as the procedure of choice for patients with PHPT as well as the preferred treatment option in patients with PHPT and negative results on sestamibi scans.<sup>1,2,14</sup> It has been shown to have many advantages over traditional bilateral 4-gland parathyroid exploration, including decreased pain, small incisions, improved cosmetic results, lower morbidity, and decreased length of hospital stay.<sup>3–5</sup> In contrast, parathyroid exploratory surgery often and unpredictably requires more extensive neck exploration, including paratracheal dissection, thymectomy, and partial thyroidectomy. Intraoperative PTH monitoring can help confirm a successful operation, leaving little to no suspicion of multiglandular disease and thereby avoiding bilateral neck exploration.<sup>14</sup> We and others have shown that intraoperative PTH monitoring is of value not only in cases involving single-gland disease but also in cases involving double adenoma and multiglandular disease.<sup>8,14,15</sup> Therefore, it has been our goal to consider more patients with PHPT as candidates for MIFP. However, it is important to emphasize that an experienced parathyroid surgeon should perform the operation after a comprehensive preoperative workup, either with an MIFP approach or with a conventional bilateral neck exploration. Treatment using the bilateral approach results in a greater than 95% cure, with a complication rate of less than 4%.<sup>16</sup>

Our study aimed to assess the feasibility of MIFP in patients with PHPT who have negative results on preoperative sestamibi scanning. The results of our study emphasize several important points. First, in patients who had negative sestamibi scan results, we found a high incidence of single parathyroid gland disease. Most of these patients (85.7%) had a single adenoma. This finding contradicts the common perception that a negative sestamibi scan result indicates a diagnosis of parathyroid hyperplasia/multiglandular disease and thus requires 4-gland operative exploratory surgery.<sup>17</sup> Second, further localization with comprehensive cervical ultrasonography will reveal a single adenoma in most cases, as in our study, in which cervical ultrasonography demonstrated a positive predictive value of 86.9% in the preoperative detection of a single adenoma when the results of sestamibi

scanning were negative. Comprehensive neck ultrasonography is beneficial because it allows more patients who were previously excluded to be candidates for MIFP. This concept was advocated in some previous studies, but little has been done to evaluate its efficacy in cases involving negative sestamibi scan results.<sup>18-21</sup> Furthermore, we are able to achieve a success rate of 98.4% in resolving PHPT by starting with MIFP in this challenging patient subgroup. One of the limitations of our current study involved the difficulty in reporting an accurate cure rate in our study cohort. Therefore, we used intraoperative PTH testing as a predictor of cure. However, most surgeons agree that a decrease of more than 50% in PTH level from the highest preincision or preexcision level is associated with a predictive cure in 94% to 97% of cases.<sup>6,7,22</sup> Future studies are needed to specifically address the cure rate in this interesting group of patients with negative preoperative sestamibi scan results.

We recently reported on independently evaluating both ultrasonography and sestamibi scanning as single-modality preoperative screening tools in cases of PHPT. We reported that the sensitivity for correct localization of a single parathyroid adenoma was 83% for sestamibi scanning vs 72% for ultrasonography.<sup>23</sup> Therefore, when patients have negative results on a sestamibi scan, we recommend that they undergo comprehensive cervical ultrasonography before the option of MIFP is excluded. Using this approach, many more patients with PHPT will be considered for MIFP.

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