Objective: To assess the role of high-resolution ultrasonography in the preoperative evaluation of patients with hyperparathyroidism.

Design: Retrospective cohort.

Setting: Tertiary care university hospital.

Patients: Three hundred seventeen patients with hyperparathyroidism who underwent preoperative assessment with ultrasonography and/or sestamibi scan and surgical treatment between October 2003 and October 2006.

Main Outcome Measures: Descriptive statistics of localization imaging studies and detection of concomitant thyroid disease in patients presenting with hyperparathyroidism.

Results: Ultrasonography correctly localized the parathyroid adenoma(s) in 148 (69.4%) of the 229 patients with these lesions. Sestamibi scans correctly localized the parathyroid adenoma(s) in 133 (58.1%) of the 229 patients. The agreement between the 2 imaging procedures was moderate (κ = 0.23; 95% confidence interval, 0.12-0.36). Of 317 patients with hyperparathyroidism, 96 (30.3%) had clinically significant concomitant thyroid disease requiring partial or total thyroidectomy. Histopathologic examination revealed benign thyroid disease in 80 (83.0%) of the 96 patients and thyroid carcinoma in 16 (16.6%).

Conclusion: Ultrasonography is a useful tool in the preoperative evaluation of patients with hyperparathyroidism both for localization of parathyroid adenomas and for the diagnosis of concomitant thyroid disease.

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Minimally invasive surgery is gaining popularity in head and neck endocrine surgery, and bilateral neck exploration is no longer routinely performed at the time of parathyroidectomy. Therefore, preoperative localization of parathyroid adenomas is increasingly important. Given the 95% success rate with no localizing studies and the performance of bilateral neck exploration, the use of localization studies is still controversial.1 Successful localization with imaging and intraoperative parathyroid hormone assays provides an acceptable alternative to routine bilateral neck exploration. A sestamibi scan is the most commonly used localization study and has a reported sensitivity range of 54% to 84%.1-3 Ultrasonography, which is also used for the localization of parathyroid adenomas, has a sensitivity range of 57% to 89%.2,3 Without routine bilateral neck exploration at the time of parathyroidectomy, concomitant incidental thyroid disease can be missed. Historically, the prevalence of associated thyroid disease found at the time of bilateral neck exploration for parathyroidectomy has been 20% to 60%.4-8 Thyroid malignancy has been found in 2% to 19% of patients who present with hyperparathyroidism compared with less than 1% in autopsy reports.7,9 The aim of this study was to assess the role of ultrasonography in the preoperative assessment of patients presenting with hyperparathyroidism both for the localization of parathyroid adenomas and for the preoperative diagnosis of concomitant thyroid disease.

Methods

Patient Population

The medical charts of all patients who underwent parathyroidectomy between October 2003 and October 2006 at the University of Alabama at Birmingham were reviewed. Three hundred thirty-one patients were identified, and 14 patients were excluded who did not receive preoperative ultrasonography. A total of 317 patients were used to assess for concomitant thyroid disease. Of these 317 patients, only 260 had primary hyperthyroidism. Of these 260 patients, 249 underwent both ultrasonography and sestamibi scanning. Of those 249, 229 had adenomas found at the time of surgery. Therefore, these 229 patients were used to assess localization by ultrasonography and ses-
tamibi scanning. Information collected from chart review included patients' age, sex, type of hyperparathyroidism, preoperative imaging results (sestamibi scanning and ultrasonography), operative findings, and histopathologic findings. The study was approved by the institutional review board of the University of Alabama at Birmingham.

**IMAGING STUDIES**

A sestamibi scan was performed on all patients with primary hyperparathyroidism. Patients were injected with 20 mCi (740 MBq) of technetium Tc 99m sestamibi. Early images were obtained 10 to 15 minutes after injection, and delayed images were obtained 2 and/or 4 hours later. The sestamibi scan results used for this study were read by the attending radiologist. A localizing sestamibi scan was defined as one that localized and identified hyperfunctioning abnormal parathyroid tissue by retaining the technetium Tc 99m after the delayed washout in the thyroid at 2 and/or 4 hours was complete. This abnormal parathyroid tissue seen on sestamibi scans was presumed to be a single adenoma by definition (Figure 1).

Ultrasonography, which was performed by the department of radiology, was used to carefully examine the thyroid gland and surrounding soft tissue of the neck for both parathyroid and thyroid disease. Ultrasonography was performed with a high-frequency (5-15 MHz) transducer equipped with spectral and color duplex Doppler imaging capabilities. Ultrasonographic images were read by the attending radiologist. Ultrasonographic localization of parathyroid disease was assessed. A localizing ultrasonographic scan was defined as one that identified a hypoechoic mass adjacent to the thyroid that was hypervascular on color flow Doppler imaging (Figure 2). Patients with clinically significant thyroid nodules (dominant nodules >8 mm and nodules with hypoechogenicity, irregular margins, calcifications, and increased vascularity) were identified.

**TREATMENT PLAN**

Patients with primary hyperparathyroidism with localizing studies were offered a minimally invasive approach. Using a skin crease, a small curvilinear transverse cervical incision (2.0-2.5 cm) was made over the area indicated by the localization study. A unilateral neck exploration was performed, and the enlarged parathyroid gland(s) was excised. Successful excision of hyperfunctioning parathyroid tissue was defined as a decrease of 50% or more from the baseline intraoperative parathyroid hormone level 20 minutes after surgery. In patients with nonlocalizing scans, bilateral neck exploration was performed.

Patients with concomitant thyroid disease were offered fine-needle aspiration or thyroid lobectomy at the time of parathyroidectomy for diagnosis. If fine-needle aspiration indicated a suspicious, a malignant, or an indeterminant lesion, thyroid lobectomy was performed at time of parathyroidectomy. Frozen-section analysis was performed on all thyroid lobectomy specimens, allowing total thyroidectomy to be performed for any malignant or suspicious lesions at the same operation.

**DATA REVIEW AND STATISTICAL ANALYSIS**

The sensitivity and specificity of sestamibi scans and ultrasonography in the localization of parathyroid adenomas were cal-
A true positive was defined as a study that correctly localized the parathyroid adenoma(s). A false positive was defined as a study that was read as localizing in a patient with 4-gland hyperplasia. A true negative was defined as a study that was read as nonlocalizing in a patient who was found to have 4-gland hyperplasia. A false negative was defined as a study that was read as nonlocalizing in a patient who was found to have a parathyroid adenoma at the time of surgery.

Categorical variables were reported as proportions. Continuous variables were reported as means and standard deviations. The prevalence of localization was calculated using each imaging test independently. Using the reference standard of histologically confirmed parathyroid adenomas, the sensitivity, specificity, positive and negative predictive values, and accuracy of ultrasonography and sestamibi scans were calculated. The exact binomial confidence intervals were computed for each estimate. The accuracy of ultrasonography vs sestamibi scans was compared by the \( \kappa \) statistic. The percentage of patients with hyperparathyroidism and a concomitant diagnosis of benign and malignant thyroid disease was determined by review of pathology reports.

**RESULTS**

Of the 317 patients included in the study, 78 (24.6%) were male (age range, 16-86 years; mean ± SD age, 54.3 ± 15.8 years) and 239 (75.4%) were female (age range, 17-87 years; mean ± SD age, 58.1 ± 13.6 years). Two hundred sixty patients (82%) had the preoperative diagnosis of primary hyperparathyroidism, 40 (12.6%) were diag-

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**Table. Characteristics of Ultrasonography and Sestamibi Scanning in Localization of Parathyroid Adenomas**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasonography</td>
<td>69.8 (63.6-76.0)</td>
<td>56.8 (40.8-72.7)</td>
<td>90.2 (85.7-94.8)</td>
<td>24.7 (15.5-33.9)</td>
</tr>
<tr>
<td>Sestamibi scanning</td>
<td>62.7 (56.2-69.2)</td>
<td>62.1 (46.5-77.8)</td>
<td>90.5 (85.7-95.2)</td>
<td>22.5 (14.4-30.6)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.
nosed as having secondary hyperparathyroidism, and 17 (5.3%) had tertiary hyperparathyroidism. The most common parathyroid histologic diagnosis was single adenoma (65.6%), followed by 4-gland hyperplasia (23.0%). Double adenomas were found in 30 patients (9.4%). A diagnosis of normal parathyroid tissue or a diagnosis other than parathyroid disease occurred less than 1% of the time. Only 2 patients (0.6%) had no parathyroid tissue.

Two hundred forty-nine of the 260 patients diagnosed as having primary hyperparathyroidism underwent both sestamibi scanning and ultrasonography before surgery. Of these patients, 229 were found to have parathyroid adenoma(s) at the time of surgery. The sestamibi scan was read as localizing in 147 of these 229 patients (64.2%) and correctly localized the parathyroid adenoma(s) in 133 (58.1%). Ultrasonography was read as localizing in 159 of the 229 patients (69.4%) and correctly localized the lesion in 148 (64.6%).

The classification of the individual test results, compared with the reference standard of histologic diagnosis, is shown in the Table. Sestamibi imaging had a sensitivity of 62.7% and a specificity of 62.1%. Ultrasonography had a sensitivity of 69.8% and a specificity of 56.8%. There was no statistical difference in the sensitivity or specificity of the 2 imaging procedures, and the results of both were in moderate agreement (κ=0.23; 95% confidence interval, 0.11-0.36). For the patients who underwent both procedures, which were considered parallel tests, the combined sensitivity and specificity was 88.7% and 35.3%, respectively.

Ultrasonography was able to correctly localize the parathyroid adenoma in 46 patients with nonlocalizing or incorrectly localizing sestamibi scans. Sestamibi scanning was able to correctly localize the parathyroid lesion in 31 patients with nonlocalizing or incorrectly localizing ultrasonographic examination findings. Of the 229 patients who were found to have parathyroid adenoma(s) intraoperatively, 102 (41.0%) had correct localization on both ultrasonography and sestamibi scan, and 34 (13.7%) patients had incorrectly localizing or nonlocalizing studies by both imaging modalities.

Ninety-six of the 317 patients (30.3%) in the study were found to have clinically significant concomitant thyroid disease, which was identified preoperatively with ultrasonography in 66 patients (68.8%), intraoperatively in 12 patients (12.5%), and incidentally when the thyroid gland was removed for intrathyroidal parathyroid tissue in 18 patients (18.8%). Of the patients with concomitant thyroid disease, 80 (83.3%) were found to have benign disease, while 16 (16.7%) were diagnosed as having thyroid carcinoma. Nearly half of the patients diagnosed as having benign thyroid disease were found to have nodular hyperplasia (49.0%). The next most common diagnosis was thyroiditis with fibrosis and chronic inflammation (13.5%). Follicular adenoma (9.4%), Hurthle cell adenoma (1.0%), and normal thyroid tissue (8.3%) were found less commonly. All 16 patients diagnosed as having malignant disease were found to have papillary carcinoma.

This study highlights the role of ultrasonography in the preoperative assessment of patients with hyperparathyroidism. Although some authors still believe that “the only localizing study is to locate an experienced parathyroid surgeon,”5 preoperative localizing studies have reported a success rate similar to that reported for routine bilateral neck exploration at our institution.6 Sestamibi imaging is considered the localization study with the greatest sensitivity but is less accurate in patients with multiglandular disease, small adenomas, or concomitant thyroid disease.9,11 Ultrasonography, which has also been used for parathyroid adenoma localization, has a sensitivity and a specificity similar to those of sestamibi scanning. In our study, there was no statistically significant difference between the 2 tests in the localization of parathyroid adenomas. The accuracy of the 2 tests was compared by the κ statistic (κ=0.23).

Ultrasonography offers the advantages of being less expensive, noninvasive, less time consuming, and widely available. The disadvantages are that it is widely operator dependent and that it relies on newer models with color flow Doppler imaging capabilities. The advantages of a sestamibi scan include a decrease in operator dependence and a reported increase in sensitivity. Also, sestamibi scans have the ability to localize mediastinal disease. The disadvantages of sestamibi scanning include cost, time, and increased invasiveness. The coexistence of thyroid disease affects the ability of both ultrasonography and sestamibi to detect parathyroid adenomas, with a reported decrease in sensitivity ranging from 53% to 77% for ultrasonography and from 71% to 80% for sestamibi scanning.9

While the difference between ultrasonography and sestamibi scanning in identifying parathyroid adenoma(s) was not significant in this study, the combination of the 2 studies produced better results (κ=0.23). When the advantages and disadvantages of each test and their individual and combined accuracy in identifying parathyroid adenomas are being considered, we propose evaluating patients with primary hyperparathyroidism initially with ultrasonography and then with sestamibi scan-
ning if they have not undergone a localizing ultrasono-
graphic examination.

Our review again recognized the coexistence of thy-
roid and parathyroid disease, which was first reported in
1956.13 Our finding of a 30.3% prevalence of coexis-
ting lesions is consistent with previous studies.6,8 Inter-
estingly, of the thyroid nodules that were diagnosed in
our study, 16.6% were malignant compared with the gen-
eral malignancy risk of 5% assigned to thyroid nodules
that is found in the general population.13 The incidence
of concomitant thyroid malignant neoplasms found in
this study demonstrates the importance of exploring the
thyroid gland before surgery in order to avoid missed di-
agnosis or delayed diagnosis requiring reoperation in the
same surgical field.

High-resolution ultrasonography is the modality of
choice for the evaluation of concomitant thyroid dis-
ease. Nodules with certain characteristics (>8 mm, hy-
poechochogenicity, irregular margins, calcifications, and
increased vascularity) are at increased risk for being
malignant and should be biopsied with fine-needle as-
piration before the neck is entered or with thyroid lo-
bectomy and frozen-section analysis at the time of para-
thyroidectomy.11,14 Controversy does exist over the
management of incidental, nonpalpable thyroid nod-
ules found in the general population owing to the un-
certainty about the biological behavior of well-
differentiated thyroid microcarcinomas, which are often
diagnosed retrospectively after thyroidectomy has been
performed because of other diagnoses.11 However, pa-
tients with hyperparathyroidism differ from the general
population in that they will undergo a surgical proce-
dure that includes the thyroid region. Also, our retro-
spective study indicates that there is an increased rate of
malignancy for concomitant thyroid nodules, a finding
that is supported in the literature.7,9,11

In conclusion, ultrasonography plays an important role
in the preoperative evaluation of patients with hyper-
parathyroidism. For patients with primary hyperpara-
thyroidism, preoperative localization allows the sur-
geon to use a minimally invasive approach. While we
advocate the use of ultrasonography for parathyroid ad-
enoma localization, a role for sestamibi scanning still ex-
ists. For patients with nonlocalizing ultrasonographic ex-
amination findings, sestamibi scans still may be able to
localize the parathyroid adenoma. Also, when newer, more
advanced ultrasonographic models with color flow Dop-
pler imaging are unavailable, sestamibi scans may be su-
perior. For all patients with hyperparathyroidism, identi-
fication of concomitant thyroid disease before surgery
allows proper counseling and planning, reduces the num-
ber of missed diagnoses, and decreases the risk of reop-
eration in the same surgical field. Ultrasonography plays a
valuable role in the preoperative evaluation of patients
with hyperparathyroidism both for localization of para-
thyroid adenomas and for identification of concomitant
thyroid disease.

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