The Cost of Screening for Synchronous Thyroid Disease in Patients Presenting With Primary Hyperparathyroidism

Christopher S. Hollenbeak, PhD; Irina Lendel, MD; Kirt S. Beus, MD; James M. Ruda, MD; Brendan C. Stack Jr, MD

Objective: To use decision analysis to compare the costs associated with minimally invasive parathyroidectomy (MIP) and bilateral neck exploration (BNE) in patients with primary hyperparathyroidism with regard to treatment of incidental synchronous thyroid disease.

Design: We developed a decision tree model to evaluate the cost of managing thyroid pathology in primary hyperparathyroidism with the following 3 approaches: MIP, MIP with preoperative ultrasonography, and routine BNE with intraoperative thyroid evaluation. We tested the robustness of the optimal decision with sensitivity analyses.

Setting: A tertiary care academic medical center.

Main Outcome Measure: Total costs from a provider perspective.

Results: Minimally invasive parathyroidectomy without an active search for thyroid abnormalities was determined to have the lowest expected cost ($5275 per patient). Parathyroid surgery with routine preoperative thyroid ultrasonography and further thyroid treatment as indicated had an expected cost of $5910 per patient. Bilateral neck exploration with intraoperative thyroid evaluation and treatment of the thyroid gland had an expected cost of $5916 per patient. Sensitivity analyses confirmed the robustness of the results across a reasonable range of surgical and imaging costs.

Conclusions: Minimally invasive parathyroidectomy is not contraindicated on the basis of cost by an inability to screen for synchronous thyroid disease. In addition, ultrasonographic screening of the thyroid glands of patients undergoing MIP is not cost prohibitive and, in fact, is less costly than BNE. Ultrasonography has the added advantage of confirming the location of the offending parathyroid.


SYNCHRONOUS THYROID AND parathyroid disease was first described in 1947.1 Since that time, many reports have observed this association. Among patients with primary hyperparathyroidism (PHPT), synchronous thyroid disease has been detected in 12.6% to 80% and synchronous thyroid carcinoma has been reported in 1.7% to 10.7%.2-5 These diseases may coexist because of similar demographics (ie, both affect women more often), and no pathophysiological link has been established (except in cases of multiple endocrine neoplasia).

A trend toward minimally invasive parathyroidectomy (MIP) has gained momentum. Minimally invasive parathyroidectomy is defined as the removal of a parathyroid adenoma through a small incision, which precludes full thyroid examination. The noted correlation between PHPT and thyroid carcinoma has been used as an argument against the MIP approach in the surgical management of parathyroid disease. The argument stems from the ability to palpate and inspect the thyroid gland intraoperatively during conventional bilateral parathyroid exploration, allowing for the detection of coexisting thyroid abnormalities. This approach supposes that thyroid observation and palpation are specific for thyroid disease, cannot be done through a small incision, and will lead to appropriate additional thyroid surgery when indicated. Most minimally invasive techniques do not allow for a thorough intraoperative thyroid evaluation.

Minimally invasive parathyroidectomy has been proliferating as the pre-
ferred method for parathyroid surgery because of patient comfort, operative time, and resource utilization. A systematic underdiagnosis or undertreatment of synchronous thyroid disease might undermine any convenience or cost advantage.

In this study, we performed a cost analysis (within a decision analysis framework) of patients with PHPT that includes identification, preoperative diagnostic testing, and surgical management of coexistent thyroid lesions. The costs of additional diagnostic testing and ultimate

![Figure 1. Decision tree for the bilateral neck exploration (BNE) with palpation parathyroid surgery strategy relative to the ultrasonography (US) and minimally invasive parathyroidectomy (MIP) strategies. Circles indicate chance nodes; square, choice node (ie, the point at which a clinician makes a decision); and triangles, terminal nodes representing end points.](image1)

![Figure 2. Decision tree for the minimally invasive parathyroidectomy (MIP) strategy with no preoperative imaging of the thyroid gland. Thyroid evaluation and treatment are included in the decision analysis if thyroid abnormalities are discovered during the treatment. BNE indicates bilateral neck exploration; UNE, unilateral neck exploration; circles, chance nodes; minus sign, negative; plus sign, positive; and square, choice node (ie, the point at which a clinician makes a decision).](image2)
thyroid treatment were compared with those of conventional bilateral neck exploration (BNE), without preoperative imaging for the PHPT alone.

**METHODS**

**DECISION ANALYTIC MODEL**

A decision tree model was developed for the evaluation and treatment of PHPT and included definitive management of thyroid nodules if discovered during the respective strategy (Figure 1). We compared the following 3 strategies at the time of the diagnosis of PHPT: (1) MIP (with previous sestamibi imaging) with no preoperative imaging of the thyroid gland (Figure 2, MIP strategy); (2) preoperative ultrasonography (US) of the thyroid gland for nodules and areas of sestamibi uptake followed by the surgical approach dictated by the results of imaging (Figure 3, US strategy); and (3) traditional BNE with thyroid palpation (Figure 1, BNE strategy). (The complete decision tree is very large and is available on request from the authors.) Simplified versions of the treatment strategies are presented in Figure 1 to Figure 4. The full decision analysis takes into account the failure of sestamibi imaging and US, the presence of multiple adenomas and parathyroid hyperplasia, and the incidence of conversion of minimally invasive approaches to more invasive procedures. The decision analysis framework was used to estimate expected costs for each of the 3 clinical approaches.

**PROBABILITIES**

The probabilities of each management outcome in the decision tree and the model variables were determined by a comprehensive review of the literature. The data for parathyroid evaluation and treatment were obtained from a previous study that performed an evidence synthesis of the literature for sensitivity and specificity of sestamibi scanning, incidence of multiple adenomas and hyperplasia, and cure rates of the surgical approaches. These values were used to populate the decision tree for the parathyroid variables.

Probabilities used in the decision tree included the probabilities of achieving cure of hyperparathyroidism using MIP, unilateral neck exploration (UNE), BNE, BNE completion, the probability of sestamibi imaging or US localizing single- or multiple-gland disease, and the probability of encountering single-gland disease associated with PHPT (Table 1). In addition, the literature was reviewed extensively to establish model variables for the evaluation and treatment of thyroid disease. Weighted averages were computed for the incidence of thy-

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*Figure 3.* Decision tree for the ultrasonography (US) strategy followed by the surgical approach dictated by the results of imaging, including thyroid evaluation and treatment. BNE indicates bilateral neck exploration; FNA, fine-needle aspiration biopsy; MIP, minimally invasive parathyroidectomy; UNE, unilateral neck exploration; circles, chance nodes; minus sign, negative; plus sign, positive; and square, choice node (ie, the point at which a clinician makes a decision).
To populate the decision tree, a meta-analysis of the literature was performed to determine the incidence of synchronous thyroid disease and synchronous thyroid malignant neo-

Figure 4. Subtree for negative results on sestamibi imaging. This subtree is the topmost branch in Figures 2 and 3. BNE indicates bilateral neck exploration; FNA, fine-needle aspiration biopsy; UNE, unilateral neck exploration; US, ultrasonography; circles, chance nodes; minus sign, negative; plus sign, positive; and square, choice node (ie, the point at which a clinician makes a decision).

roid abnormalities and carcinoma in patients with PHPT and the incidence of various fine-needle aspiration biopsy (FNA) results for thyroid lesions (Table 2).
Table 1. Baseline Values Used in the Model in Sensitivity Analyses

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value, %</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure rates, % (range)</td>
<td>97.0 (0-100.0)</td>
<td>MIP</td>
</tr>
<tr>
<td></td>
<td>95.0 (0-100.0)</td>
<td>UNE</td>
</tr>
<tr>
<td></td>
<td>99.0 (0-100.0)</td>
<td>BNE completion</td>
</tr>
<tr>
<td></td>
<td>98.0 (0-100.0)</td>
<td>BNE</td>
</tr>
<tr>
<td>Costs, $ (range)</td>
<td>5594 (3000-7000)</td>
<td>BNE</td>
</tr>
<tr>
<td></td>
<td>1776 (1000-5000)</td>
<td>BNE completion</td>
</tr>
<tr>
<td></td>
<td>3779 (2000-6000)</td>
<td>Completion thyroidectomy</td>
</tr>
<tr>
<td></td>
<td>1006 (500-3000)</td>
<td>Hemithyroidectomy</td>
</tr>
<tr>
<td></td>
<td>5000 (3000-10000)</td>
<td>Median sternotomy</td>
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<tr>
<td></td>
<td>4006 (2000-7000)</td>
<td>Total thyroidectomy</td>
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<tr>
<td></td>
<td>1626 (1000-5000)</td>
<td>UNE</td>
</tr>
<tr>
<td></td>
<td>3939 (2500-6000)</td>
<td>UNE completion</td>
</tr>
<tr>
<td></td>
<td>387 (500-3000)</td>
<td>US</td>
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<tr>
<td></td>
<td>320 (100-500)</td>
<td>US-guided FNA</td>
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<tr>
<td></td>
<td>1078 (750-1500)</td>
<td>Sestamibi imaging</td>
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Prevalence

<table>
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<tr>
<th>Variable</th>
<th>Value, %</th>
<th>Source</th>
</tr>
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<tbody>
<tr>
<td>Single-gland disease</td>
<td>89.6 (0-100.0)</td>
<td>Hawkins et al, 1987</td>
</tr>
<tr>
<td>Multiple-gland disease</td>
<td>9.8 (0-20.0)</td>
<td>Hawkins et al, 1987</td>
</tr>
</tbody>
</table>

Probabilities (sestamibi imaging)

| Detect 0 glands if 1 gland is abnormal | 1.0 | Hawkins et al, 1987 |
| Detect 0 glands if 2 glands are abnormal | 55.0 | Hawkins et al, 1987 |
| Detect 1 gland if 1 gland is abnormal | 86.0 | Hawkins et al, 1987 |
| Detect 1 gland if 2 glands are abnormal | 44.0 | Hawkins et al, 1987 |
| Detect 2 glands if 1 gland is abnormal | 1.0 | Hawkins et al, 1987 |
| Detect 2 glands if 2 glands are abnormal | 36.0 | Hawkins et al, 1987 |

Probabilities (US)

| Detect 0 glands if 1 gland is abnormal | 20.0 | Hawkins et al, 1987 |
| Detect 0 glands if 2 glands are abnormal | 21.0 | Hawkins et al, 1987 |
| Detect 1 gland if 1 gland is abnormal | 79.0 | Hawkins et al, 1987 |
| Detect 1 gland if 2 glands are abnormal | 55.0 | Hawkins et al, 1987 |
| Detect 2 glands if 1 gland is abnormal | 1.0 | Hawkins et al, 1987 |
| Detect 2 glands if 2 glands are abnormal | 23.0 | Hawkins et al, 1987 |

Abbreviations: BNE, bilateral neck exploration; FNA, fine-needle aspiration biopsy; MIP, minimally invasive parathyroidectomy; UNE, unilateral neck exploration; US, ultrasonography.

In addition, extensive review of the literature was performed to establish model variables for the evaluation and treatment of thyroid disease.

A further meta-analysis for parameterization of the decision tree was performed using 54,239 FNA biopsy specimens from thyroid nodules reported in the literature. Results of cytologic evaluation of these specimens found 43,870 to be benign (80.9%). An additional 1868 were malignant (3.4%), and 8501 were found to be insufficient, inconclusive, or indeterminate (15.7%) (Table 2).

Patients with insufficient, inconclusive, or indeterminate FNA results who underwent thyroidectomy also underwent plasms (Table 2). We found 8510 patients diagnosed as having PHPT in the literature with information regarding synchronous thyroid malignant neoplasms. Of these, 312 (3.7%) had coexisting thyroid carcinoma. We identified 4863 patients with PHPT who had information regarding types of synchronous thyroid disease, and 1261 of these (25.9%) had coexisting thyroid disease.

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evaluation to obtain variables for the decision tree. Of these, 3155 underwent thyroidectomy, with 753 (23.9%) found to have thyroid carcinoma on permanent sections (Table 2).38,40,43-50,52-67

The data for parathyroid evaluation and treatment were previously reported.6 We used additional literature review to estimate cure rates for MIP (Table 1).

COSTS

Costs were computed as direct medical costs from the perspective of the hospital, presented in 2005 dollars. No discounting was performed because we did not consider any long-term costs. Costs for the operating room, hospital admission, technical support for sestamibi imaging and US, frozen section preparation, and rapid measurement of parathyroid hormone (PTH) levels were obtained from the our institution's cost accounting database. Professional costs were determined by Medicare reimbursement rates for the surgeon, anesthesiologist, radiologist, and pathologist. Comprehensive costs of adding a hemithyroidectomy, total thyroidectomy, or conversion to a more invasive parathyroid surgical technique were added as they occurred in the decision tree (Table 2).

DETAILS OF COSTS

Operative time is the major determinant in total cost, with the operating room cost of $15 per minute at our institution. The operative time for each surgical method was reviewed at our institution, and all of the surgical procedures were performed by the senior author (B.C.S.). Operative time for radio-guided parathyroidectomy averaged 46 minutes in 47 patients. Unilateral neck exploration with rapid testing for PTH levels was found to have an average operative time of 72 minutes in 15 patients. Average operative time for BNE was 138 minutes in 11 patients. The BNE time is somewhat higher than that reported in the literature. This may be due to selection bias because one of us (B.C.S.) preferentially performs minimally invasive techniques for parathyroidectomy and selects patients with nonlocalizing sestamibi imaging and US results for BNE. The time also reflects waiting for results of intraoperative measurement of PTH levels (25-30 minutes.) We therefore used operative time data for BNE reported in the literature in a meta-analysis by Denham and Norman.7 They found an average operative time of 109 minutes.

Average total costs per patient were computed for the evaluation and treatment of PHPT, as well as for all thyroid evaluation and treatment (Table 2). The surgeon professional fees listed reflect the Medicare reimbursement amount. Reimbursements were added as incurred for parathyroidectomy ($924), hemithyroidectomy ($697), total thyroidectomy ($1008), and completion thyroidectomy ($924). The anesthesiology costs reflect the base reimbursement plus the incremental additional cost based on operative time. The base reimbursement was $504 with $84 added for each 15-minute increment. The cost of sestamibi imaging on the day of surgery for the sole purpose of use of intraoperative gamma probe guidance does not include a second radiology professional fee because this service was previously obtained in the initial diagnostic imaging. A second radiology interpretation is not necessary on the day of surgery. The cost of performing sestamibi imaging at our institution is $707 per scan. The professional fee to interpret the initial study is reimbursed from Medicare at $218. The cost of performing US is $155. The professional fee to interpret the results of the US is $165. The cost of FNA was based on the cost of a US-guided FNA on all patients undergoing this procedure. The total cost of this procedure at our institution is $1078. We used 3.4 frozen sections per patient as the average number for standard

BNE based on review of the literature by Denham and Norman.7 The cost of frozen section preparation at our institution is $93. The professional fees are $238 for the first frozen section and $74 for each of the subsequent specimens. Rapid testing of PTH levels costs $28 per test at our institution. Two tests were added to the cost of a UNE. Three tests were applied to a BNE and represent the first at the onset of the procedure, the second after the first exploration is completed, and the third after the second neck exploration. We assumed that successful excision of the parathyroid adenoma was completed each time without the need for further rapid testing of PTH levels, which we recognize is not always achievable. Recovery room charges for patients at our institution were similar for all surgical techniques at an average of $218. Hospital admission costs were evaluated for all patients undergoing parathyroidectomy. Radio-guided parathyroidectomy cost $296 on average, whereas UNE cost $406 on average; both were outpatient procedures. Patients undergoing BNE required an overnight stay and incurred a cost of $826 on average.

The incremental cost of adding a hemithyroidectomy or a total thyroidectomy to a neck exploration was not available in the literature. To make this determination, an additional operative time of 15 minutes was estimated to add a hemithyroidectomy to a neck exploration. Thirty minutes was estimated to add a total thyroidectomy to a BNE. To our knowledge, operative time data for conversion of a radio-guided parathyroidectomy to a UNE and of a UNE to a BNE are not available in the literature. Estimates for additional operative time were calculated in the cost data as 35 minutes for conversion of a radio-guided parathyroidectomy to a UNE and 45 minutes for conversion of a UNE to a BNE. Also included in the cost of the conversion was the increased hospital admission costs, the surgeon’s professional fee, the cost of performing rapid testing of PTH levels, the cost of additional frozen sections for the BNE, and the increase in anesthesia costs. The total cost of conversion from a radio-guided parathyroidectomy to a UNE is calculated at $859 and for conversion from a UNE to a BNE is $1776. The cost to perform a completion thyroidectomy as a second procedure when diagnostic hemithyroidectomy returned with a finding of malignant thyroid cancer on permanent sections was added at an average of $3779 at our institution.

Total costs per patient were based on each of the strategies of the decision tree to include all costs incurred and averaged per patient. We then compared the expected costs among the 3 treatment strategies.

SENSITIVITY ANALYSIS

To study the robustness of our results, we performed several 1-way sensitivity analyses. We changed 1 variable at a time to determine whether the results were sensitive to our estimated values for the probability of single-gland disease and the cost of UNE, MIP, BNE, US-guided FNA, sestamibi imaging, and US.

BASELINE COST ANALYSIS

With baseline model variables, MIP without an active search for thyroid abnormalities was determined to have the lowest cost at $5275 per patient. Patients with thyroid abnormalities on US in whom sestamibi imaging failed to identify parathyroid abnormalities underwent evaluation and treatment for thyroid lesions identified in the decision tree model (Figure 3). Parathyroid surgery with routine preoperative thyroid US and further treatment as indicated
was found to have a cost of $5910 per patient. Bilateral neck exploration for parathyroidectomy with intraoperative thyroid evaluation and treatment of the thyroid gland as indicated was found to have a cost per patient of $5916 (Figure 1). These estimates include all costs incurred following the algorithms described and nontypical costs such as conversion to more invasive surgical techniques when more conservative regimens fail.

SENSITIVITY ANALYSIS

The MIP strategy was associated with lower costs compared with the US and BNE strategies if the prevalence of single-gland disease in patients with PHPT remains greater than 50% (Figure 5). Furthermore, the MIP strategy was associated with lower costs compared with the US and BNE strategies at any cost of unilateral neck exploration (UNE) (Figure 6). However, if the cost of BNE was less than $4900 or the cost of MIP exceeded $4800, the MIP strategy was no longer dominant. Finally, as seen in Figure 7, the MIP strategy was associated with lower costs for all reasonably expected costs of the US-guided FNA and US. However, if the cost of sestamibi imaging exceeded $1600, the MIP strategy was no longer dominant.

COMMENT

Because the surgical management of PHPT has moved to a more minimally invasive approach, the evaluation and treatment of coexisting thyroid carcinoma has become more limited, with potentially undiagnosed thyroid cancer being left until the disease process manifests itself separately. Primary hyperparathyroidism and
thyroid carcinoma have an established relationship; therefore, arguments against MIP owing to the lack of thyroid diagnoses have surfaced.

From a cost perspective, each parathyroid surgery method has supporting arguments. Data vary widely in the literature, with operative time being the largest point of contention. There are limited reports from surgeons who maintain that a BNE is less time consuming than a minimally invasive approach, and most of the published operative times are consistent with the time values used in our cost analysis.

Expected costs from our decision analysis suggest that, even with thyroid US studies (which are being used more frequently in the ambulatory setting) and further treatment when appropriate, MIP offers an essentially equal cost alternative to conventional bilateral parathyroid exploration with a $6 difference. These results tend to support the treatment of PHPT by focused means with evaluation and treatment of coexisting thyroid disease as an equal cost alternative to conventional BNE.

We also recognize the limitations of this study. The primary limitation is that it is only a cost analysis and therefore should not provide the sole basis for clinical decision making. Expected costs can be used as part of a more comprehensive set of information that can inform decision making. Furthermore, a formal cost-effectiveness analysis would estimate how much additional cost must be incurred to have 1 additional unit of benefit for each clinical strategy.

The incremental cost to evaluate and treat the thyroid gland in patients with PHPT was found to be $635 less for an MIP approach relative to the US strategy. Further study assessing quality-adjusted life-years and the incremental cost-effectiveness ratio may be addressed in the future to more fully determine whether the additional expense of $635 per patient is worthwhile in the evaluation and treatment of the 3.0% of patients with PHPT and synchronous thyroid carcinoma.

The MIP strategy does not appear to be contraindicated on the basis of cost by an inability to screen for synchronous thyroid disease. Moreover, US screening of the thyroid glands of patients undergoing the MIP approach is not cost prohibitive; in fact, it is less costly than BNE.

Submitted for Publication: December 7, 2006; final revision received May 22, 2007; accepted May 25, 2007.

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Author Contributions: Drs Hollenbeak, Beus, Ruda, and Stack 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: Hollenbeak, Beus, and Stack. Acquisition of data: Beus and Ruda. Analysis and interpretation of data: Hollenbeak, Lendel, and Beus. Drafting of the manuscript: Hollenbeak, Beus, and Ruda. Critical revision of the manuscript for important intellectual content: Hollenbeak, Lendel, and Stack.

Statistical analysis: Hollenbeak and Lendel. Administrative, technical, and material support: Ruda and Stack.

Study supervision: Stack.

Financial Disclosure: None reported.

Funding/Support: This study was supported by salaries from the respective institutions.

REFERENCES
