Predictors of Single-Gland vs Multigland Parathyroid Disease in Primary Hyperparathyroidism

A Simple and Accurate Scoring Model

Electron Kebebew, MD; Jimmy Hwang, PhD; Emily Reiff, BS; Quan-Yang Duh, MD; Orlo H. Clark, MD

Hypothesis: Preoperative clinical, biochemical, and imaging studies could be used to reliably select patients with single-gland primary hyperparathyroidism who could undergo minimally invasive parathyroidectomy and to determine whether additional perioperative testing is necessary.

Design: Retrospective analysis.

Setting: Tertiary referral center.


Main Outcome Measures: Demographic, clinical, biochemical, and imaging factors that predict single-gland vs multigland parathyroid disease, and biochemical cure.

Results: Of the 238 patients, 75.2% had a single adenoma, 21.4% had asymmetric 4-gland hyperplasia, and 3.4% had double adenomas. A biochemical cure was achieved in 99.2% of the patients. Preoperative calcium and intact parathyroid hormone levels were significantly higher (P = .03 and .04, respectively) and ultrasound and sestamibi scan results were more likely to be positive (both P < .001) in single-gland primary hyperparathyroidism. A dichotomous scoring model based on preoperative total calcium level (≥ 3 mmol/L [≥ 12 mg/dL]), intact parathyroid hormone level (≥ 2 times the upper limit of normal levels), positive ultrasound and sestamibi scan results for 1 enlarged gland, and concordant ultrasound and sestamibi scan findings reliably distinguished single-gland vs multigland cases (P < .001). The positive predictive value of this scoring model to correctly predict single-gland disease was 100% for a total score of 3 or higher.

Conclusions: Preoperative biochemical and imaging study results reliably distinguished single-gland vs multigland parathyroid disease in primary hyperparathyroidism. Our findings suggest that patients with a score of 3 or higher can undergo a minimally invasive parathyroidectomy without the routine use of intraoperative parathyroid hormone or additional imaging studies, and those with a score of less than 3 should have additional testing to ensure that multigland disease is not overlooked.

Arch Surg. 2006;141:777-782
have PHPT due to single-gland disease. The percentage of patients who undergo limited neck surgical exploration for parathyroidectomy ranges from 39% to 70% of all patients with PHPT. Because appropriate patient selection determines which patients can undergo limited neck surgical exploration for parathyroidectomy, we sought to determine what preoperative localizing studies and demographic, clinical, and biochemical factors distinguish between single-gland and multigland (multiple parathyroid adenomas and asymmetric 4-gland hyperplasia) disease in patients with PHPT.

METHODS

STUDY DESIGN AND SUBJECTS

We retrospectively analyzed the records of 238 consecutive patients with PHPT who underwent a neck surgical exploration and parathyroidectomy at the University of California, San Francisco, between January 7, 2002, and December 23, 2004. We reviewed demographic, clinical (presence of hereditary disease and history of head and neck radiation exposure), and biochemical (total serum calcium and intact PTH levels) data, results of preoperative localizing studies (technetium Tc 99m sestamibi scans [n=224] and neck ultrasounds [n=229]), pathology reports, operative notes, IOPTH measurements, postoperative total serum calcium and intact PTH values, and clinic follow-up notes 2 to 3 weeks postoperatively.

IOPTH MEASUREMENTS

The IOPTH measurements were recorded before resection of any enlarged glands: once before dissection and again just before excising the parathyroid gland. Postexcision IOPTH levels were measured 10 minutes or longer after resection of the enlarged parathyroid gland(s). A decrease of 50% or more in the IOPTH level was used to define successful parathyroidectomy.3

DETERMINING ACCURACY OF LOCALIZING STUDIES

The accuracy of preoperative localizing studies was determined by comparing the results of these studies with the operative and pathologic findings and with the normalizaton of the postoperative total calcium and intact PTH levels. A true-positive localizing result was defined as when all of the enlarged parathyroid glands were correctly identified and the patient had low or normal postoperative calcium and intact PTH levels. A false-negative localizing result was defined as when 1 or more enlarged parathyroid glands were not identified. A false-positive result was defined as when 1 or more nonenlarged parathyroid glands were identified. No true-negative results could occur because all of the patients had biochemical evidence of PHPT consisting of elevated or inappropriately high total serum calcium levels and elevated or inappropriately high intact PTH levels. Concordant localizing study findings were defined as showing 1 enlarged parathyroid gland on the same side of the neck.

STATISTICAL ANALYSIS AND CONSTRUCTION OF A DICHOTOMOUS MODEL

Nonparametric data were compared by the Wilcoxon rank sum test, and categorical data were compared by the χ² or Fisher exact test. A difference was defined as being statistically significant where P<.05. Data are presented as mean±1 SD or as number (percentage) unless specified otherwise. For variables found to be significantly different between single-gland and multigland parathyroid disease, dichotomous scoring was used, with 1 indicating single-gland parathyroid disease and 0 indicating multigland parathyroid disease. The first significant interval was determined for continuous variables to define the cutoff level for the dichotomous score. Multigland disease refers to any PHPT due to double or triple adenomas or asymmetric 4-gland hyperplasia. The area under the receiver operating characteristic curve was calculated using SAS/STAT software (SAS Institute, Inc, Cary, NC) to measure the accuracy of the scoring model in distinguishing between single-gland and multigland PHPT. Different combinations of variables were compared to determine which combination resulted in the largest area under the receiver operating characteristic curve, indicating a more accurate test for distinguishing single-gland disease from multigland disease.

RESULTS

Two hundred thirty-eight patients with PHPT underwent parathyroidectomy at our institution, and their clinical, biochemical, and pathologic data are summarized in Table 1. Eighty-three patients (34.9%) had bilateral neck surgical exploration, 103 (43.3%) had unilateral neck surgical exploration, and 52 (21.8%) had focused neck surgical exploration for their parathyroidectomy. Of 238 patients, 179 (75.2%) had a single adenoma, 51 (21.4%) had asymmetric 4-gland hyperplasia, and 8 (3.4%) had double adenomas. Biochemical cure was achieved in 99.2% of the patients based on normal or low postoperative calcium and intact PTH levels.

There were no significant differences in age, race or ethnicity, history of head and neck radiation exposure, presence of hereditary PHPT, and sex between single-gland and multigland PHPT cases. In single-gland PHPT cases as compared with multigland PHPT, preoperative calcium levels (2.8 mmol/L [11.2 mg/dL] vs 2.6 mmol/L [10.4 mg/dL], respectively; P=.03) and intact PTH levels (22 pmol/L [211 pg/mL] vs 13 pmol/L [121 pg/mL], respectively; P=.04) were significantly higher and neck ultrasound and sestamibi scan results were more likely to be positive (both P<.001).

Single-gland PHPT cases were reliably distinguished from multigland cases when we used a dichotomous scoring model (CaPTHUS) consisting of 5 variables: (1) preoperative total serum calcium level (≥3 mol/L [≥12 mg/dL]); (2) intact PTH level (≥2 times the upper limit of normal PTH levels); (3) sestamibi scan results positive for 1 enlarged parathyroid gland; (4) neck ultrasound results positive for 1 enlarged parathyroid gland; and (5) concordant sestamibi and neck ultrasound study results (identifying 1 enlarged gland on the same side of the neck) (Table 2). A total score of 3 or greater had a sensitivity of 43.9% and specificity of 100% for correctly predicting single-gland PHPT (Table 3). The positive predictive value of this scoring model to correctly predict single-gland disease was 100% for a total score of 3 or higher. Thirty-five percent of our study cohort had a total score of 3 or higher. The positive predictive value for a total score of 3 or higher was still 100% when cases with hereditary PHPT, history of head and neck irradiation, or persistent and recurrent disease were excluded.
The area under the receiver operating characteristic curve was 0.857 for the 5-variable CaPTHUS model, indicating that it would be useful preoperatively for distinguishing single-gland disease from multigland disease in patients with PHPT (Figure 1). Different combinations of the 5 variables were compared to determine which combination results in the largest area under the receiver operating characteristic curve, indicating a more accurate test to distinguish single-gland disease from multigland disease. The area under the receiver operating characteristic curve was 0.774 for the total serum calcium level, intact PTH level, and sestamibi scan results, 0.751 for the total serum calcium level, intact PTH level, and neck ultrasound results, and 0.840 for the total serum calcium level, intact PTH level, sestamibi scan results, and neck ultrasound results.

When we compared the results of the scoring model with the results of the IOPTH level in 138 patients who had IOPTH measurement (Figure 2), we found that the scoring model was as accurate as the IOPTH measurement for predicting single-gland disease when the total score was 3 or higher. Furthermore, the scoring model would have been reassuring in 5 patients who had false-negative IOPTH measurement results because the PTH level did not decrease by 50% or more. These 5 patients underwent a repeat IOPTH measurement and surgical exploration of the contralateral neck. For 93 patients with a total score of less than 3, the results of the IOPTH measurements were helpful in predicting biochemical cure in 89.6% of cases with 8 false negatives and 2 false positives.

In this study, we determined that preoperative biochemical and imaging studies could be used to reliably select patients with single-gland PHPT to perform a minimally invasive parathyroidectomy and could be used to determine whether additional perioperative testing is necessary. We found that total serum calcium level (≥3 mmol/L, ≥12 mg/dL), intact PTH level (≥2 times the upper limit of normal PTH levels), positive sestamibi scan and neck ultrasound results for 1 enlarged parathyroid gland, and concordant sestamibi and neck ultrasound results (identifying 1 enlarged parathyroid gland on the same side of the neck) were associated with single-gland PHPT. The dichotomous scoring model (CaPTHUS) with these

### Table 1. Clinical, Biochemical, and Pathologic Characteristics of Patients With Primary Hyperparathyroidism

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, female/male, No.</td>
<td>181/57</td>
</tr>
<tr>
<td>Race or ethnicity, No. (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>181 (76.0)</td>
</tr>
<tr>
<td>Asian or Pacific Islander</td>
<td>13 (5.5)</td>
</tr>
<tr>
<td>Latino</td>
<td>19 (8.0)</td>
</tr>
<tr>
<td>African American</td>
<td>14 (5.9)</td>
</tr>
<tr>
<td>Not specified</td>
<td>11 (4.6)</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>58.0 ± 12.4</td>
</tr>
<tr>
<td>Median (range)</td>
<td>58.0 (18-88)</td>
</tr>
<tr>
<td>Calcium, mg/dL</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>10.8 ± 0.9</td>
</tr>
<tr>
<td>Median (range)</td>
<td>11.2 (9.6-14.0)</td>
</tr>
<tr>
<td>Intact PTH level, pg/mL</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>190.8 ± 284.8</td>
</tr>
<tr>
<td>Median (range)</td>
<td>129 (57-2464)</td>
</tr>
<tr>
<td>No. of times that of upper limit of normal intact PTH levels, mean ± SD</td>
<td>2.8 ± 4.3</td>
</tr>
<tr>
<td>History of head and neck irradiation, No. (%)</td>
<td>5 (2.1)</td>
</tr>
<tr>
<td>Family history of PHPT, No. (%)</td>
<td>14 (5.9)</td>
</tr>
<tr>
<td>Familial PHPT, No.</td>
<td>5</td>
</tr>
<tr>
<td>MEN type 1, No.</td>
<td>8</td>
</tr>
<tr>
<td>MEN type 2A, No.</td>
<td>1</td>
</tr>
<tr>
<td>PHPT, No. (%)</td>
<td></td>
</tr>
<tr>
<td>At initial presentation</td>
<td>194 (81.5)</td>
</tr>
<tr>
<td>Persistent disease</td>
<td>28 (11.8)</td>
</tr>
<tr>
<td>Recurrent disease</td>
<td>16 (6.7)</td>
</tr>
<tr>
<td>Histopathologic finding, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Single adenoma</td>
<td>179 (75.2)</td>
</tr>
<tr>
<td>Asymmetric 4-gland hyperplasia</td>
<td>51 (21.4)</td>
</tr>
<tr>
<td>Double adenoma</td>
<td>8 (3.4)</td>
</tr>
<tr>
<td>Sensitivity of localizing studies, %</td>
<td></td>
</tr>
<tr>
<td>Ultrasound (n = 224)</td>
<td>53.0</td>
</tr>
<tr>
<td>Sestamibi scan (n = 229)</td>
<td>75.1</td>
</tr>
<tr>
<td>Surgical approach, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Focused</td>
<td>52 (21.8)</td>
</tr>
<tr>
<td>Unilateral neck surgical exploration</td>
<td>103 (43.3)</td>
</tr>
<tr>
<td>Bilateral neck surgical exploration</td>
<td>83 (34.9)</td>
</tr>
</tbody>
</table>

Abbreviations: MEN, multiple endocrine neoplasia; PHPT, primary hyperparathyroidism; PTH, parathyroid hormone.

SI conversion factors: To convert calcium from the conventional units of milligrams per deciliter to the SI units of millimoles per liter, multiply by 0.25. To convert PTH from the conventional units of picograms per milliliter to the SI units of picomoles per liter, multiply by 0.1053.

### Table 2. Comparison of Predictive Factors Between Single-Gland and Multigland Primary Hyperparathyroidism

<table>
<thead>
<tr>
<th>Predictive Factor</th>
<th>Patients With Single-Gland Disease, %</th>
<th>Patients With Multigland Disease, %</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total serum calcium level ≥3 mmol/L [≥12 mg/dL]</td>
<td>20.9</td>
<td>4.3</td>
<td>.008</td>
</tr>
<tr>
<td>Intact PTH level ≥2 times the upper limit of normal intact PTH levels</td>
<td>45.1</td>
<td>26.1</td>
<td>.02</td>
</tr>
<tr>
<td>Neck ultrasound results positive for 1 enlarged parathyroid gland</td>
<td>62.1</td>
<td>0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sestamibi scan results positive for 1 enlarged parathyroid gland</td>
<td>69.9</td>
<td>0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Concordant sestamibi scan and neck ultrasound results for 1 enlarged gland on the same side of the neck</td>
<td>44.9</td>
<td>0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Family history of PHPT</td>
<td>10.2</td>
<td>4.5</td>
<td>.11</td>
</tr>
<tr>
<td>Persistent PHPT</td>
<td>14.0</td>
<td>5.1</td>
<td>.07</td>
</tr>
<tr>
<td>Recurrent PHPT</td>
<td>1.7</td>
<td>5.1</td>
<td>.15</td>
</tr>
</tbody>
</table>

Abbreviations: PHPT, primary hyperparathyroidism; PTH, parathyroid hormone.
Table 3. Sensitivity, Specificity, and Positive and Negative Predictive Values of the Scoring Model for Predicting Single-Gland Disease in 238 Patients With Primary Hyperparathyroidism

<table>
<thead>
<tr>
<th>Total Score*</th>
<th>Patients in Total Study Cohort, %</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1</td>
<td>80</td>
<td>89</td>
<td>59</td>
<td>90</td>
<td>57</td>
</tr>
<tr>
<td>≥2</td>
<td>50</td>
<td>60</td>
<td>89</td>
<td>96</td>
<td>35</td>
</tr>
<tr>
<td>≥3</td>
<td>35</td>
<td>44</td>
<td>100</td>
<td>100</td>
<td>30</td>
</tr>
<tr>
<td>≥4</td>
<td>18</td>
<td>23</td>
<td>100</td>
<td>100</td>
<td>26</td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>6</td>
<td>100</td>
<td>100</td>
<td>22</td>
</tr>
</tbody>
</table>

Abbreviations: NPV, negative predictive value; PPV, positive predictive value.

*Total score for the 5 variables in the CaPTHUS model was determined by the following: (1) 1 point for a total serum calcium level of 3 mmol/L or greater (≥12 mg/dL); (2) 1 point for an intact parathyroid hormone level 2 or more times the upper limit of normal intact parathyroid hormone levels; (3) 1 point for positive sestamibi scan results showing 1 enlarged gland; (4) 1 point for positive neck ultrasound results showing 1 enlarged parathyroid gland; and (5) 1 point for concordant sestamibi and neck ultrasound results (identifying 1 enlarged gland on the same side of the neck).

5 preoperative variables had a low sensitivity (44%) but a 100% positive predictive value for identifying patients with PHPT due to single-gland disease when the total score was 3 or higher.

Both total serum calcium and intact PTH levels have been previously found to correlate with parathyroid gland size, volume, or weight in patients with PHPT. Therefore, our finding that total serum calcium and intact PTH levels were higher in patients who have single-gland disease is not surprising, especially when considering that parathyroid adenomas tend to be larger than parathyroid glands in cases of asymmetric 4-gland hyperplasia.

The most commonly used preoperative localization studies in patients with PHPT are sestamibi scan and neck ultrasound because they are noninvasive and accurate for localizing enlarged parathyroid glands. Like other investigators, we had previously found that sestamibi scanning was more accurate than neck ultrasound and that both approaches were more accurate in patients who had PHPT due to single-gland disease. When the neck ultrasound and sestamibi scan results were concordant (positive for 1 enlarged parathyroid gland on the same side of the neck) in patients with PHPT, there was a high likelihood that the PHPT was due to single-gland disease. Our current study not only confirms these previous observations by our group and others but also shows that concordant neck ultrasound and sestamibi scan results can be used to reliably select patients who would be ideal candidates for a focused neck surgical exploration.

The need and cost of using routine IOPTH measurement and, less commonly, the gamma probe, to predict biochemical cure at the time of parathyroidectomy is unclear. Because IOPTH measurement is highly accurate for predicting biochemical cure in most patients, it has been widely used by most surgeons whereas the intraoperative gamma probe has not. However, IOPTH measurement is less accurate in cases of multigland disease, which...
is precisely the clinical situation in which it would be the most useful, because most patients who undergo a focused parathyroidectomy have positive localizing study results commonly showing 1 enlarged parathyroid gland.  

In this context, our finding that a CaPTHUS total score of 3 or higher has a 100% positive predictive value for identifying patients with PHPT due to single-gland disease may obviate the need for routine use of IOPTH measurement for all of the focused parathyroidectomy approaches. Instead, IOPTH measurement could be used selectively in patients who are less likely to have single-gland disease. The fact that 35.0% of our cohort had a total score of 3 or higher suggests that the time and cost associated with the use of IOPTH measurement might not be necessary for a significant proportion of patients with PHPT. Moreover, the results of the preoperative scoring model could be reassuring in cases in which the IOPTH level does not decrease by 50% or more owing to false-negative results. In such cases, another IOPTH measurement would not be needed just so that the threshold of a decrease of 50% or more is met before commencing the operation. The CaPTHUS scoring model would also reduce the need for further neck surgical exploration or conversion to a bilateral neck surgical exploration when the IOPTH level does not decrease by more than 50%, which occurs in 6% to 17% of focused parathyroidectomies.19-22

Although our study findings suggest that the CaPTHUS scoring model offers a good estimate of those patients likely to have PHPT due to single-gland disease, its usefulness needs to be confirmed by other investigators. We have begun a prospective trial to validate the CaPTHUS scoring model in patients with PHPT. The accuracy of preoperative localizing studies reported in the literature is obviously variable and may affect the number of patients who can undergo such an evaluation to determine whether a focused parathyroidectomy approach is appropriate. Our preoperative scoring model may also overestimate the number of patients for whom the focused parathyroidectomy approach is appropriate, and it is dependent on the biochemical profile of the patients with PHPT who are seen at our institution. Another limitation of our study is the relatively short follow-up, which may affect the long-term biochemical cure rate in these patients and thus overestimate the accuracy of the proposed scoring model. However, we do not believe that the accuracy of the scoring model would decrease by more than 5%, even after long-term follow-up, because recurrent PHPT is uncommon and occurs in only 1% to 5% of cases in which normal postoperative calcium and PTH levels are observed.23 Furthermore, recurrent PHPT most commonly occurs in patients with hereditary PHPT and/or a history of head and neck irradiation.1,2,3 Only 8.0% of our cohort had hereditary PHPT or a history of head and neck irradiation, and the accuracy of the scoring model was not affected when we excluded these cases.

In summary, preoperative biochemical and imaging study results can be used to reliably distinguish single-gland vs multigland parathyroid disease in PHPT. Our findings suggest that a patient with a CaPTHUS score of 3 or higher can undergo a focused parathyroidectomy without the routine use of IOPTH measurement or additional imaging studies, and those with a score of less than 3 should have additional testing to ensure that multigland disease is not missed.

Accepted for Publication: April 13, 2006.

Correspondence: Electron Kebebew, MD, Department of Surgery, Box 1674, University of California, San Francisco/Mt Zion Medical Center, San Francisco, CA 94143-1674 (kebebewe@surgery.ucsf.edu).

Funding/Support: This work was supported in part by the Harold Amos Medical Faculty Development Program of the Robert Wood Johnson Foundation, American Cancer Society, University of California Cancer Research Coordinating Committee, and a Hellman Family Grant.

Previous Presentation: This paper was presented at the 77th Annual Meeting of the Pacific Coast Surgical Association; February 17, 2006; San Francisco, Calif; and is published after peer review and revision. The discussions that follow this article are based on the originally submitted manuscript and not the revised manuscript.

REFERENCES


©2006 American Medical Association. All rights reserved.

Downloaded From: by a Non-Human Traffic (NHT) User on 10/25/2018
are weighted equally, with 1 point for each. At our institution, ul-
in single-gland disease. What might the pathophysiologic ex-
tigland disease, the levels of calcium and PTH are lower than

**DISCUSSION**

Philip D. Schneider, MD, Sacramento, Calif: Dr Kebebew and his colleagues have presented an important paper that has the laud-
able goal of attempting to simplify the decision making and treat-
ment of primary hyperparathyroidism at a time when the field is,
as Dr Kebebew pointed out, undergoing a sea change in man-
agement philosophy. Two hundred thirty-eight consecutive pa-
tients undergoing parathyroid neck exploration were assessed for
features of their presentation and diagnostic workup that pre-
dicted single- vs multi-gland parathyroid disease. Statistically
significant single variables were then subjected to multivariate
analysis in the form of seeking combinations or variables that maxi-
mized receiver operating characteristic curves. The 5 variables
(CaPTHUS) were preoperative serum calcium and parathyroid
hormone levels and localizing parathyroid scan and ultrasound,
particularly when the imaging studies were concordant. The pre-
diction of single-gland disease improves operative logistics and
confidence that multigland disease is not being overlooked.

There are several interesting facets of this study. Three, in par-
icular, summarize the changing nature of parathyroid surgery
in the US [United States]. First, preoperative imaging is now an
important aspect of the evaluation of candidates for initial neck
exploration. Second, imaging is now a part of first-time explo-
ration because a majority of endocrine surgeons in the US now
consider minimally invasive approaches to initial parathyroid neck
exploration to be entirely reasonable. Third and finally, the suc-
cess of the operation is defined as biochemical cure and not by
identification and size estimates of the parathyroid glands. This
latter point is emphasized by the 3.4% incidence of double ad-
enomas, when series based on surgical evaluation of glands at
surgery yield an incidence of nearly double that percentage. The
authors therefore are very careful to caution that more time and
additional experience may be required to validate their scoring
system, yet the known pathophysiology of parathyroid disease
only strengthens their conclusions.

I wish to pose these questions to Dr Kebebew and his col-
leagues. For the generation of this model, 22% of patients un-
derwent focused exploration, 43% underwent a unilateral explo-
ration, and 33% underwent bilateral exploration. With this model,
what percentage of the 238 patients would actually have been able
to undergo focused exploration? When the CaPTHUS score is less
than 3, what is your group’s preferred operative strategy? What
is the postresection time point at which the parathyroid hor-
monal level should be determined? Since biochemical cure is the
endpoint and 6% to 17% of explored patients may experience a
false-negative, persistently elevated parathyroid hormone level,
timing appears critical for documenting cure.

This lucid presentation offers a greatly simplified, modern
approach to primary hyperparathyroidism with widespread ap-
pliability and great practicability.

John A. Ryan, MD, Seattle, Wash: It appears that in mul-
tigland disease, the levels of calcium and PTH are lower than
in single-gland disease. What might the pathophysiologic ex-
planation for this be?

Philip I. Haigh, MD, Los Angeles, Calif: All of the parameters
are weighted equally, with 1 point for each. At our institution, ul-
trasound is not a great test when compared to the sestamibi scan.
I am wondering if there is perhaps any weighting that could be
done for each test. An ultrasound that was negative, at least in our
hands, wouldn’t really bother me too much in the setting of a posi-
tive sestamibi scan. So, at least at our institution, an ultrasound
result would be weighted less than a sestamibi scan.

Ronald G. Latimer, MD, Santa Barbara, Calif: Just a ques-
tion about ionized calcium vs total calcium: would that have
made any difference in your results?

Unknown Discussant: We all continue to learn from Pro-
fessor Clark and his group, and I have several questions for Dr
Clark. First, can you predict your failures? You have a very low
failure rate, and at our institution, it’s in the order of 1% as well.
Why do we have failure rates now? With IOPTH, with this in-
credible improvement in preoperative localization, can you pre-
dict which patients from your model are more likely to fail?
How do you define a biochemical cure? Are you looking at post-
operative total calcium, ionized calcium, or postoperative PTH
level, or hopefully all 3?

How do you account for the false-negative or false-positive
IOPTH levels? We are seeing those as well, and I am at a loss to
explain them. Sometimes, it makes the intraoperative manage-
ment very difficult.

Finally, how would you have us use this information next
week when we return to the operating room?

Theodore X. O’Connell, MD, Los Angeles: Why would you
ev even use IOPTH? Certainly from your data, you are so good at
predicting disease, either adenoma or hyperplasia, and using a
localized approach finding the disease, it does not seem that
IOPTH is necessary. The false-positive IOPTH, although a small
number, leads to unnecessary exploration. It seems like IOPTH
produces more of a negative effect rather than a positive effect
in dealing with your patients.

Dr Kebebew: I will start with Dr Schneider. The first ques-
tion is, how many of the patients could have had an initial fo-
cused approach? Because sestamibi scanning was most accu-
rate and positive in 75% of patients, 75% of the study cohort
could have had an initial focused approach with the use of
IOPTH to confirm biochemical cure. Forty-one percent of the
study cohort had a score of 3 or more and would not have needed
IOPTH. We measure the PTH 10 minutes post resection.

Dr Ryan asked what could account for the difference in the
calcium and PTH levels between patients with single-gland and
multigland disease. There have been several studies that sug-
gest a correlation between parathyroid gland size or weight to
the serum calcium levels and PTH. Because parathyroid ad-
enomas tend to be much larger than hyperplastic parathyroid
glands, this may explain our finding.

I am not sure if ionized calcium levels would be valid in the
model since it was not studied.

There was also a question regarding how failure was de-
\led. Biochemical cure was defined as both total serum cal-
cium and PTH levels that were either low or normal at least 2
weeks at follow-up. Also, there was a question about why
IOPTH results in a false-positive or false-negative result. This
is certainly something that creates a lot of anxiety in the oper-
ating room for us where it appears that a patient has just 1
enlarged gland and we have waited 10 minutes and the PTH has
not dropped. Although the half-life of intact PTH is anywhere
from 3 to 5 minutes, the kinetics might be different for each
individual patient and/or parathyroid gland. In addition, I think
it depends at what time the postexcision PTH is measured and
what percent decrease in the PTH is used.

Lastly, Dr O’Connell had asked, why use IOPTH? I think, yes,
we don’t need to use it all of the time. It is really in those cases
where we are not absolutely sure or as sure as we can be that the
patient doesn’t have single-gland disease that it would be useful.

19. Lorenz K, Miccoli P, Monchik JM, Duren M, Dralle H. Minimally invasive video-assisted
20. Lo CY, Chan WF, Luk JM. Minimally invasive endoscopic-assisted parathyroid-
21. Burkey SH, Snyder WH III, Nwariaku F, Watumull L, Mathews D. Directed para-
thyroidectomy: feasibility and performance in 100 consecutive patients with pri-
23. Cameiro OM, Solorzano CC, Irvin GL III. Recurrent disease after limited para-
199:849-855.


©2006 American Medical Association. All rights reserved.

Downloaded From:  by a Non-Human Traffic (NHT) User  on 10/25/2018