PAPER

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

A Simple and Accurate Scoring Model

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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.

Patients: A total of 238 patients who underwent neck surgical exploration and parathyroidectomy for primary hyperparathyroidism from January 7, 2002, to December 23, 2004.

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.

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PRIMARY HYPERPARATHYROIDism (PHPT) is a common endocrine disorder, with approximately 100 000 new cases diagnosed each year in the United States.[1] Patients with PHPT have a single parathyroid adenoma (80%-87% of patients), multiple adenomas (2%-5% of patients), asymmetric 4-gland hyperplasia (10%-15% of patients), or carcinoma (<1% of patients) that secretes an inappropriately high parathyroid hormone (PTH) level relative to the serum calcium level.[1] Parathyroidectomy is the only curative treatment for PHPT that resolves metabolic complications and improves symptoms and quality of life.[2]

Many surgeons now use focused, limited, or minimally invasive parathyroidectomy approaches instead of traditional bilateral neck surgical exploration to identify all of the 4 parathyroid glands and remove the enlarged, hyperfunctioning parathyroid gland(s).[3] Limited neck surgical exploration approaches for parathyroidectomy have been successfully used, mainly because of better preoperative localizing studies (commonly, technetium Tc 99m sestamibi and neck ultrasound scanning) that allow for accurate identification of the enlarged parathyroid gland(s). Furthermore, measurement of intraoperative PTH (IOPTH) levels to detect a decrease greater than 50% in the PTH level can be used to predict biochemical cure in most patients.[4,5] The short-term results of limited surgical exploration for parathyroidectomy suggest that the biochemical cure and complication rates are similar to those for traditional bilateral neck surgical exploration.[3,6,7]

The use of limited surgical exploration for parathyroidectomy depends on the ability to reliably select those patients who

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.[6-9] 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.[5]

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 normalization 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 χ^2 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 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 mmol/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.

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

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

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.

*Focused approach refers to when the enlarged gland was excised without visualization of the other (upper or lower) gland. In the unilateral approach, the other lower or upper gland was visualized.

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 158 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.

COMMENT

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

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

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

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

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).

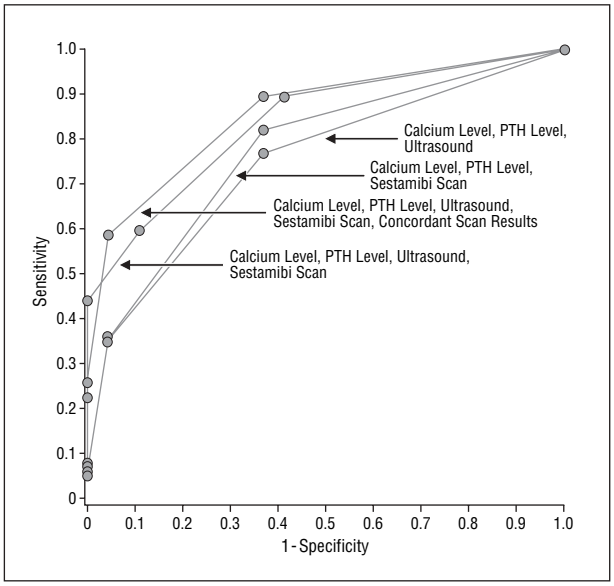

Figure 1. The receiver operating characteristic curve for the 5-variable CaPTHUS scoring model to distinguish between single-gland and multigland primary hyperparathyroidism compared with receiver operating characteristic curves for other combinations of variables (in addition to serum total calcium and intact parathyroid hormone [PTH] levels). The curve with the largest area under the curve indicates a more accurate test. A perfect test without any false-positive results or false-negative results would have an area under the curve equal to 1.

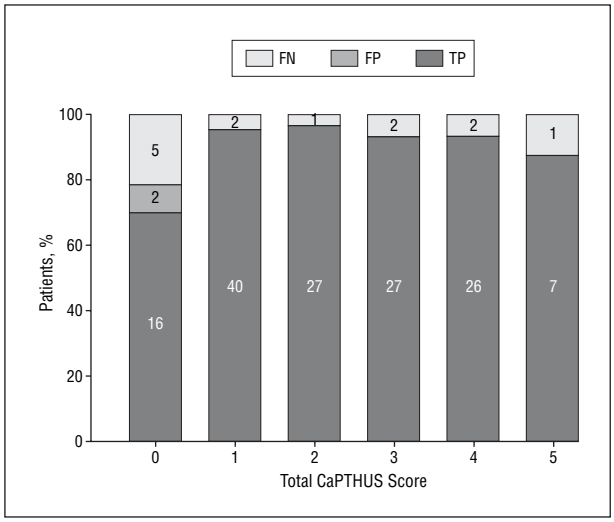

Figure 2. Intraoperative parathyroid hormone and CaPTHUS scoring model results. For cases with a total score of 3 or higher, the intraoperative parathyroid hormone measurement did not add additional information for confirming biochemical cure. Five patients had false-negative intraoperative parathyroid hormone measurement results and a total score of 3 or higher. For patients with a total score of less than 3, intraoperative parathyroid hormone measurement was useful for confirming biochemical cure in 89.6% of cases. FN indicates false negative; FP, false positive; and TP, true positive.

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.[10-15] 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 localizing studies in patients with PHPT are sestamibi scan and neck ultrasound because they are noninvasive and accurate for localizing enlarged parathyroid glands.[3] 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.[9,12,16,17] 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.[9,12,17] 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.[6,18] 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.[16] 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.[1,23] 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.

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DISCUSSION

Philip D. Schneider, MD, Sacramento, Calif: Dr Kebebew and his colleagues have presented an important paper that has the laudable goal of attempting to simplify the decision making and treatment of primary hyperparathyroidism at a time when the field is, as Dr Kebebew pointed out, undergoing a sea change in management philosophy. Two hundred thirty-eight consecutive patients undergoing parathyroid neck exploration were assessed for features of their presentation and diagnostic workup that predicted 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 maximized 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 prediction 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 particular, 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 exploration 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 success 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 adenomas, 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 colleagues. For the generation of this model, 22% of patients underwent focused exploration, 43% underwent a unilateral exploration, and 35% 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 hormone 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 applicability and great practicality.

John A. Ryan, MD, Seattle, Wash: It appears that in multigland disease, the levels of calcium and PTH are lower than in single-gland disease. What might the pathophysiologic explanation 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, ultrasound 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 positive 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 question about ionized calciums vs total calciums: would that have made any difference in your results?

Unknown Discussant: We all continue to learn from Professor 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 incredible improvement in preoperative localization, can you predict which patients from your model are more likely to fail? How do you define a biochemical cure? Are you looking at postoperative 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'm at a loss to explain them. Sometimes, it makes the intraoperative management 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 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 question is, how many of the patients could have had an initial focused approach? Because sestamibi scanning was most accurate 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 suggest a correlation between parathyroid gland size or weight to the serum calcium levels and PTH. Because parathyroid adenomas 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 defined. Biochemical cure was defined as both total serum calcium and PTH levels that were either low or normal at least 2 to 3 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 operating 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.