PAPER

Maximizing Outcomes While Minimizing Exploration in Hyperparathyroidism Using Localization Tests

John A. Ryan, Jr, MD; Faye T. Lee, RN

Hypothesis: Preoperative localization (ultrasonography and scintigraphy) can be used to limit operative exploration in primary hyperparathyroidism while providing a high rate of success.

Design: Prospective cohort analysis of 3 types of exploration (1-gland, unilateral, or 4-gland), as directed by localization.

Results: In 185 consecutive patients who underwent operations, the final diagnoses were solitary adenoma in 87% and multigland disease in 13%. Ultrasonography (75%) and scintigraphy (83%) demonstrated an enlarged parathyroid gland and, together with operative findings, resulted in 61 1-gland, 63 unilateral, and 61 4-gland explorations, with an initial success rate of 96% and an ultimate success rate of 99%. Limiting exploration resulted in a significant decrease in operative time and hospitalization.

Conclusion: Localization can limit exploration with success.

Arch Surg. 2004;139:838-843

THE EXTENT OF OPERATIVE EXploration in patients with primary hyperparathyroidism is controversial. The standard of bilateral, 4-gland exploration is being challenged by unilateral and 1-gland explorations. We report the outcomes of a cohort analysis of these 3 types of exploration. The type of operation was determined by demonstrating abnormally enlarged parathyroid glands with the use of preoperative ultrasonography and parathyroid scintigraphy.

Our operative strategy consisted of limiting exploration to 1 parathyroid gland when only 1 gland was localized preoperatively and that gland proved during operation to be abnormal. Our strategy, however, was flexible in that we explored all demonstrated glands, we always found and removed an abnormal gland, we explored bilaterally if 2 abnormal glands were found on 1 side, and we resected thyroid pathologic features as necessary.

METHODS

A total of 185 consecutive patients who underwent operations by 1 surgeon (J.A.R.) at Virginia Mason Medical Center for primary sporadic hyperparathyroidism between September 1999 and August 2003 were evaluated prospectively. Mean age was 62 years with a range from 17 to 88 years. Women comprised 67% of the patients. Patients with renal failure, familial hyperparathyroidism, multiple endocrine neoplasia, parathyroid cancer, persistent or recurrent hyperparathyroidism, or prior thyroidectomy were not included. All 185 patients had high-resolution real-time ultrasonography performed in both transverse and longitudinal images from the hyoid bone to the sternal notch with a variety of ultrasound probes.

The type of parathyroid scintigraphy was variable based on referral patterns. Thallium 201-Cl and technetium Tc 99m pertechnetate subtraction scans were available for 101 patients. Dual-phase Tc 99m sestamibi scans were available for 92 patients. Neck and chest survey images were obtained with parallel hole collimators, and magnified images of the neck were obtained with pinhole collimators. Seven patients did not have nuclear scintigraphy, and 15 patients had both thallium and sestamibi scans.

All patients were given a standardized informed-consent brochure explaining the rationale of the 3 types of operations. One-gland exploration was recommended to the patient when the ultrasonography and scintigraphy demonstrated only 1 enlarged parathyroid gland, particularly when both imaging tests showed the same finding. Unilateral exploration was performed when localization tests suggested enlarged upper and lower glands on the same side, were questionably positive on 1 side, suggested a huge upper gland that might require full mobilization of the thyroid to be safely resected, or when ipsilateral thyroid pathologic fea-

From the Department of Surgery, Virginia Mason Medical Center, Seattle, Wash.

©2004 American Medical Association. All rights reserved.
Downloaded From: http://archsurg.jamanetwork.com/ on 05/24/2015

Table 1. Results of 185 Initial Operations for Primary Hyperparathyroidism

Exploration Type	No. of Patients	Ultimate Diagnosis Adenoma	Ultimate Diagnosis Multigland Disease	Success	Failure*
1-gland	61	59	2	59	2
Unilateral	63	59	4	59	4
4-gland	61	43	18	59	2
Total	**185**	**161** (87%)	**24** (13%)	**177** (96%)	**8** (4%)

*Seven of the 8 failures had a second operation leading to eucalcemia.

Table 2. Operative Time and Length of Stay in 185 Patients With Primary Hyperparathyroidism

Exploration Type	No. of Patients	Mean Operative Time,* min (Range)	Length of Stay, Day†	Length of Stay, 23^{59}‡	Length of Stay, Admit§
1-gland	61	41 (13-89)	35	26	0
Unilateral	63	72 (47-135)	14	48	1
4-gland	61	124 (35-335)	1	53	7
Total	**185**	79 (13-335)	**50**	**127**	**8**

*Operative time, $P<.001$.
†The number of patients whose length of stay was less than 1 day, $P<.05$.
‡The number of patients whose stay included 1 night but was less than 24 hours.
§The number of patients whose stay was more than 24 hours.

tures existed. Four-gland exploration (bilateral) was performed if neither imaging test revealed an enlarged gland, if imaging tests revealed abnormal glands on both sides, if 2 abnormal glands were found on 1 side, for patients with thyroid cancer or dominant contralateral thyroid nodules, and for ill patients in whom leaving behind a potentially diseased gland would not be tolerated. If intraoperative findings did not confirm the correctness of positive localization images, then exploration was continued to identify all 4 glands. The operations were performed by 20 surgical residents under the direct supervision of the senior author. All operations were performed under general endotracheal anesthesia in the Joel W. Baker operating rooms at Virginia Mason Medical Center. Neither operative radioguided handheld nuclear mapping by γ probe[1] nor intraoperative parathyroid hormone (PTH) monitoring was used.[2]

A standard diagram describing the thyroid and the fate of each parathyroid gland was made at the completion of the operation. Operative time was defined as the period from incision to skin closure. Complications were recorded.

Patients' calcium levels were determined on the first postoperative day and 1 to 2 weeks later on their return visit to the office and then serially by their primary care providers during the follow-up period. Patients whose calcium levels had returned to normal on the first postoperative day were given calcium replacement to avoid symptomatic temporary hypocalcemia. At least 1 year of calcium follow-up was available for all patients operated on before September 2002, and patients operated on after September 2002 had calcium follow-up by September 2003. Patients with persistent hypercalcemia were reevaluated and reoperated, if appropriate.

The study was approved by the institutional review board of the Virginia Mason Research Center. Data was collected prospectively but was analyzed retrospectively. Statistical analysis by *t* tests was performed when appropriate, with a *P* value $<.05$ considered significant.

RESULTS

The ultimate diagnosis was parathyroid adenoma in 161 patients (87%). Multigland parathyroid disease was found in 24 patients (13%), including 13 cases of double adenoma, 3 cases of triple adenoma, 7 cases of 4-gland hyperplasia, and 1 case of 5-gland hyperplasia. **Table 1** notes the type of exploration, the ultimate diagnosis, and success or failure in achieving eucalcemia. **Table 2** reports operative time and length of stay. Eight patients for whom the intention was to limit exploration were converted to 4-gland exploration because we did not find the abnormal parathyroid gland as demonstrated (5 patients) or we found 2 abnormal parathyroid glands on 1 side (3 patients). During the initial operation, at least 1 abnormal parathyroid gland was removed from each patient, except for 1 patient in whom the abnormal parathyroid gland was later found to be in the chest.

The initial operation was successful in 96% of the patients. Eight patients (4%) had persistent hyperparathyroidism. The reasons for persistent hyperparathyroidism as confirmed by successful reoperation in 7 of the 8 patients are as follows. For initial 1-gland operation, 1 patient had a double adenoma, and 1 patient had a triple adenoma. For initial unilateral exploration, 3 patients had double adenomas, and 1 patient had 4-gland hyperplasia. For 4-gland exploration, 1 patient had biopsy performed on 3 normal parathyroid glands and a thyroid lobectomy. A postoperative sestamibi scan localized a solitary parathyroid adenoma in the left anterior mediastinum, which was successfully removed thorascopically. The final patient had all 4 glands identified; 3 underwent biopsy, and the largest (1.2 cm) was removed. Final histologic examination revealed the largest gland to be normal but with a microadenoma in 1 of the glands that underwent biopsy. The patient has declined further pursuit. This patient represents the only long-term failure to achieve eucalcemia in the entire series.

In patients with a single parathyroid adenoma, 159 (99%) of 161 were cured by the initial operation. In patients with multigland disease, 18 (75%) of 24 were cured

©2004 American Medical Association. All rights reserved.
Downloaded From: http://archsurg.jamanetwork.com/ on 05/24/2015

by the initial operation. Six patients (25%), all of whom had a single abnormal parathyroid gland removed during the initial operation, remained hypercalcemic, and all were cured with a second operation. In these 6 patients, the initial localizing test demonstrated only 1 abnormal gland, and it was confirmed to be abnormal when removed. With a second nuclear scan, 5 of the 6 patients demonstrated new abnormal glands. Further ultrasonography was not helpful.

In this series, 2 thyroid cancers required total thyroidectomy, and 3 thyroid cancers (<1 cm each) were found incidentally during thyroid lobectomies. Concomitant thyroid resections were performed, with 36 nodules excised, 6 thyroid lobectomies, and 4 total thyroidectomies. Thirty of these 46 thyroid excisions were performed for the purpose of looking for parathyroid glands. Three cases of intrathyroidal parathyroid adenomas were discovered, 1 of which was a fifth gland parathyroid adenoma. Thirty-seven thyroid resections were performed with 4-gland explorations, contributing to increased operative times.

No complications of recurrent laryngeal nerve damage, permanent hypoparathyroidism, bleeding, infection, or death occurred. A 79-year-old patient hospitalized with congestive heart failure and severe confusion underwent 3½ gland resections for hyperplasia. While still hospitalized, he suffered a cardiac arrest on the second postoperative day, and he was successfully resuscitated.

During the initial operations, 217 abnormal parathyroid glands were excised; 142 normal parathyroid glands underwent biopsy, including 20 excisional biopsies; 34 normal glands were identified; 40 glands were searched for but not found; and 309 glands were intentionally not surgically explored, for a total of 742 glands. Of note, 2 patients had 5 glands each. Of the 433 glands that were surgically explored, 40 (9%) were not found. All but 1 of the 40 glands that were not found turned out to be normal glands. The only exception was a parathyroid adenoma that was subsequently found thorascopically in the chest.

Thallium/technetium scans were used in 101 patients and correctly identified an abnormal parathyroid gland in 82 patients (81%). Sestamibi scans were used in 92 patients and correctly identified an abnormal parathyroid gland in 78 patients (85%). In 15 patients, both thallium/technetium and sestamibi scans were performed. Twelve of these patients each had a solitary adenoma. The sestamibi scans correctly identified the adenoma in 6 patients and were false negative in 6 patients. The thallium scans identified it correctly in 7 patients and were false negative in 5 patients. Results from the thallium scan were positive in 3 cases when the sestamibi scan results were negative, and the sestamibi scan results were positive in 2 cases when the thallium scan results were negative. In our analysis, there was no superiority of one of the nuclear medicine scintigraphy tests over the other, and consequently in this report outcomes from scintigraphy will be grouped.

Overall, scintigraphy was used in 178 patients, with an abnormal parathyroid gland identified in 83% of the scans. Ultrasonography was used as a preoperative localization in all 185 patients and correctly identified an abnormal parathyroid gland in 139 patients (75%). The combined use of ultrasonography and scintigraphy correctly demonstrated an abnormal parathyroid gland in 88% of the patients.

In 161 patients whose ultimate diagnosis was a single parathyroid adenoma, ultrasonography correctly identified the abnormal parathyroid gland in 109 patients (68%). Scintigraphy was used in 155 patients and correctly identified the abnormal parathyroid gland in 125 patients (81%). With the combined use of ultrasonography and scintigraphy, 140 (87%) of 161 single adenomas were correctly identified. However, ultrasonography did not identify abnormal solitary parathyroid adenomas in 52 cases (false negatives). In 18 of these 52 cases, not only did ultrasonography fail to identify the abnormal parathyroid gland, but it erroneously suggested that a normal parathyroid gland was the culprit (a false positive). In 15 cases in which ultrasonography correctly identified the abnormal solitary parathyroid adenoma, it also identified a normal gland as abnormal (false positive). Likewise, scintigraphy had 30 cases of false negative identification of the ultimate culprit, coexisting with 13 false positives and 17 cases of correct identification that also had a false positive. False positives were usually secondary to thyroid nodules and occasional lymph nodes.

In the 24 patients with ultimately confirmed multigland disease, 68 abnormal parathyroid glands were ultimately removed. Preoperatively, only 38 (56%) of these abnormal glands were identified with a combination of ultrasonography and scintigraphy. In 13 cases of confirmed double adenomas, ultrasonography demonstrated both enlarged parathyroid glands 4 times, 1 enlarged parathyroid gland 6 times, and no enlarged parathyroid glands 3 times.

Scintigraphy did not perform any better; it identified both enlarged parathyroid glands 4 times, 1 enlarged parathyroid gland 7 times, and no enlarged parathyroid glands 2 times. Used together, ultrasonography and scintigraphy identified both abnormal adenomas in 6 cases, only 1 in 5 cases, and none in 2 cases.

In 8 cases with confirmed parathyroid hyperplasia, the results of preoperative localization tests were not favorable. In none of the cases did either ultrasonography or scintigraphy identify 4 or 3 abnormal parathyroid glands. Ultrasonography did demonstrate 2 abnormal glands 3 times and 1 abnormal gland 5 times. Scintigraphy was able to identify 2 abnormal glands in 3 patients and 1 abnormal gland in 4 patients. Used together, however, ultrasonography and scintigraphy did dictate bilateral explorations in 7 of 7 patients.

COMMENT

Is it wise to attempt to reduce exploration in patients with primary hyperparathyroidism, or would it be better to explore all 4 glands in every case? This is a central question in the treatment of hyperparathyroidism today because new technology, including preoperative imaging, intraoperative radioguided nuclear mapping, and intraoperative parathyroid hormone monitoring, may help identify cases of single adenoma in which limited explo-

©2004 American Medical Association. All rights reserved.
Downloaded From: http://archsurg.jamanetwork.com/ on 05/24/2015

ration would be satisfactory. Ideally, if the 87% of patients with a single adenoma in our series could be identified reliably, we could perform 1-gland exploration and reserve bilateral 4-gland exploration for patients who have multigland disease and/or coexisting thyroid pathologic features. Perceived benefits of reduced exploration include a smaller incision with better cosmesis, no likelihood of permanent hypoparathyroidism, and decreases in anesthesia, operative trauma, operative time, hospitalization, pain, and overall expense. Patients are gratified to have a 40-minute operation, walk away that same day with a bandaid on a small incision, and enjoy a meal at home that evening with their family. The 1-gland "bandaid" operation appeals to patients and referring physicians, but it does so at a cost; currently, we are unable to ensure that all of the unexplored glands are normal. In our series, we limited the exploration to 1 gland or 1 side in 124 patients (67%) with 6 failures (5%) due to undisclosed abnormal parathyroid glands in areas intentionally not explored, all of whom required reoperation to achieve eucalcemia.

Unfortunately, the clinician is unable to identify patients with multigland disease by parameters of age, sex, symptoms, indications for operation, levels of calcium, levels of PTH, or duration of hyperparathyroidism.[3,4] Preoperative imaging in our series identified only 56% of abnormal glands in multigland-disease patients and only directed bilateral exploration in 18 (75%) of 24 patients.

Others have advocated the use of intraoperative PTH monitoring because theoretically a 50% drop in PTH levels from baseline 10 minutes after removing a single adenoma would ensure that no other abnormal parathyroid gland existed. Unfortunately, recent reports on patients with double adenoma have shown a greater than 55% false-positive rate for intraoperative PTH results.[5-7] This means that the intraoperative PTH has falsely reassured the surgeon to stop exploring even though other abnormal glands exist. In patients with a single adenoma, a recent report showed that a 13% false-negative rate of intraoperative PTH assay existed.[8] False negatives occur when the only abnormal parathyroid gland has been removed, but the intraoperative PTH level did not drop sufficiently. This would lead to continued exploration because a surgeon would believe that another enlarged parathyroid gland existed even though it did not. This might encourage aggressive exploration with thymectomy and hemithyroidectomy, potentially jeopardizing normal parathyroid glands leading to permanent hypoparathyroidism. The considerable expense, strategies of obtaining blood samples, and timing problems of intraoperative PTH (in our 1-gland exploration the patients are routinely in the recovery room 10 minutes after removal of a single adenoma) also discourage routine use. We have preferred to evaluate patients' calcium and PTH levels the morning after operation, a strategy that can advise physicians concerning postoperative calcium replacement and can identify the rare patient who may not have been cured by the first operation.

We have not used operative nuclear mapping with handheld gamma probes because of its added expense, timing problems in relation to the injection of sestamibi and operative scheduling, and unreliability in detecting multigland disease or differentiating thyroid adenomas from parathyroid glands.[6] Using the gamma probe through a small incision would seem to block normal anatomic vision.

Our strategy allowed us to limit exploration in 118 (73%) of 161 patients with solitary adenomas. In all, 309 (42%) of 740 potential parathyroid glands were not explored intentionally. Limiting exploration significantly decreased operative time and length of stay and therefore overall resource use and cost.

The normal suppressed parathyroid gland may be difficult to find during an operation (9% in our series) because of ectopic position or because it is hidden in fat or confused by thyroid nodules. Surgeons who routinely explore all 4 glands have an obligation to identify normal parathyroid glands because a cursory examination leading to scarring may make any later reexploration difficult, with increased complication rates. Our strategy consists of limiting the initial operation when appropriate to 1 gland or 1 side with all of its benefits, but with a recognition that persistent hyperparathyroidism may exist in a small percentage of patients. When our strategy fails, resulting in persistent or recurrent hyperparathyroidism, repeat operation takes place in an unoperated field and proceeds easily, but with the surgeon convinced that further abnormalities exist. Our overall strategy has resulted in long-term cure in 184 of 185 consecutive patients with primary sporadic hyperparathyroidism without any long-term complications and with overall decreased resource use.

Accepted for publication April 9, 2004.

This paper was presented at the 75th Annual Meeting of the Pacific Coast Surgical Association; February 14, 2004; Maui, Hawaii; 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.

We thank Jim Randall, RN, validating statistician.

Correspondence: John A. Ryan, Jr, MD, Department of Surgery, Virginia Mason Medical Center, 1100 Ninth Ave, Seattle, WA 98111 (john.ryan@vmmc.org).

REFERENCES

1. Norman J, Chheda H. Minimally invasive parathyroidectomy facilitated by intraoperative nuclear mapping. *Surgery*. 1997;122:998-1004.
2. Irvin G, Deriso G. A new practical intraoperative parathyroid hormone assay. *Am J Surg*. 1994;168:466-468.
3. Szabo E, Lundgren E, Juhlin C, Ljunghall S, Akerstrom G, Rastad J. Double parathyroid adenoma, a clinically nondistinct entity of primary hyperparathyroidism. *World J Surg*. 1998;22:708-713.
4. Mozes G, Curlee KJ, Rowland CM, et al. The predictive value of laboratory findings in patients with primary hyperparathyroidism. *J Am Coll Surg*. 2002;194:126-130.
5. Gauger PG, Agarwal G, England BG, et al. Intraoperative parathyroid hormone monitoring fails to detect double parathyroid adenomas: a 2-institution experience. *Surgery*. 2001;130:1005-1010.
6. Jaskowiak NT, Sugg SL, Helke J, Koka MR, Kaplan EL. Pitfalls of intraoperative quick parathyroid hormone monitoring and gamma probe localization in surgery for primary hyperparathyroidism. *Arch Surg*. 2002;137:659-669.
7. Haciyanli M, Lal G, Morita E, Duh QY, Kebebew E, Clark OH. Accuracy of preoperative localization studies and intraoperative parathyroid hormone assay in patients with primary hyperparathyroidism and double adenoma. *J Am Coll Surg*. 2003;197:739-746.

©2004 American Medical Association. All rights reserved.
Downloaded From: http://archsurg.jamanetwork.com/ on 05/24/2015

8. Miura D, Wada N, Arici C, Morita E, Duh QY, Clark OH. Does intraoperative quick parathyroid hormone assay improve the results of parathyroidectomy? *World J Surg*. 2002;26:926-930.

DISCUSSION

Orlo H. Clark, MD, San Francisco, Calif: The authors are to be congratulated on the results of their operative treatment of 185 consecutive patients with primary sporadic hyperparathyroidism (HPT) treated during a 4-year period at Virginia Mason Medical Center. In their investigation, patient data was prospectively collected and retrospectively analyzed. Using a selective approach based on the results of preoperative radionucleide and ultrasound localization studies, 96% of these patients were successfully treated at the initial operation and no patient developed permanent hypoparathyroidism or injuries to the recurrent laryngeal nerve. Seven of the 8 patients who had persistent HPT were successfully treated at a second operation.

As the authors state, there is currently considerable controversy regarding the best surgical approach for patients with primary sporadic HPT. What do we currently know about these patients? (1) About 85% of patients with primary sporadic HPT have 1 abnormal parathyroid gland. In the current investigation, it was 87%. Interestingly, the authors found multiple abnormal parathyroid glands in only 2 (3.3%) of 61 patients having a focal approach and in 18 (29.5%) of 61 patients having a bilateral approach. As in this investigation, more abnormal parathyroid glands were demonstrated when a bilateral approach was used, even where preoperative localization investigations suggest only 1 abnormal parathyroid gland [Haciyanli M, Lal G, Morita E, Duh QY, Kebebew E, Clark OH. Accuracy of preoperative localization studies and intraoperative parathyroid hormone assay in patients with primary hyperparathyroidism and double adenoma. *J Am Coll Surg*. 2003;197:739-746]. This observation suggests that some macroscopically and histologically abnormal parathyroid glands such as oxyphilic adenomas may not cause persistent disease, but longer-term follow-up is required to determine whether some of these patients may develop recurrent HPT. (2) Preoperative localization tests are essential when a focal or unilateral exploration is planned. Sestamibi scanning with or without SPECT, and ultrasound, are the most cost-effective and generally used techniques. Sestamibi scanning is most helpful for identifying ectopically situated parathyroid glands and ultrasound for parathyroid tumors immediately adjacent to or within the thyroid. The authors removed 3 intrathyroidal glands in their patients. The combined use of these investigations provides useful information to direct a focused approach and also to determine where to position the surgical incision. CT [computed tomography], MRI [magnetic resonance imaging], and invasive localization techniques are not recommended prior to initial parathyroid operations. Regarding the value of localization techniques for the selective approach to patients with HPT, they may be helpful when negative and also when they suggest more than 1 abnormal parathyroid gland. Thus, when no tumor is identified or more than 1 tumor is identified, a bilateral approach is indicated. In the current investigation using both ultrasound and radionucleide testing, 8 of 13 tests in patients with multiple abnormal parathyroid glands were helpful, whereas in 5 patients only 1 gland was demonstrated so that if only 1 gland were removed the patient would have persistent hyperparathyroidism.

Such failures have led to the use of intraoperative PTH [IOPTH] testing. Although Dr Ryan and many other surgeons do not use IOPTH testing, there is little doubt that it is helpful in preventing persistent HPT. Unfortunately, it is only about 50% accurate in patients who have double adenomas [Gauger PG, Agarwal G, England BG, et al. Intraoperative parathyroid hormone monitoring fails to detect double parathyroid adenomas. *Surgery*. 2001;130:1005-1010; Haciyanli M, Lal G, Morita E, Duh QY, Kebebew E, Clark OH. Accuracy of preoperative localization studies and intraoperative parathyroid hormone assay in patients with primary hyperparathyroidism and double adenoma. *J Am Coll Surg*. 2003;197:739-746]. Overall, Dr Ryan successfully treated 99% of patients with a solitary adenoma but only 18 (75%) of 24 patients with multiple gland disease. By using IOPTH testing, Dr Ryan's overall results would probably improve to about 98% at the initial operation. As he mentioned, IOPTH testing is expensive, and it also takes about 20 minutes to perform.

I have several questions for Dr Ryan. (1) Do you use preoperative localization studies to select the site and size of the incision, and what size incision are you using? (2) Why wasn't the mediastinal parathyroid tumor seen on the initial radionucleide study? (3) Did you find more multiple adenomas in patients over 60 as we, and Dr Norman Thompson from the University of Michigan, have previously described [Tezelman S, Shen W, Siperstein AE, Duh QY, Clark OH. Persistent or recurrent hyperparathyroidism in patients with double adenomas. *Surgery*. 1995;118:1115-1124]? (4) How will you improve your surgical results in the future? How does one make excellent results even better?

I congratulate you and your team for your superb results and continued important contributions regarding the management of patients with HPT.

Lawrence A. Danto, MD, Truckee, Calif: A quick comment. Over 2 hours for an average bilateral 4-gland exploration in experienced hands like yours seems a little on the long side, especially with preoperative imaging. Why in your study did simply exploring the other side apparently increase the operative time by what appears to be a factor of 3? Even so, although this difference is numerically significant, is it really clinically significant? Did these patients really do any worse than those undergoing a unilateral exploration? In current surgical practice, most patients with typically bilateral exploration are able and ready to go home the same day of operation. Even postoperative calcium metabolism is not adversely affected in most patients with a bilateral exploration. Staying overnight has more to do with inadequate preparation for same-day discharge and/or uncontrollable circumstances such as unusual infirmity or long travel distances. What conditions led to all but 1 of your patients with a bilateral exploration having to stay overnight in the hospital?

Finally, the incidence of multiple gland disease in your 124 patients having a unilateral exploration was about 5%, yet remarkably, as Orlo has noticed, it rose to almost 30% in the 61 patients undergoing a 4-gland exploration. It seems the more you looked, the more you found, that in fact maximizing exploration leads to maximizing outcome. Could this be contrary to your paper's conclusion? Despite this nice study, I think the basic question remains. Is it better practice to operate on 98% of primary hyperthyroid patients once with an adequate operation or to reoperate on about 15% after a failed first exploration? Are we really maximizing patient outcome by minimizing exploration? From a practice standpoint, might not the best place for a so-called minimal exploration be in a patient with persistent or recurrent hyperparathyroidism?

Quan-Yang Duh, MD, San Francisco: I have 2 questions. The first question is, how was the decision made as to when to discharge the patient? I think there is likely some bias in the surgeon's thinking that patients who had lesser exploration will be at lower risk for hypocalcemia or bleeding. However, in our own study, analyzing the same 3 groups as Dr Ryan has (focused, unilateral, and bilateral explorations), we found no difference in postoperative calcium levels, changes in calcium levels, or hypocalcemic symptoms, or bleeding among the

©2004 American Medical Association. All rights reserved.
Downloaded From: http://archsurg.jamanetwork.com/ on 05/24/2015

3 groups. As Dr Danto has mentioned, the decision to discharge patients earlier or later may reflect our bias that may or may not be supported by data.

The second question is, do you use intraoperative ultrasound before the incision? Do you have the radiologist do the ultrasound preoperatively or do you do the ultrasound in the operating room yourself, and if you do, have you found it helpful?

James J. Peck, MD, Portland, Ore: These are excellent results, a remarkable 96% success rate at the initial exploration. Dr Ryan is a very experienced endocrine surgeon. Can a limited exploration be done safely by a less experienced surgeon? How many full neck explorations must be done before attempting minimal invasive surgery?

In those patients who had day surgery, how many had a general anesthetic and how many a local cervical block? Do you routinely identify the recurrent laryngeal nerve when you are doing the limited exploration?

Finally, is there a role for radioguided sestamibi?

Earl S. Schuman, MD, Portland: I was also wondering about the difference between your unilateral and bilateral explorations and the amount of time to discharge. We found that with appropriate preparation of the patient, appropriate handling of the tissues, minimizing incisions even for bilateral exploration, and on occasion, when appropriate, use of NSAID and Cox-2 inhibitors for pain relief and an antinausea protocol, that the majority of patients can get home the same day. In that regard, I was wondering, what are your specific criteria for discharge for patients after either unilateral or bilateral exploration? Do you think just a single calcium test postoperatively is adequate prior to discharge?

Electron Kebebew, MD, San Francisco: I am curious as to why the distinction between a focused and a unilateral approach. Oftentimes, the focused approach ends up being a unilateral approach. Looking at either the upper or lower parathyroid gland gives one an idea if the patient is at risk for having multiglandular disease. I am wondering about what factors determine whether you select a focused vs a unilateral approach and if that has made a difference in you going on to do a bilateral neck exploration.

Dr Ryan: Thanks to the PCSA for accepting the paper, and I appreciate the comments of the endocrine surgeons in the audience and especially to Dr Clark for his excellent remarks and his many contributions to understanding hyperparathyroidism. The operation for hyperparathyroidism used to be simple. We explored all 4 glands, and either we found the abnormal gland or we did not. Now, however, we have new technologies to integrate into our practice, and we have to decide which to use and how to use them. At Virginia Mason Hospital, the resource that is under tightest constraint is our operating room time. Using the operating room unnecessarily is not good for our medical center, and, of course, unnecessarily prolonging a patient's anesthetics is not good for the patient. We have used the new technology of localizing tests to attempt to limit the exploration and reduce the operating room time. We have not used the γ probe and intraoperative PTH measurements and explain our reasoning in the manuscript. The importance of our paper is that we are reporting the results of a large group of consecutive patients treated with a uniform strategy of selection and not just the cases treated by limited exploration.

Drs Clark, Peck, and Kebebew have asked about our operative technique. Our 1-gland exploration is distinctly different than a unilateral approach. For an abnormal upper parathyroid gland, we make a small incision just inside the border of the sternocleidomastoid muscle on the side indicated by the preoperative localization tests. Dissection is carried medial to the sternocleidomastoid and lateral to the strap muscles in a plane medial to the jugular vein and carotid artery, often dividing the middle thyroidal vein until the spine is reached. The enlarged upper gland is found posterior to the thyroid. In this instance, no attempt is made to search for the lower gland.

In exploration for an enlarged lower parathyroid gland, a small incision is made horizontally between the 2 clavicular tendons of the sternocleidomastoids, and a small flap is raised subplatysmally. The strap muscles are removed from the lower pole of the thyroid, and by retracting the thyroid the parathyroid is found usually behind the thyroid or when indicated in the thymic gland. No attempt is made to mobilize the thyroid further or to observe the upper gland.

We agree with Dr Peck that familiarization of the anatomy of the neck is important for any parathyroid surgeon. Since our approach is flexible to 4-gland exploration, unilateral exploration, and 1-gland exploration, our residents learn the relative anatomy. We do not specifically identify the recurrent laryngeal nerve in every case but are careful to get within the sheath of the parathyroid so that the nerve is not damaged. Although all of our operations have been done under general anesthesia, we have no qualms about others' use of local, which might be particularly suited to the removal of an enlarged lower gland. However, we fear too much infusion of local anesthesia may distort anatomy.

We have not measured the length of our incisions, but as in all operations try to keep them small. Incision size depends on the size of the patient, the length of the neck, coexisting thyroid pathology, and the decision for localized or 4-gland exploration.

Drs Danto, Duh, Peck, and Schuman have all asked questions about the decision and planning for timing of discharge, and I agree with all of their comments. I am sure with a more aggressive attitude we could have discharged more patients earlier, but many social, geographic, and medical factors influence those decisions. We have patients' serum calcium checked on the first postoperative day either at the time of discharge or by returning to the medical center, and when we know the calcium has returned to normal we treat almost all patients with prophylactic calcium carbonate tablets up to 2 g per day in order to prevent the occasional patient whose temporary hypocalcemia can be symptomatically troublesome.

We agree with Dr Clark's and Dr Danto's comments that finding more abnormal parathyroid seems to occur with extending exploration and that there may be certain parathyroid glands that are enlarged and are nonfunctioning, as we see in all other endocrine tumors. However, we were not surprised to find multiple enlarged parathyroid glands in our 4-gland exploration because our ultrasound and scintigraphic tests often demonstrated more than 1 enlarged gland.

We did not find double adenomas more common in the older age group or in the upper glands, Dr Clark.

Dr Danto, extended time for 4-gland exploration was due to the fact that many of these patients had thyroid pathology and extensive dissection was mandatory if more than 1 gland was abnormal in order to ensure that all glands were identified. When surgeons carefully record the operative times, they are always longer than in their memory or their best-case time.

Dr Duh, all of our ultrasounds were done by ultrasonographers preoperatively.

Improved results long-term will depend upon future developments in the field. I am not optimistic that routine use of intraoperative PTH monitoring will greatly change results.

©2004 American Medical Association. All rights reserved.
Downloaded From: http://archsurg.jamanetwork.com/ on 05/24/2015