ORIGINAL ARTICLE

Impact of Localization Studies and Clinical Scenario in Patients With Hyperparathyroidism Being Evaluated for Reoperative Neck Surgery

Joyce J. Shin, MD; Mira Milas, MD; Jamie Mitchell, MD; Eren Berber, MD; Louis Ross, BS; Allan Siperstein, MD

Background: Previous studies have focused on the success of localization studies (LSs) in patients undergoing reoperative parathyroid surgery; however, patients who did not undergo reexploration surgery have been excluded from analysis. In addition, the concept of whether clinical scenario (CS) suggests single- vs multiple-gland disease in reoperative strategy is often underemphasized.

Objective: To evaluate how LSs and CS direct operative strategy in patients being considered for reexploration.

Design: Retrospective review of a prospective database.

Setting: Tertiary referral center.

Patients: Two hundred three patients with hyperparathyroidism who underwent previous neck surgery. The CS stratified patients as candidates for single- or multiple-site exploration (or unknown).

Main Outcome Measure: Ability of CS and LSs to direct successful reexploration.

Results: Of 203 patients, 27 were not explored owing to nonlocalizing studies. Of the remaining 176 patients, LSs accurately guided reexploration in 85%. However, when including the 27 nonexplored patients, the success of LSs decreased to 73%. The cure rate in reoperated patients was 96% but was reduced to 83% when including nonexplored patients. Of the reoperated patients, 83% had single-site disease and 17% had multiple-site disease. The positive predictive value of LSs in predicting single- or multiple-site disease was 92% and 73%, respectively. However, when stratified by CS, the positive predictive value increased to 95% for single-site disease and to 100% for multiple-site disease.

Conclusions: Failure to cure patients was 4 times more likely to be due to nonlocalizing studies than to a failed reexploration. Stratification by CS was useful in the interpretation of LSs and in determining the most accurate reoperative approach.

Arch Surg. 2011;146(12):1397-1403

PREOPERATIVE LOCALIZATION studies (LSs) for parathyroid reexploration, unlike for initial parathyroid surgery, are crucial for operative success. Numerous studies[1-10] in the literature have reported favorable outcomes of reoperative parathyroid surgery, as high as 97%, and have focused on the accuracy of LSs in directing surgeons where to explore. However, the success rates of curing patients with persistent or recurrent hyperparathyroidism (HPT) and the accuracy of LSs have been derived only from patients who do, in fact, undergo reoperative parathyroid surgery after LSs have successfully localized the site(s) of the abnormal parathyroid gland(s). On the other hand, those who do not meet the criteria for reexploration owing to nonlocalizing studies have been excluded from the analysis, skewing the actual success of reoperative parathyroid surgery and LSs in previous series.

See Invited Critique at end of article

Although there is a general consensus that LSs are a prerequisite for reexploration, conscientious surgeons also expend a great amount of time and effort reviewing the patient's clinical history, such as the initial diagnosis, type of surgical approach used in previous explorations, operative findings, and surgical pathology results, before performing reoperative parathyroid surgery.[10,11] Clinical history can help provide information about the

Author Affiliations: Department of Endocrine Surgery, Endocrinology and Metabolism Institute, Cleveland Clinic, Cleveland, Ohio.

Table 1. Stratification of Disease Status and Reoperative Approach by Clinical Scenario

Type of Clinical Scenario
Clinical scenario in which the patient is strongly suspected of having a single remaining abnormal gland
Previous negative parathyroid exploration with persistent hyperparathyroidism (HPT)
Previous thyroid or esophageal surgery
Previous neck exploration for primary HPT with excision of 1 abnormal parathyroid gland and identification of ≥1 normal parathyroid gland
Previous neck exploration for primary HPT with excision of ≥3 abnormal parathyroid glands
Previous neck exploration for secondary, tertiary, or multiple endocrine neoplasia–associated HPT with excision of ≥3 abnormal parathyroid glands
Clinical scenario in which the patient is strongly suspected of having multiple remaining abnormal glands
Previous neck exploration for primary HPT with excision of 2 abnormal parathyroid glands
Previous neck exploration for secondary, tertiary, or multiple endocrine neoplasia–associated HPT with excision of <3 abnormal parathyroid glands
Clinical scenario in which the patient could have either a single or multiple remaining abnormal glands
Previous neck exploration with excision and identification of 1 abnormal parathyroid gland
Insufficient or no information from previous exploration(s)

disease status, stratifying the patient as having a single diseased gland or multiple diseased glands remaining in the neck and/or mediastinum. Consequently, patients who are predicted to have single-site disease (SSD) by clinical history are candidates for single-site exploration (SSE), and those who are predicted to have multiple-site disease (MSD) are candidates for multiple-site exploration (MSE). Clinical scenario (CS) can assure surgeons that the LSs correspond to their clinical expectations and is a helpful strategy in decision making for the reoperative approach. Although this clinical stratification process may be obvious and already practiced by many surgeons, it is an important concept that is often not systematically scrutinized or reported in the literature.

This study was designed to analyze our clinical strategies in the management of patients with HPT requiring reoperative neck surgery. Information provided by LSs and clinical history was applied in the stratification of patients by disease status and reoperative approach. To our knowledge, this is the first study to consider a very critical view of the success rates of LSs and reoperative parathyroid surgery by including all patients with HPT being evaluated for reoperative neck surgery in an intent-to-treat analysis, even those who were not reexplored owing to nonlocalizing studies.

METHODS

Between May 1, 2000, and November 30, 2009, 203 patients with HPT being evaluated for reoperative neck surgery at the Cleveland Clinic (Cleveland, Ohio) by 4 endocrine surgeons (M.M., J.M., E.B., and A.S.) were studied from a prospective database. These patients had symptoms and/or associated conditions of HPT that warranted reoperation. They also had a history of neck operations involving the same surgical territory as in parathyroid exploration (previous parathyroid, thyroid, and esophageal surgical procedures). Diagnoses of primary, secondary, persistent, and recurrent HPT were confirmed. *Persistent HPT* was defined as hypercalcemia (serum calcium level >10.5 mg/dL [to convert to millimoles per liter, multiply by 0.25]) occurring within 6 months of parathyroidectomy, and *recurrent HPT* was defined as hypercalcemia recurring after at least 6 months of postoperative normocalcemia. Clinical scenario (determined by the type of HPT and findings at previous exploration[s] obtained from referring notes, operative notes, and surgical pathology reports) stratified patients into the following disease categories: (1) strongly suspected of having a single remaining abnormal gland, (2) strongly suspected of having multiple remaining abnormal glands, and (3) unknown (inadequate clinical information to determine clinical status). The various clinical conditions used to stratify these patients are listed in **Table 1**.

All 203 patients underwent surgeon-performed ultrasonography and sestamibi-iodine subtraction scan (MIBI) with or without computed tomography (CT) (co-registration of single-photon emission CT with CT images performed with MIBI starting in July 2005). When the results of these studies were negative or inconclusive, parathyroid fine-needle aspiration biopsy under ultrasonographic guidance, magnetic resonance imaging, CT (before the use of single-photon emission CT/CT with MIBI), and/or selective venous sampling for intact parathyroid hormone (PTH) was performed. The success rates of each LS were evaluated on a per-patient basis, as previously described by Shen et al.[4] A study was defined as *completely correct* if it identified all abnormal parathyroid glands in a patient with no false-positive or false-negative findings. The term *correct with false-positive results* was used if the LS identified all abnormal glands in a patient but also had false-positive results (imaged suspected tumors not identified at surgery). The term *correct with false-negative results* was used if the localization study identified all abnormal glands in a patient but also had false-negative results (additional nonimaged tumors found at exploration). Finally, a study was defined as *completely incorrect* if it produced the following results: (1) a completely negative study result in a patient with an abnormal gland(s), (2) a completely false-positive study result that localized all abnormal glands in incorrect positions, or (3) the localization of the abnormal gland(s) remaining unknown after reexploration. The sensitivity of LSs was defined as the proportion of studies that correctly located all abnormal parathyroid glands (completely correct and correct with false-positive results) in patients with abnormal glands.

In addition, the accuracy of these LSs in guiding the surgeon to perform an appropriate and curative exploration was assessed based on the aggregate interpretation of LSs for each patient. For this study, LSs were considered to be accurate if a focal signal led to a curative exploration and excision of only the single localized gland (completely correct) or if multifocal signals guided the surgeon to perform a curative exploration and excision of at least 2 localized glands (completely correct or correct with false-negative results). Surgical cure was determined by the assessment of serial serum calcium and PTH values at least 6 months postoperatively (range, 6 months to 9 years), in which the patient did not meet the criteria for persistent or recurrent primary HPT. After reexploration and from surgically confirmed pathology laboratory findings, the positive predictive value (PPV) of disease status (SSD or MSD) derived only from the CS was analyzed. Last, the PPV of disease status based on the interpretation of LSs in the context of the patient's CS was also evaluated.

Statistical analysis was performed using a commercially available statistical software package (JMP 8.0; SAS Institute, Inc). We determined statistical significance between the PPVs using a z score for proportions. The level of statistical significance for this study was defined as $P < .05$.

RESULTS

Of the 203 patients, 147 were women and 56 were men (female to male ratio of 2.6 to 1). Their mean age was 58 years (age range, 21-87 years). Indications for previous cervical operations are listed in **Table 2**. Previous surgical procedures included parathyroid surgery in 126 patients (62.1%), parathyroid and thyroid surgery in 24 (11.8%), and nonparathyroid surgery (thyroid or esophageal) in 53 (26.1%). Indications for reoperative parathyroid surgery included persistent HPT (primary, secondary, and tertiary HPT and multiple endocrine neoplasia type 1) in 110 patients (54.2%), recurrent HPT (primary, secondary, and tertiary HPT and multiple endocrine neoplasia types 1 and 2A) in 40 (19.7%), primary HPT in 52 (25.6%), and secondary HPT in 1 (0.5%). Of the 203 patients, 176 (86.7%) were candidates for reexploration due to concordance on 2 LSs (n=165, 93.8%), localization by only selective venous sampling when all other study results were negative (n=6, 3.4%), or localization by only 1 study when also undergoing thyroid surgery (n=5, 2.8%). On the other hand, 27 patients (13.3%) did not meet the criteria for reexploration due to nonlocalizing studies. Of the 176 reoperative candidates, localization by only ultrasonogram and MIBI (with or without co-registration of CT images) was achieved in 63 patients (35.8%). Thirty-seven patients (21.0%) required fine-needle aspiration biopsy as the only additional preoperative study, and 46 (26.1%) needed other noninvasive imaging modalities (CT and/or magnetic resonance imaging) with or without fine-needle aspiration biopsy. Magnetic resonance imaging was used more frequently in the earlier years of this study and is now rarely used owing to its low sensitivity, and CT alone without MIBI was performed before July 2005. Thirty patients (17.0%) underwent selective venous sampling for PTH. A total of 517 LSs were performed in these reoperative candidates. The success rates of these LSs analyzed individually are demonstrated in **Table 3**.

For the 176 reoperative candidates, their CSs as previously described were reviewed, and they were stratified as having SSD (n=145, 82.4%), MSD (n=16, 9.1%), or unknown disease status (SSD or MSD) (n=15, 8.5%). For each group, the aggregate interpretation of LSs (focal or multifocal signal), surgical approach (SSE or MSE), operative success (cure, fail, or negative exploration), and surgically confirmed outcome (SSD, MSD, or no disease) were evaluated. For details, refer to the Appendix and eFigures 1, 2, and 3 (http:/www.archsurg.com).

Surgically confirmed outcomes of HPT in reoperative neck surgery in 176 patients who were candidates for reexploration were as follows: SSD removed in 144 cured patients (81.8%), MSD excised in 25 cured patients (14.2%), SSD removed in 4 failed patients (2.3%), and no disease found in 3 patients (1.7%). The SSE group achieved cure by removing 90% SSD and 6% MSD (with the last 4% representing 3 failures and 3 negative explorations), the MSE group achieved cure by excising 19% SSD and 81% MSD, and the unknown disease status group achieved cure by removing 67% SSD and 27% MSD (with the last 6% representing 1 failure). The LSs accurately guided reexploration (either SSE or MSE) in 84.7% of patients (149 of 176), consisting of 88% in the SSE group, 75% in the MSE group, and 67% in the unknown disease status group. However, when including the 27 patients who were not reexplored owing to nonlocalizing studies, the success of LSs to direct reexploration was decreased to 73%. The cure rate in reoperated patients was 96% (3 negative explorations and 4 persistent disease). When including the 27 nonexplored patients, the overall cure rate of the entire cohort was reduced to 83%.

Table 2. Indications for Previous Cervical Explorations

Indication	Patients, No. (N = 203)
Primary hyperparathyroidism (HPT)	96
Secondary HPT	6
Tertiary HPT	9
Parathyroid cancer	1
Multiple endocrine neoplasia type 1	12
Multiple endocrine neoplasia type 2A	2
Thyroid disease (benign or cancer)	48
Thyroid disease and primary HPT	22
Thyroid disease and secondary HPT	1
Thyroid disease and tertiary HPT	1
Esophageal disease	5

Of the 173 reexplored patients in whom pathologic abnormalities were found (excluding 3 negative explorations), 83.2% (n=144) were found to have SSD and 16.8% (n=29) MSD (**Table 4**). The PPV of the disease status derived only from the CS was then evaluated. When patients were strongly suspected of having a single remaining abnormal gland and, therefore, were candidates for SSE based on CS alone, 92.3% (131 of 142) had surgically confirmed SSD and 7.7% (11 of 142) had MSD. Conversely, when patients were strongly suspected of having multiple remaining abnormal glands and, therefore, were candidates for MSE based on the CS alone, 81.3% (13 of 16) had surgically confirmed MSD and 18.8% (3 of 16) had SSD. Therefore, when patients were stratified by CS, 92% actually had SSD (increased from 83%, $P = .008$) and 81% actually had MSD (increased from 17%, $P < .001$). Although the stratification process could not be applied in the group with unknown or unclear history, 66.7% (10 of 15) had surgically confirmed SSD, and 33.3% (5 of 15) had MSD.

The PPV of the disease status from the interpretation of LSs in the context of the patient's CS was then analyzed (**Table 5**). From the entire cohort with a focal signal on LSs, 91.8% of patients (135 of 147) were found to have SSD based on completely correct LSs alone. However, when an accurate focal signal was seen in the SSE

Table 3. Success Rates of Localization Studies Analyzed Individually in 176 Reoperated Patients

		MIBI (n = 176)					
Results[a]	Ultrasound (n = 176)	MIBI (n = 103)	MIBI + CT (n = 73)	FNAB (n = 62)	MRI (n = 53)	CT (n = 20)	SVS (n = 30)
Completely correct, No.	119	69	56	57	18	9	24
Correct + FP, No.	2	7	7	0	0	0	2
Correct + FN, No.	11	7	0	0	3	0	1
Completely incorrect, No.	44	20	10	5	32	11	3
Sensitivity, %[b]	69	74	86	92	34	45	87

Abbreviations: CT, computed tomography; FN, false-negative results; FNAB, fine-needle aspiration biopsy; FP, false-positive results; MIBI, sestamibi-iodine subtraction scan; MIBI + CT, MIBI with co-registration of CT; MRI, magnetic resonance imaging; SVS, selective venous sampling.
[a] See the "Methods" section of the text for definitions.
[b] Sensitivity was calculated as (completely correct + correct with FP) / total.

Table 4. Surgically Confirmed Disease Status When Stratified by Clinical Scenario

Disease Status	Total, No. (%) (n = 173)	Candidate for SSE, No. (%) (n = 142)[a]	Candidate for MSE, No. (%) (n = 16)	Unknown Disease Status, No. (%) (n = 15)
Surgically confirmed SSD	**144** (83)	131 (92)	3 (19)	10 (67)
Surgically confirmed MSD	**29** (17)	11 (8)	13 (81)	5 (33)

Abbreviations: MSD, multiple-site disease; MSE, multiple-site exploration; SSD, single-site disease; SSE, single-site exploration.
[a] Excluding 3 negative explorations.

Table 5. Accuracy of Disease Status Based on the Interpretation of Localization Studies in Context of the Clinical Scenario

Variable	Total, No. (%) (n = 173)	Candidate for SSE (n = 142)[a]	Candidate for MSE (n = 16)	Unknown Disease Status (n = 15)
Accuracy of focal signal on LSs in predicting SSD[b]	135/147 (92)	123/129 (95)	3/5 (60)	9/13 (69)
Accuracy of multifocal signals on LSs in predicting MSD[c]	19/26 (73)	7/13 (54)	11/11 (100)	1/2 (50)

Abbreviations: LSs, localization studies; MSD, multiple-site disease; MSE, multiple-site exploration; SSD, single-site diseases; SSE, single-site exploration.
[a] Excluding 3 negative surgical explorations.
[b] No. of patients with SSD/No. of patients with focal signal on LSs.
[c] No. of patients with MSD/No. of patients with multifocal signals on LSs.

group, 95.3% of patients (123 of 129) had surgically confirmed SSD. When a focal signal was seen in the MSE group, 60.0% of patients (3 of 5) had SSD. Lastly, when a focal signal was seen in the group with unknown disease status, 69.2% of patients (9 of 13) actually had SSD. On the other hand, from the entire cohort with multifocal signals on LSs, 73.1% (19 of 26) were found to have MSD based on LSs alone (completely correct or correct with false-negative results). However, when accurate multifocal signals were seen in the SSE group, 53.8% of patients (7 of 13) had surgically confirmed SSD. When multifocal signals were seen in the MSE group, 100% of patients (11 of 11) had MSD. Lastly, when multifocal signals were seen in the group with unknown disease status, 50.0% of patients (1 of 2) actually had MSD. From this analysis, we can conclude that a focal signal on LSs has a PPV for SSD of 92%. However, if the patient can be stratified by CS to have SSD, the PPV of the focal signal on LSs is increased to 95% ($P = .12$). Conversely, multifocal signals on LSs have a PPV for MSD of 73%. However, if the patient can be stratified by CS to have MSD, the PPV of the LSs is increased to 100% ($P = .03$). Although the PPV of disease status improved for both groups, it was statistically significant only for the MSE group, supporting previous studies[12-14] that have shown LSs to be superior at detecting single adenomas vs multigland disease.

Thirty-four of 176 patients (19.3%) had more extensive exploration than indicated by LSs due to concomitant thyroid surgery (29 in the SSE group and 5 in the unknown disease status group). However, for this study, patients were considered to have SSE if a completely correct focal signal on LSs guided the surgeon to explore only the index site, and, therefore, the concomitant thyroid surgery would not have changed the surgical approach. Only 3 of 34 patients were considered to have MSE due to completely or partially incorrect LSs that led the surgeon to explore other nonlocalized sites, even if no thyroidectomy was being performed.

Intraoperative PTH assays were used in 171 of 176 patients (97.2%). After excision of a single abnormal parathyroid gland, operative cure was achieved in 120 pa-

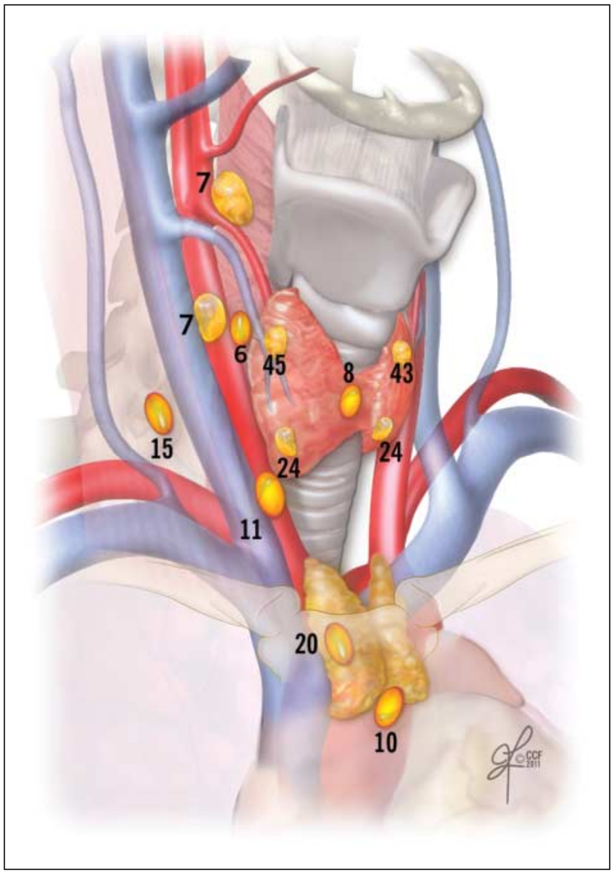

Figure. Distribution of 220 parathyroid specimens: 136 parathyroid glands (61.8%) located in their normal anatomical positions and 84 ectopic parathyroid glands (38.2%). Reprinted with permission from Cleveland Clinic Center for Medical Art & Photography 2011. All rights reserved.

tients, where the Miami criterion[15] (an intraoperative PTH decline ≥50% from the highest of either the preincision or preexcision level 10 minutes after gland excision) was met in 110 patients (64.3%) but was not satisfied in 10 (5.8%). In patients with multiple abnormal glands removed, operative cure was achieved in 28, where the Miami criterion was met in 26 patients (15.2%) but was not satisfied in 2 (1.2%). In 11 patients, the preincision or preexcision value was within the reference range and decreased at least 50% after gland excision in 8 patients (4.7%) but fell less than 50% after gland excision in 3 (1.8%). Of the remaining 12 patients, intraoperative PTH measurements were not interpretable in 6 (3.5%), 3 (1.8%) failed postoperatively (2 met the Miami criterion and 1 did not), and 3 (1.8%) had negative explorations and did not meet the Miami criterion. Overall, the Miami criterion correctly predicted postoperative cure in 144 of 159 interpretable intraoperative PTH values (90.6%).

From this cohort, 220 parathyroid specimens were excised in 173 patients (excluding 3 negative explorations). As shown in the **Figure**, 136 parathyroid glands (61.8%) were located in their normal anatomical positions (24 left lower, 43 left upper, 24 right lower, and 45 right upper). Of the remaining 84 ectopic parathyroid specimens (38.2%), 15 were previously autotransplanted parathyroid tissue in the sternocleidomastoid or

Table 6. Anatomical Locations of 84 Ectopic Parathyroid Specimens

Location	Ectopic Parathyroid Glands, No.
Intrathymic	**20**
RL thymus	8
LL thymus	8
Superiormost aspect of RL thyrothymic ligament	2
Superiormost aspect of LL thyrothymic ligament	2
Descended	**11**
RU	5
LU	3
LU and within tracheoesophageal groove	2
LU and retroesophageal	1
Undescended	**7**
LU	2
RU	2
LU and retroesophageal	1
LU and within carotid sheath	1
RU and within carotid sheath	1
Intrathyroidal	**8**
Left	5
Right	3
Carotid sheath	**7**
LL	4
LU	2
RU	1
Esophageal	**6**
LU paraesophageal	2
RU retroesophageal	3
RL retroesophageal	1
Mediastinum	**10**
Right ventricular outflow tract	1
Adjacent to brachiocephalic artery	1
Aortic arch	3
Anterior mediastinum and within thymus	2
Posterior mediastinum	3
Autotransplants	**15**
Left sternocleidomastoid muscle	9
Right sternocleidomastoid muscle	3
Left strap muscle	2
Right strap muscle	1

Abbreviations: LL, left lower; LU, left upper; RL, right lower; RU, right upper.

strap muscles, and the most common ectopic location was intrathymic (**Table 6**).

COMMENT

Reoperative neck surgery for HPT in patients with previous cervical explorations can pose diagnostic and technical difficulties.[1-6,8,9,16-21] With the higher risk of morbidity, surgeons need to rely heavily on the patient's clinical history and LSs to perform curative reexploration. When sufficient data can be obtained from both clinical information and imaging studies, reoperative parathyroid surgery can have success rates that are comparable with those of initial parathyroidectomy.[4,5,8,10] However, most of the recognition has been given to the success of LSs, whereas the wealth of data that can be gained from the clinical history has not been as well acknowledged. In addition, previous studies[1-10] in the literature have not analyzed patients in whom the LSs are unable to localize the abnormal gland(s), and, therefore, only report the success of LSs in those who actually undergo reoperative parathyroid surgery. In this study, we took an intent-to-treat approach by evaluating all patients presenting for reoperative neck surgery. The ability of LSs to accurately direct reexploration was 85% in those who met the criteria for reexploration; however, it was decreased to 73% when including those who never underwent reexploration. Similar to other series, the present cure rate in reoperated patients was 96%; however, 27 nonexplored patients remain with disease, thereby reducing the overall cure rate to 83%. In conclusion, the failure to cure patients with HPT and previous neck surgery was 4 times more likely to be due to nonlocalizing studies than to a failed reexploration.

One of the aims of this study was to emphasize the importance of clinical history in this patient population. From the entire cohort of patients who were reexplored and in whom pathologic abnormalities were found, 83% had SSD and 17% had MSD. However, by applying CS to the stratification of disease status, the likelihood of actually having either a single or multiple remaining abnormal glands was improved (from 83% to 92% in the SSE group and from 17% to 81% in the MSE group). Furthermore, the PPV of the disease status based on LSs also increased when a patient was stratified as having either a single or multiple remaining abnormal glands (from 92% to 95% in the SSE group and from 73% to 100% in the MSE group). Therefore, the CS allows surgeons to categorize patients according to their disease status, aids in the interpretation of LSs, and helps correctly direct the reoperative approach.

The incidence of concomitant thyroid and parathyroid diseases is growing.[22-25] Twenty-four percent of this patient population initially underwent thyroid surgery, and 12% had simultaneous parathyroid and thyroid operation as their previous cervical exploration. Furthermore, 19% of patients had concomitant thyroidectomy during reexploration for HPT, which meant requiring more extensive exploration than indicated by LSs. This represents realistic groups of patients who are being evaluated for reoperative neck surgery, and our approach to these patients is extremely relevant to the true clinical setting.

Although the best strategy is to prevent reoperative surgery, failures do occur after initial surgery for HPT. Owing to the potential difficulties of reoperative neck explorations, surgeons must seek data that can help reduce the complexity and morbidity of these operations. These results demonstrate the significance of LSs and clinical history used in conjunction to achieve operative cure. With the use of all available information, the success of reexploration for HPT has the potential to equal that of initial parathyroid surgery in patients with concordant LSs. However, there remain many patients with unsuccessful LSs who continue to live with the disease.

Accepted for Publication: June 24, 2011.

Correspondence: Joyce J. Shin, MD, Department of Endocrine Surgery, Endocrinology and Metabolism Institute, Cleveland Clinic, 9500 Euclid Ave, Ste F20, Cleveland, OH 44195 (shinj2@ccf.org).

Author Contributions: Dr Shin had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Shin, Milas, Mitchell, Berber, and Siperstein. *Acquisition of data:* Shin. *Analysis and interpretation of data:* Shin, Milas, Mitchell, Ross, and Siperstein. *Drafting of the manuscript:* Shin, Milas, Mitchell, and Siperstein. *Critical revision of the manuscript for important intellectual content:* Shin, Milas, Mitchell, Berber, Ross, and Siperstein. *Statistical analysis:* Shin, Ross, and Siperstein. *Administrative, technical, and material support:* Shin, Milas, Mitchell, Berber, and Siperstein. *Study supervision:* Shin, Milas, Mitchell, Berber, and Siperstein.

Financial Disclosure: None reported.

Online-Only Materials: The eAppendix and 3 eFigures are available at http://www.archsurg.com.

REFERENCES

1. Yen TW, Wang TS, Doffek KM, Krzywda EA, Wilson SD. Reoperative parathyroidectomy: an algorithm for imaging and monitoring of intraoperative parathyroid hormone levels that results in a successful focused approach. *Surgery*. 2008;144(4):611-621.
2. Reidel MA, Schilling T, Graf S, et al. Localization of hyperfunctioning parathyroid glands by selective venous sampling in reoperation for primary or secondary hyperparathyroidism. *Surgery*. 2006;140(6):907-913.
3. Jones JJ, Brunaud L, Dowd CF, Duh QY, Morita E, Clark OH. Accuracy of selective venous sampling for intact parathyroid hormone in difficult patients with recurrent or persistent hyperparathyroidism. *Surgery*. 2002;132(6):944-951.
4. Shen W, Düren M, Morita E, et al. Reoperation for persistent or recurrent primary hyperparathyroidism. *Arch Surg*. 1996;131(8):861-869.
5. Jaskowiak N, Norton JA, Alexander HR, et al. A prospective trial evaluating a standard approach to reoperation for missed parathyroid adenoma. *Ann Surg*. 1996;224(3):308-321.
6. Hessman O, Stålberg P, Sundin A, et al. High success rate of parathyroid reoperation may be achieved with improved localization diagnosis. *World J Surg*. 2008;32(5):774-783.
7. Rotstein L, Irish J, Gullane P, Keller MA, Sniderman K. Reoperative parathyroidectomy in the era of localization technology. *Head Neck*. 1998;20(6):535-539.
8. Udelsman R, Donovan PI. Remedial parathyroid surgery: changing trends in 130 consecutive cases. *Ann Surg*. 2006;244(3):471-479.
9. Richards ML, Thompson GB, Farley DR, Grant CS. Reoperative parathyroidectomy in 228 patients during the era of minimal-access surgery and intraoperative parathyroid hormone monitoring. *Am J Surg*. 2008;196(6):937-943.
10. Feingold DL, Alexander HR, Chen CC, et al. Ultrasound and sestamibi scan as the only preoperative imaging tests in reoperation for parathyroid adenomas. *Surgery*. 2000;128(6):1103-1110.
11. Brennan MF, Doppman JL, Marx SJ, Spiegel AM, Brown EM, Aurbach GD. Reoperative parathyroid surgery for persistent hyperparathyroidism. *Surgery*. 1978;83(6):669-676.
12. Bhansali A, Masoodi SR, Bhadada S, Mittal BR, Behra A, Singh P. Ultrasonography in detection of single and multiple abnormal parathyroid glands in primary hyperparathyroidism: comparison with radionuclide scintigraphy and surgery. *Clin Endocrinol (Oxf)*. 2006;65(3):340-345.
13. Haber RS, Kim CK, Inabnet WB. Ultrasonography for preoperative localization of enlarged parathyroid glands in primary hyperparathyroidism: comparison with (99m)technetium sestamibi scintigraphy. *Clin Endocrinol (Oxf)*. 2002;57(2):241-249.
14. Heller KS, Attie JN, Dubner S. Parathyroid localization: inability to predict multiple gland involvement. *Am J Surg*. 1993;166(4):357-359.
15. Carneiro DM, Solorzano CC, Nader MC, Ramirez M, Irvin GL III. Comparison of intraoperative iPTH assay (QPTH) criteria in guiding parathyroidectomy: which criterion is the most accurate? *Surgery*. 2003;134(6):973-981.
16. Shaha AR. Parathyroid re-exploration. *Otolaryngol Clin North Am*. 2004;37(4):833-843, x.
17. Simental A, Ferris RL. Reoperative parathyroidectomy. *Otolaryngol Clin North Am*. 2008;41(6):1269-1274, xii.
18. Hasse C, Sitter H, Brune M, Wollenteit I, Nies C, Rothmund M. Quality of life and

patient satisfaction after reoperation for primary hyperparathyroidism: analysis of long-term results. *World J Surg*. 2002;26(8):1029-1036.
19. Ghaheri BA, Koslin DB, Wood AH, Cohen JI. Preoperative ultrasound is worthwhile for reoperative parathyroid surgery. *Laryngoscope*. 2004;114(12):2168-2171.
20. Brennan MF, Norton JA. Reoperation for persistent and recurrent hyperparathyroidism. *Ann Surg*. 1985;201(1):40-44.
21. Weber CJ, Sewell CW, McGarity WC. Persistent and recurrent sporadic primary hyperparathyroidism: histopathology, complications, and results of reoperation. *Surgery*. 1994;116(6):991-998.
22. Prinz RA, Barbato AL, Braithwaite SS, et al. Simultaneous primary hyperparathyroidism and nodular thyroid disease. *Surgery*. 1982;92(3):454-458.
23. Strichartz SD, Giuliano AE. The operative management of coexisting thyroid and parathyroid disease. *Arch Surg*. 1990;125(10):1327-1331.
24. Sidhu S, Campbell P. Thyroid pathology associated with primary hyperparathyroidism. *Aust N Z J Surg*. 2000;70(4):285-287.
25. Wang TS, Roman SA, Cox H, Air M, Sosa JA. The management of thyroid nodules in patients with primary hyperparathyroidism. *J Surg Res*. 2009;154(2):317-323.

INVITED CRITIQUE

The Bayes Theorem Wins

"Torture numbers and they will confess to anything,"
(Gregg Easterbrook, 1999, *New Republic*)

"There are three kinds of lies: lies, damned lies, and statistics." (misattributed to Disraeli by Mark Twain, 1906)

Endocrine surgeons are known to be friendly, humble, and thoughtful intellectuals rather than chestthumpers. The main socially acceptable mode of competition among endocrine surgeons is their excellence in surgical outcome. One measure of endocrine surgeons' prowess is their parathyroidectomy success rate. For primary operations, the success rate is expected to be 96% to 99%. Even for reoperations, the success rate is expected to be 90% to 95%. Success rate is a simple fraction with a numerator and a denominator. As surgeons, we try to improve the percentage by having more accurate diagnosis and localization studies (LSs) and better knowledge of anatomy and embryology. Usually, we concentrate on improving the outcome of individual patients (the numerator). Shin et al[1] remind us that the denominator is just as important. They analyzed a large series of reoperative parathyroidectomy from Cleveland Clinic, a center of excellence for complex parathyroid surgery. They show that the expected success rate depends on how and when you measure it. For a patient already scheduled for a reoperative parathyroidectomy, the expected success rate is 96%, but for a patient who has an indication for reoperative parathyroidectomy who has not yet undergone LSs, the expected success rate is only 83% because those with negative LSs usually could not undergo parathyroidectomy. Similarly, the PPVs of their LSs depended on whether nonoperated patients were included in the calculation and whether clinical scenarios (CSs) were considered.

It may seem artificial or a trivial point that "patient selection" and "exclusion criteria" would significantly affect the success rate of an operation. Patients and referring physicians, however, reading Web site postings and surgical literature may, nevertheless, have different perceptions about the 2 statistically equivalent statements of "we have an 83% chance of curing you" vs "we have a 96% chance of curing you if your LSs are positive." Adding such conditional statements allows for a more optimistic interpretation of the same facts.

So, are endocrine surgeons guilty of minimizing their denominators to improve their success rates or of "torturing the numbers" and "lying with statistics"? I do not think that is the message of this article. I think this article shows the importance of thinking and talking about probability precisely, on a time continuum, and in a clinically relevant manner. As additional information is accumulated about a patient, the expected probability of an outcome needs to be adjusted.

The Bayes theorem tells us that posttest probability is determined by pretest probability. To evaluate statistical numbers appropriately, complete clinical context is absolutely necessary. In the end, the Bayes theorem wins.

Quan-Yang Duh, MD

Author Affiliation: Department of Surgery, University of California, San Francisco, VA Medical Center, San Francisco, California.
Correspondence: Dr Duh, Department of Surgery, University of California, San Francisco, VA Medical Center, 4150 Clement St, San Francisco, CA 94121 (Quan-yang.duh@va.gov).
Financial Disclosure: None reported.

1. Shin JJ, Milas M, Mitchell J, Berber E, Ross L, Siperstein A. Impact of localization studies and clinical scenario in patients with hyperparathyroidism being evaluated for reoperative neck surgery. *Arch Surg*. 2011;146(12):1397-1403.