ORIGINAL ARTICLE

# Reoperative Parathyroidectomy

## *Location of Missed Glands Based on a Contemporary Nomenclature System*

*Eric J. Silberfein, MD; Ruijun Bao, MD; Adriana Lopez, MS; Elizabeth G. Grubbs, MD; Jeffrey E. Lee, MD; Douglas B. Evans, MD; Nancy D. Perrier, MD*

**Objectives:** To evaluate and categorize the locations of missed parathyroid glands found during reoperative parathyroidectomy and to determine any factors associated with these locations.

**Design:** Retrospective cohort study.

**Setting:** Tertiary referral center.

**Patients:** Fifty-four patients who underwent reoperative parathyroidectomy for persistent or recurrent hyperparathyroidism from January 1, 2005, through January 1, 2009.

**Main Outcome Measures:** Location of missed parathyroid glands and their association with continuous variables were analyzed using a Kruskal-Wallis test, and associations between gland location and categorical variables were evaluated using the Fisher exact test.

**Results:** Among 54 patients, 50 abnormal parathyroid glands were identified, resected, and classified as follows: 5 (10%) were type A (adherent to the posterior thyroid capsule); 11 (22%), type B (behind the thyroid in the tracheoesophageal groove); 7 (14%), type C (close to the clavicle in the prevertebral space); 3 (6%), type D (directly over the recurrent laryngeal nerve); 9 (18%), type E (easy to identify; near the inferior thyroid pole); 13 (26%), type F (fallen into the thymus); and 2 (4%), type G (gauche, within the thyroid gland). No demographic, biochemical, or pathological factors were significantly associated with gland location. Among the 43 patients followed up for 6 months, 40 (93%) had documented cures.

**Conclusions:** Missed glands after parathyroidectomy for hyperparathyroidism can be found in standard locations in most cases. A standardized nomenclature system based on the regional anatomy and the embryology of the parathyroid glands can guide a systematic exploration for parathyroid adenomas that are not easily identified and facilitate communication about gland locations.

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**Author Affiliations:**
Departments of Surgical Oncology (Drs Bao, Grubbs, Lee, Evans, and Perrier) and Biostatistics (Ms Lopez), The University of Texas M.D. Anderson Cancer Center, and Division of Surgery, Baylor College of Medicine (Dr Silberfein), Houston.

THE MOST COMMON CAUSE OF persistent and recurrent hyperparathyroidism (HPT) after parathyroidectomy is a missed abnormal parathyroid gland.[1,2] Because reoperative parathyroidectomy has higher complication and failure rates than initial parathyroidectomy,[3-5] preventing persistent or recurrent HPT by resecting all adenomas during the initial surgery is important. However, when reoperation is necessary, a thorough understanding of the common locations of missed parathyroid glands can aid in the planning and success of the surgery. The existing medical literature[1,6-8] uses inconsistent terminology to describe gland locations, making interpretation difficult. The purpose of this study is to evaluate and categorize the locations of missed parathyroid glands during reoperative parathyroidectomy and to determine any factors associated with these locations. To categorize the gland locations and facilitate use of the data by other surgeons, we applied a nomenclature system developed at our institution.[9,10]

## METHODS

From a prospectively collected database of all patients who underwent parathyroid surgery at The University of Texas M.D. Anderson Cancer Center, we identified 76 patients who underwent reoperative parathyroid surgery for persistent or recurrent HPT from January 1, 2005, through January 1, 2009. Patients with clinical or laboratory confirmation of multiple endocrine neoplasia type I or IIa (n=21) and patients with parathyroid carcinoma (n=1) were excluded, leaving 54 patients. This study was approved by our institutional review board.

Data extracted for each patient from the database and medical records included patient age, sex, body mass index (calculated as weight in

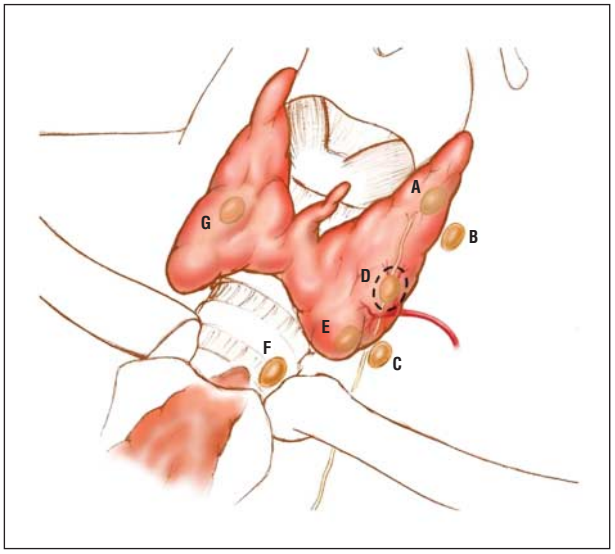


**Figure.** Schematic of types A through G locations of parathyroid glands. Locations are described in the "Results" section. Reprinted from Rodgers et al,[9] with permission from Elsevier.

kilograms divided by height in meters squared), results of biochemical studies and preoperative localization studies, previous surgical operative notes and pathology reports, intraoperative findings, resected parathyroid gland weight, and outcomes. The number and types of preoperative localization studies, including 4-dimensional computed tomography, sestamibi scanning, and ultrasonography, and the operative approach were at the discretion of the surgeon. Operative approaches included a directed approach, a planned bilateral neck exploration, or a conversion to a bilateral neck exploration from a directed approach. Surgical procedures were performed by 1 of 4 endocrine surgeons (E.G.G., J.E.L., D.B.E., and N.D.P.). A procedure was considered minimally invasive if the surgery was limited to 1 anatomic location in the neck based on the preoperative localization studies. The locations of adenomatous glands resected during reoperation were categorized using a previously published nomenclature system[9,10] coauthored by 2 of us (**Figure**). Cure was defined as eucalcemia 6 months after surgery.

We calculated descriptive statistics for the variables of interest, including age, sex, body mass index, preoperative serum calcium level, type of surgery, parathyroid gland weight, parathyroid gland location, and biochemical cure. Associations between gland location and continuous variables were analyzed using a Kruskal-Wallis test, and associations between gland location and categorical variables were evaluated using the Fisher exact test. Statistical significance was defined as $P < .05$. All analyses were performed using commercially available software (SAS, version 9.1.3; SAS Institute Inc, Cary, North Carolina).

## RESULTS

Among the 54 patients included in the study, 50 abnormal parathyroid glands were identified, resected, and classified as follows: 5 (10%) as type A (adherent to the posterior thyroid capsule); 11 (22%), type B (behind the thyroid in the tracheoesophageal groove); 7 (14%), type C (close to the clavicle in the prevertebral space); 3 (6%), type D (directly over the recurrent laryngeal nerve); 9 (18%), type E (easy to identify; near the inferior thyroid pole); 13 (26%), type F (fallen into the thymus); and 2 (4%), type G (gauche, within the thyroid gland) (**Table 1**). In 4 patients, no parathyroid tissue was found at the time of reoperative parathyroidectomy or on final pathological examination if suspected abnormal tissue was resected.

**Table 1. Patient and Disease Characteristics and Missed Parathyroid Gland Locations**

| Characteristic | Finding |
|---|---|
| Sex, No. (%) of patients | |
| Female | 43 (80) |
| Male | 11 (20) |
| Missing parathyroid location, No. (%) of patients[a] | |
| A | 5 (10) |
| B | 11 (22) |
| C | 7 (14) |
| D | 3 (6) |
| E | 9 (18) |
| F | 13 (26) |
| G | 2 (4) |
| Age, y | |
| Mean (SD) | 64.3 (11.4) |
| Median (range) | 65.7 (36.0-83.0) |
| BMI | |
| Mean (SD) | 29.5 (7.0) |
| Median (range) | 28.7 (17.8-49.2) |
| Parathyroid gland weight, g | |
| Mean (SD) | 0.8 (0.8) |
| Median (range) | 0.5 (0.0-3.2) |
| Preoperative serum calcium level, mg/dL | |
| Mean (SD) | 10.8 (0.7) |
| Median (range) | 10.6 (9.6-12.8) |

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by the square of the height in meters).
SI conversion factor: To convert calcium to millimoles per liter, multiply by 0.25.
[a] Locations are depicted in the Figure. Parathyroid adenomas were found in 50 patients.

**Table 2. Patient and Disease Characteristics by Missed Parathyroid Gland Location[a]**

| Characteristic | *P* Value |
|---|---|
| Age | .67[b] |
| BMI | .24[b] |
| Parathyroid gland weight | .20[b] |
| Preoperative serum calcium level | .93[b] |
| Sex | .33[c] |

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by the square of the height in meters).
[a] Locations are depicted in the Figure.
[b] Calculated by means of the Kruskal-Wallis test.
[c] Calculated by means of the Fisher exact test.

Patient and disease characteristics are summarized in Table 1. The mean age of the patients was 64 years, and most of the patients (80%) were women. There were no significant associations between gland location and patient age, sex, body mass index, preoperative serum calcium level, or gland weight (**Table 2**). Of the 43 patients who had 6 months of follow-up, 40 (93%) had a documented cure. Of these 40 patients, 22 (55%) had a minimally invasive reoperative parathyroidectomy.

## COMMENT

In our study, abnormal parathyroid glands could be identified and resected in 93% of patients who underwent reoperative parathyroidectomy for persistent or recurrent HPT. This finding is consistent with 2 recent reviews[1,6] that confirmed that the most common cause of a failed parathyroidectomy is a missed abnormal gland at the time of initial resection. We also found that previously missed glands were most often located in the tracheoesophageal groove, thyrothymic ligament, or superior mediastinum (**Table 3**).

In a retrospective study of reoperative parathyroidectomy, Gough[1] found that 8 of the 18 single glands (44%) causing persistent or recurrent HPT were in "normal" locations, whereas 10 (56%) were in "ectopic" locations. In a similar study, Yen et al[6] found that 25 of the 38 single glands causing persistent or recurrent HPT of the 38 (66%) were in normal locations and 13 (34%) were in ectopic locations. These studies highlight the fact that most cases of persistent or recurrent HPT after parathyroidectomy are owing to missed glands in normal or ectopic locations. Furthermore, several researchers have reported on the locations of ectopic parathyroid glands found during reoperative parathyroidectomy. Shen et al[7] found that of 54 ectopic glands identified at reoperation, half were located in the neck and half in the mediastinum. A large percentage (78%) of the specific ectopic locations identified were paraesophageal, mediastinal, or intrathymic. Similarly, Thompson et al[5] found that of the 26 glands not in normal positions at reoperation, 18 (69%) were located in the mediastinum, within the thyroid, or anterior to the trachea. Cheung et al[8] found a large proportion 6 (86%) of "aberrant" glands in the reoperative setting to be in the tracheoesophageal groove or the retropharyngeal or retroesophageal space. However, the terminology in prior studies is inconsistent, even as to what constitutes normal and ectopic, and this inconsistency makes interpretation of the literature difficult.

In an attempt to standardize reporting, 2 of us[9,10] recently published a nomenclature system to describe the most common positions of parathyroid adenomas. This easily reproduced system provides a consistent means of communicating exact gland location without lengthy descriptions. The system takes into account the embryology of the parathyroid glands and the regional anatomy. The descent of the inferior glands from the third branchial pouch and the descent of the superior glands from the fourth branchial pouch during fetal development result in variability in the locations of parathyroid glands. Superior glands are usually located on the posterior surface of the thyroid gland approximately 1 cm above the intersection of the recurrent laryngeal nerve and the inferior thyroid artery. If they are not in this location, they most likely are confined within the thyroid capsule (type A gland) or have fallen posteriorly into the tracheoesophageal groove (type B or C gland). The normal inferior glands are more variable in location but are most commonly found on the posterolateral aspect of the inferior pole of the thyroid gland medial to the recurrent laryngeal nerve (type D or E gland). During embryologic migration, enlarged, heavy inferior glands originally situated in the neck may gradually descend into the anterior mediastinum (type F gland) as a result of gravity[11]; in fact, autopsy studies have documented parathyroid tissue within the thymus or adjacent organs in more than 20% of patients.[12]

**Table 3. Missed Parathyroid Gland Location by Patient Sex**

| Parathyroid Location[a] | Patients, No. (%) Female (n=41) | Male (n=9) | *P* Value[b] |
|---|---|---|---|
| A | 3 (7) | 2 (22) | |
| B | 9 (22) | 2 (22) | |
| C | 7 (17) | 0 | |
| D | 2 (5) | 1 (11) | 0.3259 |
| E | 6 (15) | 3 (33) | |
| F | 12 (29) | 1 (11) | |
| G | 25 | 0 | |

[a] See the Figure. Locations of 50 parathyroids in 50 patients were identified.
[b] From Fisher exact test.

Our system is useful in helping to clarify and report gland location, and most of the previously described locations[5,7,8] can be characterized by this system. In fact, when we applied our system to other reports, the locations of most previously described single glands corresponded with our B and F locations, as in our study. Furthermore, gland location in our system can often be determined preoperatively on the basis of imaging studies, with the location communicated between the radiologist and surgeon using the system. The system thus is helpful for planning initial and reoperative parathyroidectomy and perhaps can be used to guide a search when the adenomatous gland is not easily identified. Maneuvers to uncover such glands could include incision of the posterior capsule of the thyroid gland to reveal a type A gland; methodical evaluation of the dorsal surface of the thyroid gland, tracheoesophageal groove, prevertebral space, inferior pole of the thyroid gland, thyrothymic ligament, and thymus to detect type B through F glands; and, rarely, a thyroidotomy or even a thyroid lobectomy to locate a type G gland.

Preventing failure of parathyroidectomy is important because repeated parathyroid exploration is associated with more complications, including recurrent laryngeal nerve injury and hypocalcemia, and fewer cures compared with initial exploration.[3-5,13] The reported cure rate after reoperative parathyroidectomy varies from 87% to 93%.[2,6,14,15] Therefore, these procedures should be undertaken after careful review of previous operative and pathology reports by an experienced surgeon in a center that can provide expert preoperative localization, intraoperative biochemical monitoring, and cryopreservation of parathyroid tissue. Because gland locations are predictable, however, experienced surgeons can often perform reoperations via a minimally invasive approach. In fact, a minimally invasive approach was possible in 55% of the cured patients in this series.

In conclusion, missed glands after parathyroidectomy for HPT can be found in standard locations in most cases. Thorough knowledge of the embryology of the parathyroid glands and the regional anatomy is essential for successful parathyroid gland surgery. A standardized no-

menclature system can eliminate inconsistencies in the ways gland locations are reported by surgeons at different institutions, simplify location descriptions, and guide a systematic exploration for parathyroid adenomas.

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**Correspondence:** Nancy D. Perrier, MD, Department of Surgical Oncology, The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd, Unit 444, Houston, TX 77030 (NPerrier@mdanderson.org).
**Author Contributions:** *Study concept and design:* Silberfein and Perrier. *Acquisition of data:* Silberfein, Bao, and Grubbs. *Analysis and interpretation of data:* Silberfein, Bao, Lopez, Lee, Evans, and Perrier. *Drafting of the manuscript:* Silberfein, Lopez, Evans, and Perrier. *Critical revision of the manuscript for important intellectual content*: Grubbs, Lee, Evans, and Perrier. *Statistical analysis:* Bao and Lopez. *Administrative, technical, and material support:* Grubbs. *Study supervision:* Lee.
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