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## The Incidence of Concomitant Hyperparathyroidism in Patients with Thyroid Disease Requiring Surgery

Sara Murray, M.D., Rebecca S. Sippel, M.D., FACS, and Herbert Chen, M.D., FACS

Section of Endocrine Surgery, Department of Surgery, University of Wisconsin, Madison, WI

### Abstract

**Introduction**—Thyroid disease and hyperparathyroidism (HPT) are among the most common endocrine disorders, though their association has not been well established. The aim of this study was to determine the incidence of concomitant HPT in patients with thyroid disease requiring surgery, as a single definitive surgery should ideally be performed.

**Methods**—We retrospectively reviewed a prospectively maintained database of patients who underwent thyroidectomy at a single institution. Data was collected on patients' initial indication for surgery, pre-operative workup, and operative findings.

**Results**—Of the 1,049 patients who underwent thyroidectomy, 56 (5%) had concomitant HPT and underwent a simultaneous parathyroidectomy. Of these 56 patients, 36 initially presented with thyroid disease, and the other 20 with HPT. The mean age was  $59 \pm 2$  years and 79% were female. The mean pre-operative calcium and PTH were elevated at  $10.4 \pm 0.1$  mg/dL and  $87 \pm 7$  pg/mL, respectively. The majority of these patients had primary HPT ( $n=54$ , 96%). Of the 36 patients presenting initially with thyroid disease, 26 had an elevated calcium or PTH value and were pre-operatively diagnosed with HPT. However, the remaining 10 patients had normal labs, yet a pathologically enlarged parathyroid gland was found at the time of thyroidectomy. The overall cure rate for HPT within this series was 96%.

**Conclusion**—The incidence of concomitant HPT in patients with thyroid disease requiring surgery is significant at 5%. Recognition of concurrent disease is important as it allows for a single definitive surgery to treat both pathologies.

### Keywords

thyroid disease; thyroidectomy; hyperparathyroidism; parathyroidectomy; calcium; parathyroid hormone

### Introduction

Thyroid disease and hyperparathyroidism (HPT) are among the most common endocrine disorders<sup>1</sup>. The rate of HPT is higher in patients with thyroid disease than in the general medical population, and the association between these two pathologies has been described in

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Address for Correspondence: Herbert Chen, M.D., FACS, University of Wisconsin, Department of Surgery, Section of Endocrine Surgery, K3/705 Clinical Science Center, 600 Highland Avenue, Madison, WI 53792, USA, Tel.: 608-263-1387, Fax: 608-263-7652, chen@surgery.wisc.edu.

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several series<sup>2-12</sup>. While the etiology of this relationship is unknown, in patients with thyroid disease requiring surgery the recognition of concomitant HPT is essential because surgery is the only definitive therapy for HPT. Surgical intervention is nearly always recommended for symptomatic primary HPT (PHPT), and guidelines for asymptomatic HPT have been established which recommend that surgery be performed if any of the following are present: 1) serum calcium of 1.0 mg/dL above the normal, 2) 24-hour urinary calcium >400 mg, 3) creatinine clearance reduced by 30%, 4) bone mineral density t-score <-2.5 at any of three sites, 5) age <50, or 6) if medical surveillance is not possible or desirable in a patient. Although non-operative management is an option for asymptomatic PHPT, no convincing data support long-term efficacy of medical therapy<sup>13,14</sup>.

Ideally, patients with HPT in conjunction with thyroid disease requiring surgery should be treated with a simultaneous thyroidectomy and parathyroidectomy. Performing a single definitive surgery has several advantages, including the avoidance of surgical complications during neck re-exploration, cost effectiveness, and patient preference.

The aim of this study was two fold. The first was to report the incidence of concomitant HPT in patients who underwent thyroidectomy at our institution. The second objective was to assess the utility of routine pre-operative calcium and parathyroid hormone (PTH) testing in patients referred for thyroidectomy, in order to determine whether this would be beneficial in identifying patients with coexistent HPT pre-operatively.

## Methods

We performed an institutional review board-approved retrospective review of a prospectively maintained database of patients who underwent a thyroidectomy (total, subtotal, or lobectomy) at our institution between October 2000 and July 2011. All operations were performed by one of two endocrine surgeons. Patients who had previously undergone parathyroid surgery were excluded. Furthermore, patients requiring more than one thyroid surgery at our institution during this time period were only included once in this series. Routine pre-operative calcium and PTH testing was performed on all patients. We reviewed data including the following: patient demographics, clinical presentation, indication for thyroidectomy, pre-operative calcium and PTH levels, and surgical procedure performed. If HPT was known pre-operatively or discovered intra-operatively by visualization of an enlarged parathyroid gland, simultaneous parathyroidectomy was performed at the time of thyroidectomy. If the patient's parathyroid adenoma was located on the same side as the thyroid lesion, both parathyroid glands on that side were visualized. Alternatively, if the patient underwent a total thyroidectomy, all 4 parathyroid glands were identified. Intra-operative PTH was measured in patients with known HPT pre-operatively to confirm successful removal of the pathologic gland. Results are reported as mean  $\pm$  standard error of the mean. Comparison of continuous variables were made using Student's T-test, with values of  $p < 0.05$  considered significant.

## Results

Of the 1,049 patients who underwent thyroid surgery, 56 (5%) had concomitant HPT and underwent a simultaneous parathyroidectomy (Figure 1). The remaining 993 patients in the series did not have parathyroid disease and underwent solely a thyroidectomy. Focusing exclusively on the 56 patients with concomitant disease, the mean age of this group was  $59 \pm 2$  years (range 20–83) and 79% were female (female: 44, male: 12). The mean preoperative calcium and PTH were elevated at  $10.4 \pm 0.1$  mg/dL and  $87 \pm 7$  pg/mL, respectively (Table 1). The indication for thyroid surgery in these patients is shown in Table 2, with goiter and malignancy being the most common, accounting for 84% of the

pathology. Additionally, 54 (96%) patients had PHPT, and two (4%) had either secondary or tertiary HPT. On further characterization of these patients, 42 (75%) had a single adenoma, 7 (12.5%) had double adenomas, and 7 (12.5%) had parathyroid hyperplasia necessitating a subtotal parathyroidectomy. The mean parathyroid gland weight was  $453 \pm 58$  mg (range 80–2600 mg).

Of 56 patients with concomitant disease, 20 initially presented with HPT and were found on further pre-operative evaluation to have concurrent thyroid disease necessitating thyroidectomy. As shown in Table 1, the mean pre-operative calcium and PTH levels in this group were elevated at  $10.6 \pm 0.1$  mg/dL and  $112 \pm 13$  pg/mL (one outlier of 2,429 pg/mL was excluded), respectively. The remaining 36 patients in the series of 56 with concomitant disease initially presented with thyroid disease and were subsequently found to have HPT. The mean pre-operative calcium and PTH levels were also elevated at  $10.3 \pm 0.1$  mg/dL and  $72 \pm 5$  pg/mL (Table 1), although significantly lower than the pre-operative levels in the 20 patients presenting with HPT ( $p < 0.01$ ). Based on an elevated pre-operative calcium or PTH, 26 of these 36 patients were known or suspected to have co-existent HPT at the time of surgery. However, the other 10 patients in this group had normal pre-operative calcium and PTH values and were found at the time of thyroidectomy to have an incidental parathyroid adenoma necessitating parathyroidectomy. All 10 of these patients had a single parathyroid adenoma. These data demonstrate that in total, 46 patients were known to have concomitant HPT preoperatively. This amounts to 4% of all patients who underwent a thyroidectomy at our institution.

Lastly, the overall cure rate for HPT within this series of 56 patients with concomitant disease was high at 96%. Two patients required a neck re-exploration for persistent disease. There were no reported recurrences, and the complication rate was low, with two (4%) patients experiencing transient hypocalcemia.

## Discussion

The incidence of concomitant hyperparathyroidism in patients who underwent thyroidectomy at our institution is significant at 5%. Previous studies have evaluated the frequency of thyroid disease in patients with hyperparathyroidism, with reported rates ranging from 12% to 84.3%<sup>4–9</sup>. However, far fewer studies have examined the incidence of HPT in patients with thyroid disease requiring surgery, and our result of 5% incidence is consistent with previously reported series quoting between 2% to 6%<sup>10–12</sup>. Our study is the largest cohort reported in the literature, and is also unique because of its inclusivity. We included all patients who underwent either a lobectomy, subtotal or total thyroidectomy, as compared to only including total thyroidectomies in two of the above-mentioned studies.

Notably, 4% of all patients undergoing thyroidectomy at our institution had known concomitant HPT prior to surgery based on abnormal pre-operative calcium or PTH. The utility of measuring pre-operative calcium in thyroid patients has long been suggested, though is not universally performed<sup>2</sup>. More recently, Del Rio *et al.* recommended pre-operative PTH measurement as a cost-effective screening tool for concurrent HPT, particularly given that pre-operative ultrasound and sestamibi scintigraphy are less sensitive in patients with concurrent disease compared to those without<sup>11,15</sup>. While we did not address imaging modalities in this study, we do believe that routine calcium and PTH testing in patients undergoing thyroid surgery is useful, as it lead to pre-operative diagnosis of HPT in the majority of patients with concomitant disease in our series. Had these biochemical markers not been obtained, it is possible that parathyroid pathology could have been missed intra-operatively in asymptomatic patients, particularly during lobectomies. The consequences of overlooking a parathyroid adenoma causing HPT can be serious. Rubin *et*

*al.* determined that 37% of patients with asymptomatic PHPT who did not undergo parathyroidectomy showed evidence of disease progression over a 15-year follow-up period<sup>16</sup>. Abbrogini *et al.* alternatively demonstrated that patients with asymptomatic PHPT who underwent parathyroidectomy had improvements in bone mineral density and quality of life, which has been reproduced in additional series<sup>17–19</sup>.

An added advantage of recognizing concurrent HPT prior to thyroidectomy and performing a simultaneous operation is the avoidance of a second neck operation. Re-operative neck surgery is challenging because there is often dense scar tissue and distorted tissue planes<sup>20</sup>. Consequently, operations for HPT in patients with previous neck surgery have lower cure rates and higher complication rates<sup>21–23</sup>. Two significant complications associated with redo surgery include bleeding and damage to the recurrent laryngeal nerves at a rate of 10% in redo operations, compared to 1% in initial neck operations<sup>24</sup>. In our case series we had no occurrences of either of these complications.

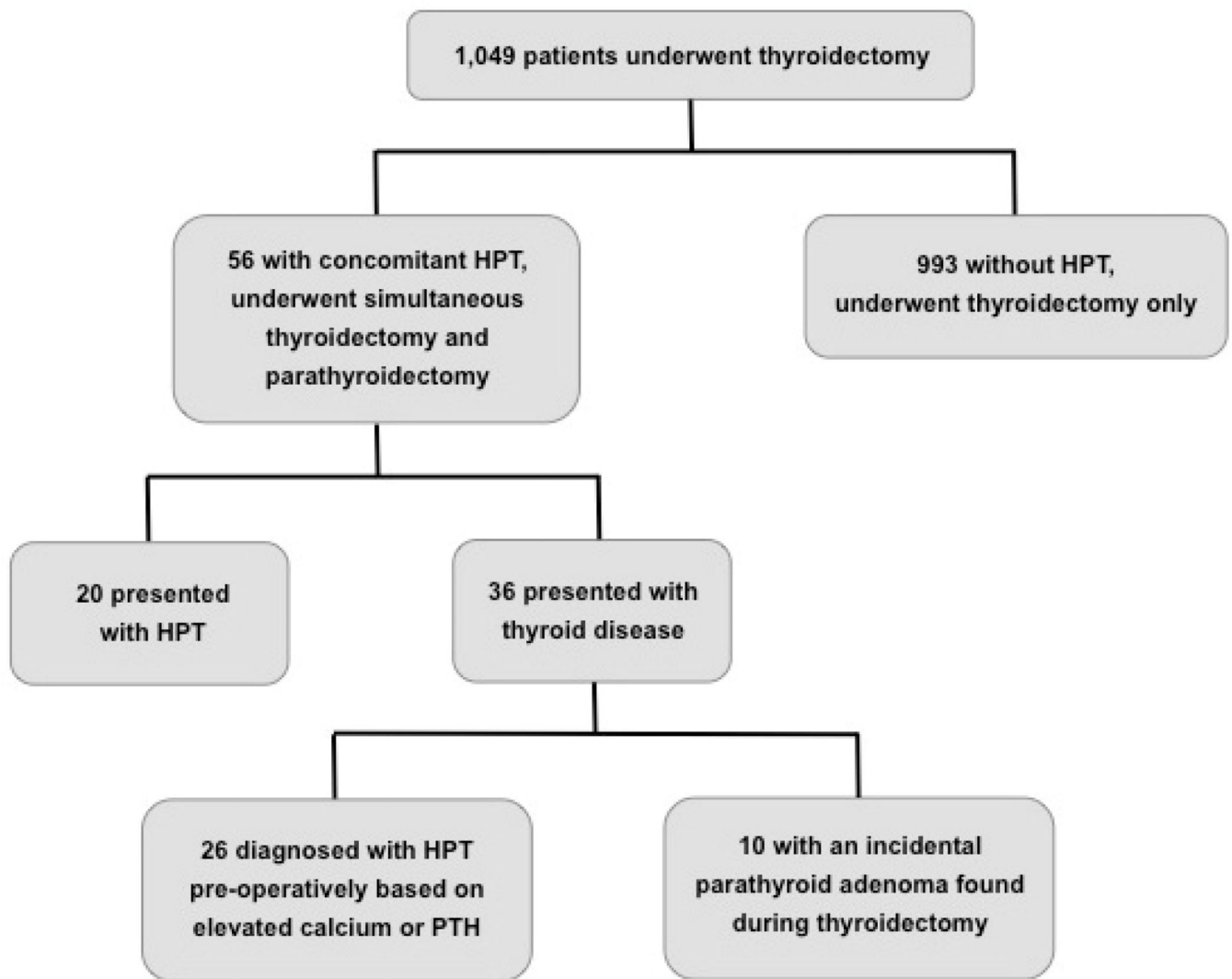
The major limitation of this study was that it used retrospective methods of data collection. Therefore, the true incidence of concomitant HPT in patients with thyroid disease remains unknown, as this was a retrospective analysis of patients who underwent thyroidectomy and had simultaneous HPT. Additionally, we were unable to provide quantitative differences of biochemical markers between patients with and without concomitant HPT. While our data suggests the utility of pre-operative PTH to diagnose concomitant disease, the lack of quantitative comparison to those without HPT may reduce the positive predictive value of pre-operative PTH. It is also possible that some cases of HPT were missed in these patients, which would increase our incidence of reported concomitant disease. Despite these shortcomings, this study was a preliminary investigation to characterize the relationship between these two pathologies. It raises additional questions that require further investigation, such as characterizing the initial clinical presentation of patients with concomitant disease.

Based on this large cohort, we conclude that concomitant HPT occurs in a small but significant number of patients with thyroid disease requiring surgery (5%). As the treatment for PHPT is predominantly surgical, pre-operative recognition of simultaneous HPT in patients requiring a thyroidectomy is ideal. It allows for improved operative planning leading to a single definitive surgery to treat both pathologies, and avoids a re-operation and its associated complications. Given the frequent occurrence of concomitant disease, pre-operative calcium and PTH testing is a useful initial screening method for HPT and should be routinely performed on all patients undergoing thyroidectomy.

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**Figure 1.**  
The incidence, presentation, and clinical outcome of concomitant HPT in 1,049 thyroidectomized patients.

**Table 1**

Pre-operative mean biochemical values in 56 patients with concomitant HPT and thyroid disease requiring thyroidectomy.

	Calcium (mg/dL) <sup>‡</sup>	PTH (pg/mL) <sup>‡</sup>
<b>Total 56 patients</b>	10.4 ± 0.1 (8.7–13.9)	87 ± 7 (26–263) <sup>*</sup>
20 patients presenting with HPT	10.6 ± 0.1 (8.7–11.6)	112 ± 13 (45–263) <sup>*</sup>
36 patients presenting with thyroid disease	10.3 ± 0.1 (9.2–13.9)	72 ± 5 (26–133)

<sup>‡</sup> Mean ± SEM (range)

<sup>\*</sup> One patient was excluded as an outlier, PTH 2,429 pg/dL.

**Table 2**

Indication for thyroid surgery in 56 patients with concomitant thyroid disease requiring surgery and HPT.

Thyroid Pathology	Patients (%)
Goiter	25 (45)
Malignancy	22 (39)
Indeterminate Fine Needle Aspiration	7 (12)
Acute Thyroiditis	1 (2)
Graves Thyrotoxicosis	1 (2)