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Evaluation of clinical significance and risk factors of incidental parathyroidectomy due to thyroidectomy

A single-center retrospective clinical study

Jianwei Zheng, BS, Huimin Song, MD*, Shuyan Cai, BS, Yunlei Wang, BS, Xiaofeng Han, MD, Haoliang Wu, BS, Zhigang Gao, BS, Fanrong Qiu, BS

Abstract

We assessed the clinical significance and risk factors of incidental parathyroidectomy during total thyroidectomy with or without central neck dissection or subtotal thyroidectomy.

Retrospective analysis of clinical and pathological features of 548 consecutive thyroidectomy cases was compared by grouping into inadvertent resection (IR, n = 86) with IR of parathyroid glands, non-IR (n = 462) without, and then into postoperative hypoparathyroidism (PH, n = 140) with PH and non-PH (n = 408) without.

Two hundred ninety-eight patients had total thyroidectomy and 250 had subtotal thyroidectomy. IR had higher malignant disease ($P < .001$), total thyroidectomy ($P = .016$), T3 and T4 classification ($P = .005$), central neck dissection ($P < .001$), recurrent laryngeal nerve palsy ($P = .003$), postoperative transient hypoparathyroidism ($P < .001$), duration of disease prior to thyroidectomy ($P < .001$), and weight of excised thyroid tissue ($P < .001$) than non-IR.

Preoperative diagnosis of malignant disease, duration of disease prior to thyroidectomy, and central neck dissection were independent risk factors for incidental parathyroidectomy. Preoperative diagnosis of malignant disease, central neck dissection, duration of disease prior to thyroidectomy, weight of excised thyroid tissue, and incidental parathyroidectomy were correlated with PH.

Abbreviations: CND = central neck dissection, iPTH = intact parathyroid hormone, IR = inadvertent resection, PH = postoperative hypoparathyroidism, PTH = parathyroid hormone, SD = standard deviation.

Keywords: complications, hypoparathyroidism, parathyroidectomy, risk factors, thyroidectomy

1. Introduction

Thyroid disorders such as thyroid cancer, benign multinodular goiter, toxic multinodular goiter, and Graves disease are very common in adults.[1] Despite advances in conservative management, treatment often involves surgery.[1] Nowadays, thyroidectomy is a relatively safe surgical procedure, which is associated with a morbidity <5%.[2] The surgical procedure itself demands both perfect knowledge of the anatomical structures of the neck and a meticulous surgical technique.

However, there remains some debate about the suitability of thyroidectomy in the treatment of some diseases because of the risk of complications.[3] The most significant operative complications include injury to the recurrent or superior laryngeal nerve and to the parathyroid glands. Devascularization, trauma, and inadvertent removal of 1 or more parathyroid glands will probably result in hypoparathyroidism and hypocalcemia; however, the cause of postoperative hypocalcemia is multifactorial, and can be transient or permanent. Meticulous identification of the anatomy and preservation of the blood supply to the parathyroid glands is of utmost importance for avoiding these complications. According to the existing literature the incidence of temporary hypocalcemia after thyroid surgery is reported to be between 10% and 46% whereas permanent hypocalcemia occurs after 1.5% to 4% of surgeries.[4]

The associated morbidity of these complications includes hypocalcemia symptoms such as perioral numbness and tingling in the fingers, and also calcification of basal ganglia and renal impairment.[3] Postoperative hypocalcemia increases the use of medicine and biochemical tests, and results in a prolonged hospital stay, and so adds to the overall cost of thyroidectomy.[5] Incidental parathyroidectomy during thyroidectomy occurs at a rate between 5.2% and 21.6%, depending mainly on the

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Department of General Surgery, Beijing Chaoyang Hospital Affiliated Capital Medical University, Beijing, China.

* Correspondence: Huimin Song, Department of General Surgery, Beijing Chaoyang Hospital Affiliated Capital Medical University, No. 5 Jingyuan Street, Beijing 100043, China (e-mail: songhuimin3828@163.com).

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surgeon's experience,[6] although the risk is not completely eliminated in the hands of high-case-volume endocrine surgeons. Autotransplantation of at least 1 parathyroid gland, with or without histological confirmation, has been found by some,[7] but not all,[8] to avoid long-term hypoparathyroidism.

Although incidental parathyroidectomy is considered a minor complication of thyroid surgery, there are controversies about its risk factors.[9] Furthermore it is very difficult to obtain adequate evidence about the correlation between incidental parathyroidectomy and postoperative hypoparathyroidism (PH) due to the variable incidence of hypoparathyroidism reported in literature and the lack of consensus on the clinical significance and the risk factors of incidental parathyroidectomy.[10]

The aim of this present study was to evaluate the frequency, risk factors, and clinical significance of incidental extirpation of the parathyroid glands during thyroid surgery as well as the incidence and risk factors of PH and to evaluate their potential correlation. The results of this study are likely to provide information that will assist clinicians in predicting the risk of incidental parathyroidectomy at an early stage after surgery. This would help prevent risks of hypo- and hypercalcemia and guide patients on their individual prognosis. Identification of patients at risk is important because improved recovery of parathyroid function may be possible with therapy such as aggressive vitamin D and calcium substitution[5] and recombinant parathyroid hormone (PTH) may successfully treat hypoparathyroidism.[11]

2. Methods

2.1. Patients

A retrospective review was performed of 548 consecutive patients who underwent primarily transcervical total thyroidectomy with or without central neck dissection (CND), or subtotal thyroidectomy for malignant thyroid disease or benign diseases, performed by 4 surgeons in the Department of General Surgery of Beijing Chaoyang Hospital Affiliated Capital Medical University, Beijing, China, in the period between July 2005 and May 2016. To be included in the study, patients had to fulfil the inclusion criteria: diagnosed with a benign thyroid disease or with thyroid cancer, confirmed using imaging, pathology, and/or blood biochemistry (tumor markers); no history of thyroid or neck surgery; available blood results on postoperative 1 day; and underwent total thyroidectomy with or without CND[12] or subtotal thyroidectomy (bilateral benign lesions). Exclusion criteria included previously known parathyroid disease, previous cervical surgery, lobectomy, completion thyroidectomy in the area of the neck for thyroid carcinoma, intentional parathyroidectomy, lost to follow-up, and parathyroid autotransplantation. The patients with abnormal preoperative laboratory findings, including serum albumin, total calcium, alkaline phosphatase, intact PTH, were also excluded.

This study was conducted in accordance with the Declaration of Helsinki. This study was approved by the Ethics Committee of Beijing Chaoyang Hospital, Capital Medical University. Written informed consents were obtained from the patients.

2.2. Study design

We excluded 42 (42/590, 7.1%) patients who had undergone parathyroid gland autotransplantation. In our hospital, we do not routinely excise and transplant the parathyroid glands, especially in the dissection of inferior parathyroid glands. Therefore, we excluded cases with autotransplantation to reduce bias. The included patients were categorized into 2 groups according to the presence of incidental parathyroidectomy in the excised thyroid specimen. Patients in group inadvertent resection (IR) (n = 86) had IR of parathyroid glands, whereas patients in group non-IR (n = 462) had not had their parathyroid glands removed. The same patients were also divided into 2 other groups according to the presence of PH. Patients in group PH (n = 140) had PH (transient or permanent) after operation, whereas patients in group non-PH (n = 408) had not. This information is represented in a flowchart (Fig. 1).

All of the patients underwent operations performed by 4 consultant surgeons in our hospital who have a particular interest in and experience with thyroid surgery, using methods based on the 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer.[12] The follow-up period was >1 year, and all patients' medical records were reviewed to obtain clinicopathologic information. Preoperative evaluation was done in detail in each patient. Thyroid and central and lateral neck lymph nodes were examined by ultrasound. Ultrasonography-guided fine needle aspiration was performed to confirm if a malignant or metastatic lesion was suspected. Vocal cord function was obtained by direct or indirect laryngoscopy. In addition, thyroid hormone function, PTH, calcitonin, and serum calcium were also measured.

To identify risk factors for incidental parathyroidectomy, patients with and without incidental parathyroidectomy in the pathology specimen were compared in terms of age, sex, preoperative diagnosis, duration of the disease prior to thyroidectomy (defined as the time to diagnosis of the thyroid disorder until the thyroidectomy was undertaken), type of operation (total or subtotal thyroidectomy), excised thyroid weight, T classification, CND, tumor location, operation time, PTH, PH, and recurrent laryngeal nerve palsy. The surgical procedure involved total thyroidectomy with CND in patients with the following indications: patients with papillary thyroid carcinoma with clinically uninvolved central neck lymph nodes who had advanced primary tumors (T3 or T4); patients with lateral neck lymph node metastasis; or patients for whom the tissue sample pathological information was needed to clarify the lymph node status to plan further therapeutic steps.

2.3. Laboratory measurements and definitions

Parathyroid function was measured as intact parathyroid hormone (iPTH), because iPTH has a short biological half-life and so is an appropriate index of parathyroid gland function.[13]

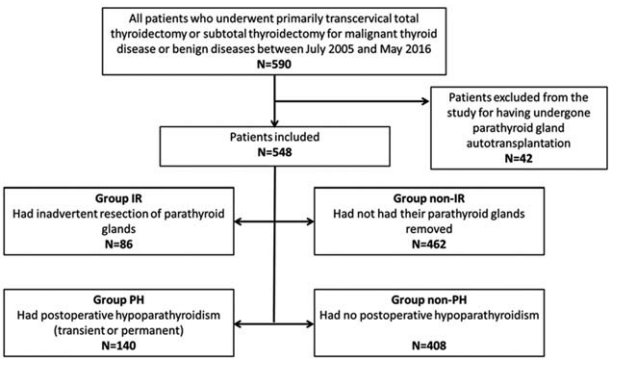

Figure 1. Flow chart showing the patient inclusion in the study and the patient groupings.

Intact PTH was estimated using an automated electrochemiluminescent immunoassay analyzer (Modular E170; Roche Diagnostic GmbH, Mannheim, Germany). The reference range was 15 to 65 pg/mL (according to the manufacturer's normative data). Serum calcium was determined using an automatic analyzer (Cobas c711; Roche Diagnostics). Serum calcium was measured using a colorimetric *o*-cresolphthalein assay with a reference range of 2.10 to 2.55 mmol/L. Baseline levels of iPTH, serum calcium were evaluated preoperatively, and their postoperative levels were measured on postoperative day 1, 1 week, and 6 months, and when necessary. PH was defined as any hypocalcemic symptom with decreased serum calcium level (<1.9 mmol/L). Calcium and vitamin D were administered according to the laboratory findings and hypocalcemic symptom. Hypocalcemic symptoms included perioral or facial numbness, a tingling sensation or paresthesia of the hands and/or feet, positive Chvostek or Trousseau signs, muscular cramp, and tetany. A diagnosis of permanent hypoparathyroidism was defined as postoperative serum PTH level below the normal value that required >12 months of calcium and vitamin D supplementation.[14] Hypoparathyroidism that healed within 12 months was considered transient. All patients were followed up for at least 12 months after surgery.

2.4. Determining incidental parathyroidectomy

The histological reports of all thyroid specimens were reviewed to identify those which described the presence of associated parathyroid tissue, the histological features of the thyroid and parathyroid glands, and the weight of the excised thyroid tissue. Incidental parathyroid excision was defined as the microscopic identification of parathyroid tissue in the resected thyroid specimen which is distant from any thyroid tumor, benign or malignant.[6] For the specimens that included parathyroid tissue, the slides were scrutinized to identify the location (intrathyroidal, extracapsular, or in the central node compartment), the number, and the histological features of the excised parathyroid glands. Extracapsular was defined as lying outside the thyroid capsule; intracapsular was defined as being encased within the thyroid capsule or lying just beneath the capsule, and intrathyroid was defined as being completely surrounded by thyroid parenchyma.

2.5. Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (version 20.0, SPSS, Inc, Chicago, IL). Measurement data are presented as mean ± standard deviation (SD) or median (range). Categorical data are presented as frequencies and percentage. Fisher exact test was used to evaluate the differences of incidences and Mann-Whitney *U* test was used to evaluate differences in means of variables between groups according to the parathyroid gland numbers excised. Multivariate analysis was performed to assess the independent risk factor for incidental parathyroidectomy and hypoparathyroidism. For multivariate analysis, binary logistic regression analysis was performed employing the variables that were statistically significant in univariate analysis. Forward logistic regression was used for the multivariate analysis. *P* values <.05 were considered statistically significant.

3. Results

3.1. Patients' characteristics

Of the 548 patients, 180 (32.8%) were male and 368 (67.2%) were female, with a male-to-female ratio of 1:2.0. Mean age was 42.4 ± 10.9 years. The mean excised thyroid weight was 35.5 ± 9.1 g. The patient diagnoses are presented in Table 1. Surgical indication was benign thyroid disease in 236 patients (43.1%), including nontoxic multinodular goiter in 198, toxic nodular goiter in 28, and toxic adenoma in 10. In the remaining 312 patients, malignant thyroid disease had been diagnosed preoperatively (Table 1). Most of them (295 cases) had papillary carcinoma (53.8%). A total of 548 thyroidectomies were performed and were included in the study. Total thyroidectomy was performed in 298 (54.4%); 86 patients (28.9%) without CND, 70 (23.5%) with unilateral CND, and 142 (47.7%) with bilateral CND, whereas subtotal thyroidectomy for benign thyroid disease was performed in 250 (45.6%). The duration of the disease prior to thyroidectomy was performed ranged from 1 to 10 years with a median of 3 years.

Table 1

Patient diagnosis.

Diagnosis	No. (%) of patients (n = 548)
Benign	
Nontoxic nodular goiter	198 (36.1)
Toxic nodular goiter	28 (5.1)
Toxic adenoma	10 (1.8)
Malignant	
Papillary carcinoma	295 (53.8)
Follicular carcinoma	11 (2.0)
Medullary carcinoma	5 (0.9)
Anaplastic carcinoma	1 (0.2)

Histopathological analysis identified incidentally excised parathyroid tissue in 86 (15.7%). One parathyroid gland was found in 78 cases (78/86, 90.7%), and 2 parathyroid glands were found in 8 cases (8/86, 9.3%). Neither case of malignant parathyroid disease, nor hyperplasia was identified. Incidentally excised parathyroid tissue was found to be intrathyroid in 24 (27.9%), extracapsular in 62 (72.1%), and in 14 cases (16.3%) parathyroid gland was identified in tissue that was considered to be lymph node, during the operation. PH occurred in 140 cases (25.5%). Transient hypoparathyroidism was found in 122 cases (22.3%) and permanent in 18 cases (3.3%). Transient laryngeal nerve palsy was identified in 15 cases (2.7%) whereas permanent palsy was found in 3 cases (0.5%).

3.2. Factors related to incidental parathyroidectomy

In comparing patients with and without incidental parathyroidectomy, univariate analysis revealed that in group IR, the patients with preoperative diagnosis of malignant disease ($P < .001$), total thyroidectomy ($P = .016$), weight of the excised thyroid tissue ($P < .001$), duration of the disease prior to thyroidectomy ($P < .001$), T classification (T3 and T4) ($P = .005$), CND ($P < .001$), recurrent laryngeal nerve palsy ($P = .003$), and postoperative transient hypoparathyroidism ($P < .001$) were all at significantly higher rates than in group non-IR. On the other hand, subtotal thyroidectomy ($P = .016$), duration of the disease prior to thyroidectomy ($P < .001$), T classification (T1 and T2) ($P = .005$), absence of CND ($P < .001$), no recurrent laryngeal nerve palsy ($P = .003$), and postoperative permanent hypoparathyroidism ($P < .001$) were at significantly higher rates in group non-IR than group IR.

There was no association between the incidental parathyroidectomy and age, gender, bilateral tumors, tumor location, and

Table 2

Univariate analysis of factors in the groups with and without incidental parathyroidectomy.

Variable	N	Incidental parathyroidectomy (n = 86) No. (%) group IR	No parathyroidectomy (n = 462) No. (%) group non-IR	*P*
Sex				
Male	180	26 (30.2)	154 (33.3)	
Female	368	60 (69.8)	308 (66.7)	.574
Age, y				
Mean ± SD		41 ± 8.0	42 ± 11.4	.63
Diagnosis				
Benign	236	20 (23.3)	216 (46.8)	
Malignant	312	66 (76.7)	246 (53.2)	<.001
Disease duration, y				
Mean ± SD		4 ± 1.7	3 ± 1.9	<.001
Procedure				
Total	298	57 (66.3)	241 (52.3)	.016
Subtotal	250	29 (33.7)	221 (47.7)	
Excised thyroid weight				
Mean ± SD		43 ± 12.5	34 ± 7.5	<.001
T classification	312			
T1	165	27 (31.4)	138 (29.9)	.005
T2	19	2 (2.3)	17 (3.7)	
T3	124	34 (39.5)	90 (19.5)	
T4	4	3 (3.5)	1 (0.2)	
CND	298			<.001
None	86	4 (4.7)	82 (17.7)	
Unilateral	70	9 (10.5)	61 (13.2)	
Bilateral	142	53 (6.2)	89 (19.3)	
Multiple tumors				
Yes	161	31 (36.0)	130 (28.1)	.139
No	387	55 (64.0)	332 (71.9)	
Bilateral tumor				
Yes	264	46 (53.5)	218 (47.2)	.283
No	284	40 (46.5)	244 (52.8)	
Tumor location				
Right	148	17 (19.8)	131 (28.4)	.189
Left	136	23 (26.7)	113 (24.5)	
Operation time, min				
Mean ± SD		129.6 ± 58.5	122.5 ± 52.7	.301
PTH, preop, pg/mL				.457
Mean ± SD		37.84 ± 11.47	39.01 ± 12.67	
PTH, postop 1 d				.091
Mean ± SD		14.34 ± 3.60	14.94 ± 3.22	
PTH, postop 1 wk				
Mean ± SD		19.70 ± 3.31	19.01 ± 3.39	.165
PTH, postop 6 mo				
Mean ± SD		29.44 ± 6.57	28.25 ± 7.85	.653
Parathyroid				
Intrathyroidal		24 (27.9)	0	
Extrathyroidal		62 (72.1)	0	
As lymph node		14 (16.3)	0	
Hypoparathyroidism	140			
Temporary	122	57 (66.3)	65 (14.1)	<.001
Permanent	18	7 (8.1)	11 (2.4)	
Nerve palsy				
Present	18	8 (9.3)	10 (2.2)	.003
Absent	530	78 (90.7)	452 (97.8)	

CND = cervical neck dissection, IR = inadvertent resection, PTH = parathyroid hormone, SD = standard deviation.

operation time. There were no differences in iPTH levels between patients with no inadvertent parathyroid glands and incidental parathyroid gland removed on day 1 after operation, or 1 week, and 6 months postoperatively (Table 2).

Multivariate analysis showed that preoperative diagnosis of malignant disease (OR = 1.766, 95% CI: 1.099–2.869, $P = .019$), duration of the disease prior to thyroidectomy (OR = 1.729, 95% CI: 1.066–2.805, $P = .027$), and CND (OR = 2.380, 95% CI: 1.475–3.840, $P < .001$) were independent risk factors in the development of incidental parathyroidectomy during thyroidectomy. However, the weight of the excised thyroid tissue, total thyroidectomy, T classification, postoperative transient hypopara-

Table 3

Logistic regression predicting the occurrence of incidental parathyroidectomy.

Variable	*P* value	Odds ratio	95% Confidence interval
Duration of the disease	.027	1.729	1.066–2.805
Diagnosis of malignant disease	.019	1.776	1.099–2.869
CND	<.001	2.38	1.475–3.840

CND = central neck dissection.

thyroidism, and recurrent laryngeal nerve palsy were not significant predictors when all 8 variables were considered together (Table 3).

3.3. Factors related to postoperative hypoparathyroidism

In comparing patients with or without hypoparathyroidism, the PH and non-PH groups, univariate analysis revealed that in the PH group, the rate of the patients with preoperative diagnosis of malignant disease, total thyroidectomy, the weight of the excised thyroid tissue, the duration of the disease prior to thyroidectomy, CND, recurrent laryngeal nerve palsy, and incidental parathyroidectomy were all significantly higher than in non-PH group. Patients with preoperative diagnosis of benign disease, subtotal thyroidectomy, the duration of the disease prior to thyroidectomy, the absence of CND, no recurrent laryngeal nerve palsy, and no incidental parathyroidectomy were all higher in the non-PH group than the PH group (all *P* values < .05) (Table 4). Patient's sex, localization of incidentally excised parathyroid tissue, T classification, and operation time were not significantly correlated with PH.

Multivariate analysis showed that preoperative diagnosis of malignant disease (OR = 1.725, 95% CI: 1.156–2.573, *P* = .008), CND (OR = 1.612, 95% CI: 1.056–2.461, *P* = .027), the duration of the disease prior to thyroidectomy (OR = 1.707, 95% CI: 1.144–2.548, *P* = .009), the weight of the excised thyroid tissue (OR = 1.644, 95% CI: 1.097–2.466, *P* = .016), and incidental parathyroidectomy (OR = 1.907, 95% CI: 1.280–2.842, *P* = .002) were independent risk factors of PH (Table 5). Incidental

Table 4

Univariate analysis of PH.

Variable	N	Postoperative hypoparathyroidism (n = 140) No. (%) group PH	Normal (n = 408) No. (%) group non-PH	*P*
Sex				
Male	180	41 (29.3)	139 (34.1)	
Female	368	99 (70.7)	269 (65.9)	.298
Age, y				.179
Mean ± SD		45 ± 10.9	44 ± 10.7	
Diagnosis				
Benign	236	42 (30.0)	194 (47.5)	
Malignant	312	98 (70.0)	214 (52.5)	<.001
Disease duration, y				
Mean ± SD		4 ± 1.7	3 ± 1.8	<.001
Procedure				
Total	298	92 (65.7)	206 (50.5)	.002
Subtotal	250	48 ((34.3)	202 (49.5)	
Excised thyroid weight				
Mean ± SD		39 ± 11.6	34 ± 7.7	<.001
T classification	312			.717
T1	165	77 (55.0)	88 (21.6)	
T2	19	4 (2.9)	15 (3.7)	
T3	124	57 (40.7)	67 (16.4)	
T4	4	2 (1.4)	2 (0.5)	
CND	298			.298
Unilateral	70	22 (15.7)	48 (11.8)	
Bilateral	142	55 (39.3)	87 (21.3)	
CND	298			.012
No	86	19 (13.6)	67 (16.4)	
Yes	212	79 (56.4)	133 (32.6)	
Operation time, min				.667
Mean ± SD		156.6 ± 46.5	155.6 ± 43.4	
Range		50.1–276.8	50.1–253.2	
Parathyroid				
Intrathyroidal	24	19 (13.6)	5 (1.2)	
Extrathyroidal	62	56 (40.0)	6 (1.5)	.165
As lymph node	14	12 (8.6)	2 (0.5)	
Nerve palsy				
Yes	18	11 (7.9)	7 (1.7)	.001
No	530	129 (92.1)	401 (98.2)	
Parathyroidectomy				
Yes	86	57 (40.7)	29 (7.1)	<.001
No	462	83 (59.3)	379 (92.9)	

CND = cervical neck dissection, PH = postoperative hypoparathyroidism, SD = standard deviation.

Table 5

Logistic regression predicting PH.

Variable	*P* value	Odds ratio	95% Confidence interval
Duration of the disease	.009	1.707	1.144–2.548
Diagnosis of malignant disease	.008	1.725	1.156–2.573
Incidental parathyroidectomy	.002	1.907	1.280–2.842
Excised thyroid weight	.016	1.644	1.097~2.466
CND	.027	1.612	1.056~2.461

CND = central neck dissection.

parathyroidectomy was significantly positively correlated with PH.

In comparing patients with transient hypoparathyroidism and those with permanent hypoparathyroidism, univariate analysis revealed that permanent hypoparathyroidism was more common than transient hypoparathyroidism for males ($P=.003$), and those with a higher excised thyroid weight ($P=.002$) (Table 6). Because of the small number of cases, however, we could not compare transient hypoparathyroidism with permanent hypoparathyroidism using logistic regression analysis.

4. Discussion

The aim of this study was to evaluate the frequency, risk factors, and clinical significance of incidental parathyroidectomy during thyroid surgery. In addition, the incidence and risk factors of post-procedure hypoparathyroidism and their potential correlation were investigated. The results show that 15.7% patients experienced incidental parathyroidectomy and 25.5% had PH. Total thyroidectomy and the weight of the excised thyroid tissue during thyroidectomy and preoperative diagnosis of malignant disease, duration of the disease prior to thyroidectomy, and concomitant CND were significant predictors of incidental parathyroidectomy.

Although the morbidity of thyroid surgery has significantly decreased during the last decades, inadvertent parathyroidectomy during thyroidectomy continues to challenge even experienced surgeons. According to recent literature, the rate of presence of parathyroid tissue in histopathologic examination varies widely from 5.2% up to 21.6%.[4,5] In the present trial, it was identified in 15.7% of the cases. In the literature, it is reported that in most cases only 1 parathyroid gland is resected incidentally. However, there are several reviews where 2 parathyroid glands were identified at a significant rate.[5] In the present study 1 parathyroid gland was found in 78 cases (78/86, 90.7%), and 2 parathyroid glands were found in 8 cases (8/86, 9.3%). Incidentally excised parathyroid glands were reported in an intrathyroidal location in 27.9% of the cases, in extracapsular location in 72.1%, and in a subcapsular location in 16.3%.[11] Because intrathyroidal location of incidentally excised parathyroid glands was found in 27.9% of the cases in our study, this high rate makes complete avoidance of incidental parathyroidectomy during thyroid operation virtually impossible. This conclusion has also been reached by another study that found 57.7% of resections were of intrathyroid location.[15]

Most authors agree that identifying parathyroid glands during thyroid surgery may help to reduce the incidence of parathyroid excision. A significant association between intraoperative identification of parathyroid glands and incidental removal of the glands was found. To prevent inadvertent injury devascularization, or resection of the parathyroid parenchyma, it is

Table 6

Univariate analysis: transient versus permanent hypoparathyroidism.

Variable	N 140	Transient hypoparathyroidism (n=122) No. (%) group TH	Permanent hypoparathyroidism (n=18) No. (%) group PH	*P*
Sex				
Male	41	30 (24.5)	11 (61.1)	0.003
Female	99	92 (75.5)	7 (38.9)	
Age, y				0.881
Mean ± SD		45 ± 8.3	46 ± 9.9	
Diagnosis				0.826
Benign	42	37 (30.3)	5 (27.8)	
Malignant	98	85 (69.7)	13 (72.2)	
Disease duration, y				
Mean ± SD		4 ± 1.9	4 ± 1.7	0.735
Procedure				
Total	92	79 (64.8)	13 (72.2)	0.533
Subtotal	48	43 ((35.2)	5 (27.8)	
Excised thyroid weight				
Mean ± SD		34 ± 7.2	41 ± 10.7	0.002
T classification	312			0.217
T1	77	70 (63.1)	7 (38.9)	
T2	4	3 (2.5)	1 (5.6)	
T3	57	48 (39.3)	9 (50.0)	
T4	2	1 (0.8)	1 (5.6)	
Operation time, min				0.377
Mean ± SD		122.9 ± 54.4	133.5 ± 55.2	
Range		53.3–261.5	63.0–238.8	
Parathyroidectomy				
Yes	57	51 (41.8)	6 (33.3)	0.495
No	83	71 (58.2)	12 (66.7)	

PH = postoperative hypoparathyroidism, SD = standard deviation, TH = transient hypoparathyroidism.

important to have a detailed anatomical understanding of parathyroid glands and their vasculature.[16] However, even with a surgeon of many years' experience undertaking extremely careful dissection an incidental parathyroid gland can be identified in thyroid specimens. Identification of the glands during surgery may be tricky even with a careful capsular dissection technique due to various locations of parathyroid tissue. It is usual for the location of the superior parathyroid glands to be at the superior pole of the posterior thyroid gland close to the cricothyroid junction, and though the inferior parathyroid glands are mostly located in the lower pole of the thyroid gland, they are sometimes in a different location such as the thymus and mediastinum. However, dissection in search of all parathyroid glands during surgery seems unwarranted and may be hazardous, and it may compromise their blood supply. Thus, it is not always possible to identify all 4 parathyroid glands. Hence, even with improvement in surgical techniques, the risk of incidental parathyroidectomy cannot be eliminated. Therefore, it is advised by various authors to carefully inspect the specimen for the presence of parathyroid glands and autotransplant them onto an adjacent sternomastoid muscle.[4] In the present study, the pathology specimens were reviewed after the operation so there was no possibility of their being reimplanted. There was a careful examination of the thyroid glands intraoperatively to identify the parathyroid glands and avoid injury of the parathyroid tissue or its blood supply. Although the various locations of parathyroid glands make the intraoperative identification a difficult procedure, our rate of incidental parathyroidectomy was 15.7% and the incidence of PH was 25.7%, within the normal range considering the related literature. However, the effort to salvage parathyroid glands at the time of surgery is a procedure that is expected to be widely used in future. It might be useful to identify a high-risk group to scrutinize more carefully during surgery. However, currently there is no consensus concerning the significant predictors of incidental parathyroidectomy. There are no risk factors that are common to all the related reviews and so further investigation is warranted in this area.

Total thyroidectomy is regarded as the treatment of choice for a variety of thyroid conditions, benign or malignant. However, total thyroidectomy is considered to be a significant predictor for incidental parathyroidectomy in many studies.[17] Univariate analysis of our results indicated that total thyroidectomy, although positively correlated ($P = .016$) with increased incidence of parathyroidectomy, was not an independent risk factor in multivariate analysis. In contrast to previous reports,[18] in our study, preoperative diagnosis of malignant disease, duration of the disease prior to thyroidectomy, and concomitant CND were significantly correlated with increased risk of incidental parathyroidectomy in multivariate analysis. However, preoperative diagnosis of malignancy was also found to be an independent predictor by some of the most recent related reviews.[19] These results demonstrate that incidental parathyroidectomy occurs more often when a patient undergoes a more aggressive thyroid approach for malignancy. Delay between the onset of the disease and the operation can lead to advanced thyroid disease, making the use of a more extensive surgical procedure necessary.

The wide variation in inadvertent parathyroidectomy rates[4,5] suggests that detection of the inadvertent parathyroidectomy rate is likely to be linked to the degree of rigor with which surgical specimens are analyzed. Paolo et al[17] have postulated that thyroid disease may influence the ability to find parathyroid tissue in a thyroid specimen. If a large number of sections are obtained and the specimen is examined very carefully the likelihood of identifying parathyroid tissue will increase. When a malignant disease is suspected the thyroid specimens may be sliced into thinner sections than when benign disease is suspected, this will increase the chance of finding incidental parathyroid glands in those specimens that contain malignant disease, which may partly explain the association of malignancy with higher rates of inadvertent parathyroidectomy. There were 5 cases in the present study where incidentally excised parathyroid gland was found in tissue that was thought to be lymph nodes intraoperatively. In 4 of these cases there was also malignant thyroid disease. CND is the most frequently identifiable risk factor of incidental parathyroidectomy in the related literature.[15,20] Radical neck dissection is also assessed as a risk factor by various authors.[21] Therefore, increased awareness during the dissection of the central compartment is necessary to avoid inadvertent excision of parathyroid tissue. The need for elective neck dissection should be considered, particularly in the prophylactic setting of well-differentiated thyroid cancer. Our study implies that elective neck dissection VI might be an interesting option in some types of thyroid malignancy to reduce the risk of incidental parathyroidectomy. Hence, surgeons should take care not to resect any of the parathyroid glands during CND, and especially, to preserve the inferior parathyroid gland. Total thyroidectomy without CND in patients with malignancy is appropriate for small (T1 or T2), noninvasive, clinically node-negative papillary thyroid cancers and for most follicular cancers. However, oncological principle must always be considered and complied with first. Completion thyroidectomy and reoperation have also been correlated with an increased risk of unintentional parathyroidectomy. A second dissection neck operation is complicated by scarring, inflammation, and bleeding, making accurate identification of the critical structures more difficult.[22] In our case patients who were reoperated on for recurrent or persistent thyroid disease were excluded from the study.

Postoperative hypocalcemia is the most frequent complication after thyroidectomy and can significantly increase the overall cost of operation due to prolongation of the hospital stay and the need for biochemical tests.[23] Injury, devascularization, and unintentional excision of parathyroid tissue have all been described as causes of postoperative hypocalcemia. Although many other factors have been studied, the cause of postoperative hypocalcemia seems to be multifactorial. In the literature,[11] it is reported that in most cases only 1 parathyroid gland is resected. There are also a number of reviews where 2 parathyroid glands were incidentally removed in a notable rate (from 13% up to 32.3%).[24] It is hard to find a review where IR of >2 parathyroid glands has been described. However, the occurrences of PH range widely and are often above 10%. The majority of patients will have 4 parathyroid glands or more, so it is likely that problems with calcium homeostasis will not result from removal of 1 or its fragments. But, removal of some parathyroid tissue is more likely when the surgery is difficult or particularly aggressive, so unintended removal of parathyroid tissue can be used to indicate the likelihood of damage to the other glands. This might lead to a notable decrease in parathyroid function. Thence, it arises that hypoparathyroidism is affected not only by incidental excision of parathyroid glands. It seems that in most cases of hypoparathyroidism, inadvertent excision is also combined with injury of the remaining parathyroid glands and their blood supplies. The incidence of PH cited in the literature range from 1.6% to 50% for temporary cases and from 1.5% to 4% for permanent cases.[9] In the present study, transient hypoparathyroidism occurred in 22.3% and it was permanent in 3.3% of the cases, which is within

the range of the international studies. Most reports concerning multivariate analysis on PH consider modified neck dissection, reoperations, and the surgical extent, in general, as independent predictors.[25] Total thyroidectomy and female sex have also been considered as risk factors.[5] In the present study, PH was significantly and positively correlated with preoperative diagnosis of malignant thyroid disease, concomitant CND, duration of the disease prior to thyroidectomy, the weight of the excised thyroid tissue, and incidental parathyroidectomy in multivariate analysis. A long duration of the disease before surgery is undertaken may lead to a potentially more problematic thyroid pathology, which requires an extensive operation with higher risk of damaging the parathyroid glands and leading to hypoparathyroidism. In contrast to previous studies,[20] we found a significantly positive correlation between PH and incidental parathyroidectomy during thyroidectomy.

The present study has some limitations. The study was retrospective and without randomization of the surgical extent. Also, the viability and vascularization of the preserved parathyroid glands was not confirmed. The number of intact or impaired parathyroid glands could not be assessed, which reflects actual parathyroid gland function. This highlights the risk of parathyroid-related complications in thyroid surgery and demonstrates the need for more prospective studies in this field. A further study involving the evaluation of the viability and vascularization of the preserved parathyroid glands and the comparison with cases of parathyroid autotransplantation is needed. As the numbers of patients undergoing CND increases, cases of incidental parathyroidectomy also increase; the incidental parathyroidectomy would be better analyzed in populations divided into those with benign and malignant tumors. However, because of limitations with the sample sizes this analysis was not possible in this present study.

The weight of the excised thyroid tissue and total thyroidectomy increase the incidence of unintentional parathyroidectomy; however, the preoperative diagnosis of malignant disease, concomitant CND, and the duration of the disease prior to thyroidectomy are significant predictors of unintentional parathyroidectomy. Incidental parathyroidectomy seems to be the result of the use of aggressive surgical procedures due to advanced thyroid disease. Delay of the operation, which leads to a more advanced thyroid disease, and preoperative diagnosis of malignancy make the use of extensive surgical procedures necessary. Delay of the operation seems to be also critical for the development of postoperative morbidity such as hypoparathyroidism. The correlation between inadvertent excision of parathyroid tissue and hypoparathyroidism is yet to be fully considered. We suggest that to avoid hypoparathyroidism, attempts to preserve the parathyroid glands in situ and their blood supply should be made, by meticulous isolating techniques during thyroid surgery. The present study suggests that prevention of incidental parathyroidectomy will decrease substantially postoperative morbidity.

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