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ORIGINAL ARTICLE

Predictive factors for longer operative times for thyroidectomy

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Summary *Background/Objective:* Conventional open thyroidectomy is considered as a safe surgery nowadays. However, surgeons sometimes encounter unexpected difficulty when performing thyroidectomies. The aim of this paper was to identify the predictors of a difficult thyroidectomy for the management of patients with papillary thyroid carcinoma.
Methods: A database of patients who underwent open conventional thyroidectomy with cervical lymph node dissection after diagnosed papillary thyroid carcinoma between July 2008 and June 2013 was examined. In addition, the patients were subgrouped by difficult thyroidectomy (DT) and nondifficult thyroidectomy to determine the predictors of DT according to operation time. Clinicopathologic characteristics, surgical outcomes, and postoperative morbidities were investigated.
Results: No between-group differences in clinicopathologic factors and postoperative complications, except for male sex ($p < 0.001$) and tumor size ($p = 0.039$), were noted. Male sex [odds ratio (OR) 4.158, 95% confidence interval (CI) 2.020–8.559, $p = 0.043$] and age < 45 years (OR 2.239, 95% CI 1.304–3.843, $p = 0.003$) were independent factors associated with DT in a multivariate logistic regression model. Elevated antithyroglobulin antibody (OR 1.004, 95% CI 1.000–1.008, $p = 0.030$) was a variable which is statistically significant, but not clinically significant.

Conflicts of interest: The authors have declared no conflicts of interest.
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Discussion: Young age and male sex might be regarded as predictors of DT. Expecting DT before surgery might help surgeons, especially beginners, prevent troublesome situations.

1. Introduction

Thyroid cancer is the most frequently occurring endocrine cancer, and its incidence is increasing worldwide.[1,2] Thyroidectomy was regarded as a dangerous surgery with high mortality even in the early 20th century.[3] However, with improved operative techniques and the understanding of the thyroid anatomy and physiology, thyroidectomy has become a safe surgery. Today, thyroidectomy is granted as an operation with low morbidity and rare mortality, especially in a high-volume hospital.[4,5] Although complications of thyroidectomy, such as recurrent laryngeal nerve palsy or hypothyroidism, are rare, they still occur. Experts report permanent complications in 1–2% of patients.[6,7] Transient problems occur much more frequently, but the rates vary depending on the indication for thyroidectomy, patient factors, etc.[8]

Most thyroid surgeons agree that higher complication rates are associated with certain thyroid diseases with difficult resections. These conditions include increased gland size, fibrosis, vascularity, and inflammation.[9–11] Although certain thyroid diseases such as hyperthyroidism, goiter, and thyroiditis lead to a more difficult operation, the degree of difficulty varies and is hard to predict preoperatively. Literature describing the quantification of difficulty for thyroidectomy is limited.[8,12] Hence, more objective methods for a difficulty scale are needed.

The prevalence of thyroiditis among papillary thyroid carcinoma (PTC) patients who had thyroidectomy has been reported to be > 40% in a noncase controlled study.[13] However, the degree of difficulty is questionable before the operation begins. Therefore, the need to identify predictors of difficult thyroidectomy for the management of patients with PTC seemed inevitable.

2. Methods

2.1. Study design and setting

A prospective database of 1293 patients who underwent thyroid surgery by an experienced single endocrine surgeon between July 2008 and June 2013 at the Department of Surgery, Korea University College of Medicine, Seoul, Korea, was reviewed. Inclusion criteria were patients who underwent conventional open thyroidectomy after a diagnosis of PTC or suspected PTC upon preoperative fine needle aspiration. All patients were offered either lobectomy or total thyroidectomy with cervical lymph node (LN) dissection according to the standard protocols used in Anam Hospital, Seoul, Korea. Of 714 total patients, 548 patients (75.8%) had total thyroidectomy and 166 (24.2%) had lobectomy. The study protocol was approved by our Institutional Review Board of Korea University, Anam Hospital.

2.2. Protocols

The surgical extent of the operation was chosen based on the thyroid nodule size and the status of the LN both with preoperative studies and frozen section analysis. If the nodule was > 1 cm and no LN metastasis was seen, a total thyroidectomy with ipsilateral central LN dissection was performed. If the tumor size was > 1 cm and LN enlargement was observed before or during surgery, a total thyroidectomy with bilateral central LN dissection was performed. However, if the size was < 1 cm and no extrathyroidal extension or LN enlargement was noted, a lobectomy with ipsilateral central LN dissection was performed. The patient underwent either total thyroidectomy or lobectomy with the identification of the recurrent laryngeal nerves and conservation of the parathyroid glands. A wound drain (100 mL, 3.2 mm diameter, Barovac Sewoon Medical Co., Seoul, Korea) was placed in patients undergoing thyroidectomy and was removed when the amount of liquid drained was < 20 mL. We measured parathyroid hormone (PTH) levels during the immediate postoperative period (beginning 3 hours after the thyroidectomy was complete) and serum calcium and ionized calcium levels daily. The patients typically left the department 3 days after surgery when they had undergone total thyroidectomy and 2 days after surgery in the case of lobectomy.

Perioperative complications such as hematoma, seroma, infection, vocal cord palsy observed by stroboscopy, and hypoparathyroidism (serum ionized calcium < 4.4 mg/dL or PTH < 8 pg/mL) were assessed. We especially examined the number of incidentally resected parathyroid glands in each group, based on pathologic results. All patients were followed-up in the same manner, which included clinical examinations within 1 week of discharge and a 3–6-month follow-up. The minimum follow-up period was 6 months to confirm or rule out persistent sequelae. Any complications still noted after 6 months were regarded as permanent.

Patients with permanent hypoparathyroidism were defined as those with nonnormalization of laboratory data, which includes the PTH level (normal range: PTH > 8 pg/mL) and calcium level 1 year after the surgery, who required extrinsic calcium uptake. Using laryngoscopy, we evaluated vocal cord palsy in patients complaining of hoarseness, difficulty in voicing high tones, and tracheal aspiration. All patients underwent indirect laryngoscopy with stroboscopy before and after the operation.

2.3. Outcomes

The data recorded for each patient included the following: age, gender, body mass index (kg/m^2), thyroid surgery type (e.g., total thyroidectomy), dominant nodule size (cm) on ultrasound, operative time, hospitalization duration in days, number of retrieved LNs, and number of metastatic LNs. The thyroid function test in our institution includes T3, free T4, thyroid stimulating hormone, thyroglobulin antigen, antithyroglobulin antibody (anti-Tg Ab), and anti-microsomal antibody.

2.4. Difficult thyroidectomy

Operating time was regarded as a scale for difficulty of open conventional thyroidectomy. A longer operation time was set as the parameter for difficulty in thyroidectomy in the same surgical setting. Therefore, only the subgroups of patients who had undergone total thyroidectomy with cervical LN dissection ($N = 548$) were further analyzed. Those with operation times above the 75th percentile were regarded to have had a difficult thyroidectomy (DT; $N = 137$), while those with operation times below the 25th percentile were classified as nondifficult thyroidectomy (NDT). The surgeon who had performed the thyroidectomies (H.Y.K.) had experienced > 100 cases of thyroidectomy, which meant he had already overcome the turning point of learning curve in prior institutions. Patient demographics were also analyzed to predict "difficulty" in open conventional thyroidectomy before surgery.

2.5. Operative procedures

Open conventional thyroidectomy was performed using a 5–6 cm collar incision on the anterior neck. After dissecting an adequate subplatysmal flap, the midline of the strap muscle was divided to expose the thyroid gland. Thyroidal vessels were individually ligated by coagulation with a Harmonic scalpel close to the thyroid gland to preserve the superior laryngeal nerve and parathyroid glands. The entire cervical course of the ipsilateral recurrent laryngeal nerve was traced and preserved. Therapeutic or prophylactic cervical LN dissection was performed in all cases.

2.6. Statistical analysis

The Chi-square test was used to compare categorical variables, and independent two-sample *t* tests were used to compare the values of continuous variables between the DT and NDT groups. The results are presented as mean ± standard deviation or *n* (%) as appropriate. Variables with statistically significant predictors in the univariate analysis were assessed in a multivariate analysis with a binary logistic regression model. Results are presented as an odds ratio (OR) with a 95% confidence interval (CI). All statistical tests were two-sided, and $p < 0.05$ was considered statistically significant. Statistical analyses were performed with IBM SPSS software version 20.0 (SPSS Inc., Chicago, IL, USA) for Windows.

3. Results

3.1. Clinicopathologic characteristics

Table 1 shows the clinicopathologic characteristics of the patients who underwent thyroidectomy. In this analysis, no factors were significantly different between the DT and NDT groups except for sex ($p < 0.001$) and older than 45 years. Body mass index was higher in the DT group, but this difference was not statistically significant ($p = 0.437$). The dominant nodule size on ultrasound ($p = 0.400$) and thyroid function test including T3 ($p = 0.626$), free T4 ($p = 0.192$), thyroid stimulating hormone ($p = 0.474$), thyroglobulin antigen ($p = 0.541$), anti-Tg Ab ($p = 0.688$), and anti-microsomal antibody ($p = 0.530$) were also comparable between the two groups. We added the comparison between the 90th percentile and 10th percentile in order to find out whether the results are solid (Table 2). In this comparison, we had a similar outcome.

Table 1 Comparison of the preoperative characteristics between the difficult thyroidectomy group and nondifficult thyroidectomy group.

Characteristics	DT ($n = 137$)	NDT ($n = 137$)	p
Age (y)	48.26 ± 14.08	54.80 ± 11.39	0.420
Age (y)			
< 45	61 (44.5)	34 (24.8)	0.001
≥ 45	76 (45.5)	103 (75.2)	
Sex			<0.001
Female	99 (72.3)	125 (91.2)	
Male	38 (27.7)	12 (8.8)	
BMI (kg/m^2)	25.10 ± 4.05	24.74 ± 3.30	0.437
T3 (ng/dL)	116.90 ± 32.52	109.69 ± 30.37	0.626
fT4 (ng/dL)	2.08 ± 9.52	1.26 ± 0.25	0.192
TSH (uIU/mL)	2.02 ± 1.59	2.21 ± 2.64	0.474
Tg Ag (ng/mL)	62.72 ± 268.71	17.15 ± 28.47	0.541
Anti-Tg Ab (IU/mL)	74.19 ± 121.23	48.01 ± 56.08	0.688
Anti-MIC Ab (U/mL)	131.89 ± 385.85	105.09 ± 361.68	0.530
Predicted thyroiditis	48 (35.0)	44 (32.1)	0.609
Dominant nodule size on ultrasound (cm)	1.24 ± 0.92	0.99 ± 0.68	0.400

Data are presented as *n* (%) or mean ± SD.
Anti-MIC Ab = antimicrosomal antibody; Anti-Tg Ab = antithyroglobulin antigen; BMI = body mass index; DT = difficult thyroidectomy; fT4 = free T4; NDT = nondifficult thyroidectomy; SD = standard deviation; Tg Ag = thyroglobulin antigen; TSH = thyroid stimulating hormone.

3.2. Surgical outcomes and postoperative morbidities

Patients with DT showed a higher T-stage than those with NDT ($p = 0.039$). Other surgical outcomes, including hospitalization duration ($p = 0.420$), pathologic tumor size ($p = 0.063$), multiplicity ($p = 0.606$), and the number of metastatic LNs ($p = 0.258$) and retrieved LNs ($p = 0.154$) showed no statistically significant difference (Table 3). A comparison of the postoperative complications also showed no significant differences between the two groups (Table 4).

Table 2 Comparison of the preoperative characteristics between the difficult thyroidectomy group and nondifficult thyroidectomy group with above the 90th percentile and below the 10th percentile.

Characteristics	DT (n = 54)	NDT (n = 54)	p
Age (y)	46.00 ± 15.07	55.87 ± 12.82	0.341
Age (y)			0.003
< 45	29 (53.7)	14 (25.9)	
≥ 45	25 (46.3)	40 (74.1)	
Sex			<0.001
Female	39 (72.2)	51 (94.4)	
Male	15 (27.8)	3 (5.6)	
BMI (kg/m^2)	24.62 ± 4.30	24.79 ± 3.08	0.454
T3 (ng/dL)	110.42 ± 29.93	108.80 ± 31.11	0.500
fT4 (ng/dL)	2.29 ± 15.17	1.23 ± 0.23	0.781
TSH (uIU/mL)	2.28 ± 2.11	1.95 ± 1.16	0.424
Tg Ag (ng/mL)	113.60 ± 416.51	17.15 ± 28.47	0.453
Anti-Tg Ab (IU/mL)	73.48 ± 124.04	43.49 ± 45.03	0.662
Anti-MIC Ab (U/mL)	155.53 ± 447.45	84.66 ± 188.82	0.487
Predicted thyroiditis	21 (38.9)	17 (31.5)	0.420
Dominant nodule size on ultrasound (cm)	1.45 ± 1.04	1.10 ± 0.78	0.544

Data are presented as n (%) or mean ± SD.
Anti-MIC Ab = antimicrosomal antibody; Anti-Tg Ab = antithyroglobulin antigen; BMI = body mass index; DT = difficult thyroidectomy; fT4 = free T4; NDT = nondifficult thyroidectomy; SD = standard deviation; Tg Ag = thyroglobulin antigen; TSH = thyroid stimulating hormone.

Table 3 Comparison of surgical outcomes between the difficult thyroidectomy group and nondifficult thyroidectomy group.

Characteristics	DT (n = 137)	NDT (n = 137)	p
Hospitalization duration (d)	3.48 ± 1.02	3.46 ± 1.19	0.420
Tumor size (cm, pathological)	1.19 ± 0.93	0.84 ± 0.57	0.063
T stage			0.039
T0	5 (3.6)	3 (2.2)	
T1	50 (36.5)	74 (54.0)	
T2	2 (1.5)	1 (0.7)	
T3	78 (56.9)	59 (43.1)	
T4	2 (1.5)	0	
No. of resected PTG			0.670
0	96 (70.1)	100 (73.0)	
1	29 (21.2)	29 (21.2)	
2	11 (8.0)	8 (5.8)	
3	1 (0.7)	0	
Multiplicity			0.606
Single	75 (54.7)	81 (59.1)	
Multifocal, unilateral	19 (13.9)	14 (10.2)	
Multifocal, bilateral	43 (31.4)	42 (30.7)	
Thyroiditis	15 (10.9)	9 (6.6)	0.200
No. of retrieved lymph nodes	10.89 ± 7.09	7.62 ± 5.45	0.154
No. of metastatic lymph nodes	1.88 ± 2.90	1.00 ± 1.97	0.258
LNR	0.17 ± 0.24	0.13 ± 0.23	0.637

Data are presented as n (%) or mean ± SD.
DT = difficult thyroidectomy; LNR = lymph node ratio (the number of positive lymph nodes divided by the total amount of retrieved lymph nodes); NDT = nondifficult thyroidectomy; PTG = parathyroid gland; SD = standard deviation.

3.3. Multivariate analysis

A univariate analysis was performed using a logistic regression model to determine which clinicopathologic factors were associated with DT. The variables found to be significant on univariate analysis ($p < 0.05$) and those assumed to be associated predictors of DT were then included in the final multivariate model (Table 5). The variables included in the final model were male sex (OR 4.158, 95% CI 2.020–8.559, $p = 0.043$), age < 45 years (OR 2.239, 95% CI 1.304–3.843, $p = 0.003$), preoperative size > 1 cm (OR 1.338, 95% CI 0.960–1.864, $p = 0.086$), and elevated anti-Tg Ab (OR 1.004, 95% CI 1.000–1.008, $p = 0.030$).

4. Discussion

In the current study, we analyzed the outcomes of patients who underwent open conventional thyroidectomy and assessed the predictors of complications during thyroidectomy. However, literature that investigates the predictors of difficult thyroid surgery is scarce. A few recent studies reported the thyroidectomy difficulty scale to be associated with a longer operation time and complications.[8,12]

Table 4 Comparison of the postoperative morbidities between the difficult thyroidectomy group and nondifficult thyroidectomy group.

Characteristics	DT (n = 137)	NDT (n = 137)	p
Hypoparathyroidism			
Transient	19 (13.9)	15 (10.9)	0.538
Permanent	1 (0.7)	0	0.316
Vocal cord palsy			
Transient	1 (0.7)	0	0.316
Permanent	0	0	—
Hematoma	1 (0.7)	1 (0.7)	1.000
Chyle leakage	0	0	—
Wound infection	1 (0.7)	0	0.316
Seroma	0	1 (0.7)	0.316

Data are presented as n (%).
DT = difficult thyroidectomy; NDT = nondifficult thyroidectomy.

Table 5 Multivariate analysis of associations between clinicopathologic factors and difficult thyroidectomy.

Characteristics	p	OR	CI
Male	< 0.001	4.158	2.020–8.559
Age < 45 y	0.003	2.239	1.304–3.843
Preoperative size > 1 cm	0.086	1.338	0.960–1.864
Elevated anti-Tg Ab	0.030	1.004	1.000–1.008

Anti-Tg Ab = antithyroglobulin antibody; CI = confidence interval; OR = odds ratio.

However, the thyroidectomy difficulty scale is a subjective scale that is graded after the surgery. Therefore, it is still hard to predict before the surgery whether the thyroid surgery will be difficult.

Predicting difficulty on a scale with objective preoperative factors would be meaningful for evaluating DT. In our study, preoperative clinical factors and laboratory tests in subgroup analyses were evaluated to identify the predictors of DT: male sex (OR 4.158, 95% CI 2.020–8.559, $p = 0.043$) and younger than 45 years (OR 2.239, 95% CI 1.304–3.843, $p = 0.003$) were estimated to be predicted independent factors in a multivariate analysis. Elevated anti-Tg Ab (OR 1.004, 95% CI 1.000–1.008, $p = 0.030$) was a variable which is statistically significant, but not clinically significant.

A possible reason why the operation time is longer in young men might be related to tough neck tissue. Hence, it takes longer to create a flap and dissect in the field of operation. It may be estimated that the operation of larger sized nodules would be difficult to perform. Nevertheless, our result showed that there is no significant difference in relationship between the nodule size and DT. With larger numbers, however, the results might show significance between the size and DT.

Thyroiditis is a common disease of the thyroid in which the immune system mostly reacts against a variety of thyroid antigens.[14] Therefore, the physiological, protective process used by the organism in response to tissue damage results in inflammation. It is well known that thyroiditis might be a risk factor for potentially more difficult thyroid surgery.[11,15] Patients with elevated anti-Tg Ab were more related to DT in our study than NDT statistically but not clinically (OR 1.004, 95% CI 1.000–1.008, $p = 0.030$).

With regard to adequate LN dissection, our data revealed that the number of retrieved LNs (10.99 ± 7.09 nodes vs. 7.62 ± 5.45 nodes, $p = 0.154$) and metastatic LNs (1.88 ± 2.90 nodes vs. 1.00 ± 1.94 nodes, $p = 0.258$) was larger and the lymph node ratio (0.17 ± 0.24 vs. 0.13 ± 0.23, $p = 0.637$) was higher in the DT group compared with the NDT group. This result enabled us to assume that the status of LNs did not affect operation time in total thyroidectomy.

The incidence of transient ($p = 0.538$) and permanent hypoparathyroidism ($p = 0.316$) did not differ between the two groups, although the numbers were small. In the present study, the incidences of either transient or permanent vocal cord palsy were even lower, but no significant difference between the two groups was noted. The results are comparable to those of previous studies, which showed that transient hypocalcemia after open thyroidectomy ranges from 0.3% to 49% and permanent hypocalcemia ranges from 0% to 13%.[16] In addition, the incidence of transient vocal cord palsy was reported to range from 0% to 6%, and the incidence of permanent vocal cord palsy is <1%.[17]

With all of these efforts, the major limitations of the present study are the retrospective design with a small number of patients from a single institution in Korea. Therefore, the concept of difficulty in thyroidectomy in other ethnic groups could be different. This research is difficult to perform in a prospective randomized clinical trial, in that operating time itself cannot be randomized before the surgery. To overcome selection bias and heterogeneity, we tried a multivariate analysis to see if there is an association between DT and any other clinicopathologic factors. Another limitation is the fact that other unknown factors for which we had no records of might have affected the results. Lastly, difficult operations lead to longer operative times. However, our study has its own strength in that this study was the first to describe objective predictive factors of DT.

In conclusion, our retrospective analysis showed that young age and male sex were predictive factors for DT in terms of operating time. However, complication rates after DT might not be higher than those after NDT. Expecting DT before surgery might help surgeons, especially beginners, prevent troublesome situations.

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