

# Postoperative Complications of Thyroid Cancer in a Single Center Experience

The aim of this study was to investigate the complications following surgical treatment of thyroid cancer and the association between the extent of surgery and complication rates. A total of 2,636 patients who underwent surgery due to thyroid cancer were retrospectively reviewed to identify surgical complications. Complication rates were assessed according to the extent of surgery, which was classified as follows; less-than-total thyroidectomy with central compartment node dissection (CCND) (Group I, n=636), total thyroidectomy with CCND (Group II, n=1,390), total thyroidectomy plus ipsilateral neck dissection (Group III, n=513), and total thyroidectomy plus bilateral neck dissection (Group IV, n=97). The most common surgical complication was symptomatic hypoparathyroidism, of which 28.4% of cases were transient and 0.3% permanent. The other surgical complications included vocal cord palsy (0.7% transient, and 0.2% permanent), hematoma (0.5%), seroma (4.7%), chyle fistula (1.8%), and Horner's syndrome (0.2%). The complication rates increased significantly with increasing the extent of surgery from Group I to Group IV. The more extensive surgery makes more complications, such as hypoparathyroidism, seroma, and others.

**Key Words :** *Intraoperative Complications; Thyroid Neoplasms; Thyroidectomy; Lymph Node Excision*

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## INTRODUCTION

Surgical resection is the treatment of choice for patients with thyroid cancer; however, the optimal extent of thyroid resection and lymph node dissection remain controversial. Based on the extent of disease, total thyroidectomy or less-than-total thyroidectomy is chosen. Central compartment node dissection (CCND) is usually performed with thyroidectomy for prophylactic purposes, whereas lateral neck dissection is performed only in patients in whom metastasis is clinically evident. In cases of follicular cancer, a hemithyroidectomy is usually performed for minimally invasive cancers, and a total thyroidectomy for widely invasive cancers, although the optimal approach for these cancers remains controversial. In patients with medullary cancer, total thyroidectomy with compartment-oriented node dissection is usually considered adequate (1).

Although the benefits of extended resection are an increased survival rate and a decreased recurrence rate, all surgical procedures have the potential to cause complications, and more extensive resections may be associated with substantially increased complication rates (2, 3).

We therefore investigated surgical complications after thyroid cancer surgery and the association between the extent of surgery and complication rates.

## MATERIALS AND METHODS

Approval to conduct a retrospective review of the images and medical records of patients was obtained from the Institutional Review Board of Yonsei University College of Medicine. Medical records of 3,137 patients who underwent thyroid surgery at the Thyroid Cancer Clinic, Department of Surgery, Yonsei University College of Medicine between January 2006 and December 2007 were retrospectively reviewed.

Patients who had a recurrent or persistent thyroid cancer and who underwent thyroid surgery for benign thyroid disease were excluded, and 2,636 (84.0%) patients were enrolled in the present study. Of the 2,636 patients, 2,596 (98.5%) had papillary cancers, 22 (0.8%) follicular cancers, and 18 (0.7%) medullary cancers. Patients could be divided into four groups according to the extent of surgery; less-than-total thyroidectomy with central compartment node dissection (CCND) (Group

I, n=636); total thyroidectomy with CCND (Group II, n=1390); total thyroidectomy plus ipsilateral neck dissection (Group III, n=513) and total thyroidectomy plus bilateral neck dissection (Group IV, n=97).

The extent of surgery was determined according to the American Thyroid Association (ATA) guidelines (4). A total thyroidectomy was performed if any of the following criteria were met: age <15 yr or >45 yr, a history of radiation exposure in the head and neck, known distant metastases, contralateral thyroid nodules, extrathyroidal extension, cervical lymph node involvement, and a first-degree family history of thyroid carcinoma. A less-than-total thyroidectomy was selected for patients with small, isolated, intrathyroidal carcinomas without gross nodal involvement. Central compartment clearance was performed routinely for prophylactic purposes, whereas lateral neck dissection was performed only in patients with clinically positive lateral neck nodes.

All patients underwent preoperative examination of vocal cord movement by direct laryngoscopy and routine preoperative measurements of serum calcium, phosphorus, and parathyroid hormone levels. During surgery, all parathyroid glands were identified and preserved as much as possible. Postoperative laryngoscopy was performed only in patients who experienced symptomatic voice changes after surgery.

Postoperative complications including hypoparathyroidism, recurrent laryngeal nerve (RLN) injury or palsy, hematoma, seroma, chyle fistula, and Horner's syndrome were assessed based on clinical findings. Hypoparathyroidism was considered permanent when calcium and vitamin D therapy was required more than 6 months after surgery. Regarding RLN palsy, permanent palsy included direct injury to the nerve and cord palsy more than 6 months.

The surgical complications and complication rates were assessed for each of the four patient groups and comparisons among groups were made using Fisher's exact test; when nec-

essary, data were transformed to obtain results distributed with equal variance. Pearson's chi-square test was used to assess the relationship between each group and the following potential predictors of surgical complications: age, sex, tumor size, nodal status, extracapsular invasion, underlying thyroiditis, multiplicity, hospital stay and postoperative complications. Statistical significance was defined as a *P* value <0.05.

## RESULTS

Demographic and clinicopathologic characteristics of the total patient population and of the four patient groups are listed in Table 1. The proportion of male patients, mean tumor diameter, number of dissected and metastatic lymph nodes, and mean hospital stay increased significantly with increasing extent of surgery (*P*<0.001). However, mean age at diagnosis had no differences between each group (*P*<0.001) (Table 1).

Assessment of complications showed that symptomatic hypoparathyroidism occurred in 757 patients (28.7%), of whom 749 (28.4%) cases were transient and 8 (0.3%) were permanent hypoparathyroidism. And the incidence rates increased with increasing extent of surgery (Table 2). The incidence of incidentally removed parathyroids during surgery was not different between groups (*P*=0.002). However, the incidence of parathyroid autotransplantation increased significantly with increasing the extent of surgery (Table 3).

The incidence of RLN palsy, which was 0.8% in all patients, was also significantly related to the extent of surgery, with incidences of 0.5%, 0.6%, 1.2%, and 3.1% in Groups I, II, III, and IV, respectively (*P*=0.026). By contrast, the incidence of hematoma, which was 0.5% overall, was not associated with the extent of surgery (*P*=0.744).

The incidence rates of other complications were also significantly associated with the extent of surgery. For example,

Table 1. Demographic and clinicopathologic characteristics of patients

Parameters	Total (n=2,636)	Group I (n=636)	Group II (n=1,390)	Group III (n=513)	Group IV (n=97)	<i>P</i> value
Age (mean, yr)	46.8±11.6	44.0±10.9	48.3±11.1	46.4±12.8	45.1±14.0	<0.001
Male:female	360:2276 (1:6.3)	68:568 (1:8.4)	172:1228 (1:7.1)	95:418 (1:4.4)	25:72 (1:2.9)	<0.001
Tumor size (mean, cm)	1.02±0.77	0.66±0.51	0.99±0.65	1.43±0.97	1.70±1.12	<0.001
Capsular invasion	53.5%	30.4%	55.9%	72.3%	72.2%	<0.001
Multiplicity						<0.001
Unilateral	10.5%	11.4%	10.6%	9.0%	10.4%	
Bilateral	23.9%	2.8%	29.3%	30.5%	50.0%	
Underlying thyroiditis	5.2%	5.9%	5.2%	3.6%	9.7%	0.080
Nodal status (mean)						
Dissected lymph nodes	11.3±15.1	5.2±4.6	5.3±4.1	25.2±18.1	48.1±22.0	<0.001
Metastatic lymph nodes	2.1±4.6	0.4±1.0	0.9±1.7	5.0±6.4	11.1±10.5	<0.001
Hospital stay (mean, days)	5.6±2.7	4.8±1.9	5.3±2.2	6.9±3.2	9.0±4.6	<0.001

Group I, less-than-total thyroidectomy with central compartment node dissection; Group II, total thyroidectomy with central compartment node dissection; Group III, total thyroidectomy plus ipsilateral neck dissection; Group IV, total thyroidectomy plus bilateral neck dissection.

**Table 2.** Complication rates according to the extent of thyroid surgery

Parameters	Total (n=2,636)	Group I (n=636)	Group II (n=1,390)	Group III (n=513)	Group IV (n=97)	P value
Hypoparathyroidism						<0.001
Transient	28.4%	6.6%	30.7%	44.4%	53.6%	
Permanent	0.3%	0%	0.3%	0.6%	1.0%	
RLN palsy						0.026
Transient	0.7%	0.5%	0.4%	1.0%	3.1%	
Permanent	0.2%	–	0.2%	0.2%		
Hematoma	0.5%	0.3%	0.4%	0.6%	1.0%	0.744
Seroma	4.7%	3.9%	3.7%	7.7%	8.3%	0.002
Chyle fistula	1.8%	0.5%	0.8%	5.1%	6.2%	<0.001
Horner's syndrome	0.2%	–	–	0.8%	1.0%	0.001

Group I, less-than-total thyroidectomy with central compartment node dissection; Group II, total thyroidectomy with central compartment node dissection; Group III, total thyroidectomy plus ipsilateral neck dissection; Group IV, total thyroidectomy plus bilateral neck dissection; RLN, recurrent laryngeal nerve.

**Table 3.** Parathyroid glands removed by surgery

	Total (n=2,636)	Group I (n=636)	Group II (n=1,390)	Group III (n=513)	Group IV (n=97)	P value
Parathyroid removal	379 (14.4%)	95 (14.9%)	194 (14.0%)	76 (14.8%)	14 (14.4)	0.002
One	334 (88.1%)	79 (83.2%)	173 (89.2%)	69 (90.8%)	13 (92.9%)	
Two	42 (11.1%)	14 (14.7%)	20 (10.3%)	7 (9.2%)	1 (7.1%)	
Three	3 (0.8%)	2 (2.1%)	1 (0.5%)	0 (0%)	0 (0%)	
Autotransplantation	17 (0.6%)	2 (0.3%)	8 (0.6%)	5 (1.0%)	2 (2.1%)	0.037

Group I, less-than-total thyroidectomy with central compartment node dissection; Group II, total thyroidectomy with central compartment node dissection; Group III, total thyroidectomy plus ipsilateral neck dissection; Group IV, total thyroidectomy plus bilateral neck dissection.

seroma, which was reported in 4.7% of all patients, was 3.9%, 3.7%, 7.7%, and 8.3% of patients in Groups I, II, III, and IV, respectively ( $P=0.002$ ). Chyle fistula, which had an overall incidence of 1.8%, was reported in 0.5%, 0.8%, 5.1%, and 6.2% of patients in Groups I, II, III, and IV, respectively ( $P<0.001$ ); and Horner's syndrome, which had an overall incidence of 0.2%, was reported in 0%, 0%, 0.8%, and 1.0% of patients in Groups I, II, III, and IV, respectively ( $P=0.001$ ) (Table 2).

## DISCUSSION

Postoperative complications following thyroid surgery can include transient and permanent hypoparathyroidism, RLN injury or palsy, hematoma, seroma, chyle fistula, Horner's syndrome, and injury to some motor nerves in the neck. The incidence of transient hypoparathyroidism has been reported to range from 0.3% to 49%, and that of permanent hypoparathyroidism from 0% to 13% (5, 6). In addition, the incidence of RLN palsy has been found to range from 0% to 5% (5-7), and those of hematoma, seroma, chyle fistula, and Horner's syndrome from 0% to 3%, 0% to 6%, 1.0% to 2.5% and 1.8% to 7.8%, respectively (6, 8, 9). In our institution, we

found that the incidence rates of transient hypoparathyroidism, permanent hypoparathyroidism, transient RLN palsy, permanent RLN palsy, hematoma, seroma, chyle fistula, and Horner's syndrome were 28.4%, 0.3%, 0.7%, 0.2%, 0.5%, 4.7%, 1.8%, and 0.2%, respectively all of which are in good agreement with previous reports (5-9).

Hypoparathyroidism is the most common complication after total or near-total thyroidectomy due to the unintentional removal of parathyroid glands or poor blood flow to the glands. Patients with permanent hypoparathyroidism require life-long treatment with calcium and vitamin D, so this complication is considered serious. Transient hypoparathyroidism, however, rarely affects quality of life.

Studies that have performed multivariate analysis on factors predictive of postoperative hypoparathyroidism have shown differences in terms of the effects of surgical extent, surgeon's experience, and method of study (10-12). In our series, the incidence rates of transient and permanent hypoparathyroidism increased significantly with increasing extent of surgery. The incidence of incidental parathyroid removal during surgery showed no differences between groups, which indicated that the incidental removal of parathyroid glands did not affect the incidence of hypoparathyroidism. On the contrary, the incidence of parathyroid autotransplantation during surgery

increased significantly with increasing the extent of surgery. This result revealed that more extended surgery caused more ischemic changes to parathyroids. Thus, hypoparathyroidism following thyroid surgery is likely to be due to the decrease of blood flow to the parathyroid glands with increasing extent of surgery.

Similar to permanent hypoparathyroidism, RLN palsy also has marked effects on patient quality of life. The causes of transient RLN palsy include excessive nerve skeletonization, neuritis caused by scar tissue and myelinic lesion, axon damage caused by excessive strain, "a frigore" or "a calore" paralysis, thermic lesions caused by electrocoagulation, viral neuritis, and difficult endotracheal intubation (13). Patients with vocal cord palsy should start logopedic rehabilitation as early as possible. The injured RLNs are usually treated by voice therapy, laryngeal reinnervation procedures, injection laryngoplasty with materials such as gelfoam, fat and collagen, arytenoid adduction, or medialization laryngoplasty with expanded polytetrafluoroethylene (EPTTE, Gore-Tex) (14-16). Although intraoperative RLN monitoring using an electrode inserted into the endotracheal tube has been suggested, it does not seem to decrease the incidence of RLN palsy (17, 18). In our series, the rate of transient RLN palsy increased significantly with increasing extent of surgery, whereas permanent RLN palsy was not related to the extent of surgery; this is likely that permanent palsy was caused by invasion of the RLN nerve or accidental injuries.

Hematoma after thyroidectomy is a potentially fatal complication. Acute respiratory embarrassment due to hematoma formation is lethal unless the hematoma is immediately removed surgically. Meticulous hemostasis is therefore mandatory in thyroid surgery, and the level of care taken during the surgery cannot be compromised (19). Seroma may require aspiration to make the patients comfortable; aspiration can be easily performed by inserting a needle above the incision when fluid collection is noted (19). In our series, 0.5% of the patients experienced postoperative hematoma and 4.7% of the patients experienced seroma. The incidences of these complications also increased with increasing extent of surgery.

Chyle fistula is a rare and troublesome complication. If untreated, it can cause severe disturbances in fluid and electrolyte balance, protein loss, delayed wound healing, abnormal metabolic status, shock, and even death (8). The most common cause of chyle fistula is thoracic duct injury, mainly on the left side (responsible for 75-92% of cases) (20). Most chyle fistulas (75%) are detected during surgery, or detected after surgery (21, 22). Chyle fistula is usually found upon postoperative commencement of an oral diet and is indicated by milky drainage, a sudden increase in drainage volume, bulging supraclavicular fossa, and induration or erythema of the skin (22, 23). Low output fistulas (<500 mL/day) can usually be conservatively managed by fasting or maintenance of a low-fat diet, a semi-Fowler's position, a diet of medium-chain fatty acids, total parenteral nutrition, compression dressing on the

supraclavicular fossa, and the use of somatostatin analogues (such as octreotide) (24, 25). High output fistulas (>500 mL/day), however, require surgical intervention for direct closure of the fistula or thoracic duct ligation (26, 27).

Horner's syndrome is usually associated with unique clinical features based on the anatomical location of the underlying pathologic process. Classical symptoms include miosis, ptosis, anhidrosis, and in some cases, nasal stuffiness. Horner's syndrome results from paralysis of the ipsilateral sympathetic chain due to extensive surgical dissection around the sympathetic trunk lying along the deep posterior and medial to the carotid artery, between the prevertebral fascia and the carotid sheath (9, 28). There is no specific treatment for Horner's syndrome; however, postoperative ophthalmic problems can be managed by ophthalmic supportive care, ptosis can be treated with blepharoplasty or administration of  $\alpha_2$ -adrenaline receptor agonists, and nasal stuffiness can be treated with turbinectomy. Careful dissection around the prevertebral fascia and the carotid sheath is necessary to avoid injury to the sympathetic chains when performing a radical neck dissection. In our series, the Horner's syndrome only occurred in patients the lateral neck dissection groups. Rare complications such as injury to the spinal accessory nerve, hypoglossal nerve, vagus nerve, and phrenic nerve were not seen in our patients.

The dilemma associated with the surgical principles of thyroid cancer surgery includes achieving the proper oncologic outcomes while reducing postoperative complications. Although extended resection increases survival rate and decreases the recurrence rate, all surgical procedures have the potential to cause complications and more extensive resections may be associated with substantially increased complication rates.

In conclusion, the results of our study suggest that most thyroid cancer surgeries are safe and can be performed with minimal morbidity, but an increased risk of surgical complications, particularly hypoparathyroidism, is still a problem that needs to be solved in patients who require more extensive surgery. Therefore, an understanding of the relationship between complication patterns and the extent of surgery seems to be crucial for thyroid cancer surgery.

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