**Learning curve for endoscopic thyroidectomy using video-assisted neck surgery:
retrospective analysis of a single surgeon's experience of 100 cases**

Running title: Learning curve in 100 cases of VANS

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50

51 **Abstract**

52 **Background:** Endoscopic thyroidectomy offers excellent cosmetic outcomes, but
53 requires a period of time for surgeons to become proficient. We examined the learning
54 curve for the first 100 cases experienced by a single surgeon using a video-assisted neck
55 surgery (VANS) subclavian approach.

56 **Methods:** We retrospectively studied 100 patients (99 women, 1 man; mean age, 36.2
57 years) with both benign and malignant thyroid diseases treated between 2016 and 2020.

58 **Results:** Preoperative diagnosis was papillary thyroid carcinoma (PTC) in 36 cases and
59 other (non-PTC) in 64 cases. All patients underwent lobectomy, with unilateral central
60 node dissection added for patients with PTC. Mean operative time was 125 min for non-
61 PTC cases and 129 min for PTC cases ($p = 0.43$), with blood loss of 33.8 ml and 7.6 ml,
62 respectively ($p = 0.01$). Recurrent laryngeal nerve paralysis (RNP) was observed in 12
63 patients (12%) and hemorrhage in 2 patients (2%). Comparing the first 30 cases with the
64 last 70 cases, no significant differences in operative time or blood loss were evident,
65 although tumor size of non-PTC cases was significantly greater among later cases (32.4
66 mm vs. 39.5 mm, $p = 0.039$). RNP was significantly decreased in later cases (26.7% vs.
67 5.7%, $p = 0.003$). Multivariate analysis revealed tumor size as a significant risk factor for
68 increased blood loss, and increased experience correlated significantly with the decrease
69 in RNP.

70 **Conclusions:** In VANS, a certain surgical level was reached after experiencing 30 cases.

71

72 **Key Words:** endoscopic thyroidectomy, gasless lifting method, learning curve, video-

73 assisted neck surgery, papillary thyroid carcinoma

74

Introduction

Thyroid tumors are particularly common among young women, and conventional thyroid surgery requires a collar-like incision in the neck. This incision poses a problem in terms of cosmetic appearance. In 1997, Huscher et al. reported the first endoscopic thyroid surgery¹, and Shimizu et al. reported video-assisted neck surgery (VANS) using a subclavian approach in 1998². Various approaches have subsequently been reported, including axillary³, breast⁴, anterior chest⁵, and transoral approaches⁶. The indications for surgery are currently being expanded to include not only benign conditions, but also malignant diseases.

Among these techniques, we have been performing VANS using a subclavian approach since 1998. This is because this approach: 1) is closer to the neck than other approaches and relatively easy to perform; 2) is less invasive in terms of the extent of skin flap creation than other approaches; and 3) does not need air insufflation and does not show complications such as CO₂ embolism or subcutaneous emphysema. In addition, as mentioned in our previous report⁷, the level of satisfaction with the scar is higher among younger patients, especially those in their 20s and 30s, compared to the conventional approach.

However, as a new surgical technique, this method requires a period of time for surgeons to become proficient. Several reports have described the learning curve for endoscopic thyroid surgery and have suggested a need for surgical experience with about

30 cases to attain proficiency⁸⁻¹². However, those studies only examined operative time and blood loss, and either only benign or only malignant diseases. This study examined the learning curve for the first 100 cases experienced by a single surgeon using the VANS subclavian approach, including both benign and malignant diseases. We compared the rate of postoperative complications as well as operative time and blood loss between the former 30 cases and the latter 70 cases.

Materials and Methods

1) Patients

Subjects were 107 patients with benign and malignant thyroid diseases who underwent surgery by a single surgeon between May 2016 and July 2020. A total of 100 cases were retrospectively reviewed, after excluding 6 cases that underwent procedures other than lobectomy (total thyroidectomy, n=3; isthmectomy, n=3) and 1 case of malignancy with recurrent laryngeal nerve invasion. The institutional review board approved this retrospective study (approval number R1-05-1126) and informed consent for participation was obtained using an opt-out method for the study. Indications for surgery were as follows: benign tumors with longitudinal diameter ≤ 6 cm; malignant tumors preoperatively diagnosed as papillary thyroid carcinoma (PTC) only, with tumor diameter ≤ 4 cm, no extrathyroidal invasion or invasion limited to the sternothyroid muscle, and no lymph node metastasis or with central node metastasis (N1a).

115

116 2) Study protocol

117 Tumors were evaluated by palpation, ultrasound, and computed tomography.

118 Fine-needle aspiration cytology was performed in all cases to obtain a preoperative

119 diagnosis. On the day after the surgery, otolaryngologists checked the vocal cord

120 movement using a laryngeal fiber. Prolonged recurrent laryngeal nerve paralysis (RNP)

121 for >6 months was defined as permanent, and otherwise as transient. Preoperative vocal

122 cord movement confirmation was performed only by ultrasound.

123

124 3) Operative techniques

125 Intraoperative neuro-monitoring (IONM) was used for the 14th case (April

126 2018) and thereafter for malignant disease and from the 63rd case (July 2020) and

127 thereafter for benign disease. An ultrasonic coagulation incision device was used in all

128 cases. Lobectomy was performed in all cases, with additional central node dissection

129 (CND) on the affected side in cases of malignant disease.

130 The operative method was based on a previous report⁷. In summary, a 30- to 35-

131 mm skin incision (depending on the size of the tumor) was placed in the subclavian area

132 on the affected side, and a lifting technique using a lifting retractor with an aspirator was

133 applied. A 5-mm camera port was created in the lateral neck (**Fig. 1**). After the thyroid

134 gland was exposed, the superior thyroid artery and the inferior thyroid artery were

dissected in that order, and the parathyroid glands were confirmed and preserved (**Fig. 2**).

All the vessels were dissected using an energy device. The recurrent laryngeal nerve was identified and preserved by careful dissection with the use of IONM. When dissecting around the recurrent laryngeal nerve, the energy device was operated at least 2 mm away from the nerve to prevent thermal injury (**Fig. 3**). In addition, the perineural tissues were periodically cooled by the infusion of saline solution.

4) Statistical analysis and evaluation

Data are expressed as mean $\pm$ standard deviation. Clinical characteristics were compared between groups using the chi-square test for categorical variables and the Mann-Whitney U-test for continuous variables. Multivariate analysis was carried out by multiple and logistic regression analyses. All analyses were performed using JMP for Windows version 10.0.2 software (SAS Institute, Cary, NC). Values of $P < 0.05$ were considered statistically significant.

Results

Ninety-nine patients were female, with a mean age of 36.2 years (range, 12–71 years; median, 36.5 years). The preoperative diagnosis was PTC in 36 cases and non-PTC in 64 cases. All patients underwent lobectomy, and unilateral CND was added for patients with PTC. Postoperative pathological diagnosis was malignant in 45 cases (37 PTCs; 7

follicular thyroid carcinomas, including 4 minimally invasive tumors, 2 encapsulated angioinvasive tumors, and 1 widely invasive tumor; and 1 poorly differentiated thyroid carcinoma), benign in 55 cases (46 adenomatous goiters; and 9 follicular adenomas). The relationship between preoperative diagnosis and pathological diagnosis is shown in **Table 1**. The relationship between clinical characteristics and preoperative diagnosis of the 100 cases is shown in **Table 2**. No significant difference in age was evident between non-PTC cases (35.4 years) and PTC cases (37.7 years, $p = 0.34$). Chronic thyroiditis was significantly more frequent in PTC cases (42%) than in non-PTC cases (16%, $p = 0.004$). IONM was used in a total of 25 cases, including 2 non-PTC cases (3%) and 23 PTC cases (64%, $p < 0.001$). Mean operative time was 126 min (range, 83–179 min). Operative time did not differ significantly between non-PTC cases (125 min; range, 83–179 min) and PTC cases (129 min; range, 91–166 min; $p = 0.43$). The approximation curve of operative time showed a slight upward trend in non-PTC cases and a flat trend in PTC cases (**Fig. 4**). Blood loss was 33.8 ml (range, 0–400 ml) in non-PTC cases and 7.6 ml (range, 0–53 ml) in PTC cases (**Fig. 5**), showing a significant difference ($p = 0.01$). Mean tumor size was 37.6 mm (range, 13–60 mm) in non-PTC cases with the approximation curve showing a rightward increase, and 13.1 mm (range, 5–27 mm) in PTC cases with the approximation curve remaining almost unchanged (**Fig. 6**). Excised thyroid weight showed similar results to tumor size. (**Fig. 7**). The mean number of dissected lymph nodes in PTC cases was 1.2 (range, 0–5; median, 1).

Regarding postoperative complications, RNP was observed in 12 patients (12%) and hemorrhage in 2 patients (2%). RNP occurred in the 6th, 9th, 12nd, 18th, 22nd, 25th, 28th, 30th, 38th, 57th, 72nd and 80th cases, and hemorrhage occurred in the 20th and 52nd cases. One case of RNP was permanent, and the remaining 11 cases were transient. No cases suffered nerve transection. Physical damage from traction or forceps manipulation, or thermal damage from energy devices were considered possible causes. No significant difference in frequency of RNP was seen between non-PTC cases (9%) and PTC cases (17%, $p = 0.28$). The source of postoperative bleeding in all cases was a vein in the skin flap, and hemostasis was obtained endoscopically.

We then divided the patients into the first 30 cases and the last 70 cases for comparison. The distribution of non-PTC and PTC cases is shown in **Table 3**. While no significant difference was apparent between the first 30 and last 70 cases in operative time (125 min vs. 127 min, $p = 0.60$) or blood loss (20.6 ml vs. 26.0 ml, $p = 0.62$); tumor size of non-PTC cases (32.4 mm vs. 39.5 mm, $p = 0.039$) and excised weight of non-PTC cases (16.0 g vs. 23.4 g, $p = 0.009$) were significantly increased among the last 70 cases. Numbers of dissected lymph nodes in PTC cases were 0.7 and 1.5 ($p = 0.099$) in the first 30 and last 70 cases, respectively. RNP decreased significantly in the last 70 cases (26.7% vs. 5.7%, $p = 0.003$). Among the 25 patients for whom IONM was used, one case developed RNP (4%).

Multivariate analysis using multiple regression analysis was performed for five factors (age, sex, chronic thyroiditis, tumor size and total number of cases experienced) to predict operative time and blood loss (**Table 4A, B**). Variance inflation factors for each factor in multiple regression analyses were all less than 1.2. No significant predictors were seen for operative time, while tumor size was a significant risk factor for increased blood loss. We then performed multivariable analysis using logistic regression analysis for the occurrence of RNP with two factors: tumor size and total number of cases experienced (**Table 4C**). Increasing number of cases experienced correlated significantly with decreased frequency of RNP.

Discussion

In VANS surgery, tumors with larger diameter are generally more difficult to operate on. This is because large tumors limit forceps manipulation and field-of-view development, and are more prone to bleeding due to abundant blood flow. Shimizu et al. reported that in benign tumors, operative time (120.7 min vs. 98.1 min, $p = 0.0028$) and blood loss (82.9 ml vs. 36.3 ml, $p = 0.0084$) were significantly greater for tumor diameter ≥ 5 cm compared to < 5 cm¹³. In this series, non-PTC tumors were significantly larger than PTCs. The amount of blood loss was significantly higher in non-PTC cases, while no significant difference in operative time was evident between groups. This may be due to

the addition of CND in PTC cases. Moreover, the tendency toward a greater frequency of RNP in PTC cases was attributed to perineural manipulation during CND.

In non-PTC cases, tumor size and excised weight tended to increase with the number of cases, indicating that the number of difficult cases is gradually increasing. The reason why operative time did not follow the general downward learning curve was thought to be unevenness in the degree of difficulty. Operative time and blood loss alone therefore should not be used to evaluate the learning curve.

Regarding the learning curve of endoscopic thyroid surgery, Shimizu et al. reported that the operating time and amount of bleeding could be reduced as surgeons gain experience with more than 30 cases⁸. Although differing in approach, several recent papers have examined endoscopic thyroidectomy using cumulative summation analysis. Previous studies investigating the learning curve for endoscopic thyroidectomy and number of cases required for surgeons to attain proficiency are summarized in **Table 5**. Based on these reports, we hypothesized that mastery in VANS could be attained within about 30 cases, and we therefore divided the study into the first 30 and last 70 cases.

For non-PTC in the last 70 cases, operative time and blood loss did not increase, despite the increase in tumor size. Among PTC cases, although no significant differences were identified in operative time, blood loss, tumor size or excised weight, the number of dissected lymph nodes tended to increase in the last 70 cases of the study. This might be due to improvements in surgical techniques.

The causes of recurrent nerve palsy include transection, ligation, constricting, clamping, traction, and thermal injury¹⁴. The frequency of RNP decreased significantly to 5.7% in the last 70 cases, comparable to previous reports from Japan (conventional surgery, 4.4%; VANS, 8.9%)¹⁵. We have been applying IONM since 2018. Among the 25 cases treated with IONM, RNP was seen in only 4% of cases. IONM may facilitate safer surgery.

Multiple regression analysis revealed increased tumor size as a significant risk factor for increased blood loss. However, tumor size was not a significant risk factor for prolonged operative time, as previously reported¹³. This would be because of the additional time required for CND in PTC cases. Excised weight is considered to more accurately reflect tumor volume than tumor diameter. However, we judged tumor diameter, which is easily measured preoperatively by ultrasound, as a clinically preferable variable, and adopted tumor diameter rather than excised weight as the item for multiple regression analysis. In cases with chronic thyroiditis, thyroid tissue becomes diffusely hard and is generally difficult to grasp during endoscopic surgery. However, no significant effect on operative time or blood loss was seen. Multivariate analysis showed that the total number of cases experienced was significantly related to reduced frequency of RNP. The more cases experienced, the lower the risk of RNP.

As a limitation to this study, analyzing the learning curve for the first 100 cases from the start of VANS required mixing benign and malignant diseases in this study. In

clinical practice, the number of difficult cases will naturally increase with experience. Thus, surgical difficulty was not even during the study period. In addition, the cumulative summation (CUSUM) analysis would be used to evaluate the learning curve, however, it is not applicable in this study due to the mixture of benign and malignant cases, and the skewed distribution of surgical difficulty and IONM use.

In conclusion, surgical proficiency could be attained after performing surgery in about 30 cases using VANS. The risk of RNP fell significantly with an increasing number of cases experienced.

Acknowledgements: We wish to acknowledge and thank Dr. Toshiaki Otsuka, Department of Hygiene and Public Health, Nippon Medical School, Tokyo, Japan for assistance with statistical analysis.

Conflict of interest: None declared.

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314 **Figure legends**

315 Fig. 1

316 Skin incision design

317 (1) 30-mm skin incision, (2) 5-mm camera port

318

319 Fig. 2

320 Intraoperative findings 1

321 The recurrent laryngeal nerve is identified after dissecting the superior thyroid artery. The
322 surrounding tissue is carefully dissected and intraoperative neuromonitoring is used to
323 identify the recurrent laryngeal nerve.

324 (1) thyroid gland, (2) trachea, (3) recurrent laryngeal nerve, (4) inferior thyroid artery

325

326 Fig. 3

327 Intraoperative findings 2

328 The tissue surrounding the recurrent laryngeal nerve should be dissected away from the
329 nerve as far as possible and be cooled as necessary to prevent thermal damage.

330 (1) trachea, (2) recurrent laryngeal nerve

331

332 Fig. 4

333 Operative time in non-PTC and PTC cases

334 *dotted line, logarithmic approximation curve

335 **arrow, the 30th case the surgeon experienced in total

336

337 Fig. 5

338 Blood loss in non-PTC and PTC cases

339 *dotted line, logarithmic approximation curve

340 **arrow, the 30th case the surgeon experienced in total

341

342 Fig. 6

343 Tumor size in non-PTC and PTC cases

344 *dotted line, exponential approximation curve

345 **arrow, the 30th case the surgeon experienced in total

346

347 Fig. 7

348 Excised weight in non-PTC and PTC cases

349 *dotted line, exponential approximation curve

350 **arrow, the 30th case the surgeon experienced in total

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352

353

Fig. 1 Skin incision design

Figure. 2 Intraoperative findings 1

Figure. 3 Intraoperative findings 2

Fig. 4 Operative time in non-PTC and PTC cases

Fig. 5 Blood loss in non-PTC and PTC cases

Fig. 6 Tumor size in non-PTC and PTC cases

Fig. 7 Excised weight in non-PTC and PTC cases

Table 1 Relationship between preoperative and pathological diagnosis

Preoperative diagnosis			Pathological diagnosis		
non-PTC					
AG	27		AG		26
			FA		1
FT	37		AG		20
			FA		8
			PTC		2
			FTC	minimally invasive	3
				encapsulated angioinvasive	2
				widely invasive	1
		PDTC		1	
PTC					
PTC	36		PTC		35
			FTC	minimally invasive	1
Total	100				100

AG, adenomatous goiter; FT, follicular tumor; FA, follicular adenoma;

PTC, papillary thyroid carcinoma; FTC, follicular thyroid carcinoma;

PDTC, poorly differentiated thyroid carcinoma

Table 2 Preoperative diagnosis and clinical characteristics of patients

		Total (n = 100)	non-PTC (n = 64)	PTC (n = 36)	p
Age (years)	mean ± SD	36.2 ± 12.7	35.4 ± 13.9	37.7 ± 10.2	0.34
	range	(12-71)	(12-71)	(23-59)	
	median	36.5	34	38.5	
Sex (female)		99	63 (98%)	36 (100%)	0.45
Chronic thyroiditis		25	10 (16%)	15 (42%)	0.004
Use of IONM		25	2 (3%)	23 (64%)	<0.001
Operative time (min)	mean ± SD	126 ± 23.1	125 ± 24.8	129 ± 19.8	0.43
	range	(83-179)	(83-179)	(91-166)	
	median	125	122.5	126.5	
Blood loss (ml)	mean ± SD	24.4 ± 64.4	33.8 ± 78.6	7.6 ± 11.6	0.01
	range	(0-470)	(0-470)	(0-53)	
	median	5	9	4.5	
Tumor size (mm)	mean ± SD	28.8 ± 15.6	37.6 ± 12.2	13.1 ± 4.8	<0.001
	range	(4-60)	(13-60)	(4-27)	
	median	26.5	39	12	
Excised weight (g)	mean ± SD	17.1 ± 10.4	21.5 ± 10.2	9.4 ± 5.1	<0.001
	range	(4-49)	(9-49)	(4-29)	
	median	15.2	18.2	8.0	
Complications					
RNP		12 (12.0%)	6 (9%)	6 (17%)	0.28
Postoperative bleeding		2 (2%)	1 (2%)	1 (3%)	0.68

PTC, papillary thyroid carcinoma; SD, standard deviation; IONM, intraoperative neuro-monitoring;
RNP, recurrent laryngeal nerve paralysis

Table 3 Clinical characteristics of patients in first 30 and last 70 cases

			First 30 cases	Last 70 cases	p
			(n = 30)	(n = 70)	
Preoperative diagnosis	non-PTC		17 (57%)	47 (67%)	0.37
	PTC		13 (43%)	23 (33%)	-
Age (years)		mean ± SD	40 ± 12.9	34.6 ± 12.3	0.053
		range	(13-71)	(12-65)	
		median	41	33	
Sex (female)			29 (97%)	70 (100%)	0.30
Chronic thyroiditis			11 (37%)	14 (20%)	0.09
Use of IONM			0 (0%)	25 (36%)	<0.001
Operative time (min)	Total	mean ± SD	125 ± 23.2	127 ± 23.2	0.6
		range	(83-174)	(84-179)	
		median	122	127.5	
	non-PTC	mean ± SD	120 ± 26.4	127 ± 24.2	0.35
		range	(83-174)	(84-179)	
		median	114	128	
	PTC	mean ± SD	127 ± 18.0	129 ± 20.9	0.81
		range	(105-166)	(85-164)	
		median	125	128	
Blood loss (ml)	Total	mean ± SD	20.6 ± 33.0	26.0 ± 74.0	0.62
		range	(0-164)	(0-400)	
		median	6	5	
	non-PTC	mean ± SD	29.9 ± 40.8	35.2 ± 88.8	0.75
		range	(0-164)	(0-400)	
		median	10	9	
	PTC	mean ± SD	8.4 ± 12.6	7.3 ± 11.4	0.81
		range	(0-35)	(0-53)	
		median	5	4	
Tumor size (mm)	Total	mean ± SD	23.8 ± 13.2	30.9 ± 16.1	0.035
		range	(8-55)	(4-60)	
		median	20.5	30.0	
	non-PTC	mean ± SD	32.4 ± 10.8	39.5 ± 12.2	0.039
		range	(13-55)	(14-60)	
		median	33	40	
	PTC	mean ± SD	11.4 ± 4.1	13.8 ± 5.0	0.15
		range	(8-21)	(4-27)	
		median	12	12	
Excised weight (g)	Total	mean ± SD	13.2 ± 7.2	18.8 ± 11.2	0.004
		range	(4-36)	(4-29)	
		median	11.1	16.5	
	non-PTC	mean ± SD	16.0 ± 7.2	23.4 ± 10.4	0.009
		range	(9-36)	(4-29)	
		median	14.3	19.5	
	PTC	mean ± SD	9.4 ± 5.9	9.4 ± 4.9	0.99
		range	(4-23)	(5-29)	
		median	6.6	8.3	
Complications					
	RNP		8 (26.7%)	4 (5.7%)	0.006
	Postoperative bleeding		1 (3.3%)	1 (1.4%)	0.51

PTC, papillary thyroid carcinoma; SD, standard deviation; IONM, intraoperative neuro-monitoring;
RNP, recurrent laryngeal nerve paralysis

Table 4A Multivariate analysis for predictors of operative time

Independent variables	Estimated regression coefficient	Standardized partial regression coefficient	Standard error	t value	p
(Intercept)	120.17	0	15.00	8.01	<0.001
Age	-0.23	-0.13	0.19	-1.23	0.22
Sex	5.15	0.04	11.62	0.44	0.66
Chronic thyroiditis	0.67	0.03	2.81	0.24	0.81
Tumor size (mm)	0.22	0.15	0.16	1.42	0.16
No. of cases experienced	0.06	0.07	0.08	0.68	0.50

The adjusted R2 was 0.01.

Table 4B Multivariate analysis for predictors of blood loss

Independent variables	Estimated regression coefficient	Standardized partial regression coefficient	Standard error	t value	p
(Intercept)	29.84	0	41.17	0.72	0.47
Age	-0.38	-0.07	0.52	-0.73	0.46
Sex	-14.34	-0.04	31.90	-0.45	0.65
Chronic thyroiditis	0.96	0.01	7.70	0.13	0.90
Tumor size (mm)	1.19	0.29	0.43	2.77	0.007
No. of cases experienced	-0.24	-0.11	0.23	-1.05	0.29

The adjusted R² was 0.04.

Table 4C Multivariate analysis for predictors of recurrent laryngeal nerve paralysis

Risk factors for RNP	Odds ratio	95%CI	p
Tumor size (mm)	1.01	0.97-1.06	0.55
No. of cases experienced	0.97	0.94-1.00	0.018

RNP, recurrent laryngeal nerve paralysis; CI, confidence interval

Table 5 Learning curve analysis in endoscopic thyroidectomy

Year	Author	Approach	Disease	CO ₂ insufflation	CUSUM analysis	Main evaluation items	No. of cases reaching sufficient proficiency
2001	Shimizu [8]	Subclavian	Benign	-	-	OT, bleeding	30
2014	Liao [9]	Breast	Mainly benign	+	+	OT	27
2014	Kwak [10]	Axillary	Mainly malignant	-	+	OT, complications, no. of LN removed	60
2017	Yu [11]	Axillary	Benign	+	+	OT, complications, no. of LN removed, removal of PTG	31
2019	Cho [12]	Breast	Malignant	+	+	OT, tumor size	35

CUSUM, cumulative summation; OT, operative time; LN, lymph node; PTG, parathyroid gland