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Transoral robotic thyroidectomy versus transoral endoscopic thyroidectomy: a propensity-score-matched analysis of surgical outcomes

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Abstract

Background Transoral endoscopic thyroidectomy vestibular approach (TOETVA) has been shown to be safe and has similar outcomes as open thyroidectomy for selected patients. It is not clear if transoral robotic thyroidectomy (TORT) may extend transoral endoscopic thyroidectomy to more complex thyroid operations. The study aimed to compare the safety and outcomes of TORT with those of TOETVA.

Methods We retrospectively reviewed all patients who had TORT and TOETVA performed by a single surgeon from June 2017 to May 2019. Intrathoracic goiter and combined operations were excluded. Surgical outcomes were compared after propensity score matching. Learning curves, as measured by operating time, were evaluated.

Results A total of 150 patients underwent 154 transoral (55 TORT and 99 TOETVA) thyroidectomy. Of the 154 operations, 28 (18.2%) were bilateral total thyroidectomy and 126 (81.8%) were unilateral thyroid lobectomy. After propensity score matching, we found a longer operative time (median [interquartile range]) for TORT ($n = 53$) than for the TOETVA (308 [284–388] vs 228 [201–267] min, $P < 0.001$). Blood loss and visual analog scale scores for pain were not significantly different between the two groups. Central neck lymph node dissection was performed more frequent in the TORT group (28 of 53 [52.8%] vs 10 of 53 [18.9%], $P = 0.001$), and when performed, the numbers of total and positive lymph nodes did not differ significantly between the two groups. The rates of hypoparathyroidism and recurrent laryngeal nerve injury did not differ significantly between the two groups. There was no conversion to open thyroidectomy, mental nerve injury, or surgical site infection. The learning curve for TORT was 25 cases, but no obvious learning curve was observed for TOETVA.

Conclusions TORT requires a longer operative time, but is as safe as TOETVA and may be useful for more complex thyroid operations.

Keywords TOETVA · TORT · Transoral endoscopic thyroidectomy · Transoral robotic thyroidectomy

Thyroidectomy through an anterior neck incision is the current standard approach because of its efficiency and low complication rate. However, scars from anterior neck incisions may impair patients' quality of life [1] and is associated with negative social attention [2]. Various remote-access thyroidectomy, including transaxillary and trans-areolar endoscopic and robotic thyroidectomy, have been developed to address this issue; however, concerns remain because some are unilateral approaches, most require more extensive flap dissection and scaring remains in the remote approach sites [3–7]. Transoral endoscopic thyroidectomy vestibular approach (TOETVA) was developed to overcome some of these drawbacks [8, 9].

TOETVA has been shown to be safe and has similar outcomes as open thyroidectomy (OT) for selected patients

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[10–13]. Although TOETVA has a longer operating time than open thyroidectomy, the complication rates are similar, including hypocalcemia, recurrent laryngeal nerve (RLN) injury, blood loss, and surgical site infections. Patients who underwent TOETVA had less postoperative pain, as measured by visual analog scale (VAS) scores, than those who had open thyroidectomy [14]. Other studies have compared the safety, and perioperative, functional, and oncologic outcomes of transoral robotic thyroidectomy (TORT) with open thyroidectomy and with other endoscopic and robotic approaches [15–17]. Some have found the robot system to be especially useful in the dissection of lymph nodes in the central compartment [18]. These early studies have reported only the preliminary feasibility and safety of TORT compared with that of TOETVA in limited case series [19, 20]. To our knowledge, this is the largest study comparing TORT and TOETVA by a single surgeon in a single institution. The influence of confounding factors is reduced by propensity score matching. In addition, we studied the learning curves of the techniques in a surgeon without previous experience in endoscopic or robotic remote-access thyroid surgery.

Materials and methods

Study cohort

We retrospectively reviewed 154 operations (99 TOETVA and 55 TORT) performed in 150 patients by a single surgeon from June 2017 to May 2019. The inclusion criteria for transoral thyroidectomy were benign or indeterminate thyroid nodules (< 8 cm), Graves' disease, and malignant or suspicious nodules (< 3 cm). Exclusion criteria for transoral thyroidectomy were major comorbidities causing high risk for general anesthesia, a history of neck radiation, extrathyroidal extension or lateral neck lymph node metastasis on preoperative evaluation, and concurrent transoral parathyroidectomy.

Experience of surgeon and surgical team before first case of transoral thyroidectomy

The surgeon (YHC) is a general and endocrine surgeon trained at a tertiary medical center with a surgical volume of more than 450 open thyroidectomies annually—and also experienced in laparoscopic surgery. He had completed a TOETVA fellowship at Police General Hospital, Bangkok, Thailand, and a TORT observership at the Korea University Hospital, Seoul, Korea. He did not have experience in other remote-access endoscopic or robotic thyroidectomy before his first transoral thyroidectomy.

Before the first TORT, the surgeon already had done 10 cases of TOETVA and more than 30 robotic general surgical procedures using the da Vinci Xi surgical system. The surgical team included rotating assistants with different skill levels in endoscopic and robotic surgery.

Perioperative preparation and surgical procedures

Preoperative preparation

The oral hygiene and mucosal health of eligible patients were examined. Dental procedures, when needed, were completed 2 weeks before operation. Patients were treated to assure euthyroidism. Prophylactic antibiotics were used within 30 min before incision.

Operative procedures of the TOETVA and TORT

The patient was placed in supine position with the neck slightly extended and intubated, with or without a nerve monitor. The surgical site was disinfected, prepared, and draped as routine thyroidectomy.

For the transoral procedure, three trocars (one 11 mm trocar at midline and two 5 mm trocars bilaterally near the angle of the mouth for TOETVA [8, 9, 21, 22]; three 8 mm trocars at midline and bilaterally for TORT [23]) were inserted at the lower lip vestibular area. Subplatysmal working space was created in the mid- to lower neck defined superiorly by the thyroid cartilage, inferiorly by the sternal notch, and laterally by the medial margin of the sternocleidomastoid muscles. The CO_2 insufflation pressure was set at 6 to 8 mmHg with a high flow rate.

In the initial vestibular central incision, we defined a safety triangle with a standardized inverted-V incision for central trocar insertion to minimize mental nerve injury (Fig. 1a, b). The safety triangle in the oral vestibula was an isosceles triangle, with the vertex at the central lower margin of the orbicularis oris marginalis muscle of the lower lip. The sides of the triangle were the imaginary lines connecting the vertex to the mental foramens, which are located between the first and second premolar teeth. The base of the triangle was a line just above the mentalis muscle. Within the safety triangle, we created an inverted-V incision. The vertex of the inverted-V incision was at the middle point of the height of the safety triangle. The 2 sides of the inverted-V incision were extended obliquely forming a vertex angle of 110°, and the total length of the mucosal incision was 1.5 to 2 cm.

For TORT, after creating the subplatysmal working space the da Vinci Xi robotic arms were docked through the oral ports. Routinely, an additional 8-mm blunt-tip trocar was inserted through a right axillary incision and directed into the subplatysmal space for a fourth robotic arm [23] (Fig. 2). In contrast, no additional working port was used for TOETVA.

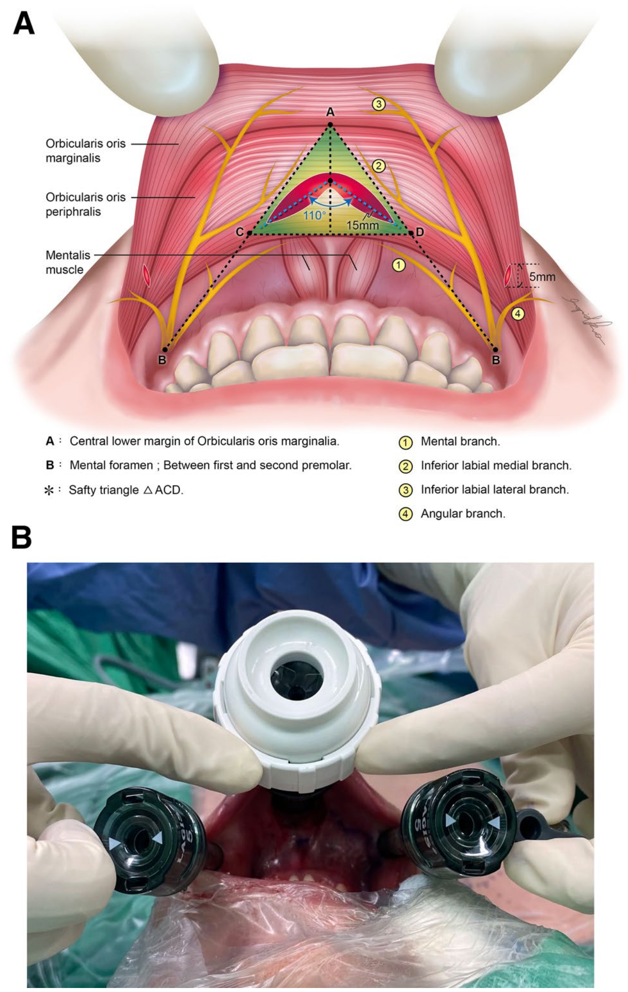

Fig. 1 **A** Safety Triangle and Standardized Central Incision. A safety triangle with a standardized inverted-V incision for central trocar insertion to minimize mental nerve injury. (A) Central lower margin of Orbicularis oris marginalis. (B) Mental foramen, defined between first and second premolar. *Safety triangle △ACD. 1: Mental branch of mental nerve. 2: Inferior labial medial branch of mental nerve. 3: Inferior labial lateral branch of mental nerve. 4: Angular branch of mental nerve. **B** Trocar placement in oral vestibular area

The strap muscles were separated at the midline and retracted with an external hanging suture laterally to expose the thyroid gland. The pyramidal lobe and isthmus were dissected free from the trachea and the isthmus divided.

The vessels at the superior pole were divided individually, and the external branch of the superior laryngeal nerve was preserved. The thyroid gland was rotated anteromedially to expose the recurrent laryngeal nerve. The parathyroid glands were preserved. The ligament of Berry was divided and thyroid lobectomy was completed. Prophylactic unilateral level VI lymph node dissection is typically performed in patients with cancer. If a total thyroidectomy was performed, the contralateral lobe was resected using the same approach.

Fig. 2 Axilla incision. A 1.5-cm-long incision along with the skin crest at the right axilla fossa. Hydrodissection was then performed along the tract from axilla to the imaginary lower end of thyroid isthmus. A long trocar with a working length of 150 mm was then inserted from axilla to the anterior neck working space after blunt dissection. The dissection space is just large enough for trocar placement, usually about 2 cm wide. Arrowhead: 1.5 cm axilla incision. Dotted line: dissection tract

The specimens were placed in a plastic endo-bag for retrieval. In the robotic group, we routinely extracted the specimens through the axilla port site. In the endoscopic group, we extracted the specimens through the central oral incision if the thyroid nodule was smaller than 2 cm. Otherwise, a right axilla incision was created in the same manner as that in the robotic group for specimen extraction.

A drainage tube was not routinely used. The midline raphe of the strap muscles was closed. Bacterial cultures were acquired at the central oral incision just before wound closure. The incisions at the oral mucosa and right axilla were closed by absorbable sutures.

Postoperative management

A compression gauze was used to compress the chin and submental area. A liquid diet was started postoperatively, followed by a soft diet on postoperative day 1 and regular diet on postoperative day 2. Oral analgesics were administered for pain control. Intravenous analgesics (Dynastat, 40 mg) were used for patients with a VAS score more than 3. Oral antibiotics were continued for 7 days.

Outcome measurement

Outcome measured included operative time, blood loss, intraoperative complications, postoperative complications (hypothyroidism, surgical site infection, RLN injury, and mental nerve injury), and VAS pain scores.

Hypoparathyroidism was defined as symptoms of hypoparathyroidism and hypocalcemia (serum calcium concentration less than 8.6 mg/dL). Permanent hypoparathyroidism was defined as hypoparathyroidism with a low parathyroid hormone level (less than 15 pg/mL) lasting more than 6 months.

RLN injury was recognized by postoperative hoarseness and confirmed through laryngoscopic identification of vocal cord palsy. Permanent RLN injury was defined if a patient's injury lasted more than 6 months or if the patient received permanent treatment such as autologous fat or hyaluronate intracordal injection.

Mental nerve injury was defined as hemi-lower or total lower lip numbness. Injury to the inferior labial branch of the mental nerve was defined as lip numbness occurring only in the midline (0.5- to 1-cm) region. Injury to the mental branch of the mental nerve was defined as hemichin or total chin numbness. Mental nerve injury, inferior labial branch injury, and mental branch injury were routinely evaluated from the 71st to 154th cases after we standardized the central incision.

Statistical analysis

Patient demographics, preoperative fine needle aspiration (FNA) cytology, perioperative information, intraoperative oral bacterial culture reports, pathological reports, and complications were recorded. We conducted propensity score matching using the nearest neighbor matching method; accordingly, we matched the TORT and TOETVA groups at a 1:1 ratio. Confounding variable such as age, sex, tumor size, extent of thyroidectomy, and Bethesda score were included in the propensity score model. Continuous variables were summarized as means with standard deviations (SD) if the data were normally distributed by the Shapiro–Wilk normality test, otherwise as medians with interquartile ranges (IQRs). Categorical variables were presented as frequencies and percentages. In the univariate analysis, baseline characteristics of the TORT and TOETVA groups were compared using the chi-squared test, Fisher exact test, *t* test, or Wilcox rank sum test where appropriate. To analyze the learning curve, operative time was used as a surrogate for procedural proficiency. Operative time was plotted as a function of case number. A simple moving average of order 7 was then calculated for all cases. The slope of the linear regression of the skill acquisition period was compared with the slope of the linear regression of the proficiency period using a plot of operative time versus case number. All reported confidence intervals and tests were 2-sided with a 5% significance level. All analyses were performed with R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria) using the MatchIt, tableone, and TTR packages.

Results

Patient characteristics and surgical outcomes before propensity score matching

Table 1 presents a summary of the overall characteristics of patients who underwent transoral thyroidectomy. A total of 150 patients (median age, 45 [IQR 36–56]; 88% female; mean body mass index, 23.6 [SD 3.56]) were included, with 4 patients undergoing completion total thyroidectomy, 3 patients undergoing transoral thyroidectomy after previous open thyroidectomy several years ago (Table 1). Of the patients, 94 (61%) had benign thyroid nodules (single or multinodular), 45 (29%) had thyroid cancer, 9 (6%) had Graves' disease, and 8 (5%) had non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

Table 2 lists the baseline characteristics of the two groups. Among the 154 transoral thyroidectomies, 99 were TOETVA and 55 were TORT. Sex, nodular size, preoperative FNA cytology, operative time, central neck lymph node dissection, and cancer were significantly different between the two groups.

Patient characteristics and surgical outcomes after propensity score matching

After propensity score matching, each group comprised 53 patients (Table 3). Age, sex, nodular size, Bethesda score, and the extent of thyroidectomy were comparable between the two groups.

Operative time was longer in the TORT group than in the TOETVA group (308 [IQR 284–388] vs 228 [IQR 201–267] min, $P < 0.001$). Although the proportion of patients with cancer was comparable between the two groups, the TORT group had more patients with prophylactic central neck dissection. Intraoperative blood loss, VAS score, and complications were not different between the two groups. One patient in the TOETVA group had a subclavian vein injury, which was repaired successfully without conversion to open.

Bacterial profile of surgical sites

In 145 of the 154 procedures, we obtained bacterial cultures from the central oral incision site immediately before closure. Of these, 115 (75%) had no bacterial growth, 22 (14%) had anaerobic bacterial growth, and 8 (5%) had aerobic bacterial growth (Table 1).

Table 1 Demographic, clinicopathologic, and treatment characteristics of patients who underwent transoral thyroidectomy

Characteristic	Overall (*n* = 154)
Age (median [IQR]), years	45.0 [36.0, 56.0]
Sex (%)	
Female	136 (88.3)
BMI (mean (SD))	23.62 (3.56)
Nodular size (median [IQR]), cm	3.13 [1.71, 4.26]
Preoperative FNA cytology (%)	
Bethesda class 4, 5 and 6	69 (44.8)
Bethesda class 2 and 3	85 (55.2)
Operative time (median [IQR]), min	251 [213, 308]
Extent of surgery (%)	
Bilateral total thyroidectomy	28 (18.2)
Unilateral thyroidectomy	126 (81.8)
Central neck lymph node dissection (%)	40 (26.0)
Number of retrieved lymph nodes (mean (SD))	4.35 (2.79)
Positive central neck lymph node (%)	10 (27)
Previous operation (%)	
No	147 (95.5)
Open	3 (1.9)
TOETVA	3 (1.9)
TORT	1 (0.6)
Blood loss (median [IQR]), mL	3.0 [2.0, 5.0]
Type of antibiotic (%)	
Augmentin	146 (94.8)
Clindamycin + Ciprofloxacin	5 (3.2)
Clindamycin	3 (1.9)
Intraoperative complication (%)	1 (0.6)
VAS score (median [IQR])	
POD1	2.0 [2.0, 3.0]
POD2	2.0 [2.0, 2.0]
Length of stay (median [IQR]), days	3.0 [2.0, 3.0]
Postoperative complication	
Mental nerve injury (%)	0
Inferior labial branch of mental nerve injury (%)	0
Mental branch of mental nerve injury (%)	0
Temporary hypoparathyroidism (%)	8 (5.2)
Permanent hypoparathyroidism (%)	1 (0.6)
Temporary RLN injury (%)	3 (1.9)
Permanent RLN injury (%)	1 (0.6)
Surgical site infection (%)	0
Bacterial culture strains (%)	
Aerobic	8 (5.2)
Anaerobic	22 (14.3)
No bacterial growth	115 (74.7)
No culture data	9 (5.8)
Final pathology (%)	
Benign	94 (61.0)
Cancer	45 (29.2)
Graves' disease	9 (5.8)
NIFTP	8 (5.2)

BMI body mass index, *FNA* fine needle aspiration, *IQR* interquartile range, *SD* standard deviation, *TOETVA* transoral endoscopic thyroidectomy vestibular approach, *TORT* transoral robotic thyroidectomy, *VAS* visual analog scale for pain, *RLN* recurrent laryngeal nerve, *NIFTP* non-invasive follicular thyroid neoplasm with papillary-like nuclear features

Learning curves for TORT and TOETVA

We studied the learning curve of TORT in 44 consecutive lobectomies. Figure 3 shows a flattening of operating time at 25 cases. The mean operative time for TOETVA was steady through the study.

Discussion

In this study, we present a series of transoral thyroidectomy performed by a single surgeon using endoscopic (TOETVA) or robotic (TORT) techniques and compare the outcomes between the two.

Before matching, the clinical characteristics showed that the TORT group had more men, higher Bethesda score, higher rate of cancer, and more prophylactic central neck lymph node dissection. In contrast, the TOETVA group had bigger benign nodules.

After controlling for age, sex, tumor size, extent of thyroidectomy, and Bethesda score by propensity score matching, we showed that TORT is as safe as TOETVA. However, the operative time for TORT was longer. The longer operating time may partially be explained by more prophylactic central neck dissection in the TORT group.

Complications were rare but can be instructive. Overall, the rate of temporary hypoparathyroidism was 5.2%, and permanent hypoparathyroidism was 0.6%, similar to open and other endoscopic or robotic thyroidectomy [24–29]. The rate of temporary RLN injury was 1.9% and permanent RLN injury was 0.6%, also comparable to the other approaches [30–35]. There was no mental nerve injury or surgical site infection.

One patient with cancer who underwent TOETVA had left subclavian vein injury during prophylactic central neck lymph node dissection. The injured vein was successfully repaired by an intracorporal suture without conversion to open thyroidectomy. One patient who had TORT sustained permanent injury of RLN, which was adherent to a posteriorly located cancer. The paralyzed cord was injected with hyaluronate with adequate voice recovery.

Although surgical time was longer for TORT than TOETVA, there was no difference in adverse event, such as surgical site infection or hypoparathyroidism. The longer surgical time for TORT likely included the need for preconsole time, docking time, instrument changing time, and lack of effective suction system. The surgeon's learning curve, shown by the decrease in operating time, likely also includes the learning curve of the surgical assistance team.

Robotic system can provide several advantages including a magnified 3-dimensional vision and tremor elimination, the additional arm allowing tissue countertraction, which

Table 2 Demographic, clinicopathologic, and treatment characteristics of patients before propensity score matching

Characteristic	TORT group ($n=55$)	TOETVA group ($n=99$)	P value
Age (median [IQR]), years	41.0 [35.0, 54.0]	45.0 [37.0, 57.5]	0.154
Sex (%)			
Female	43 (78.2)	93 (93.9)	0.008
BMI (mean (SD))	23.48 (3.56)	23.69 (3.58)	0.729
Nodular size (median [IQR]), cm	2.19 [1.36, 3.70]	3.56 [2.15, 4.58]	0.001
Preoperative FNA cytology (%)			
Bethesda class 4, 5 and 6	37 (67.3)	32 (32.3)	<0.001
Bethesda class 2 and 3	18 (32.7)	67 (67.7)	
Operative time (median [IQR]), min	308 [284, 391]	227 [201, 266]	<0.001
Extent of surgery (%)			
Bilateral total thyroidectomy	11 (20.0)	17 (17.2)	0.827
Unilateral thyroidectomy	44 (80.0)	82 (82.8)	
Central neck lymph node dissection (%)	28 (50.9)	12 (12.1)	<0.001
Number of retrieved lymph nodes (mean (SD))	4.00 (2.48)	5.18 (3.40)	0.244
Positive central neck lymph node (%)	7 (26.9%)	3 (27.3%)	0.736
Blood loss (median [IQR]), mL	3.0 [2.0, 3.5]	3.0 [2.0, 5.0]	0.949
Intraoperative complication (%)	0 (0.0)	1 (1.0)	1
Cancer (%)	23 (41.8)	22 (22.2)	0.017
VAS score (median [IQR])			
POD1	2.0 [2.0, 3.0]	2.0 [2.0 3.0]	0.884
POD2	2.0 [2.0, 2.0]	2.0 [2.0, 2.0]	0.585
Length of stay (median [IQR]), days	3.00 [2.0, 3.0]	3.0 [2.0, 3.0]	0.08
Postoperative complication			
Mental nerve injury (%)	0	0	NA
Inferior labial branch of mental nerve injury (%)	0	0	NA
Mental branch of mental nerve injury (%)	0	0	NA
Temporary hypoparathyroidism (%)	1 (1.8)	7 (7.1)	0.26
Permanent hypoparathyroidism (%)	0	1 (1.0)	1
Temporary RLN injury (%)	1 (1.8)	2 (2.0)	1
Permanent RLN injury (%)	1 (1.8)	0	0.357
Surgical site infection (%)	0	0	NA

BMI body mass index, *FNA* fine needle aspiration, *IQR* interquartile range, *SD* standard deviation, *TOETVA* transoral endoscopic thyroidectomy vestibular approach, *TORT* transoral robotic thyroidectomy, *VAS* visual analog scale for pain, *RLN* recurrent laryngeal nerve

can facilitate superior thyroid pole dissection, perineural tissue dissection, and parathyroid gland preservation [36–39]. In the first two cases of TORT we did not use the additional axilla port, as per routine in TOETVA. Without the additional axillary port for retraction, we found the robot added no benefit to endoscopy, and may have some potential hazard from the bulky robotic instrument and lack of tactile sensation. To take fully advantage of the robot, the axillary robotic arm is essential [23]. It helped in countertraction and dissection, reduced instrument change, helped as a stimulator in nerve monitoring, and as a route for suction-irrigation.

Since we removed larger specimen through an axillary incision in TOETVA, for this subgroup of patients the number of incisions was the same as in TORT. The newer da Vinci SP system uses only a single port and is under investigation for use in thyroidectomy [40–42]. The fluorescent technology in both robotic and endoscopic surgery may also help intraoperative identification and preservation of the parathyroid glands [43–46]. These may facilitate complex thyroid surgery and central neck lymph node dissection. In our experience, central neck dissection seems to be easier to perform with the robot, but a randomized study would be needed to confirm this.

It is difficult to remove larger specimens intact through small incisions. Piecemeal removal [47] risks seeding and recurrence of incidental cancer [48] and inaccurate diagnosis because of capsule disruption [49, 50]. In our series we found NIFTP in 5.2% and incidental malignancy in

Table 3 Demographic, clinicopathologic, and treatment characteristics of patients after propensity score matching

Characteristic	TORT Group (*n* = 53)	TOETVA Group (*n* = 53)	*P* value
Age (median [IQR]), year	43.38 (12.84)	45.75 (15.47)	0.391
Sex (%)			
Female	41 (77.4)	48 (90.6)	0.112
BMI (mean (SD))	23.55 (3.58)	23.66 (3.73)	0.885
Nodular size (median [IQR]), cm	2.19 [1.36, 3.70]	2.90 [1.80, 4.20]	0.144
Preoperative FNA cytology (%)			
Bethesda class 4, 5 and 6	37 (69.8)	31 (58.5)	0.311
Bethesda class 2 and 3	16 (30.2)	22 (41.5)	
Operative time (median [IQR]), min	308 [284, 388]	228.00 [201.00, 267.00]	< 0.001
Extent of surgery (%)			
Bilateral total thyroidectomy	10 (18.9)	8 (15.1)	0.796
Unilateral thyroidectomy	43 (81.1)	45 (84.9)	
Central neck lymph node dissection (%)	28 (52.8)	10 (18.9)	0.001
Number of retrieved lymph nodes (mean (SD))	4.00 (2.48)	5.50 (3.41)	0.153
Positive central neck lymph node (%)	7 (26.9)	3 (30)	0.707
Blood loss (median [IQR]), mL	3.0 [2.0, 3.0]	3.0 [2.0, 3.0]	0.144
Intraoperative complication (%)	0	1 (1.9)	1
Cancer (%)	23 (43.4)	16 (30.2)	0.227
VAS score (median [IQR])			
POD1	2.0 [2.0, 3.0]	2.0 [2.0, 3.0]	0.473
POD2	2.0 [2.0, 2.0]	2.0 [2.0, 2.0]	0.979
Length of stay (median [IQR]), days	3.0 [2.0, 3.0]	3.0 [2.0, 3.0]	0.029
Postoperative complication			
Mental nerve injury (%)	0	0	NA
Inferior labial branch of mental nerve injury (%)	0	0	NA
Mental branch of mental nerve injury (%)	0	0	NA
Temporary hypoparathyroidism (%)	0	3 (5.7)	0.243
Permanent hypoparathyroidism (%)	0	1 (1.9)	1
Temporary RLN injury (%)	1 (1.9)	2 (3.8)	1
Permanent RLN injury (%)	1 (1.9)	0 (0.0)	1
Surgical site infection (%)	0	0	NA

BMI body mass index, *FNA* fine needle aspiration, *IQR* interquartile range, *SD* standard deviation, *TOETVA* transoral endoscopic thyroidectomy vestibular approach, *TORT* transoral robotic thyroidectomy, *VAS* visual analog scale for pain, *RLN* recurrent laryngeal nerve

14.1%, reaffirming the importance of removing the specimen intact. Some surgeons use a hidden submental incision for the transoral thyroidectomy [51]. For extraction of large specimen in TOETVA, we preferred to use an axillary incision, which can be made quickly, safely and allows for removal of large nodules while preserving excellent cosmetic effect. By extraction the specimen intact from axillary incision, we could expand the size criteria for malignant nodule up to 4 cm if there is no evidence of extrathyroidal extension by preoperative evaluation. The resection margins were all negative in our patients with cancers.

Of the four patients who underwent completion total thyroidectomy after initial transoral thyroidectomy, the interval was 2, 7, 12, and 20 weeks. We routinely use anti-adhesion hyaluronic acid gel at the end of the operation and closed the strap muscle to prevent trachea adhesion to the skin. We had no specific difficulties in the completion thyroidectomy except for the case done within 2 weeks, in which we found the skin flap to be harder and there was more adhesion encountered during the operation.

For the 3 patients who underwent transoral approach after previous open thyroidectomy, we performed preoperative CT scan to confirm the extent of residual thyroid tissue. During the operations, there were no specific difficulties and the patients recovered as usual. One of these patients had a hypertrophic scar after the first operation that required scar revision and wanted to avoid the same problem.

Mental nerve injury was a major concern initially for transoral thyroidectomy [14, 52]. The risk was lowered by

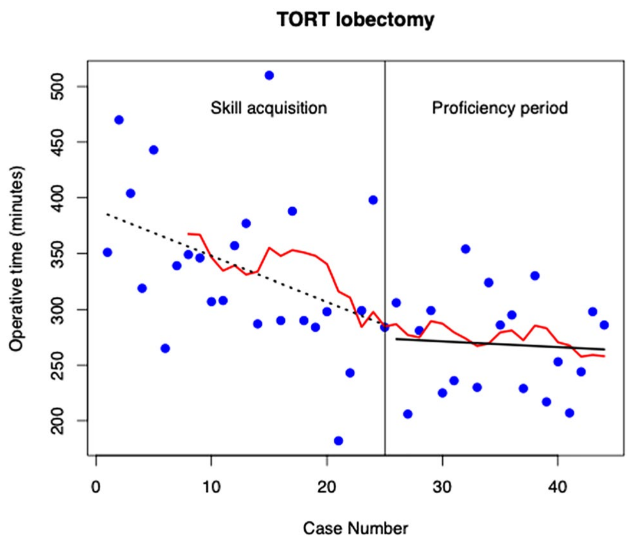

Fig. 3 Learning Curve for Transoral Robotic Thyroidectomy (TORT). The learning curve for 44 TORT lobectomy. The simple moving average curve of order 7 is depicted in red, which was used to define the proficiency case. The slope of the skill acquisition period (cases 1–25) is denoted by the dashed black line, and the slope of the proficiency period (cases 26–44) is denoted by the solid black line. The change in the slope of the line is statistically significant from zero (−4.12, 95% confidence interval [CI], 8.01–0.24, $P=0.039$). The operative time between the 2 periods is significantly different (319.0 min [IQR 290.0–377.0] vs 281 min [IQR 229.5–298.5], $P=0.001$, Kruskal–Wallis rank sum test) (Color figure online)

moving the sites of oral incision closer to the lips [22, 23]. We further improved this by standardizing the central incision through a "safe triangle" informed by the knowledge of metal nerve anatomy with its three branches [53, 54]. The safety triangle involved a standardized inverted-V incision for the central trocar. The sides of the inverted-V parallel the fiber of the inferior labial branch to prevent its injury [55]. The higher position and longer incision also allows for an increased range of movement of the central trocar.

We found the learning curve for TORT to be 25 cases, which is shorter than those reported for other robotic thyroidectomy (typically between 35 and 50 cases for transaxillary, bilateral axillo-breast, and retroauricular approaches) [56–61]. Similarly, TOETVA appears to require a shorter learning curve compared with other endoscopic thyroidectomy techniques [62–65]. We cannot explain the lack of an observable learning curve in our TOETVA series. It is possible that for a high-volume thyroid surgeon who also routinely perform other laparoscopic and endoscopic operations and had been trained in the technique of TOETVA as a fellow, the learning curve may not be observable. The training process might have helped to obscure the early learning curve for TOETVA.

Regarding the obese patients, in this series of 154 operations, we have 43 operations (27.9%) on overweight patients (BMI 25–29.9) and 7 operations (4.5%) on obese patients (BMI > 30). Despite the obesity case numbers being limited, we do not perceive the difference between obese and non-obese patients during the operation or during postoperative care. The result is compatible with previous literature [47, 66]. In our view, we suggest that transoral thyroidectomy has the potential benefit in obese patients compared to open thyroidectomy or at least another remote-access thyroidectomy (Trans-axilla, BABA, facelift access, etc.) because of less skin flap needs to be elevated and smaller incision wound. However, this hypothesis needs to be investigated in a further well-designed study.

Considering the costs related to surgery, transoral endoscopic surgery only needs a conventional laparoscopic instrument and energy device. The cost is very similar to that of an open thyroidectomy. Also, as there are more and more robotic surgical systems being announced, the cost of robotic surgery will continue to drop. In a previous publication concerning the U.S. population, casual observers were willing to pay an average of $10,116 to avoid having a neck scar, suggesting that society highly values avoiding them [2].

The length of stay is slightly higher in our study. As an innovative procedure, we have been initially more conservative. The length of stay is now almost the same as our open thyroidectomy. Even with an open thyroidectomy, our patients do not prefer same-day surgery or an over-night stay. The longer length of stay in Asia rather than in a western country might be due to the difference in culture and the insurance system. There is only an over-night stay for a TOETVA performed in US. In a previous study, the average length of stay in the US has been described as 0.2–1.6 days [67].

The infection rate in transoral thyroidectomies is low in reported literature [68, 69]. However, it is a major concern when we change the thyroidectomy technique from clean wound to clean-contaminated wound. Using the prophylactic bacterial culture, we were able to better understand the possible pathogen, the antibiotic sensitivity in the transoral thyroidectomy, and the suitable empiric antibiotic treatment for the patient. Our data showed that 74.7% of cultures were without bacterial growth, and 14.3% of cultures had slow growing anaerobic bacteria. This might partially explain the low infection rate in transoral thyroidectomies.

Our study has several limitations. First, although propensity score matching was conducted, observational study can have selection bias. Second, retrospective analyses have limited information available. Third, this study is from a single Asian institute, and the findings may not be generalizable. Finally, we have no data on the long-term oncological outcomes of transoral thyroidectomy for cancer.

In conclusion, transoral thyroidectomy, both endoscopic (TOETVA) and robot assisted (TORT), are safe and have relatively short learning curve. TORT is associated with longer operating time but may be helpful for surgeon to perform more complex thyroid operations. Future prospective studies are needed to confirm our findings.

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Compliance with ethical standards

Disclosures Drs. Yu-Hsien Chen, Hoon-Yub Kim, Angkoon Anuwong, Ting-Shuo Huang, and Quan-Yang Duh have no conflicts of interest or financial ties to disclose.

Ethical approval This study was approved by the Ethics Committee of the Chang Gung Medical Foundation Institutional Review Board (no. 201901376B0) and was conducted in accordance with the Declaration of Helsinki (of the World Medical Association). Informed consent was waived because the data were analyzed retrospectively.

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