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ORIGINAL SCIENTIFIC REPORT

Transoral Robotic Thyroidectomy for Papillary Thyroid Carcinoma: Perioperative Outcomes of 100 Consecutive Patients

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Abstract

Background Endoscopic transoral thyroidectomy is a recently introduced technique of remote access thyroidectomy. We previously reported the feasibility of the robotic approach (TORT). Nevertheless, experience to date is limited, with scant data on outcomes in patients with papillary thyroid carcinoma (PTC).

Methods This was a retrospective analysis of prospectively collected data. Patients with PTC, who underwent TORT at a single center between March 2016 and February 2017, were analyzed.

Results There were a total of 100 patients (85 women, 15 men) with a mean age of 40.7 ± 9.8 years, and a mean tumor size of 0.8 ± 0.5 cm. Nine patients underwent a total thyroidectomy, and 91 underwent a lobectomy. The operative time for a total thyroidectomy and lobectomy was 270.0 ± 9.3 and 210.8 ± 32.9 min, respectively. Ipsilateral prophylactic central neck compartment dissection was performed routinely with retrieval of 5.0 ± 3.6 lymph nodes. Perioperative morbidity was present in nine patients including transient recurrent laryngeal nerve palsy (n = 1), postoperative bleeding requiring surgical intervention (n = 1), zygomatic bruising (n = 2), chin flap perforation (n = 1), oral commissure tearing (n = 2), and chin dimpling (n = 2). There was no conversion to endoscopic or conventional open thyroid surgery.

Conclusion In this study, TORT could be safely performed in a large series of patients with PTC without serious complications. In selected patients, TORT by experienced surgeons could be considered an alternative approach for remote access thyroidectomy.

Hong Kyu Kim and Young Jun Chai contributed equally to this study as co-first authors.

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Abbreviations

TORT	Transoral robotic thyroidectomy
PTC	Papillary thyroid carcinoma
RLN	Recurrent laryngeal nerve
VAS	Visual analog scale
AJCC	American Joint Committee on Cancer
CND	Central neck dissection
TSH	Thyroid stimulating hormone
Tg	Thyroglobulin

Introduction

Since its original description in 2010 [1], various transoral thyroidectomy approaches have been reported [2–4]. Nevertheless, the approaches through the floor of the mouth did not gain popularity because of high complication and conversion rates [2, 5]. Instead, a vestibular approach has become more successful because of a better surgical exposure and less risk of injury to the mental nerve [6, 7]. The feasibility of the vestibular approach was first reported in humans in 2014 [8], and since then numerous studies have shown the safety of this approach [9–15].

The growing interest to the transoral approach can be attributed to a number of advantages. First of all, compared to conventional and other endoscopic procedures, it yields better cosmetic results because the incisions are placed within oral mucosa. Secondly, there is a more limited flap dissection compared to other remote access approaches [16]. Furthermore, it utilizes a midline approach, thereby providing an easier access to both thyroid lobes in contrast to the transaxillary and retro-auricular techniques that employ a lateral approach [16].

Compared to endoscopic thyroid surgery, robotic thyroid surgery is four times more expensive in South Korea and needs more time for docking of robotic system. However, it has become a popular procedure over the last decade since robotic systems offer high-definition three-dimensional imaging, articulation, and a more stable surgical platform. Recognizing these benefits, we developed a robotic transoral robotic thyroidectomy (TORT) technique in 2011 [17, 18]. We have previously described the technique and early results [19]. The aim of this study is to analyze the perioperative outcomes in a large series of patients with papillary thyroid carcinoma (PTC).

Methods

Patients

This study was approved by the Institutional Review Board of Korea University Hospital (IRB No. ED14085). Indications for surgery were fine needle aspiration biopsy showing suspicious malignancy or malignant (Bethesda category V or VI) less than 3 cm with no evidence of extrathyroidal extension or bulky lymphadenopathy on preoperative ultrasound. Exclusion criteria were history of neck surgery and lymph node metastasis at the lateral neck compartment. Patients who opted to undergo surgery were extensively counseled regarding the approaches utilized for thyroid surgery at our hospital (conventional transcervical, bilateral axillo-breast, and transoral). Total thyroidectomy was performed for the patients with bilateral PTC or tumor size larger than 2 cm. Of the patients who underwent TORT between March 2016 and February 2017, the patients who had PTC on the final pathologic examination were enrolled. The procedures were performed by a single surgeon (H.Y.K.).

Preoperative preparation

All patients underwent preoperative neck ultrasound to assess the thyroid and cervical lymph nodes, indirect laryngoscopy to evaluate the vocal cords and expert dental examination to optimize oral hygiene to prevent bacterial infection.

Operative procedure

Incision and flap creation

The TORT procedure has been described in detail previously [19]. A prophylactic antibiotic (cefazedone 1 g) was administered intravenously 30 min before the incision. Approximately, 10 mL of a dilute epinephrine-saline solution (1:200,000) was injected into the lower lip down to the tip of the chin via a 22-gauge spinal tapping needle. An inverted U-shaped midline incision measuring 2 cm in length was made at the end of the frenulum of the lower lip (Fig. 1a). Subcutaneous tissue of the chin was subsequently dissected using electrocautery and mosquito clamps. 30–50 mL of epinephrine-saline solution was injected into the subplatysmal space down to the sternum using a Veress needle (Medtronic, Minneapolis, MN, USA). This space was further developed using a vascular tunneler through the midline incision. A midline trocar was inserted through this space. Two lateral incisions were then made 1 cm medial to the angle of the mouth (Fig. 1a), and 5-mm

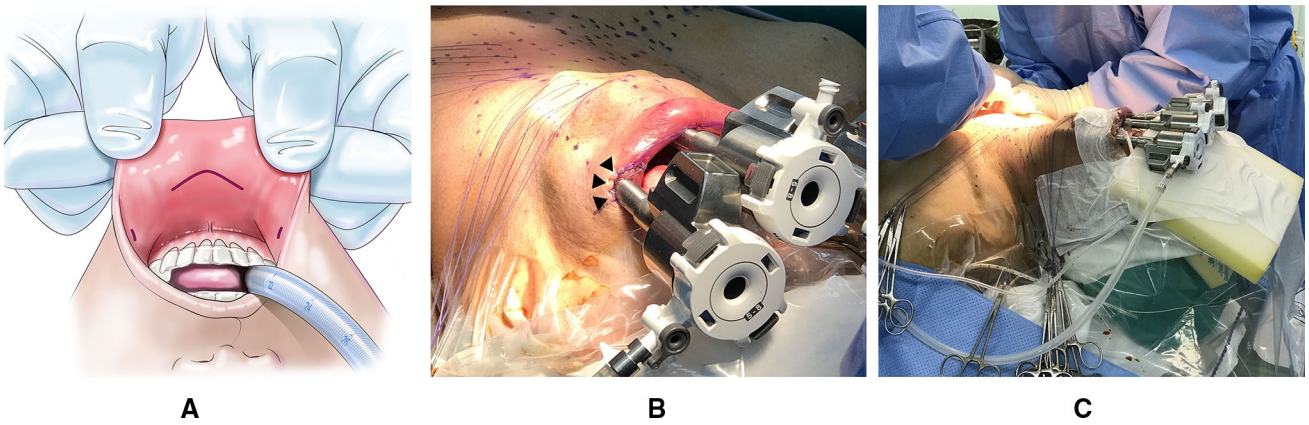

Fig. 1 Incision and flap formation of transoral robotic thyroidectomy. **a** Location of incisions. **b** Oral mucosal continuous interlocking sutures. **c** Application of plaster over oral commissures and protective sponge over zygomatic bones

trocars were inserted after injecting 10 mL of epinephrine-saline solution. Before robotic docking, further subplatysmal dissection was performed using a suction electrocautery and ultrasonic energy device (Harmonic Ace®+, Ethicon Endo-Surgery, Cincinnati, OH, USA) through the both lateral ports. The upper, lower, and lateral margins of the flap were formed by the thyroid cartilage, sternal notch, and the medial border of the sternocleidomastoid muscle, respectively. Continuous interlocking sutures were applied at both lateral aspects of the lateral trocars (Fig. 1b), and protective sponges were placed on the patient's face (Fig. 1c). An 8-mm bariatric trocar was inserted through a right axillary incision, and then the robot was docked. This additional axillary incision was used for counter-traction, specimen removal and later closed-suction drain insertion.

Da Vinci-Si and -Xi surgical systems

TORT procedures were performed using both the da Vinci-Si and -Xi Surgical Systems—the Si system was utilized for the first 58 patients and the Xi system for the remaining 42. The most notable differences between the two systems were related to the size of the ports and the docking method. With the Si system, a 12 mm camera port, 5 mm lateral working ports, and an 8-mm axillary trocar were used. In contrast, all four ports were 8 mm with the Xi system. When using the Si system, the patient was placed in the lithotomy position, and patient cart was docked in the midline between the legs (Fig. 2a). In the Xi system, the patient was supine and docking was performed from the side of the patient (Fig. 2b).

Thyroidectomy procedure

After robotic docking, the isthmus was divided in the midline and the sternothyroid muscle retracted laterally by dissecting it off the thyroid. Next, the avascular plane between the upper pole of the thyroid and the cricothyroid muscle was developed and the upper pole vessels were divided individually using ultrasonic energy device (Fig. 3a). The superior parathyroid gland was identified and dissected off the thyroid gland.

To identify the recurrent laryngeal nerve (RLN), the thyroid gland was retracted upward and a meticulous dissection performed around the site of insertion (Fig. 3b). A prophylactic unilateral central neck dissection was performed in each patient (Fig. 3c). The specimens were removed by using an endoplastic bag through the axillary incision. A Jackson-Pratt drain was placed through the axillary port. Then the strap muscles were approximated in the midline using an absorbable suture. The oral mucosal incisions were closed using interrupted absorbable sutures (4–0 polyglactin).

Postoperative management and follow-up

A clear liquid diet was started 4 h postoperatively, followed by a soft diet on postoperative day (POD) 1 and regular diet on POD 2. The Jackson-Pratt drain was removed on the day of discharge. Postoperative pain management included oral acetaminophen (650 mg) supplemented by intramuscular ketorolac tromethamine injection (30 mg) if needed.

After discharge, patients returned to the outpatient clinic for stitch removal on POD 14, when indirect laryngoscopy was also performed to assess the function of the vocal cords. Patients were again seen in follow-up at 1 and

Fig. 2 Docking of robot. **a** da Vinci-Si surgical system. **b** da Vinci-Xi surgical system

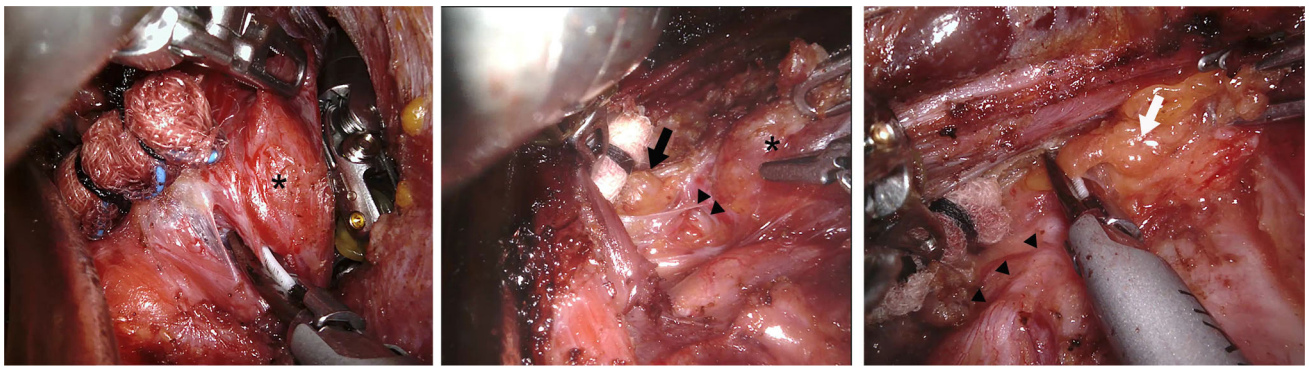

Fig. 3 The surgical steps of transoral robotic thyroidectomy. **a** Ligation of the superior thyroidal vessels of the right thyroid gland. **b** Identification of the left recurrent laryngeal nerve (arrow head) and superior parathyroid gland (black arrow). **c** Completion of left thyroidectomy preserving recurrent laryngeal nerve (arrow head) and lower parathyroid gland (white arrow). *Thyroid gland

3 months and every 6 months thereafter. Physical examination, neck ultrasonography, and serum Tg levels were examined every 6 months during the follow-up period.

RAI treatment protocol

Postoperative RAI remnant ablation was performed 9–12 weeks after thyroidectomy according to the protocol established by the Endocrinology Division of the Korea University Anam Hospital. The second RAI treatment was performed 6 months after the first RAI treatment. Serum Tg, anti-thyroglobulin antibody, and TSH levels were measured at the time of remnant ablation after thyroid hormone withdrawal or recombinant human TSH (Thyrogen, Genzyme, Cambridge, MA, USA) injection for TSH stimulation. Successful ablation was defined as a serum-stimulated Tg level <1.0 ng/mL. A dose of 100 mCi was used for patients with pathologic N1a and tumor diameter of >2 cm, or with pathologic N0 and tumor diameter of >2 cm in the presence of extra-thyroidal extension. A dose of 150 mCi was used for patients with pathologic N1b or tumor diameter of ≥4 cm. Patients with pathologic T1aN0M0 tumors were excluded from RAI treatment.

Outcome measurement

Demographic, clinical and operative data were analyzed using descriptive statistics. Postoperative pain was evaluated using a visual analog scale (VAS) ranging from 0 (no pain) to 10 (worst pain). Hypoparathyroidism was defined

as serum parathyroid hormone level the below normal range (normal range: PTH> 8 pg/mL) and/or calcium level below the normal range (normal range: total calcium > 8.8 mg/dL) with an ongoing need for calcium requirement. Vocal fold palsy or hypoparathyroidism lasting less than 6 months was defined as transient.

Results

Patient characteristics

Patient demographic and clinicopathologic details are listed in Table 1. There were 85 women and 15 men. The mean age and body mass index were 40.7 ± 9.8 years and 23.5 ± 3.6 kg/m^2, respectively. The mean tumor size was 0.8 ± 0.5 cm. Nine patients underwent a total thyroidectomy, and 91 underwent a lobectomy. The patients were followed-up for a median of 16.1 months (range, 8.2–20.4 months).

Pathology

Pathologic results of TORT are listed in Table 2. There were 78 cases of papillary microcarcinoma and 22 cases of papillary carcinoma. A mean of 5.0 ± 3.6 lymph nodes was retrieved per patient. Neck lymph node metastasis was identified in 34 patients. According to the American Joint Committee on Cancer's Cancer Staging, 8th edition, 77 patients were in stage I and 23 patients were in stage II.

Table 1 Demographics and clinical details

Variables	Value
Age (mean ± SD), years	40.7 ± 9.8 (range, 19–62)
Gender	
Male	15
Female	85
Body mass index (mean ± SD), kg/m^2	23.5 ± 3.6 (range, 16.4–36.1)
Tumor location, *n*	
Right lobe	49
Left lobe	42
Isthmus	4
Both lobes	5
Extent of surgery, *n*	
Lobectomy and CND	91
Total thyroidectomy and CND	9

SD standard deviation

Table 2 Pathologic results

Variables	Value
Tumor size, mean, cm	0.8 ± 0.5 (range 0.2–2.8)
≤1.0 cm, *n*	78
>1.0 cm, *n*	22
Number of retrieved LNs	5.0 ± 3.6 (range 0–23)
Number of involved LNs	0.9 ± 1.9 (range 0–11)
Nodal stage, *n*	
N0	66
N1a	34
N1b	0
AJCC stage, *n*	
I	77
II	23
III	0
IV	0

AJCC American Joint Committee on Cancer

Surgical outcomes

Surgical outcomes of TORT are presented in Table 3. The operative time for a total thyroidectomy and lobectomy was 270.0 ± 9.3 and 210.8 ± 32.9 min, respectively (Fig. 4). The mean serum Tg level at 3 months postoperatively was 0.92 ± 0.21 ng/mL for the patients who underwent total thyroidectomy. The mean pain score of the operative day was 3.6, which gradually decreased to 1.4 on POD#3. There was no conversion to conventional or endoscopic thyroidectomy. Of the nine patients who underwent total thyroidectomy, three patients had taken RAI ablation after the operation. The serum-stimulated Tg levels on ablation of the three patients was 0.56, 0.11 and 0.14, respectively. There was no recurrence or mortality during the follow-up.

Complications

Postoperative surgical complications of TORT are presented in Table 4. One patient developed a transient vocal cord palsy, which recovered within 3 months. Bleeding was observed in one patient who underwent right thyroid lobectomy with central neck dissection 20 min postoperatively. Bleeding from the anterior jugular vein was discovered and controlled endoscopically using ultrasonic energy device.

For TORT-specific complications, there was no incidence of mental nerve injury (paresthesia of the lower lip or chin). Zygomatic bruising was detected in two patients (case numbers #5, #13), which resolved within 10 days. In

Table 3 Operative outcomes

Variables	Number of patients	Value
Operative time (mean ± SD), min		
Lobectomy and CND	91	210.8 ± 32.9
Total thyroidectomy and CND	9	270.0 ± 9.3
Serum Tg level at post-op 3 months (ng/mL)	9[a]	0.92 ± 0.21
TSH level on ablation (uIU/mL)	3	71.2 ± 28.2
Stimulated Tg level on ablation (ng/mL)	3	0.3 ± 0.3
Serum-stimulated Tg < 1.0 ng/mL at the first ablation	3	3/3 (100%)
Pain score, visual analog scale		
Day #0		3.6 ± 1.4
Day #1		2.6 ± 1.2
Day #2		2.1 ± 1.1
Day #3		1.4 ± 1.3
Open or conventional endoscopic conversion	0	0
Recurrence, *n*	0	0

CND central neck dissection, *SD* standard deviation, *TSH* thyroid stimulating hormone, *Tg* thyroglobulin

[a]The number of the patients who underwent total thyroidectomy

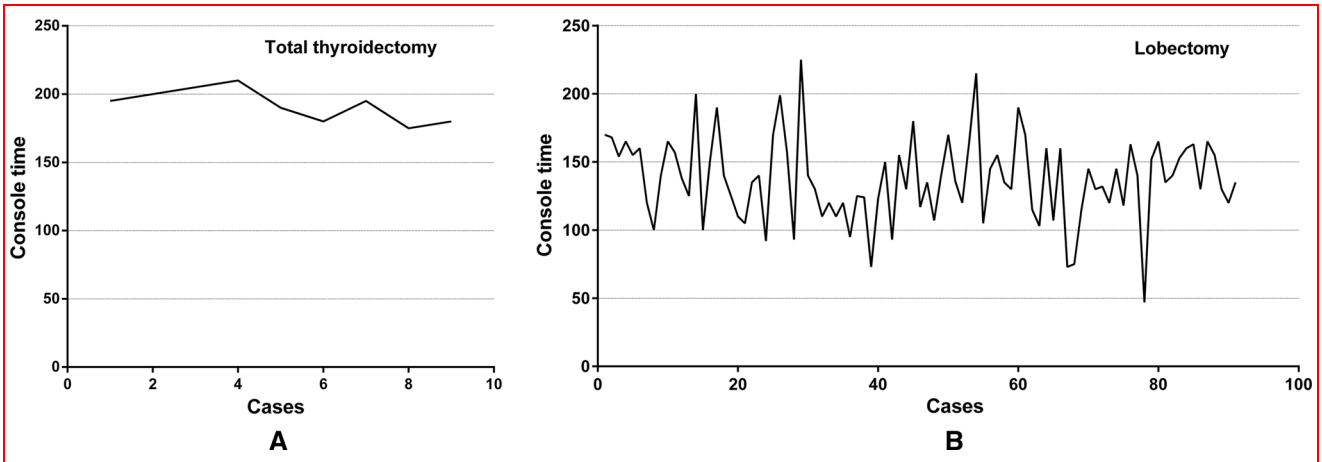

Fig. 4 Line graph showing the changes in console time (minutes) for total thyroidectomy and lobectomy chronologically in the study. **a** Total thyroidectomy. **b** Lobectomy

case number #3, a perforation of the skin over the chin occurred due to skin burn during flap dissection, which was managed with suturing. The scar at the perforation site disappeared within 30 days. In two patients (case numbers #6, #27), a skin tearing at the oral commissure (length of tear 1 cm) occurred, requiring suturing with an absorbable suture. There was complete resolution within 2 months. Dimpling of the lower chin in the midline was observed in two patients (case number #21, #34), which disappeared within 3 months.

Discussion

To our knowledge, this is the largest case series with TORT reported to date. Our results validate the feasibility and efficacy of the robotic transoral approach in a large series of patients with moderately challenging pathology. Despite concerns, this novel approach is not associated with an increased incidence of infection, flap issues, or nerve injury, and the risk of recurrent laryngeal nerve injury does not differ from that associated with other types of thyroid surgeries.

Table 4 Postoperative surgical complications

Variables	Value
General complications, n	
Bleeding	1
Surgical site infection	0
Seroma collection	0
Chyle leakage	0
Vocal cord palsy	
Transient	1
Permanent	0
Hypoparathyroidism	
Transient	0
Permanent	0
TORT-specific complications, n (case number)	
Mental nerve injury	0
Zygomatic bruising	2 (5, 13)
Chin flap perforation	1 (3)
Oral commissure tearing	2 (6, 27)
Dimpling on the chin	2 (21, 34)

Nevertheless, surgeons interesting in implementing TORT into their practice need to be aware of certain TORT-related possible complications. Mental nerve can cause significant morbidity in these patients. An injury to the nerve leads to transient or permanent numbness of the lower lip and the chin based on the severity of the injury. During the early phases of implementation of TORT, we used midline and lateral incisions at the gingival-buccal sulcus and at the first molar, respectively, which resulted in a significantly high rate of mental nerve injury [17]. It was because the incisions were too close to the nerve root and caused overstretching of the mental nerve related to the force applied by the robotic arms. Subsequently, we modified our technique to relocate the midline incision to the end of the frenulum of the lower lip, and the lateral incisions to 1 cm medial to both lateral oral commissures and this enabled us to avoid this nerve injury [19]. Patients enrolled in this study underwent TORT using this modification, and to date, no patient has reported persistent numbness in this area.

Zygomatic bruising was observed in our early experience secondary to compression of the patient's face by the robotic arms. Application of protective sponges on the patient's face prevented this complication. Another problem in our experience was a chin flap perforation related to electrocautery during initial dissection because the plane of dissection was perpendicular and not parallel to the lower lip. We resolved this problem in subsequent patients by alternating the use of electrocautery and blunt mosquito clamps for dissection. Dimpling of the skin at the level of the chin was seen in two of our patients. The dimpling could have been secondary to the wide range of movement of a large-sized (12 mm) midline trocar of the da Vinci-Si system. No instances of skin dimpling have been reported since we have switched to using an 8-mm midline trocar with the da Vinci-Xi system. Finally, we observed oral commissure tearing in two patients, which was due to excessive force on the oral commissure. Movement of the lateral trocars is maximized during upper pole dissection because of the angle of dissection at the upper pole of the thyroid while ligating superior thyroid vessels. To prevent injury to the oral commissures secondary to this lateral trocar movement, we started using continuous interlocking sutures at the lateral aspect of the lateral trocars from the 30th case onward, after which no oral commissure tearing was reported. A majority of TORT-specific complications are secondary to physical trauma; therefore, it is important for both surgeons and assistants to understand and carefully monitor movements of the robotic arms. Nevertheless, in our experience, we have seen all of these specific complications to resolve uneventfully over time.

An advantage of TORT compared to other remote access thyroidectomy procedures is that it provides an easier approach to both sides of the central neck compartment and along with a broad downward midline view. Upward midline approaches (bilateral axillo-breast) and lateral approaches (transaxillary or retro-auricular) provide limited access to the lower central neck compartment and contralateral side, respectively [20, 21]. In this study, we routinely performed central neck compartment dissection, and the number of retrieved lymph nodes was comparable to those reported by previous studies [22–24], despite the learning curve involved.

A limitation of transoral thyroidectomy could be difficulty in removing specimens through a 12 mm incision and associated oncologic risks including track recurrence in cancer patients [25]. Some surgeons have described removal of the specimen in piecemeal [26]. Track recurrence is often associated with a fractured specimen and even can occur following excision of a tumor that was preoperatively considered benign [27]. Because of these concerns, we have removed the specimens intact by placing the specimen inside a bag delivered out through a small axillary incision.

TORT utilizes a narrow flap dissection similar to that performed during conventional surgery limited to between the sternal notch and the thyroid cartilage, and therefore, is expected to cause lesser pain than other remote access approaches. In this study, mean postoperative pain scores at POD 0, 1, 2, and 3 were 3.6, 2.6, 2.1, and 1.4, respectively. These scores were at least comparable to those reported after bilateral axillo-breast and transaxillary

thyroidectomy in the literature [23, 28]. Although this is an indirect comparison, the results demonstrate that TORT does not cause excessive postoperative pain.

The 2015 ATA guidelines recommend either a lobectomy or active surveillance for micropapillary thyroid cancer. For 1–4-cm papillary cancer, lobectomy or total thyroidectomy is recommended, but prophylactic central neck dissection is discouraged. However, central neck compartment dissection is not technically difficult in TORT as mentioned earlier, and it is difficult to perform reoperation in the case of a later central lymph node recurrence. Therefore, we initially performed prophylactic ipsilateral central neck compartment dissection.

In conclusion, as a follow-up to our initial description of the technique, this large experience in a more challenging series of selected patients with PTC, we demonstrated the safety and efficacy. Standardized TORT procedures may constitute a new option for remote access thyroidectomy by experienced surgeons in carefully selected patients.

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Compliance with ethical standards

Conflict of interest Hong Kyu Kim, Young Jun Chai, Gianlorenzo Dionigi, Eren Berber, Ralph P. Tufano, Hoon Yub Kim have no conflicts of interest or financial ties to disclose.

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