Transoral periosteal thyroidectomy: cadaver to human

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Abstract

Background Although endoscopic thyroid surgery is
gaining wide acceptance, existing endoscopic methods for
thyroidectomy are blamed for the increased frequency of
flap dissections and longer surgical times. More recently,
transoral endoscopic thyroidectomy has overcome the
limitations of previous approaches. Herein, we present our
initial experience with transoral periosteal thyroidectomy
(TOPOT) in cadaver and porcine models. Using these
models, the surgical view was improved and had greater
freedom of motion; the technique was then performed in
human subjects using robotic TOPOT, which has not pre-
viously been reported.
Method TOPOTs were performed in seven fresh human
cadavers and ten live pigs. Total thyroidectomies were
performed in all cadavers and pigs. After the cadaver and
animal trials, four human patients underwent robotic TO-
POT performed using the da Vinci® surgical system at
Korea University Anam Hospital. Recurrent laryngeal
nerve function, intra- and postoperative complications, and
postoperative outcomes were assessed in all patients.
Result One left lobectomy for follicular adenoma, two
right lobectomies for nodular hyperplasia, and one left
lobectomy with a central neck dissection for papillary
thyroid microcarcinoma were performed in the human
subjects using a robotic transoral periosteal approach. In

three cases, paresthesia occurred in the mental nerve, but
this improved within 4 weeks in all cases. No local
infections occurred at the incision site or anterior neck, and
no recurrent laryngeal nerve cord palsies occurred
postoperatively.
Conclusion TOPOT may be an effective and safe
approach for robotic thyroid surgery.

Keywords Thyroidectomy · Transoral · Periosteal ·
Minimally invasive

Transoral thyroidectomy was recently introduced as an
approach for minimally invasive thyroid resection. Witzel
et al. [1] were the first to attempt this procedure in 2008
using a single access port that included an accessory
anterior neck port. This was a hybrid approach requiring a
sublingual incision and an anterior neck incision. Wilhelm
et al. have since introduced the transoral video-assisted
thyroidectomy (TOVAT) technique which is an entirely
transoral endoscopic approach and therefore a natural ori-
fice surgery (NOS) [2]. Karakas et al. [3] were the first to
perform a transoral thyroid and parathyroid surgery using a
lateral sublingual approach. Richmon et al. [4] also intro-
duced a transoral technique for robotic thyroidectomy
using the TOVAT method.

Minimally invasive thyroid surgery has evolved over the
past 10 years. Several different techniques were pioneered
to avoid neck scarring. Among them, the gasless axillary
approach [5] and the bilateral axillo-breast approach [6] are
the most widely accepted methods. However, the existing
endoscopic and robotic methods for thyroidectomy have
been criticized as not being truly minimally invasive,
because they require extensive dissection of the chest and
neck, as well as a long surgical duration. Many surgeons

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believe that these procedures are more invasive than the conventional open thyroid surgery, and thus research has continued on devising less invasive methods. Transoral thyroid surgery was developed to fill the need for a truly minimally invasive approach. Recently, Wilhelm et al. [7] conducted a clinical study of transoral thyroidectomy in eight patients. Nakajo et al. [8] also reported results from a clinical trial that evaluated transoral endoscopic thyroidectomy using a single incision without gas.

These studies inspired us to develop a new mandibular periosteal approach for thyroid surgery. Through experimentation with cadavers, we defined the anatomical spaces and developed a mandibular periosteal approach that does not limit the movement of endoscopic instruments while reducing the risk of injury to the maxillary teeth, nose, and mental nerves. The present study describes the results of transoral periosteal thyroidectomy (TOPOT) trials in human subjects.

Materials and methods

Cadaver experiments

The cadaver experiments were performed between June 10, 2011 and November 18, 2011 at the Department of Anatomy at the Korea University College of Medicine in Seoul, Korea. Seven fresh frozen human specimens (five males and two females) were used for the study.

All endoscopic procedures were performed using conventional laparoscopic instruments (Ethicon Endo-Surgery: Johnson & Johnson, Cincinnati, OH, USA) and a 30° endoscope (Vicera System, Olympus Medical, Tokyo, Japan).

Transoral thyroidectomy was performed using four ports in three cadavers and three ports in the remaining four cadavers. After the procedure, the cadavers were dissected to evaluate all defined anatomical structures for possible injuries, particularly the mental nerves, and to evaluate the procedure.

Swine experiments

This experimental trial was approved by the Korea University Institutional Animal Care and Use Committee (Seoul, Korea, KUIACUC-2011-150, 17.08.2011). Seven pigs weighing 30–40 kg (country pig, large black-Hampshire) were used to evaluate the feasibility and safety of the minimally invasive endoscopic transoral approach in the anterior neck.

A transoral thyroidectomy was performed in four pigs using four ports and in three pigs using three ports. All surgical methods in the swine experiments were identical to those in the cadaver experiments. The anatomical structures in pigs and humans are very similar, especially the thyroid region and recurrent laryngeal nerve. However, the porcine thyroid is smaller and located primarily anterior rather than lateral to the trachea, and is further away from the recurrent laryngeal nerve. As a result, additional dissection was required to locate both recurrent laryngeal nerves after the thyroidectomy in the pig experiments.

The animals were breathing spontaneously 3 h postoperatively. For the next 2 days, all animals were observed to record pain reactions and oral feeding. Possible pain reactions were estimated based on their social behavior in the sty; normally, the animals fight one another, especially during feeding. Seven days postoperatively, all animals were anesthetized and orally intubated with EMG endotracheal tubes. The oral and anterior cervical incision sites were examined, and both recurrent laryngeal nerves were assessed using intraoperative neuromonitoring [9].

Human study

After cadaveric and animal studies, four human patients underwent robotic TOPOT using the da Vinci® surgical system at Korea University Anam Hospital. The recurrent laryngeal nerve function, intra- and postoperative complications, and postoperative outcome were assessed in all patients.

Port placement and flap dissection

Under general anesthesia with nasal intubation, the patient was placed in a supine position with the neck extended. The oral cavity was prepared with betadine solution, and a tooth protector was applied to prevent dental injury. After aseptic draping, the surgical field was outlined with a skin marker to include the thyroid cartilage, cricoid cartilage, sternal notch, both anterior borders of the sternocleidomastoid muscle, midline, both superior borders of the clavicle, and for the accessory port, the ipsilateral axillary skin incision site on an existing skin fold. Dilute epinephrine solution (1:200,000) was administered subcutaneously into the subplatysmal space in the neck.

The key procedure in this study was performing the incisions for port placement. The incisions for all three ports were made through the mandibular periosteum with a periosteal elevator. For the camera port, a 1.2-cm crevicular incision was made in the buccal surface of the central incisors. Bilateral vertical incisions were then extended into the alveolar mucosa, and mucoperiosteal flaps were raised from the buccal surface at midline using a periosteal elevator. Dissection continued around the inferior mandible until the subplatysmal plane was identified. Using this technique, the camera port gained access through the

Fig. 1 Port placement in transoral periosteal thyroidectomy using three ports, **A** lateral and **B** anterior views (Color figure online)
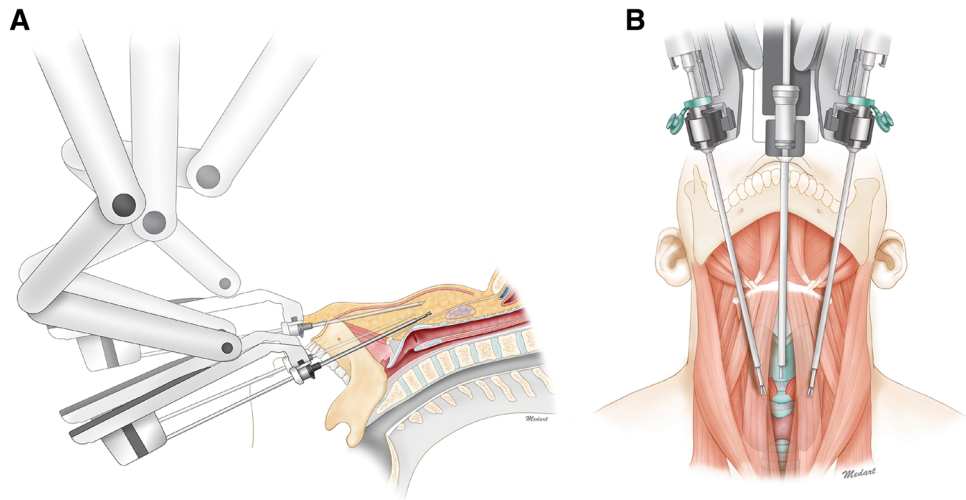
Fig. 2 Using a camera for visualization, a working space was made in the subplatysmal plane using endoscopic instruments. The 30°-angled dual-channel robotic camera was advanced through the 12-mm central port, and endoscopic instruments were inserted through the two lateral working ports (Color figure online)

mandibular periosteum. The dissection plane opened naturally within the subplatysmal area without any artificial force. To avoid injury to the mental nerves, two 0.8-cm incisions were made atin the gingival-buccal sulcus at the level of the first molar. Dissection proceeded along the periosteum of the mandible into the submental area (Fig. 1).

The 8-mm robotic trocars were placed into the two lateral incisions, and a 12-mm conventional trocar was placed into the midline incision. Carbon dioxide was insufflated at a pressure of 4–6 mmHg. The 30°-angled dual-channel robotic camera was advanced through the 12-mm camera port into the submental and subplatysmal areas. Ultrasonic shears (Harmonic Scalpel, Ethicon Endo-Surgery, Inc., Cincinnati, OH, USA) were introduced through the left lateral 8-mm port for the left lobectomy. For the

right lobectomy, ultrasonic shears were introduced through the right 8-mm port. Using a camera for visualization, a working space was made in the subplatysmal plane that extended inferior toward the suprasternal notch and lateral to the medial border of the sternocleidomastoid muscles (Fig. 2). The da Vinci robotic system was then docked at the patient's left side, and the three robotic arms were connected (Fig. 3A); the robotic camera was inserted through the 12-mm central port, the ultrasonic shears (Harmonic Scalpel, Ethicon Endo-Surgery Inc.) or the monopolar electrocauterization device was inserted through the 8-mm ipsilateral working port, and the Prograsp forceps were inserted through the 8-mm contralateral robotic trocars (Fig. 3B). After docking was complete, the surgeon's console work began. The accessory port was inserted at the ipsilateral axilla. Through this axillary port, the assistant inserted the snake retractor or endo-mini-retractor to retract the strap muscles laterally during the operation (Fig. 3C). After the operation, we inserted a drain using this axillary port (Video 1).

Operative methods

Under camera visualization, the midline raphe of the strap muscles was identified at the thyroid cartilage notch and divided. The isthmus was divided with ultrasonic shears, and the resected isthmus was then grasped and retracted medially using the Prograsp forceps in the surgeon's left hand during the right lobectomy and the right hand during the left lobectomy. The assistant retracted the ipsilateral strap muscles laterally. The upper pole of the thyroid was drawn inferiomedially by the Prograsp forceps, and the superior thyroid vessels were identified and individually ligated close to the thyroid gland using the ultrasonic shears. The superior parathyroid gland was identified during the dissection and preserved.
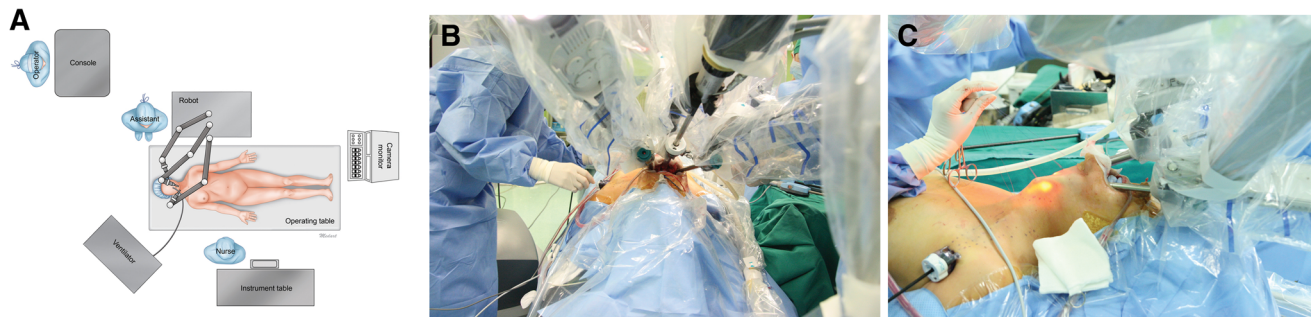
Fig. 3 View during the robotic transoral periosteal thyroidectomy. A Operating room seeting of robotic transoral periosteal thyroidectomy. B Three robotic arms were placed through the transoral ports. The da Vinci robotic system was docked at the patient's *left side*. The robotic camera was inserted through the central port. C Lateral view intraoperatively. An accessory port for the assistant was inserted through the contralateral axilla. Three robotic instruments were inserted through the transoral ports (Color figure online)
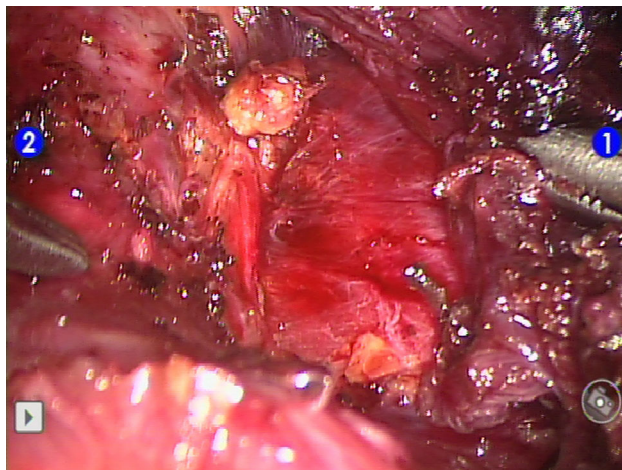
Fig. 4 Intraoperative view of the robotic transoral periosteal thyroidectomy (craniocaudal). The recurrent laryngeal nerve and upper and lower parathyroid glands were identified and preserved. *RLN* recurrent laryngeal nerve (Color figure online)

After the upper pole dissection, the thyroid gland was retracted medially using the Prograsp forceps, and the lower pole was dissected from the perithyroidal and thymic tissues. Using gentle blunt dissection, the recurrent laryngeal nerve was identified at its entry point and traced inferiorly. The surgeon identified the inferior parathyroid gland and preserved it along with its vascular pedicle. The inferior thyroid artery was ligated close to the thyroid gland using the ultrasonic shears, and the entire path of the recurrent laryngeal nerve was identified and preserved (Fig. 4). Finally, the thyroid gland was dissected from the trachea. In one patient with a papillary thyroid microcarcinoma, a central neck dissection was also performed. The resected specimen was removed transorally from the surgical field through a midline incision. Hemorrhage was precisely controlled, and a 3-mm closed suction drain was inserted through the accessory axillary port. The midline incision of the strap muscles was closed using a robotic continuous suture (Videos 2 and 3). After the thyroidectomy, the intact mentalis muscle was visualized, and the midline incisions were closed by suturing the interdental papillae together using 4-0 Vicryl. Postoperatively, a chin-neck bandage was applied to provide compression of the mandible.

Results

Through three trocars placed in the mandibular periosteal area, a working space was created underneath the platysma muscle that reached the pretracheal area. Total thyroidectomies were performed, and all recurrent laryngeal nerves were preserved in all cadavers using TOPOT. The median operative time was 89.8 (55–132) min.

In ten orally intubated live pigs, total thyroidectomies were also performed without complications using a transoral mandibular periosteal approach. Postoperatively, the white blood cell count remained normal, and both recurrent laryngeal nerves were intact in all cases.

One left lobectomy for a follicular neoplasm, two right lobectomies for nodular hyperplasia, and a left lobectomy with a central neck dissection for a papillary thyroid microcarcinoma were performed using a robotic transoral periosteal approach in four human subjects. Operation time ranged from 190 to 390 min. Intraoperatively, the ipsilateral recurrent laryngeal nerve and upper and lower parathyroid were identified and preserved in all cases. Patients were permitted water intake beginning 1 day postoperatively. All four patients began consuming a soft diet at 2 days postoperatively and a regular diet at postoperative day three. Hospitalization lasted 5 days for all patients, and drains were removed at the time of discharge (Table 1).

The ipsilateral mental nerves were torn in two cases and stretched in one case intraoperatively. The torn mental nerve was repaired intraoperatively; postoperatively, the patient suffered from paresthesia in portions of the lower

Table 1 Preoperative patient characteristics and operative findings

Case	Sex	Age	BMI	Tumor location	Tumor size (mm)	Preoperative cytologic diagnosis	Operation	Operation time (min)	Console time (min)	Weight of resected thyroid (g)	Pathologic diagnosis
1	F	38	19.9	Left	20	Benign follicular nodule	Left lobectomy	190	74	5.3	Follicular adenoma
2	F	57	27.3	Left	5	Papillary thyroid microcarcinoma	Left lobectomy With CND	390	230	5.6	Papillary thyroid microcarcinoma
3	F	46	16.3	Right	23	Nodular hyperplasia	Right lobectomy	265	132	9.9	Nodular hyperplasia
4	F	52	20.8	Right	16	Benign follicular nodule	Right lobectomy	295	132	12.5	Nodular hyperplasia

Table 2 Postoperative outcomes

Case	Hospital stay (days)	Laryngoscopic findings	Postoperative complication			
			Paresthesia of lower lip (etiology)	Transient vocal cord palsy	Infection	Hematoma or seroma formation
1	5	Normal	None	None	None	None
2	5	Normal	Existed for 4 weeks (intraoperative tearing)	None	None	None
3	5	Normal	Existed for 1 week (intraoperative stretching)	None	None	None
4	5	Normal	Existed for 1 week (intraoperative stretching)	None	None	None

lip and chin, which are innervated by the mental nerve, but this improved within 4 weeks. Prophylactic antibiotics were administered preoperatively by intravascular injection and continued until 5 days postoperatively. After discharge, patients received oral antibiotics for 7 days. There were no local infections at the incision site or within the anterior neck region, and none of the patients experienced temporary or permanent vocal cord palsy (Table 2).

The incision sites were photographed at each postoperative visit. Within 1 month, the intraoral and anterior neck incisions were completely recovered in all patients (Fig. 5).

Discussion

This is the first study reporting a clinical application of robotic transoral thyroidectomy. We developed a transoral periosteal approach for thyroidectomy and successfully performed robot-assisted surgery using this method. No patients experienced permanent recurrent laryngeal nerve palsy or other major complications. Prior to the clinical study in live humans, the feasibility and safety of the transoral periosteal approach was demonstrated in cadaver and animal studies. We performed both 3- and 4-port TOPOTs during these initial experiments, as the 4-port method is important in ensuring the safety of the endoscopic and robotic procedures. As a result, the robotic TOPOTs were performed in human subjects using three

transoral ports and one accessory port through the axilla. Postoperatively, the accessory axillary port was used for drain insertion.

The major advantage of this method is the good cosmetic result. As shown in Fig. 5, at 1 month postoperatively, there were no external scars in the anterior neck and intraoral regions in any of the four patients. Furthermore, none of the patients complained of scars, and all were satisfied with the cosmetic result. This is the most important benefit of transoral thyroidectomy compared to previous endoscopic and robotic methods for thyroid surgery such as the gasless axillary approach [5] or the bilateral axillo-breast approach [6].

The technique is also advantaged by the simplicity of the subplatysmal flap dissection. All transoral ports were made through the mandibular periosteum using a periosteal elevator to avoid transecting the mentalis muscle. Importantly, a mandibular periosteal approach enables easy access to the subplatysmal area. In other methods of endoscopic thyroidectomy such as the bilateral axillo-breast approach and the gasless axillary approach, it is very difficult to dissect a plane underneath the platysma muscle. However, the subplatysmal area can be accessed freely through the mandibular periosteum using a periosteal elevator.

Several studies have investigated transoral neck surgery, including thyroidectomy. These transoral approaches are based on the concept of the natural orifice transluminal endoscopic surgery. However, few clinical reports focus on
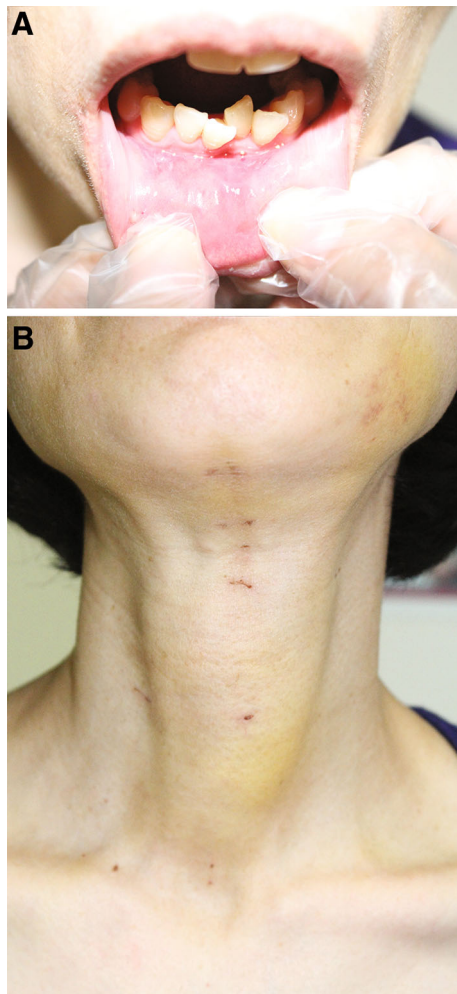
Fig. 5 Photograph of a patient 1 month postoperatively. **A** Intraoral wounds were healed. **B** The patient's anterior neck recovered completely within 1 month (Color figure online)

transoral thyroidectomy in humans. Wilhelm et al. [7] published a clinical study of transoral thyroidectomy in eight patients; three of eight cases had to be converted to open surgery, and one patient suffered permanent recurrent laryngeal nerve palsy. More recently, Nakajo et al. [8] also reported the results of clinical trials performing transoral endoscopic thyroidectomy using a single incision without gas. In this study, one patient suffered permanent recurrent laryngeal nerve palsy. These two previous studies had very high incidences of permanent recurrent laryngeal nerve palsy, raising concerns about the safety of these methods. In the present study, no patient experienced permanent or even temporary recurrent laryngeal nerve palsy. Robotic transoral periosteal thyroidectomy does not pose an undue risk to the recurrent laryngeal nerve. Nakajo et al. reported three cases of papillary thyroid microcarcinoma that underwent complete central node dissection [8]. Similarly, a complete central neck dissection was performed in the

present study in one patient with papillary thyroid microcarcinoma. Using a transoral approach for thyroid surgery, a surgeon can achieve a high-quality craniocaudal view of the central neck compartment. This method is especially useful for thyroid carcinoma surgery.

The existing endoscopic or robotic methods for thyroid surgery are disadvantaged by a longer surgical time than in conventional open thyroid surgery. A short surgical duration was initially expected for the robotic transoral thyroidectomy, but the range in operation time was from 190 to 390 min, and the console time was from 74 to 230 min. This was not a short surgical duration compared to previous reports of robotic thyroidectomy. In previous reports of other robotic thyroid surgeries, the operation time occurs as a moving average on the order of 20 [10, 11]; thus, the learning curve should stabilize after 20 procedures. In this study, only four cases were included, but at least 20 cases of robotic transoral thyroidectomy are required to average the times and achieve a short operation time.

This study is the first describing robotic transoral thyroidectomy in humans. The most important reason to use the robot is to reduce movement at the port insertion site and prevent mental nerve injury. Because the robot has an articulated wrist, it is able to perform extensive and delicate surgery even in small space such as the anterior neck. To further reduce the risk of mental nerve damage, the lateral port was positioned at the first molar. The mental foramen is most commonly located below and between the mandibular premolars; therefore, this particular placement of the lateral ports poses less of a threat to the mental nerves. Despite employing this approach, the mental nerve was torn in one case and stretched in two cases. Paresthesia of the lower chin and lip is caused by ipsilateral mental nerve injury, which occurred in all three patients. The clinical signs in the torn mental nerve case improved within 4 weeks, and in the two cases with a stretched mental nerve signs improved within 1 week. This is a much lower incidence of paresthesia in the lower chin and lip, but is still quite high. Previous clinical studies reported paresthesia in the lower chin and lip in all patients [7, 8]. This study revealed that excessive movement in the lateral port leads to mental nerve injury. Some reports have described postoperative paresthesia in the mental nerves after orthognathic surgery and other dental treatments [12, 13]. Seo et al. reported that the incidence of paresthesia decreased after 1 week postoperatively and diminished significantly by 6 weeks postoperatively [13]. Although the symptoms of paresthesia improved within 4 weeks in the present study, this problem is only indirectly related to the thyroid. Therefore, a method to prevent mental nerve injury that can be applied generally to the transoral approach is needed. This can be accomplished by minimizing movement in the lateral port, which may necessitate the development of instruments more suitable for this technique.

The transoral technique may risk possible infection within the anterior neck. A normally aseptic thyroidectomy may become contaminated due to oral microflora spread during the transoral techniques. Therefore, animal experiments were performed in advance of the clinical study. None of the treated pigs developed any severe infections, and there were no seromas in the surgical field after drain insertion [9]. In this study, prophylactic antibiotics were administered preoperatively by intravascular injection, and oral antibiotics were administered for 7 days postoperatively [9]. At surgical conclusion, a drain was inserted into the surgical field through the axillary port. The drains were later removed when the patients were discharged. No patients developed infections in the anterior neck or the oral wounds. These results suggest that, by administering prophylactic antibiotics and inserting a drain, infection after transoral endoscopic surgery can be prevented. However, because of the small sample size, strong conclusions cannot be drawn concerning the possibility of infection in the transoral thyroidectomy.

This study demonstrated the feasibility of robotic TOPOT to preserve the recurrent laryngeal nerve and allow a complete central neck dissection. However, drawbacks of the procedure include the risks of mental nerve injury and infection. This method is in the development stage; further studies are needed to evaluate its safety. Afterward, the next logical step is evaluation of the transoral thyroidectomy in a prospective, controlled clinical trial.

In conclusion, robotic TOPOT shows promise as an effective technique for thyroid surgery. Further study is needed to prove the safety of this method.

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