Surgical Endoscopy (2023) 37:7649–7657
https://doi.org/10.1007/s00464-023-10315-3

Transoral and submental endoscopic thyroidectomy (TOaST) for early stage papillary thyroid carcinoma: a real-world data retrospective cohort study

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Received: 9 May 2023 / Accepted: 15 July 2023 / Published online: 25 July 2023

Abstract

Introduction Although transoral endoscopic thyroidectomy (TOETVA) is widely utilized in clinical practice, some problems and restrictions still remain. Our study compared the perioperative features and early surgical efficacy of TOETVA and a modified transoral and submental endoscopic thyroidectomy (TOaST) in early stage papillary thyroid carcinoma (PTC).

Methods The clinical data of PTC patients who underwent endoscopic thyroidectomy, including 42 modified TOaST patients and 114 traditional TOETVA patients, were retrospectively collected. Propensity score matching was employed to reduce patient selection bias. The perioperative features and early surgical efficacy data of two groups were compared.

Results The operation time of the TOaST group was significantly shorter than that of the TOETVA group (150.00 ± 35.47 min vs. 168.75 ± 44.49 min; $P = 0.030$). Furthermore, the TOaST group required shorter days for a normal diet (3.38 ± 0.93 days vs. 4.04 ± 1.03 days; $P = 0.000$) and a shorter hospital stay than the TOETVA group (5.85 ± 2.17 days vs. 6.12 ± 2.01 days; $P = 0.003$). There was no statistical difference in complications between the two groups, but the probability of numbness of the lower lip and chin in the TOaST group was lower than that in the TOETVA group(5.12% vs. 13.04%, $P = 0.321$). The symptoms of mandibular numbness and hoarseness of most patients were relieved in both groups 6 months after surgery, and no abnormalities and recurrence were found in the thyroid ultrasound. All the patients were satisfied with the appearance of their surgical incision.

Conclusion In early stage PTC patients, TOaST had the same surgical effectiveness as traditional TOETVA but can minimize the probability of mandibular numbness and improve the perioperative quality of life.

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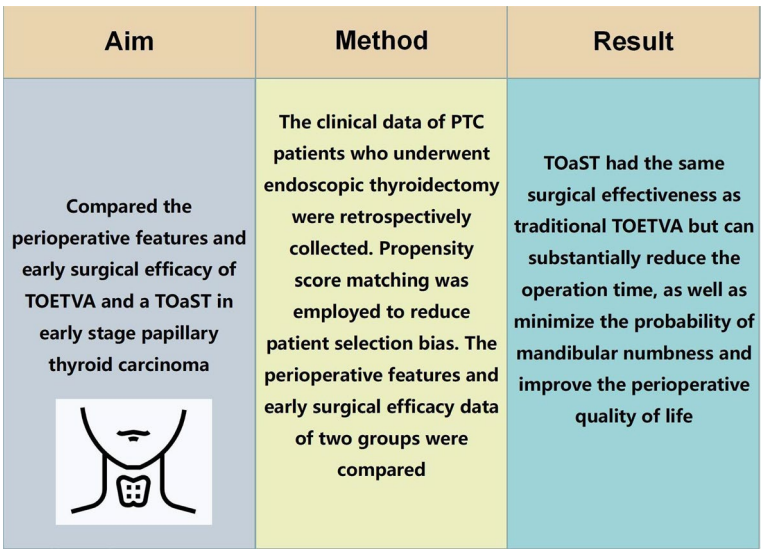
Graphical abstract



Keywords Papillary thyroid carcinoma · Endoscopic thyroidectomy · Transoral and submental approach · Transoral approach

The most frequent thyroid malignant tumour is papillary thyroid carcinoma (PTC), and surgery is the primary clinical therapy for PTC [1]. Conventional open thyroidectomy (COT) is difficult to accept by patients with high cosmetic requirements because it leaves a postoperative neck scar. In recent years, with the development of endoscopic technology, endoscopic thyroidectomy has become common. Compared with COT, endoscopic thyroidectomy has the advantages of rapid postoperative recovery and scar avoidance or minimization [2]. The surgical access of endoscopic thyroidectomy has evolved from the anterior chest approach, transaxillary approach to areola approach, and transoral approach [3]. Moreover, with the gradual popularization of natural orifice specimen extraction surgery, transoral endoscopic thyroidectomy (TOETVA) has become mainstream [4, 5].

Unlike laparoscopic surgery, TOETVA does not have a natural cavity and requires the creation and dilation of the workspace in the mandibular region [6]. Traditional TOETVA requires three oral vestibule incisions: one 10 mm observation port in front of the lower lip frenulum and two 5 mm operation ports on both sides of the buccal mucosa of the first premolars [7, 8]. For some patients with prominent mandibles, short necks, and small mouths, it is difficult to establish three oral ports and remove some large specimens through the 10 mm observation port. Furthermore, patients may experience serious intraoral discomfort after surgery and postoperative numbness of the lower lip and jaw area if the mental nerve is injured [9, 10].

Therefore, a modified transoral and submental endoscopic thyroidectomy (TOaST) has been used at our institution since December 2019. In this study, we compared the perioperative features and early surgical efficacy between the modified TOaST and the traditional TOETVA during the same period.

Materials and methods

Patient selection

The clinical data of PTC patients who underwent TOETVA in the Department of Thyroid Surgery of the Affiliated Hospital of Jining Medical University between December 2019 and June 2021 were retrospectively collected. A total of 42 patients with modified TOaST were included in the TOaST group and 114 patients with traditional TOETVA were included the TOETVA group. The inclusion criteria were as follows: (1) patients who conformed to the surgical indications in the 2018 Chinese Expert Consensus Onendoscopic thyroidectomy via oral vestibular approach (patients who have cosmetic needs, maximum differentiated thyroid carcinoma diameter ≤ 2 cm, maximum thyroid benign tumour diameter ≤ 4 cm, without lateral cervical region lymph node metastases or distant metastases, metastatic central lymph nodes ≤ 2 cm and without fused or fixed) [11], (2) PTC confirmed by preoperative fine needle aspiration biopsy and (3) patients who receive unilateral thyroidectomy. The

exclusion criteria were as follows: (1) ultrasound and computed tomography showed tumour invasion of the capsule or suggest abnormal cervical lymph nodes. (2) Poor compliance and inability to review regularly. (3) Previous neck radiotherapy and surgery. (4) Oral deformity or infection. (5) Associated with large benign nodules.

The possible advantages of both surgical methods were clearly explained to all patients preoperatively, such as TOETVA can achieve a completely external scarless and TOaST can shorten the operation time. Patients provided written informed consent and were able to choose their preferred surgical method. All operations were performed by the same surgeon. This study was approved by the ethics committee of the Affiliated Hospital of Jining Medical University (Approval No. 2022C100). The work has been reported in line with the STROCSS criteria [12].

Surgical procedure

In the TOaST group, the patients were placed in a supine position with their neck extended. The trachea was intubated through the mouth for anesthesia. The nerve monitoring endotracheal tube was fixed on the right corner of the mouth. Iodophor was used to re-disinfect the oral cavity before surgery after standard disinfection and towel spreading. A 10 mm transverse incision was made at the dermatoglyph 1.5 cm below the chin and a 10 mm trocar was inserted to accommodate a 10 mm-diameter endoscope as observation port. Two lateral incisions were created bilaterally at the buccal mucosa of the first premolars, and two 5 mm trocars were inserted to accommodate surgical apparatus as operation ports. The subcutaneous operating space was separated using a hypodermic peeling bar and an electrocoagulation hook, and the thyroid gland was visible after opening the linea alba cervicalis. The isthmus was disconnected by the ultrasonic scalpel, and the superior pole vessels were dissected and ligated. After identifying and dissecting the recurrent laryngeal nerve (RLN) and parathyroid thyroid, the involved side and isthmic gland was removed. Then the prophylactic central lymph node was dissected, the scope was superior to the hyoid bone, lateral to the carotid sheath, inferior to the sternum notch or the innominate artery, medial to the trachea and dorsal to the prevertebral fascia. Thereafter, the specimen was extracted via submental incision, and normal saline was used to wash the operations area after a careful hemostasis. Through the submental incision, the negative pressure drainage tube was inserted into the operation area, and the sutures were closed (Fig. 1). Prophylactic cefazoline sodium was administered during perioperative period. All patients were asked to gargle with chlorhexidine for seven days following surgery and was treated with 50 μg levothyroxine sodium tablets daily for suppression after surgery. An acceptable oral diet was permitted on the second day following surgery. The drainage tube was withdrawn after the drainage was less than 20 ml/day for two consecutive days and discharge was advised 1–2 days after the administration of a normal diet if no problem was encountered.

In the TOETVA group, the patients were placed in the same position, and the same tracheal cannula was inserted. After routine sterilization, a 10 mm incision was made in the center of the vestibule in front of the lower lip frenulum, and a 5 mm incision was made from the gingival root. A 10 mm trocar was then inserted to accommodate a 10 mm-diameter endoscope as an observation port. Two lateral incisions were created bilaterally at the buccal mucosa of the first premolars, and two 5 mm trocars were inserted to accommodate the surgical apparatus as operation ports. The subcutaneous operating space was separated using a hypodermic peeling bar and an electrocoagulation hook and the thyroid gland was visible after opening the linea alba cervicalis. The isthmus was disconnected by the ultrasonic scalpel, and the superior pole vessels were dissected and ligated. After identifying and dissecting the RLN and parathyroid thyroid, the involved side and isthmic gland were removed, and the prophylactic central lymph node was dissected. Thereafter, the specimen was extracted via submental incision, and normal saline was used to wash the operations area after a careful hemostasis. A negative pressure drainage tube was placed through a small port in the submental area, then closed the sutures. The same standardized treatments given to the TOaST group during the perioperative period were also given to the TOETVA group.

Efficacy comparison

Postoperative evaluation index: clinical data including operative time, intraoperative blood loss, postoperative drainage volume, number of resected lymph nodes, postoperative days for normal diet and postoperative hospital days and surgical complications such as CO_2 embolism, postoperative hemorrhage, postoperative infection, skin burns, subcutaneous effusion, postoperative hoarseness, drinking cough and mandibular numbness.

Evaluation of early surgical efficacy: Patients were recommended an outpatient review 6 months after surgery. Fiberoptic laryngoscopy and thyroid ultrasonography were performed to evaluate vocal fold mobility and the operation area and symptoms of drinking cough and numbness of the lower lip or jaw area were assessed by an outpatient doctor. Vocal cord paralysis lasting 6 months was regard permanent RLN injury, whereas mandibular numbness lasting 6 months was regard permanent mental nerve injury. Patients also completed the patient and observer scar assessment scale (POSAS) survey at this visit. The POSAS is a practical and dependable instrument for evaluating scars and is composed of the observer scar assessment scale (OSAS) and patient

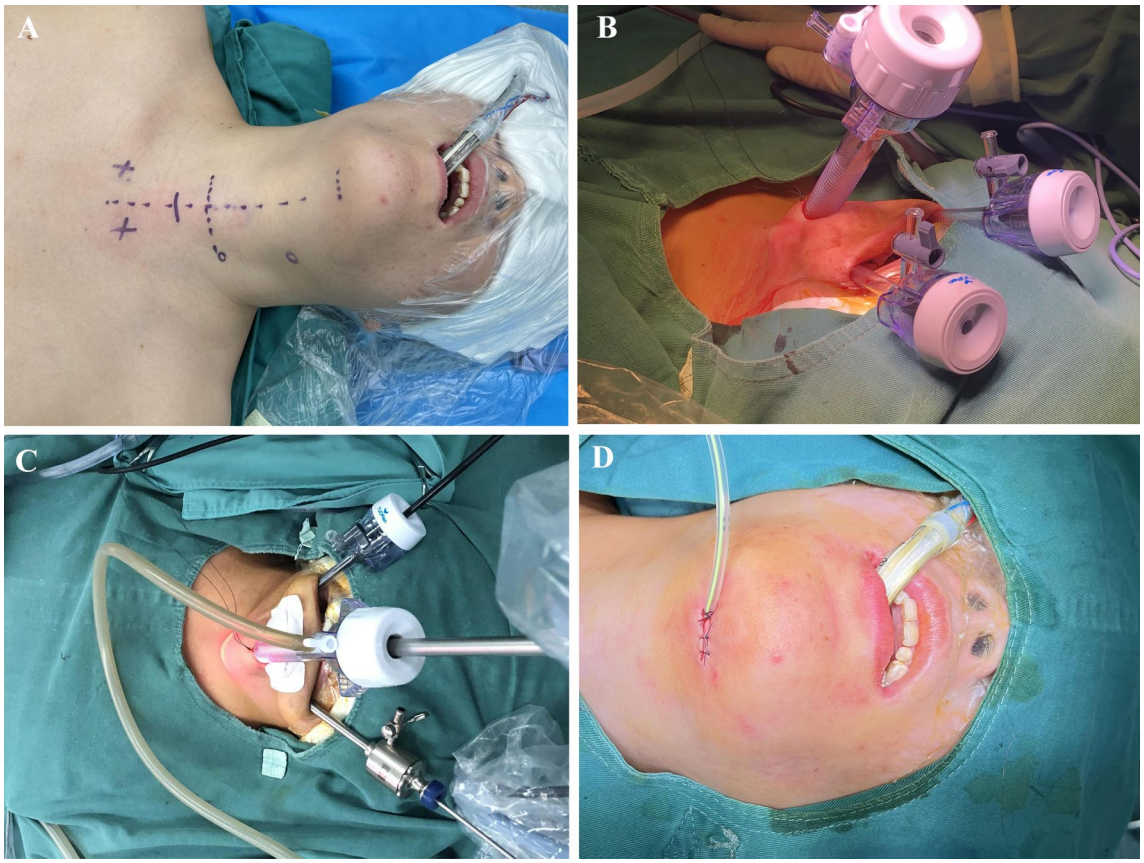


Fig. 1 The details of the submental mini-incision-assisted TOETVA**. A** Designing incisions. **B** Dilating workspace. **C** Application of the surgical apparatus. **D** Closed the sutures

scar assessment scale (PSAS). The OSAS score, which consists of five items evaluated on a 10-point scale (1 = normal skin, 10 = the worst scar imaginable), was assessed by the outpatient doctor. Normal skin is represented by a total score of 5, whereas the worst scar outcome is represented by a total score of 50. PSAS consists of 6 items that are rated on a 10-point scale, and the range from normal skin to the worst scar imaginable is represented by a total score of 6–60 [13].

Statistical analysis

Propensity score matching (PSM) was utilized to reduce patient selection bias, and logistic regression analysis was used to calculate each patient's propensity scores. Six clinicopathological traits including sex, age, tumour size, body mass index (BMI), Hashimoto's thyroiditis, extrathyroidal extension were chosen as confounders that could have influenced the surgical results. After taking into account all of the aforementioned variables, we conducted a 1:2 PSM using the closest neighbor approach and a caliper width of 0.2. Table 1 displays the general data that was matched.

Continuous data were presented as mean ± standard deviation (SD), *t* test (normally distributed data) and the Mann−Whitney test (nonnormally distributed data) were used to compare them. And the chi-square test was used to the compare categorical data. In the statistical analyses, $P < 0.05$ was considered significant. Statistical analyses were performed using SPSS (version 26.0).

Result

After PSM, 108 of 156 patients were included for analysis. The matched cohort was well balanced in the 39 TOaST group patients and 69 TOETVA group patients. All 108 patients completed the surgery successfully, and there were neither conversion to open surgery nor secondary surgery. The operation time of the TOaST group was significantly shorter than that of the TOETVA group (150.00 ± 35.47 min vs. 168.75 ± 44.49 min; $P = 0.030$), and the TOaST group required shorter days for a normal diet (3.38 ± 0.93 days vs. 4.04 ± 1.03 days; $P = 0.000$) and a shorter hospital stay (5.85 ± 2.17 days vs. 6.12 ± 2.01 days; $P = 0.003$) than the TOETVA group. Table 2 shows the postoperative outcomes. There was no statistical difference in CO_2 embolism, postoperative hemorrhage, postoperative infection, skin burns,

Table 1 Baseline characteristics of all patients

	Unmatched cohort ($n=156$)			Matched cohort ($n=108$)		
	Observation group ($n=42$)	Control group ($n=114$)	*P*	Observation group ($n=39$)	Control group ($n=69$)	*P*
Sexuality			0.018			0.550
Female	31	102		31	58	
Male	11	12		8	11	
Age (mean ± SD) (years)	30.64 ± 6.97	28.58 ± 7.81	0.135	30.36 ± 6.99	29.01 ± 7.45	0.356
Tumor size (mean ± SD) (mm)	10.57 ± 5.18	8.92 ± 4.19	0.046	9.77 ± 4.25	9.57 ± 4.47	0.815
BMI (kg/m^2)	26.94 ± 2.59	25.70 ± 3.52	0.041	26.72 ± 2.52	26.32 ± 3.46	0.525
HT			0.327			0.702
Presence	16	34		15	24	
Absence	26	80		24	45	
Extrathyroidal extension			0.968			0.574
Presence	6	16		6	8	
Absence	36	98		33	61	

Table 2 Perioperative results after propensity score matching

	Operative time (min)	Intraoperative blood loss (ml)	Postoperative drainage volume (ml)	Number of resected lymph nodes	Postoperative days for normal diet (days)	Postoperative hospital days (days)
Observation group ($n=39$)	150.00 ± 35.473	28.59 ± 13.23	156.10 ± 58.40	2.23 ± 0.95	3.38 ± 0.93	5.85 ± 2.17
Control group ($n=69$)	168.75 ± 44.487	34.04 ± 16.74	159.84 ± 56.82	3.12 ± 1.13	4.04 ± 1.03	6.12 ± 2.01
P	0.030	0.087	0.743	0.513	0.000	0.003

Table 3 Surgical complications after propensity score matching

	CO_2 embolism	Postoperative hemorrhage	Postoperative infection	Skin burns	Subcutaneous effusion	Postoperative hoarseness	Drinking cough	Mandibular numbness
Observation group ($n=39$)	0	0	0	1 (2.56%)	0	3 (7.69%)	2 (5.12%)	2 (5.12%)
Control group ($n=69$)	0	0	0	0	1 (1.45%)	2 (2.90%)	3 (4.35%)	9 (13.04%)
P	1	1	1	0.361	1.000	0.349	0.853	0.321

Table 4 Early surgical efficacy after propensity score matching

	OSAS score	PSAS score	POSAS total score	Permanent RLN injury	Permanent mental nerve injured
Observation group ($n=39$)	6.05 ± 0.324	8.08 ± 0.941	14.13 ± 1.224	1 (2.56%)	0
Control group ($n=69$)	5.75 ± 0.191	7.55 ± 0.448	13.30 ± .591	0	3 (4.35%)
P	0.414	0.352	0.443	0.361	0.552

subcutaneous effusion, postoperative hoarseness, drinking cough and mandibular numbness between the two groups, but the probability of numbness of the lower lip and chin in the TOaST group was considerably lower than that in the TOETVA group. These results are presented in Table 3.

Table 4 depicts the early surgical efficacy. The outpatient review showed that the symptoms of mandibular numbness and hoarseness of most patients were relieved in both groups 6 months after surgery, and no abnormalities and recurrence were found in the thyroid ultrasound. The OSAS

score, PSAS score, and total POSAS score in the two groups showed no statistical differences, and all the patients were satisfied with the surgical incision (Fig. 2).

Discussion

Our result showed that there were no statistical difference in intraoperative bleeding, postoperative drainage, and number of lymph nodes detected in the two groups. But the operating time of the TOaST group was considerably less than that of the TOETVA group and the TOaST group required a shorter time for a normal diet and a shorter hospital stay than the TOETVA group. There was no statistical difference in complications between the two groups. As early as 2008, Witzel [14] performed thyroidectomy using a mouth floor approach in two fresh cadavers and then in five live pigs, thus opening up a new direction in thyroid surgery and confirming the feasibility of transoral thyroidectomy. In 2010, Benhidjeb [15] successfully performed transoral unilateral thyroidectomy in a patient with benign thyroid tumour to resolve the patient's dysphagia. Nevertheless, owing to the thyroidectomy via the floor of the mouth was intrusive and frequently damaged surrounding tissues such the hypoglossal nerve, submandibular gland, sublingual gland, it had not been further popularized [7]. Until 2014, Wang [16] performed TOETVA through the oral vestibule with three incisions, including one 10 mm observation port in front of the lower lip and two 5 mm operating ports at the buccal mucosa of the first premolars on both sides, to avoid damage to the tissues at the bottom of the mouth. Thereafter, TOETVA began to be widely promoted. Although TOETVA is widely employed in clinical practice today, some problems and restrictions still remain [17]. For some patients with prominent mandibles, short necks, and small mouths, it is extremely difficult to establish three oral ports and remove some large specimens through the 10 mm observation port. Furthermore, patient may experience serious intraoral discomfort after surgery and postoperative numbness of the lower lip and jaw area often occur in patients when the mental nerve is injured. Therefore, TOaST surgery emerges [18], it transferred the observation port from the lower lip to the submental, thus separating the operating space and specimen extraction area.

TOaST significantly reduced surgery time perhaps because of the efficient operating space construction, easy flap dissection, and convenient specimen removal of the submental mini-incision. And given that the TOaST caused less damage to the oral cavity and less postoperative discomfort, most patients were able to have a half-liquid diet at the first day after surgery. By contrast, TOETVA group patients often had to eat a liquid diet on the second day. It is worth mentioning that the length-of-hospital-stay for COT is usually about 1–2 day both in Asian and Western countries, but for TOETVA and TOaST the length of stay is usually 2–3 days in Western countries and 4–5 day in China [19–21]. TOaST is a relatively new technique in our department and we allow patients return to normal diet after surgery until we make sure is it absolutely safe and provide sufficient

Fig. 2 Patient's front view of neck at the sixth-month review. **A**, **B** Traditional TOETVA. **C**, **D** Submental mini-incision-assisted TOETVA

medical resources to increase the length of stay to observe recovery and reduce post-operative complications. Despite this, the time to return to normal diet and the length of stay in hospital for patients undergoing TOaST is still less than that of TOETVA, although the difference is not obvious, such as days to normal diet (mean 3.38 days vs. 4.04 days; $P = 0.000$), and length-of-hospital-stay (mean 5.85 days vs. 6.12 days; $P = 0.003$). We believe that as TOaST matures in our centre, the time for patients to recover after surgery will be further reduced.

Although TOaST was also known as the shortest approach of all endoscopic thyroidectomy and was advantageous for central lymph node dissection [22], there was no difference in the number of lymph nodes dissected, intraoperative bleeding and postoperative drainage between the two groups in this study, probably because the extent criteria of lymph node dissection was the same in both groups and therefore the trauma caused was similar, and the convenience of lymph node dissection was only reflected in the reduction in operative time.

Intraoperative and postoperative complications including CO_2 embolism, postoperative hemorrhage, postoperative infection, skin burns, subcutaneous effusion, postoperative hoarseness, and drinking cough did not have significant difference. However, the probability of numbness of the lower lip and chin in the TOaST group was lower than the TOETVA group. This numbness was often caused by mental nerve injury. The mental nerve is the terminal branch of the inferior alveolar nerve arising from the third division of the trigeminal nerve. To provide sensory innervation to the chin, lower lip, and vestibular gingiva of the mandibular incisor, the mental nerve leaves the jaw via the mental foramen and is disseminated to the skin of the chin and the mucous membrane [23]. Numbness in the chin and lower lip can result from damage to this nerve [10]; the side effects of numbness may include lip biting, slurred speech, and decreased salivary retention [24]. There have been reports of incidents of mental nerve damage by TOETVA ranging from 0.7 to 7.1% [4, 9, 24]. The mean distance from the midline to the mental foramen is 29.2 ± 3.3 mm. Nowadays, consensus indicate that placing the 5 mm trocar at the buccal mucosa of the first premolars was safe and would not injure the mental nerve. For the observation port, the placement of the 10 mm trocar in front of the lower lip frenulum and 5 mm from the gingival root in the TOETVA group could not prevent the possibility of injury to the small terminal branches of the mental nerve [25]. In the TOaST group, the 10 mm trocar was inserted 1.5 cm below the chin, thus avoiding the mental nerve region and reducing the possibility of injury.

Other complications showed no appreciable variation. There was no case of CO_2 embolism, postoperative hemorrhage, and postoperative infection in either group. One patient in the TOaST group had significant postoperative swelling and local hardness of the submental skin, which improved after conservative treatment. These symptoms were considered related to obesity and subcutaneous fat liquefaction (BMI = 34.7 kg/m^2). One patient had drinking cough owing to damage to the cricothyroid muscle and superior laryngeal nerve during upper pole tumour resection. The symptoms of mandibular numbness and hoarseness of most patients were relieved in both groups 6 months after surgery. Furthermore, fiberoptic laryngoscopy and thyroid ultrasonography showed no abnormalities.

Although TOaST was not completely scarless, the incision was located under the chin and was only 1 cm, thus making it hard to notice without neck extension. In fact, the modified TOaST did not add an extra surface wound. The small incision could be used as an orifice for the drainage tube, whereas traditional TOETVA required a small incision in the neck to place the drainage tube [26]. Prior research had demonstrated that patients and doctor might have a different understanding about the scar evaluation [27, 28]. So we used the POSAS to evaluate visual, tactile and sensory characteristics of the scar from both patient and doctor perspectives at the same time. According to the POSAS at the sixth-month review, both the operation methods could achieve satisfactory cosmetic result. Small anterior cervical incisions were also required in thyroid surgery and modified Miccoli endoscopic-assisted thyroid surgery, both of which inevitably left significant large or small scarring in the neck and had limitations in central lymph node dissection [29]. Maybe the TOaST was not suitable for patients who require a truly external scarless operation, such with known predisposition to skin healing disorders such as keloids or hypertrophic scarring [30].

At present, our TOaST was mainly used in unilateral lobectomy for early PTC, and this study was a single-center retrospective cohort study with a small sample size and a limited follow-up period. Although PSM was used to balance some observed variables, selection bias still existed. In the future, we will extend the TOaST to bilateral thyroidectomy and design a multicenter randomized study to demonstrate its further long-term efficacy and safety.

Conclusion

In conclusion, in early stage PTC patients, TOaST had the same surgical effectiveness as traditional TOETVA but can minimize the probability of mandibular numbness and improve the perioperative life quality, particularly for patients with prominent laryngeal nodes or mandibles, short necks, and small mouths.

Author contributions TM designed the study, analysed the data and commented on the manuscript at all stages. LW, XZ collected the data. PS, ML revised the manuscript. YS provided the research direction.

Funding Academician He Lin Research Foundation of Affiliated Hospital of Jining Medical University (JYHL2022FMS10).

Declarations

Disclosures Teng Ma, Peng Shi, Xueyan Zhang, Mei Liang, Lulu Wang, Yafei Shi have no conflicts of interest or financial ties to disclose.

Ethical approval This study was approved by the Affiliated Hospital of Jining Medical University ethics committee (2022C100).

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