

Available at <http://dx.doi.org/10.21037/gs-20-147>.

**Reviewer A:**

I applaud your great challenge. It is very difficult to do thyroid operation in a small space. For patients in this study, the patient is strongly inclined and has keloid history, but this is not a recommended procedure in the general case.

1. It will be better to mention the cause of the recurrence of goiter in the discussion (World J Surg, 32 (7), 1301-12)

One of the main reason for the recurrence of goiter is incomplete surgery.

2. There is no mention of removing the specimen out after surgery. Most people who read this study will wonder how the big goiter was pulled out of the small hole.

In figure 3, the shape of the goiter was maintained.

It may be helpful to understand how to derive a specimen if a picture of the oral cavity was shown after the specimen had been removed.

Reply: Thank you very much for your suggestions. We do agree that this is not a recommended procedure in the general case. This is a special case which we intend to report. ① The cause of the recurrence of goiter is added in the discussion now. ② It is a pity that we did not took a photo to show the oral cavity after the specimen had been removed, so we add an anatomical drawing (Figure 3) to explain how to pull out a big goiter.

**Reviewer B:**

Nice case. Please add information about operative time and additional resources necessary to do the procedure.

Reply: Thank you very much for your suggestions. The operative time is 195 min, and we add it now. Additionally, an anatomical drawing (Figure 3) is added to explain how to pull out a big goiter from oral cavity.

**Reviewer C:**

This is a nice video showing TOETVA surgical technique in a patient with third-degree goiter. The novelty of this reported case is that it was successfully undertaken in a patient with a large-volume of goiter and Hashimoto's thyroiditis -

both conditions are considered as contraindications for TOETVA. Hence, to assure a clear message of this paper to the readership I would suggest to address the following issues:

1. Please add more details about the Hashimoto's thyroiditis in this patient (anti-TPO, anty-TG serum levels). Please comment on how these antibodies serum levels corelate potentially with difficulty of surgical dissection.
2. Please indicate if preoperative ultrasound with elastography was used to differentiate if the thyroid gland was stiff (which may make surgical dissection challenging) or soft (which may suggest easier surgical dissection).
3. Was intraoperative neuromonitoring used in this operation for anatomical identification and functional assessment of both the recurrent laryngeal nerves and the external branches of the superior laryngeal nerves? Irrespective if yes, or not, please comment on utility of IONM technology during TOETVA operation (safety assurance, staged planned bilateral operation in case of loss of signal with no intraoperative recovery etc).
4. Please clearly indicate the surgical experience of the principal surgeon who performed this operation (was is a high-volume surgeon > 100 thyroidectomies per year? how many TOETVA operations were done by him/her before this challenging operation?) and comment on the need of surgical experience and skills for the successful outcome of such a challenging operation.
5. Use of English should be improved through the entire manuscript.

Reply: Thank you very much for your suggestions.

① Thyroid hormones serum levels are added now (both before and after surgery) in Patients Findings and Follow-up. We add some relevant comments in discussion part.

② We are sorry to say that we did not use elastography during the preoperative ultrasound. The thyroid gland was not stiff by touching her neck in the surgeon's perspective.

③ Thanks for reminding us to mention the use of intraoperative neuromonitoring. Yes, we did use it. Here we add some comments of IONM in discussion part.

④ The principal surgeon who performed this operation has a wealth of experience (over 400 cases).

⑤ We correct some grammar mistakes .

**Reviewer D:**

Sorry for our mistakes and thank you very much for kindly offering those detailed suggestion. “√” means we correct the mistakes now.

【√】 Page 1, line 10: “hashimoto thyroiditis” should be “Hashimoto’s thyroiditis”. Same mistake also in page 1, line 37.

【√】 Page 1, line 13: suggest renaming “approach of the lateral strap muscles” to “lateral approach to the thyroid gland”. Other publications in the literature have described this method as the lateral approach to the thyroid gland, for example: Singaporewalla RM, Tan BC, Rao AD. The lateral "backdoor" approach to open thyroid surgery: A comparative study. Asian J Surg. 2018;41(4):384–388. doi:10.1016/j.asjsur.2017.05.003

Please also make the appropriate changes in other parts of the text where this technique is mentioned, namely:

page 1, line 30 page 3, line 7 page 5, line 14 & 21 page 7, line 6

【√】 Page 1, line 24: Cunchuan Wang reported endoscopic transoral vestibular approach in 2012. However, the modification of that approach, currently known as TOETVA was first reported by Angkoon Anuwong in 2016. Please can the authors add a statement on this and include the reference below in their introduction?

Anuwong A. Transoral Endoscopic Thyroidectomy Vestibular Approach: A Series of the First 60 Human Cases. World J Surg 2016;40:491-7.

【√】 Page 1, line 27: “TOTEVA” should be “TOETVA”. The mistake same mistake is also in Page 4, line 23.

【√】 Page 1, line 28: Reference 2 actually refers to a journal article published in Mandarin. A search of this article in the English language (as it is cited in this article) does not reveal any result. I would suggest that the authors cite this article in its original language (or according to the requirement of the journal Gland Surgery) or cite other similar articles that is published in English.

—— Reference 2(now Reference 3) is Chinese Experts Consensus of TOETVA(2018 version), which now represents the mainstream consensus in China. Many centers here use it as a guideline. We are very sorry that there is no English version, so it can not be searched in Pubmed in English language. However, it can be searched in other database such as CNKI or VIP (<http://qikan.cqvip.com/Qikan/Article/Detail?id=676588598>). (1)

[1] 中国医师协会外科医师分会甲状腺外科医师委员会, 中国研究型医院学会甲状腺疾病专业委员会, 海峡两岸医药卫生交流协会台海甲状腺微创美容外科专家委员会, 等. 经口腔前庭入路腔镜甲状腺手术专家共识(2018版)[J]. 中国实用外科杂志, 2018, 38(10): 1104-1107.

【√】 Page 1, line 31: suggest to reword the entire sentence as “However, with meticulous dissection of mental nerve and lateral approach to the thyroid gland, on 20 September 2019, we successfully performed TOETVA in a female patient with a history of keloid scarring and a large goitre measuring 205 ml.

【√】 Page 1, line 37: “hashimoto thyroiditis” should be “Hashimoto’s thyroiditis”

【√】 Page 1, line 41: “2019.09” should be written “September 2019” (to avoid confusion)

【√】 Page 2, line 3: “70\*46\*35mm” and “66\*43\*33mm” should be written as “70 mm x 46 mm x 35 mm” and “66 mm x 43 mm x 33 mm” respectively.

【√】 Page 2, line 4: “...upper pole of left gland was in a high level of hyoid bone...”. Is the upper pole of the left gland AT the level of the hyoid bone (as written in the text) or HIGHER THAN the level of the hyoid bone (as per label in Figure 2e)?

—— Sorry for our mistake, it is “higher than”.

【√】 Page 2, line 8: ‘electronic fiber laryngendoscope’ should be renamed ‘flexible nasopharyngolaryngoscopy’

【√】 Page 2, line 15: what do the authors mean by ‘type II incision operation’?  
—— We have reworded this term into “incision was in oral cavity (which might cause infection)”.

【√】 Page 2, line 22: it would be useful if authors could provide a picture of the incision used in the mental nerve dissection?

—— It was a pity that we did not took a photo of the incision in this case. The picture of this technique was shown in our previous article (Peng X, Li Z, Li H, et al. The clinical application of mental nerve dissection in transoral endoscopic thyroidectomy via an oral vestibular approach. Surg Endosc,2019). The appearance of incision in this case was no different from the common case, however, there are some differences in inside of the incision and we add an anatomical painting to explain (Figure 3). (Because of limited space, it is better to add some new information that we did not report before.)

【√】 Page 2, line 29: “adrenalinein” should be “adrenaline”

【√】 Page 2, line 30: can authors provide the exact name of the instrument used for creating the subcutaneous tunnel towards suprasternal fossa, instead of just calling it ‘traditional dissection stick’?

—— According to Reference15 (Jongekkasit I, Jitpratoom P, Sasanakietkul T, et al. Transoral Endoscopic Thyroidectomy for Thyroid Cancer. Endocrinol Metab Clin North Am, 2019,48:165-180.), this instrument should be called “blunt tip dilator”.

【√】 Page 2, line 34: suggest to add the word ‘diathermy’ after ‘electrocoagulation hook’. Please also consider adding this to other places in the text where the word

‘electrocoagulation hook’ appears.

【√】 Page 2, line 37: it would be useful if the authors provided a picture of the arc-shaped omnidirectional fixed device? Also, the letter ‘A’ in ‘Arc-shaped’ should not be capitalized. The authors mention patent number for this device. Which country is this patent registered under?

——This device was first mentioned in 2017 (Reference 10) and its picture was shown in 2019 (reference 9). Because of the limited space, it is better to add some new information that we did not report before. The letter “A” is replaced by “a” now. This patent is registered under China.

【√】 Page 2, line 42: suggest to rename ‘harmless grasping forceps’ as ‘atraumatic grasping forceps’.

【√】 Page 3, line 18: “In addition, there was a certain position for its taking out, which was “let the thinner part go first and vertically”, otherwise it could be “dystocia”. This phrase “let the thinner part go first and vertically” does not convey the message well, and I find it difficult to visualize how the authors manage to remove the specimen. May I suggest the authors draw a simple diagram to illustrate instead? Additionally, the use of the word “dystocia” in this sentence is inappropriate as it refers to difficult delivery in childbirth. May I suggest the authors use the word “difficult delivery of the specimen” instead?

—— We add an anatomical drawing to explain this (Figure 3) .The term “difficult delivery of the specimen” is used instead of “dystocia” according to your suggestion.

【√】 Page 4, line 22: The sentence “The limited working space and endoscopic technique unique from open thyroidectomy restrain the indication of TOTEVA” does not make much sense. If I understand correctly the message that the authors are trying to convey, may I suggest they reword the sentence to “Unlike open thyroidectomy (OT), the limited working space and endoscopic technique restricts the indication of TOETVA”.

【√】Page 4, line 33: suggest to rephrase ‘Thus, the edge of the thyroid back could not be detected clear under the ultrasound’ to ‘Thus, the boundaries of the posterior surface of the thyroid could not be detected clearly with ultrasound’.

【√】 Page 4, line 37: “This technique was first mentioned by Xiaowei Peng in 2017 (5).” However, reference (5) refers to the article by Gastka et al. Conventional Robotic Endoscopic Thyroidectomy for Thyroid Cancer. Endocrinol Metab Clin North Am, 45 (1), 153 – 163. Can the authors provide the correct reference? Also may I suggest rewording the sentence to “This technique was first reported by Xiaowei Peng and colleagues in 2017”

——Sorry for our mistake. The reference number and the sentence have been changed.

【√】 Page 4, line 38: ‘... a comparative trail..’ should be ‘...a comparative trial...’

【√】 Page 5, line 1: ‘... commonly feel a numbing lower lip...’should be ‘...commonly feel a number of the lower lip...’

【√】Page 5, line 2: ‘... this feeling will soon relieve...’ should be ‘... this feeling will soon be relieved...’

【√】 Page 5, line 2: ‘Then in the follow up, we measured the numbness of different part to represent the injury, which was feasible and straight.’ Suggest to rewrite the whole sentence as ‘Then in the follow up period, we measured the numbness of different areas of innervation of the mental nerve as a measure of nerve injury. This method was feasible and straightforward.’

【√】Page 5, line 8: “..which was enough for the big thyroid gland to remove.” Should be rewritten as “... which was wide enough for the big thyroid gland to be removed”.

【√】 Page 5, line 8: “We certainly dared not to enlarge the tunnel....”. Suggest to rewrite as “We were cautious not to enlarge the tunnel...”

【√】 Page 5, line 12: “.. according to the main surgeon’s feeling.” Suggest to rewrite as “..according to the main surgeon’s perception’.

【√】 Page 5, line 15: “... used in OT in case..” should be “...used in OT in cases..”

【√】 Page 5, line 19: “... and in a high level to hyoid bone.” Should be “...and a higher level than the hyoid bone”

【√】 Page 5, line 22: “... upper parathyroid gland was also reserved.” Should be “... upper parathyroid gland was also preserved.”

【√】 Page 5, line 243: “.. which make the dissection..” should be “..which makes the dissection..”

#### **Reviewer E:**

Very interesting case report modifying the original surgical technique with many interesting points for thyroid/ endocrine surgeons.

This is the first reported largest size of thyroid gland (Class III goitre) resected by TOETVA.

Technical variations proposed by the authors from the original described technique are original, clever and interesting.

Thank you very much for your helpful suggestions. Here are my response. “√” means the mistake is corrected now.

Suggested Minor changes:

【√】 Line 9 page 1: 53 years-old

【√】 Line 10 page 1: Hashimoto (as an Eponym)

【√】 Line 11: she underwent TOETVA instead of “she had...”

【√】 Line 27 page 1: the term TOTEVA should be changed for TOETVA

【√】 Line 9 page 2: “Thyroid function showed no hyper...neither hypothyroidism? Please specify the biochemical status

—— We add the biochemical status now.

【√】 Line 29 page 2: “adrenalin” instead of “adrenalinein”

【√】 Line 35 page 2: “sternal” instead of “sterna”

【√】 Line 43 page 2: “sternothyroid muscle” instead of “sternothyreoides”

【√】 Line 23 page 4: TOETVA instead of “TOTEVA”

【√】 Line 4 page 5: “we measured the numbness of different part to represent the injury....” what do the authors mean with this phrase? Did they test this on different anatomical areas or different potential lesions on the mental nerve?

We changed the sentence into “we measured the numbness of different areas (lower lip, chin, under the chin) of innervation of the mental nerve as a measure of nerve injury. This method was feasible and straightforward.”

【√】 Line 22 page 5: perhaps the authors mean the parathyroid gland was “preserved” instead of “reserved” is that right?

—— Sorry for the mistake, it is “preserved”.

【√】 References. It would be recommendable to uniform the reference format (for example reference 8 is different from other references)

—— The format is reedited. But reference 12 is an online published article, so we add its DOI number instead of page number.

Major changes:

1. Line 33 page 3: ¿Why the authors considered important to install a drain tube (actually a venous catheter) in this case?

—— According to our previous study of the drainage in TOETVA, the volume of her drainage would be estimated over than 150ml in total. Thus, we considered it safe to put a drain. A central venous catheter was used as a drain tube instead of a normal tube, because we’ve proved that a smaller tube would cause less scar.

2. Line 44 page 3: ¿what type of laryngoscopy was utilized on this patient? ¿Do the authors perform this routinely?

—— We used flexible nasopharyngolaryngoscopy. We did not perform this routinely, only used in patients who complained about hoarseness. However in this special case, we used it to make sure her vocal cord was normal.

3. Line 1 page 4: ¿What kind of antibiotics did the authors use on this patient? ¿Was

it a combination or a single antibiotic? ¿Why the authors employ antibiotics for 3 days?

—— Cefamandole only. We did not routinely used antibiotics for 3 days but for 1~2 d in other cases. We were afraid of her infection in this special case as the operating time was 195 minutes, so we prolonged the time of using antibiotic. Now we consider that it might be too cautious to use it for 3 days.

4. Line 2 page 4: ¿Why the authors used IV calcium for 2 days? ¿Do they use this management routinely? ¿Did they measure ionized calcium in this patient? This manoeuvre is interesting since the PTH was normal in the second postoperative day.

—— Sorry for our mistakes, we tested her PTH during the third postoperative day. Because her operation was performed in 2019.09.20 (Friday), the blood test could not be done during weekend in our hospital (unless it is a emergency). So the test was postponed to the third postoperative day. The daily need of calcium for an adult is 800 mg. It is common that temporary hypocalcemia happens after thyroidectomy especially in subtotal or total thyroidectomy. So we consider it safe to gave intravenous calcium(1g per day) for 2 days to prevent temporary low calcium. After the test was done in 2019.09.23 (Monday), the PTH showed a normal result. Now we consider that it might be too cautious to use it for 2 days.

We did not routinely gave intravenous calcium to all patients expect for those who complained hand numbness, or whose parathyroid was transplanted, or whose calcium level was low, or sometimes who underwent total thyroidectomy on Friday.

5. Line 41 page 4: It would be interesting to know the author's opinion how this "chopsticks effect" was prevented with the use of a larger incision plus mental nerve dissection when contrasted to the conventional three incisions described in the TOETVA original technique. Please describe more details.

——We put a 5 mm of working port at the inner side of the mental nerve under the large incision (usually 2.5cm to the central line ) to prevent mental nerve injury. Because a larger incision could increase more mobility of upper lip compared to the conventional three incisions (the lip could be dragged at the level of chin or even under the chin), so that the mobility of the two 5 mm trocars increased and the chopsticks effect was prevented to some extent.

6. It is interesting to note that the authors did not use IONM in cases like this, based on their experience ¿would the authors recommend the use of IONM in cases like these?

—— We used IONM in this case but forgot to mention that. Sorry about our mistake. Additionally, we add some comment on IONM in the discussion part. We highly recommend the use of IONM in cases like these.

7. What was the anatomical landmark of the inferior pole of the thyroid? ¿Did it reach the innominate artery, or it was retrosternally located? ¿How do the authors



manage this issue?

—There was no special landmark of the inferior pole of the thyroid. It nearly reached the innominate artery and was also partially hidden behind the clavicle and retrosternally located. It was a minor retrosternal goitre, so we deduced that there was no need to split the sternum and it could be completed under endoscope. As it was shown in the video, we used atraumatic grasping forceps to grasp the gland apart to create a better space, so that the endoscope and other instruments could reach the inferior pole. We grasped the tissue near the inferior pole and carefully dissected so that the hidden part could be gradually revealed and dragged out from the retrosternal area.

8. Line 19 page 5: Since the upper pole was reaching the hyoid bone level ¿how did the authors do for visualizing this point with the endoscope? ¿was it hard to visualized by means of the endoscope? ¿or was this visualization performed by direct vision through the incision?

— It was hard to visualize the upper pole with the endoscope. Nor could it be seen by direct vision through the incision. As it was shown in the video, we grasped a part of the gland, and the upper pole was dragged by its near tissue. It could not be seen thoroughly until it was fully dissected. If we loosened the grasp, the upper pole would retract back to its original position and be hidden. The first assistant also played an important role during this procedure, who had to know how to control the endoscope well to provide a better vision.

Based on the author's experience what were the main divergences of their technique (employed in this case) in contrast with the original technique? Please provide us with more details about these differences. Would you use these modifications in all goitres? Which cases would you use this modified technique on?

—The main divergences are ① The dissection of mental nerve has always been a special feature in our center compared to others. We routinely do this in almost all the cases. However, in this case, there was a difference from normal mental nerve dissection (see Fig.3). The figure 3 also shows how to pull out a large goitre from oral cavity.②The lateral approach to the thyroid gland, this technique has never been reported in TOETVA before.

We recommend mental nerve dissection in all the cases. Especially in a large goitre, mental nerve dissection and the techniques of delivery (Fig 3) are highly recommended. The lateral approach to the thyroid gland is recommended when the upper pole is high.