

Peer Review File

Article information: <https://dx.doi.org/10.21037/aot-22-5>

Reviewer A Comments

The review article entitled “A Narrative Review of Transoral Thyroidectomy – 2021 Update” surveyed English articles published between January 1, 2020 and February 1, 2022 in order to identify the most recently published updates on TOETVA. The followings are my comments:

1. Line 20: “TOETVA is the only minimally-invasive thyroid procedure that avoids a cutaneous scar.” (1) I recommend using “remote” rather than “minimally-invasive” (2) I suggest removing “only”, TOETVA is currently but will not always be the only surgical procedure without cutaneous scar.
 - a. Reply 1: Thank you for this comment, this is very true. We changed the wording and removed “only” and changed to “remote”.
 - b. Changes in text: Removed “only” and changed to “remote,” Page 2, line 38.
2. Line 21: “The rate of publication of this procedure far exceeds that of other remote access approaches to thyroidectomy.” This sentence and Figure 1 are cited from the article (Ann Thyroid 2020;5:24). Please check their original description, “While it remains to be seen whether TOETVA becomes a standard alternative to open thyroidectomy, interest in the technique is growing. Our review of the first 5 years of published remote access approach cases in the literature establishes that, at least in the academic thyroid surgery community, TOETVA has been embraced more rapidly than the trans-axillary, bilateral axillo-breast and retro-auricular approaches in their initial years” The author’s relevant narrative context in this article needs to be presented more accurately.
 - a. Reply: Changed the wording to better reflect that it is the rate of publication in the first 5 years of various remote access approaches that is being compared.
 - b. Changes in text: Clarified that we were referencing the rate of publication in the first 5 years, as reported by Banuchi et al., see Page 4, line 88-90.
3. In the “Indications” section, the authors have no 2021 updated information or consensus on surgical indications. It is recommended to summarize from the recent literature cited in this article.
 - a. Reply: Added 2020/2021 sources including a 2020 update by Russell et al. with the institutional inclusion/exclusion criteria – however, we could not find a “new” consensus published in 2021 regarding indications, as the papers all reference the previously published guidelines.

- b. **Changes in text:** Citation of Chai et al. 2021(20), Russell et al 2020 (5), on page 6 line 139 and line 143.
- 4. In Table 2 and related discussion, the risk of RLN injury should be based on nerves at risk; and the risk of transient/permanent hypoparathyroidism should be based on the proportion in bilateral surgery. Although the authors described that “Hypoparathyroidism as defined by each study. Rates of transient or permanent hypoparathyroidism calculated only for total thyroidectomy cases”. However, taking ref. 37 (Zheng et al., Eur J Surg Oncol. 2021;47(6):1346-51) for example, 96.6% patients received unilateral surgery (by the way, you can find the description “the operation times for unilateral and bilateral surgery were 135.6 ± 40.6 min and 189.3 ± 35.8 min, respectively” can be integrated to Table 3). Authors must specify which definition they use. Also, please carefully check if the data in Table 2 and Table 3 are correct.
 - a. **Reply:** Excellent point. Each study has been re-examined for the number of lobes vs total thyroidectomies (which was added as column in the Table 1 – the tables may have been incorrectly numbered before) and the risk of RLN was then calculated for each study based on the nerves at risk rather than number of cases. The operative times from Zheng et al. were also added to Table 2.
 - b. **Changes in text:** Extra column in Table 1, risk of RLN changed throughout table (page 17, line 375) and addition of operative times of Chai (20) and Zheng (39) to Table 2 (page 18, line 402).

Overall, this article is very informative and helpful for readers to update relevant data, and it can be very readable after careful revision.

Reviewer B Comments

Your paper is well done, but I have some points to be discussed:

1. I do not agree that TOETVA is a minimally-invasive thyroid procedure. To perform it there is much more dissection. Please discuss this point.
 - a. **Reply – True point.** Additional discussion has been added.
 - b. **Changes in text – Clarification** that there is more dissection required in TOETVA and therefore this should not be termed a “minimally invasive” procedure, rather “remote access.” See Page 4, line 80-84.
2. You did not show any complications in the flap of a TOETVA. But they exist and are very bad. Please would you show this kind of complications and discuss it.
 - a. **Reply – This discussion has been added.**

- b. Changes in text – Flap perforation and soft tissue injury has been added in the discussion of complications, as well as added in Table 1 as a complication (along with reported rates of incidence). See Page 11, line 229-235 and Table 1 on Page 17, line 375.
- 3. The learning curve is a problem: who will pay the costs of the complications in patients operated during the learning curve of a surgeon? Discuss please how could it be avoided and how to teach it. How much this teaching will cost to the medical services?
 - a. More discussion has been added regarded the learning curve and the necessity of considering this when implementing a program. Other important considerations for implementing a program that will hopefully decrease the complications and cost have been discussed and new references added.
 - b. Changes in text – Additional discussion added, see page 14, line 295-305.
- 4. The specimens of thyroid - you did not discuss the damage in thyroid samples during the operations (taking the specimens out). Would please do that too?
 - a. Discussion added.
 - b. Changes in text – Discussion of this point was added, see page 12, line 247 – 259.
- 5. The scars in the neck is worse in patients operated by a low volume surgeon, please discuss it too.
 - a. Reply – We could not find literature describing this, or any definitive evidence / study specifically examining this. Therefore, it was not added in our discussion.
- 6. At end: the recovering time and the use of antibiotics please discuss it in details
 - a. We agree this is an important consideration.
 - b. Changes in text – Discussion was added detailing practice patterns of prophylactic antibiotics before and after the procedure, as well as data on infection risk. See Page 11, line 236-245.

Reviewer C Comments

Perfectly written. Good review focusing on pure transoral thyroid surgery. Parathyroid surgery is not mentioned, also the potential to combine transoral with other remote access techniques (i.e., TOVARA).

Suggestion: Transoral thyroidectomy vestibular approach should not only be compared to conventional open but also to other meanwhile well-established remote access techniques especially the widespread used (robotic) trans axillary technique.

Reply: This was briefly discussed in the introduction (page 4) with the citation of Banuchi et al, discussing the rate of publication of TOETVA vs other remote access approaches in the first five years of their practice. We have also added consideration of combining remote access approaches.

Changes in text: Page 11, line 256-259.

Introduction

Page 4 Line 52: The transoral endoscopic thyroidectomy vestibular approach (TOETVA) has been increasingly studied since it was first published in 2011 by Richmon et al. (1).

Sorry to say that, but the transoral vestibular approach was not first described by Richmon et al.

Wilhelm T et al. EurArch Otorhinolaryngol 2010; 267:1285-90

Wilhelm T, Metzger A. SurgEndosc 2010; 24:1757-8

Reply: This has been corrected.

Changes in text: Correction in Page 4, line 268.

Indications

Page 6 Line 95: Change “Guidelines” to “Recommendations”. Comment: The authors should distinguish/ differentiate between absolute and relative contraindications, like former surgery in the neck (relative) vs. Lateral lymph node metastases (absolute).

Reply: This has been corrected.

Changes in text: “Recommendations” instead of “guidelines” (Page 6, line 121) and separating relative vs absolute contraindications (Page 6, Line 123 and 126).

Safety/Complications

Page 7 Line 122: “...permanent RLN palsy”-- Please add (%), not mentioned.

Reply: This has been corrected.

Changes in text: “0.6%” rate of RLN palsy has been added (page 7, line 156).

In addition, the authors do not mention the potential risk of infections at all, which is of interest and should be added (for example: Updates Surg 2022 Feb;74(1):303-308. doi: 10.1007/s13304-021-

01191-4. Epub 2021 Oct 20. Transoral thyroid surgery vestibular approach: is there an increased risk of surgical site infections? Elias Karakas, Günther Klein, Linda Michlmayr, Martin Schardey, Stefan Schopf, Endoscopic Thyroid and Parathyroid Surgery Study Group).

Reply: We agree this is an important consideration. Addition of the complication of infection and antibiotic prophylaxis / usage has been added.

Changes in text: Paragraph discussing the above has been added to page 11, line 236-245.

It is not only mental nerve injury which is a special and new complication in transoral surgery, but also injury of the skin in the chin area caused by perforation or thermal injury while implementing the access. This should also be discussed (for example: Bakkar S, Al Hyari M, Naghawi M, Corsini C, Miccoli P. Transoral thyroidectomy: a viable surgical option with unprecedented complications- a case series. J Endocrinol Invest. 2017;41(7):809-13.)

Reply: This is true and should be mentioned. Soft tissue injury has been added as a column in Table 1 as well as discussed in complications.

Changes in text: Additional column with the reported incidences of soft tissue injury in Table 1 (page 17, line 357) as well as discussion of this complication in the body of the paper (Page 11, line 229-235).

Cost

Page 12 line 220: “Although TOETVA is a more costly procedure independent 220 of operating time, the difference in energy devices alone contributed nearly \$500 USD (38.2% 221 and 43.2%) of the cost difference for lobectomies and total thyroidectomies, respectively.”

Energy devices are also used in open/ conventional thyroid surgery all around the world, especially in specialized centres in Europe. This should be considered in the discussion regarding cost.

Reply: This has been clarified, as this study attributed the difference to the different brands/types of energy devices used between TOETVA and TCA (as we agree energy devices are commonly used in both methods).

Changes in text: Clarification of the usage of energy devices in Page 13, line 285-287.

Conclusion

At the latest it is worth mentioning that it is possible and beneficial in some cases to combine other remote access techniques (transaxillary or retroauricular) with transoral surgery vestibular approach. Maybe this could be added or mentioned in the “Indication” part.

Reply: We added discussion of this, especially as being potentially beneficial in larger-size thyroid specimens.

Changes in text: Consideration for combination with other techniques added on Page 12, line 257-259.

Reviewer D Comments

You did an excellent review article about TOETVA, its safety, operating time, costs and outcomes. As a review of 2020 and 2021 as mentioned on methods you missed 2021 paper from Lira et al. (Lira RB, De Cicco R, Rangel LG, Bertelli AA, Duque Silva G, de Medeiros Vanderlei JP, Kowalski LP. Transoral endoscopic thyroidectomy vestibular approach: Experience from a multicenter national group with 412 patients. Head Neck. 2021 Nov;43(11):3468-3475. doi: 10.1002/hed.26846. Epub 2021 Aug 12. PMID: 34382715.).

Reply – Thank you for this comment, the paper by Lira et al. 2021 has been added.

Changes in text – Lira (reference 72) is now found in Table 1, page 17 line 357.

Reviewer E Comments

This paper brings a comprehensive literature review on TOETVA, focusing on the major surgical outcomes and points of debate. Very well written and direct to the point.

Reply – Thank you!