A narrative review of transoral thyroidectomy-2021 update

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Background and Objective: Transoral endoscopic thyroidectomy vestibular approach (TOETVA) is a remote-access thyroid procedure that avoids a cutaneous scar and has been adopted in countries worldwide. The early rates of publication of this procedure comparatively exceeds those of other remote access approaches to thyroidectomy. Therefore, this narrative review will overview the most influential recently published literature on the outcomes, complications, and future directions of TOETVA.

Methods: We conducted a search of three scientific databases utilizing the search terms "endoscopic transoral", "endoscopic oral vestibular", or "TOETVA" in combination with "thyroidectomy", "outcomes", or "complications". Our review was limited to English articles published between January 1, 2020 and February 1, 2022 in order to identify the most recently published updates on TOETVA.

Key Content and Findings: Several meta-analyses demonstrate that there is no significant difference in major complications between TOETVA and the transcervical approach (TCA). However, there is an increased risk of minor complications. Mental nerve injury is a complication unique to TOETVA compared to TCA, and several authors have published new methods to decrease the risk of this injury. Other authors have confirmed that this complication is rare. Oncologic outcomes as measured by median number of lymph nodes harvested and stimulated thyroglobulin (Tg) are equivalent between TOETVA and TCA respectively. A cost analysis demonstrates that TOETVA remains a more costly and lengthy procedure despite improvements in operative times.

Conclusions: TOETVA is being increasingly adopted worldwide. Current data shows that it is a safe procedure with comparable oncologic outcomes to the traditional thyroidectomy, while providing the benefit of avoiding a visible scar.

Keywords: Transoral endoscopic thyroidectomy vestibular approach (TOETVA); thyroidectomy; endoscopic oral vestibular; endoscopic transoral

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Introduction

The transoral endoscopic thyroidectomy vestibular approach (TOETVA) has been increasingly studied since it was first published in 2010 by Wilhelm *et al.* (1,2). The technique underwent subsequent modifications in order to be performed with laparoscopic instruments, and the first clinical series followed in 2015 and 2016 by Yang *et al.* (3)

and Anuwong (4) respectively. Since then, over 2,000 cases have been described in the literature (5). When examining the first 5 years of publication of various remote access thyroidectomy techniques, the early rates of adoption TOETVA comparatively exceeds that of trans-axillary, bilateral axillo-breast, and retro-auricular approaches (6) (*Figure 1*).

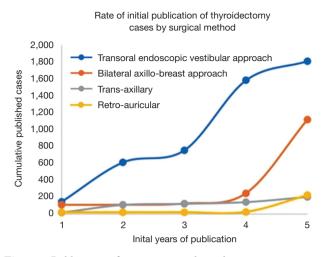


Figure 1 Publication of remote access thyroidectomy cases.

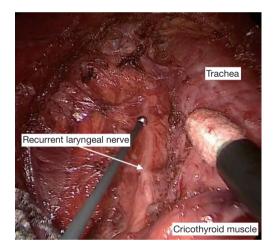


Figure 2 Recurrent laryngeal nerve at insertion.

The primary advantage to TOETVA over other remote access approaches is the avoidance of a cutaneous scar. While other approaches have moved the incision to a less conspicuous location, a cutaneous scar and dissection through extended tissue planes are still required. TOETVA utilizes three mucosal incisions above the gingivobuccal sulcus which avoids a cutaneous scar, as well as provides a more direct route to the bilateral central neck and visualization of the recurrent laryngeal nerve (RLN) at its insertion (7) (*Figure 2*). Although there is less dissection required in TOETVA than other remote access approaches, the distance of dissection from the mentum to the central neck is greater than what would be performed in an open procedure, and therefore remote access approaches cannot truly be termed "minimally invasive" procedure.

The effect of a visible scar cannot be discounted, especially as patients and clinicians may have different perceptions of a scars' appearance and what constitutes a cosmetically pleasing result (8). Several studies have found that scar concerns are a more common complication of thyroid surgery than RLN injury, hematoma, hypoparathyroidism, dysphagia or dysphonia (8,9). The impact of a cervical scar on quality of life is becoming more seriously examined. Despite the excellent prognosis of thyroid cancer, scar dissatisfaction has been found to be associated with decreased quality of life outcomes, poor self-perception, gaze distraction (10,11), and impaired social functioning (9,12,13). These disparities are still present even years after surgery (9).

This article will review the most recently published data on TOETVA in order to provide an update on the safety profile given the increasingly widespread performance of the procedure. We will also discuss new innovations and modifications to the technique. We wish to assess if current TOETVA complication rates and oncologic outcomes are comparable to transcervical approach (TCA) and identify areas of future research. We present the following article in accordance with the Narrative Review reporting checklist (available at https://aot.amegroups.com/article/ view/10.21037/aot-22-5/rc).

Methods

A systemic literature review was conducted in order to identify the most recently published outcomes and innovations in TOETVA surgery. Utilizing PubMed, SCOPUS and Google Scholar, the terms "endoscopic transoral", "endoscopic oral vestibular", and "TOETVA" were combined with "thyroidectomy" or "outcomes" or "complications" to identify studies published with greater than 5 cases between January 1, 2020–February 1, 2022. Series including robotic assisted procedures were not included (*Table 1*).

Indications

It is estimated that 55% of all patient undergoing thyroid surgery in the United States are eligible for TOETVA (14). The patient must be motivated to avoid an anterior cervical incision or have a history of keloid formation or hypertrophic scarring. Absolute size cutoffs

Table 1 The search strategy summary

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Items	Specification
Date of search	February 1, 2022
Databases and other sources searched	PubMed, SCOPUS, Google Scholar
Search terms used	"transoral" OR "endoscopic oral vestibular" OR "TOETVA" AND "thyroidectomy" OR "outcomes" OR "complications" OR "recurrence" OR "cosmesis"
Timeframe	1/2020–2/2022
Inclusion and exclusion criteria	Case series and meta-analyses published in the English language with at least 5 cases were included. Robotic assisted cases were excluded
Selection process	SAW did the article selection
Any additional considerations, if applicable	Additional articles recommended by JOR

may be institutional or surgeon specific. Published recommendations suggest a lobe no greater than 8–10 cm (4,5,7,14,15), single benign nodule no greater than 4–6 cm (3,14,16,17), and malignant nodules less than 2 cm (5,18,19). Absolute contraindications include preoperative RLN paralysis, inability to tolerate general anesthesia, lateral nodal metastases, and evidence of extrathyroidal extension into neighboring structures such as the esophagus or trachea (5,7,14,19,20). Relative contraindications include previous transoral neck surgery and radiation (5). Increased body mass index (BMI) is not a contraindication, as it does not increase the likelihood of complication (21-23), but it may make elevating skin flaps more difficult (19).

Other characteristics of the thyroid itself are critical to be considered by the surgeon before committing to a transoral approach. Conditions such as Graves' disease or chronic Hashimoto's may make the gland more friable (15,19,24) and increase the difficulty of the case. Tumors that are in close relationship with the course of the RLN may be more difficult to satisfactorily and safely remove utilizing a transoral approach. If there are concerns regarding the ability to obtain an appropriate and safe oncologic resection, TOETVA should be reconsidered.

Safety/complications

With the advent of any new technology, the concerns of safety and patient outcomes should remain paramount. As thyroid disease and thyroid malignancy are generally indolent with low disease-related morbidity and mortality (25), it is imperative that the treatment is not worse than the disease. The traditional TCA to thyroidectomy has low complication rates (26,27) and therefore the impetus is on TOETVA to perform at this level.

Appropriately, the safety profile of TOETVA is a focus of research. Previously published studies from multiple countries have demonstrated low complication rates comparable to TCA thyroidectomy (16,28-31). In a 2020 global review of 1,880 published TOETVA cases the rates of complications such as hematoma (0.4%), transient RLN palsy (3.9%), permanent RLN palsy (0.6%), transient hypoparathyroidism (16.8%), permanent hypoparathyroidism (0.9%) and infection (1.1%) were similar to a conventional approach and are reflective of the overall safety of this method (6). In Wang et al.'s 2021 meta-analysis of 478 TOETVA patients and 673 TCA patients (32), there was no significant difference in transient or permanent RLN palsy (OR, 1.01, P=0.98 and OR, 3.04, P=0.50), transient hypocalcemia (OR, 0.96, P=0.89), permanent hypocalcemia (OR, 0.32, P=0.49) or hematoma (OR, 7.93, P=0.05) between the two operative techniques. de Vries et al. also published a large meta-analysis in 2021 of several minimally invasive techniques including 736 TOETVA patients (33). The median incidence of a temporary RLN palsy was 4.0%, comparable to the 3.3% in the standard of care open thyroidectomy group (P=0.74).

With TOETVA being performed in countries worldwide, publication has become more prolific and there have been multiple large case series published within the last 2 years. The largest North American single-center study of 200 TOETVA cases was published in 2021 by Russell *et al.* (21). Their study showed no difference in the incidence of major

complications between TOETVA and TCA (1.5% vs. 2.1%, P=0.75). Temporary RLN injury occurred in 4.5% vs. 2.1% (P=0.124) and temporary hypoparathyroidism in 18.2% vs 12.5% (P=0.163) of TOETVA and TCA patients respectively. Importantly, a higher BMI was not associated with a higher odds ratio of complications. Although there was no difference in major complications of thyroidectomy, it should be noted that there was an increased risk of minor complications, defined as temporary RLN injury, temporary hypoparathyroidism, seroma formation, skin infection, and mental nerve injury. The risk of minor complications such as these was 17.5% in the TOETVA group compared to 9.3% the TCA group (P=0.007) (21). Table 2 details the complication rates in recently published case series within our inclusion criteria. However, there is a continued decrease in complication rates over time and surgeon experience, with improvement in outcomes seen well past the learning curve period (46,47).

In TOETVA, dissection of the RLN differs from the technique in open surgery. Cranial to caudal dissection is necessary, as the nerve is encountered first at its entrance into the laryngeal musculature. In a series of 145 TOETVA patients, Zhang et al. found that the majority (58%) of nerve injuries were thermal and occurred during dissection at the ligament of Berry (48). This is in contrast to several other studies examining mechanism of nerve injury in TCA, which were more commonly traction or compression injuries (49,50). Thermal injuries were found to have a longer recovery period than other methods of injury. It is possible that there is more thermal spread with the hemostatic instruments used in TOETVA compared to TCA. This information is critical for operating surgeons to be cognizant of in order to avoid excessive thermal instrumentation at the ligament of Berry and reduce the risk of nerve injury.

Another complication that may arise due to anatomic differences in how the gland is accessed during surgery is injury to the mental nerve. The mental nerve exits the mental foramen in the mandible and divides into three branches, providing sensory innervation to the chin and lower lip. Branches of the mental nerve can be at risk of injury in TOETVA during trocar placement in the oral vestibule, particularly the lateral ports. In Russell *et al.*'s review, there was a 2.5% (n=5) incidence of permanent mental nerve injury, defined as hypoesthesia persisting greater than 6 months (21). The incidence of transient mental nerve hypoesthesia is far more reported, with

Zheng *et al.* documenting varying degrees of mental nerve disturbance in 81.1% of their 297 TOETVA patients, with only 2.4% of all patients experiencing permanent mental dysesthesia (44). In addition, 12 of their patients (4.0%) experienced abnormal motor function of the lower lip and chin, all of which had resolved by 12 month follow up.

Minimizing the risk and degree of mental nerve injury or paresthesia has been a goal of surgeons since the advent of TOETVA, with Anuwong and Kim both providing modifications of port placement in 2018 (51,52) from the initially described technique (4). In 2021, Zheng et al. provided further modifications with the aim of reducing sensory and motor changes in the mental nerve distribution by proposing an arc-shaped middle mucosal incision and lateral incisions near the oral commissure adjacent to the mucosal folds (53). In the group utilizing the original incision design (Group A, n=39), 100% had sensory alterations of the lip and chin immediately post operatively, compared with 79.5% of the patients with the altered incision (Group B, n=83). The time to recovery of these changes was significantly longer in the first group $(4.5\pm3.1 \text{ months})$ compared to the second $(1.9\pm1.3 \text{ months})$, P<0.001). Complete recovery of these sensory changes at 12 months occurred in only 56.4% of Group A, compared to 97.0% of Group B. In terms of motor outcomes, 23.1% of patients in Group A had abnormal motor function of the lip and chin post operatively, including pronunciation changes, abnormal appearance during smiling, and liquid leakage while eating or drinking. In Group B, only 2.4% of patients experienced these changes. It should be noted that in both groups these motor changes resolved by 12 months, although the time to resolution was longer for Group A (53).

As evidenced by these studies, there is a wide range in the reported incidence of mental nerve injury. This may be in part due to differing definitions of true mental nerve injury, as some authors may ascribe all post-operative sensory changes to the mental area as an injury while others account only for cases with severe sensory loss. When Tae *et al.* prospectively evaluated multiple cutaneous zones of the face using a Semmes-Weinstein monofilament in 43 patients, they found that the pressure thresholds of the chin and lower lip had no significant post-operative change compared to preoperative baseline, and that there were no cases of true mental nerve injury on objective measure (54). This data suggests that varying definitions for mental nerve injury among physicians may account for the discrepancy reported in the literature, and that the incidence of true

First author, year	Ν	Extent of surgery	Temporary RLN injury [‡]	Permanent RLN injury [‡]	Temporary HPT*	Permanent HPT*	Temporary MNI	Permanent MNI	Infection	Hematoma	Soft tissue injury
Ahn, 2020 (34)	150	40 TT; 10 HT	7 (3.7%)	1 (0.5%)	5 (12.5%)	2 (5.0%)	0	0	0	1 (0.7%)	-
Dinc, 2020 (24)	56	43 TT; 13 HT	2 (2.0%)	0	10 (17.8%)	0	0	0	3 (5.4%)	-	2 (3.6%)
Fernandez Ranvier, 2020 (29)	152	38 TT; 111 HT; 3 CT	5 (2.6%)	3 (1.6%)	7 (17.1%)	0	28 (18.4%)	1 (0.7%)	1 (0.7%)	3 (2.0%)	9 (5.9%)
Fernandez- Ranvier, 2020 (35)	50	12 TT; 38 HT	2 (3.2%)	1 (1.6%)	1 (8.3%)	0	29 (58.0%)	1 (2.0%)	-	-	4 (8.0%)
Hong, 2020 (36)	82	12 TT; 70 HT	3 (3.2%)	0	1 (8.3%)	0	-	0	2 (2.4%)	0	0
Kim, 2020 (37)	132	8 TT; 124 HT	6 (4.3%)	0	1 (12.5%)	0	2 (1.5%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	-
Lira, 2020 (28)	56	37 TT; 19 HT	2 (2.1%)	0	4 (10.8%)	0	0	0	1 (1.8%)	0	0
Luna-Ortiz, 2020 (38)	46	44 TT; 2 HT	1 (1.1%)	2 (2.2%)	-	2 (4.5%)	0	0	-	-	-
Peng, 2020 (39)	105	10 TT; 95 HT	3 (2.6%)	2 (1.7%)	2 (20.0%)	0	3 (2.9%)	0	1 (0.8%)	-	-
Alsafran, 2021 (40)	4	0 TT; 4 HT	0	0	0	0	1 (25.0%)	0	0	0	-
Chai, 2021 (20)	110	3 TT; 100 HT; 7 lsth	5 (4.4%)	1 (0.9%)	1 (33.3%)	0	0	0	0	1 (0.9%)	-
Deroide, 2021 (41)	90	41 TT; 44 HT; 5 Isth	7 (5.3%)	0	8 (19.5%)	0	26 (28.9%)	1 (1.1%)	0	0	1 (1.1%)
Lira, 2021 (42)	412	265 TT; 144 HT; 3 Isth	30 (4.4%)	4 (0.6%)	19 (7.2%)	3 (1.1%)	7 (1.7%)	0	1 (0.2%)	2 (0.5%)	8 (1.9%)
Nguyen, 2022 (43)	326	47 TT; 279 HT	9 (2.4%)	0	12 (25.5%)	0	7 (2.1%)	0	0	-	-
Russell, 2021 (21)	200	36 TT; 159 HT; 5 CT	9 (3.3%)	0	14 (18.2%)	0	-	5 (2.5%)	2 (1.0%)	0	2 (1%)
Zheng, 2021 (44)	297	10 TT; 287 HT	4 (1.3%)	4 (1.3%)	3 (30.0%)	0	234 (78.8%)	7 (2.4%)	2 (0.6%)	0	-
Yap, 2022 (45)	9	9 TT; 0 HT	0	0	3 (33.3%)	2 (22.2%)	2 (22.2%)	0	0	0	-

^{*}, rates of recurrent laryngeal nerve injury calculated for total number of nerves at risk. ^{*}, hypoparathyroidism as defined by each study. Rates of transient or permanent hypoparathyroidism calculated only for total thyroidectomy and completion thyroidectomy cases. N, number; RLN, recurrent laryngeal nerve; HPT, hypoparathyroidism; MNI, mental nerve injury; TT, total thyroidectomy; HT, hemithyroidectomy; CT, completion thyroidectomy; Isth, isthmusectomy.

mental nerve injury is rare.

Another novel complication with TOETVA is the risk of flap perforation or skin burn, which may occur with placement of the ports or during flap creation (55). Although the incidence is not consistently reported in all studies, *Table 2* demonstrates that this complication occurred in 0-8.0% of published cases. Other soft tissue effects of skin dimpling, tissue tethering, or a "pulling" sensation have also been reported in the literature (28,55). While seemingly rare, these alterations in appearance may be significant in a population highly motivated to avoid visible evidence of their surgery.

Given the intra-oral access to the surgical field, the risk of post-operative infection is another variable to consider in TOETVA. While TCA thyroid surgery is deemed a "clean" procedure with no prophylactic antibiotics indicated (56), procedures involving the oral vestibule are "clean-contaminated". Therefore, antibiotic prophylaxis pre-procedure is generally recommended, with many continuing coverage for 3–7 days post operatively (4,15,52,57). However, other more recently published series have found no increased rate of infection over TCA even without extended antibiotic prophylaxis (20,58). Overall, in comparison with TCA, vestibular access does not seem have an increased rate of infection (52,58-60). A large metaanalysis completed in 2022 concurs, with only a 0.64% infection rate in the 1,887 patients studied (61).

While nodule disruption during removal is not necessarily thought of as a complication of the procedure, such an occurrence can violate oncologic principles and make assessment of capsular involvement and extrathyroidal extension difficult. Several studies have examined rates of capsular disruption on final pathology. Wu et al. found that a nodule diameter of 20 mm had a 100% sensitivity and 87% specificity for remaining intact on final pathology (18). Likewise, Smith et al. found a median nodule size of 19 mm when examining unruptured nodules (62). In both studies, there was a significant capsule disruption rate [59% (18) and 68% (62)] when considering all sizes of nodules removed. For this reason, it is imperative that surgeons adhere to published size guidelines when considering malignant or suspicious nodules for TOETVA to ensure accurate pathologic analysis. Some surgeons have combined TOETVA with other remote access incisions (submental, axillary, retro-auricular) in order to allow the benefits of a laparoscopic TOETVA dissection with a larger port for thyroid removal, allowing for larger specimens to be removed in this manner (58,63,64).

Operating time

Despite increases in implementation and increasing case volumes, TOETVA has longer operating times than the traditional approach. In Russell et al.'s review, the median operative time for a TOETVA lobectomy vs. TCA lobectomy was 123 minutes compared to 75 minutes respectively (P=0.001) (21). A TOETVA total thyroidectomy was 184 minutes, and TCA total thyroidectomy was 116 minutes (P=0.001). Similarly, de Vries et al. found a significant difference between the two methods, with the operating times of 152 vs. 105.5 minutes for TOETVA and TCA respectively (33). Although this time decreases with increased case experience (28,43), there remains a significant difference in time (28,32,65), albeit less than a robotic approach (66). Table 3 details the published operative times of TOETVA lobectomy and thyroidectomy compared to TCA.

Cost

Operative time also has an influence on the cost of the procedure. The first study of its kind was published in 2021 by Razavi et al. which examined the direct cost of TOETVA as well as time-independent costs (65). One hundred and eighteen patients underwent TOETVA and 120 underwent TCA at the same institution by the same two experienced endocrine surgeons. The mean variable direct cost was \$4,455 USD (SD 1,129, 95% CI: 4,204-4,706) for TOETVA lobectomy compared to \$3,179 USD (SD 687, 95% CI: 2,990-3,369) for TCA lobectomy (P<0.001). Independent of time, the mean cost for TOETVA lobectomy was \$3,370 USD (SD 974, 95% CI: 3,154-3,587) compared to \$2,409 USD (SD 550, 95% CI: 2,257-2,560) for TCA lobectomy (P<0.001). Although TOETVA is a more costly procedure independent of operating time, the difference in energy devices alone contributed nearly \$500 USD (38.2% and 43.2%) of the cost difference for lobectomies and total thyroidectomies, respectively. Although energy devices are commonly used in both TCA and TOETVA procedures, this institution used different instruments for each procedure, which accounted for the cost difference referenced in that study. The total difference in cost between TOETVA and TCA is considerably less than previously reported for robotic thyroidectomies (67) and is certainly an important factor in the continued implementation of TOETVA across institutions that offer remote access techniques.

Table 3 Operating time

First author, year	TOETVA lobectomy (min)	TOETVA TT (min)	TCA lobectomy (min)	TCA TT (min)
Ahn, 2020 (34)	102.1	143.6	76.4	90.7
Fernandez Ranvier, 2020 (29)	161.8	213.4	-	-
Fernandez-Ranvier, 2020 (35)	149.0	217.6	-	-
Hong, 2020 (36)	112.3	155.9	59.5	79.8
Alsafran, 2021 (40)	151.0	_	-	-
Chai, 2021 (20)	110.0	168.0	-	-
Deroide, 2021 (41)	120.6	168	-	-
Nguyen, 2022 (43)	90.7	113.4	-	-
Razavi, 2021 (65)	127	176	92	125
Russell, 2021 (21)	123	184	75	116
Zheng, 2021 (44)	135.6	189.3	-	-

TOETVA, transoral endoscopic thyroidectomy vestibular approach; TT, total thyroidectomy; TCA, transcervical approach; min, minutes.

Learning curve

As with any procedural skill, the time it takes to complete a task is expected to decrease with provider skill and experience. The learning curve for TOETVA is estimated in some series to be approximately 11-15 cases (28,68), whereas others have found proficiency can take up to 50-60 cases (20,69,70). It is critical that surgeons are aware of the possible intra-operative difficulties and complications that can arise during a novel procedure. For this reason, it is recommended that extensive preparation occurs prior to implementing TOETVA in one's practice. This preparation includes ensuring high thyroid volume, familiarity with existing literature, operative team/administration preparation, familiarity with the procedure, real-time observation of cases, cadaver dissection, and preceptor presence for initial cases (71). Careful patient selection is also critical during the learning curve, with consideration of the benefit to each patient in order to achieve optimal outcomes and limit complications. Informed consent must be obtained regarding the novel nature of this approach with the discussion of potential complications (71). With these steps in place, several series detailing their initial experience with TOETVA even during their learning curve have demonstrated acceptable outcomes (21,28,31,34,40,41,70).

Disease-related outcomes

Finally, efficacy in disease-directed treatment is a critical

element to examine. Liu et al. published a propensity scorematched analysis of outcomes in patients with papillary thyroid cancer measuring 1.0-3.5 cm (72). While they too had equivalent complication rates between the groups in line with the other papers discussed, they also examined the number of lymph nodes harvested and post-operative thyroglobulin (Tg) levels between the two groups. They found that there was no difference in the median number of central lymph nodes harvested (9 vs. 10, P=0.154) or the rate of lymph nodes metastasis (69.2% vs. 71.8%, P=0.725) between the TOETVA and TCA groups respectively. Additionally, there was no significant difference in the median stimulated Tg level (0.50 vs. 0.99 µg/L, P=0.118) and the percentage of patients with an unstimulated Tg level <1.0 µg/L (61.9% vs. 50.0%, P=0.423). While Zheng et al. did not compare their outcomes to a TCA control group, they too harvested a mean 6.6±4.1 (lobectomy) and 10.9±4.0 (total thyroidectomy) lymph nodes, with non-stimulated Tg levels in the total thyroidectomy group below 1 ng/mL at 6 months (44). These studies demonstrate appropriate oncologic clearance can be performed with TOETVA, and that malignancy (with appropriate patient selection) should not be a deterrent to the procedure. Although data does not yet exist for long term oncologic outcomes, short term recurrence rates are promising (43).

Conclusions

The TOETVA literature published in 2020-2022 includes

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data from several large case series and meta-analysis. There has been increased performance of this procedure by surgeons and pursual by patients, evidenced by the more proliferative publication and adoption of this method compared to other remote access approaches. The recently published literature further illustrates TOETVA as a safe method in patients who are motivated to avoid a cervical incision. It must be noted that while these recent studies demonstrate equivalence in major complications, there is a higher published rate of minor complications with TOETVA. Careful and appropriate patient selection remains paramount to maximize patient safety and optimize outcomes. This remains true in cases of malignancy, although there has been no difference found in short-term oncologic outcomes between TOETVA and TCA. While this is a safe and effective surgical method, the increased operative time and higher costs may hinder implementation in some practices. Further prospective research comparing quality of life and long-term disease-related outcomes between the traditional approach and TOETVA are warranted to ensure optimal patient and disease-directed outcomes.

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Footnote

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