OUTCOMES OF TRANSORAL ENDOSCOPIC THYROIDECTOMY VESTIBULAR APPROACH (TOETVA) USING NERVE INTEGRITY MONITOR (NIM) AT HANOI MEDICAL UNIVERSITY HOSPITAL

Nguyen Xuan Hau[1,2,3], Nguyen Xuan Hien[2]
Le Van Quang[1,2,3] and Nguyen Nhat Tan[1,✉]

[1]Department of Oncology, Hanoi Medical University
[2]Oncology Center, Hanoi Medical University Hospital
[3]Vietnam National Cancer Hospital

This prospective study evaluated outcomes of Nerve Integrity Monitor (NIM) application in transoral endoscopic thyroidectomy vestibular approach (TOETVA) among 30 patients (93.3% female; mean age 39.7 years old) with benign tumors or differentiated thyroid carcinoma. Among 31 nerves at risk, anatomical variations were identified in 27.3%, including 22.6% penetrating Berry's ligament, 22.6% passing between inferior thyroid artery branches, and 16.1% with extralaryngeal branching. NIM achieved 100% successful signal detection for initial vagus and RLN stimulation. Signal interference occurred in 46.6% but decreased with experience. Temporary RLN palsy occurred in one patient (3.3%) due to thermal injury during Berry's ligament dissection, with complete recovery within 3 months; no permanent injury occurred. Stable intraoperative signals provided 100% negative predictive value for normal postoperative vocal cord function. NIM application in TOETVA is feasible and safe, providing reliable intraoperative guidance for RLN preservation. The high rate of anatomical variations underscores the importance of routine neuromonitoring in this approach.

Keywords: TOETVA, transoral thyroidectomy, nerve integrity monitor, NIM.

I. INTRODUCTION

Thyroid tumors are a common clinical pathology, accounting for over 90% of endocrine system tumors, with an ultrasound detection rate ranging from 19% to 68%.[1] Currently, surgery remains the mainstay of treatment for thyroid tumors. The transoral endoscopic thyroidectomy vestibular approach (TOETVA), first described by Anuwong in 2016, offers a significant advancement by eliminating visible cervical scarring. This technique meets patients' high aesthetic expectations without compromising treatment efficacy.[2]

Corresponding author: Nguyen Nhat Tan
Hanoi Medical University
Email: nguyennhattan1708@gmail.com
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Although surgical techniques have made significant progress in recent decades, injury to the recurrent laryngeal nerve (RLN) remains a severe complication, significantly affecting the patient's quality of life with sequelae related to voice and respiration. In TOETVA, the rate of this complication is recorded at approximately 1-20%.[3,4] Furthermore, the craniocaudal approach to the surgical field and two-dimensional endoscopic visualization present certain challenges in dissecting and identifying the RLN compared to open surgery, especially in case of anatomical variations.

To assist surgeons in identifying and preserving the nerve, the Nerve Integrity Monitor

(NIM) has been applied and developed globally. This device not only aids to identify the RLN more accurately through electromyographic signals but also supports prognosticate nerve conduction function intraoperatively.[5] In Vietnam, the NIM device has been utilized in some head and neck surgeries. However, there are currently few studies in terms of evaluating the results of applying NIM in TOETVA.

This study aimed to describe the clinical and paraclinical characteristics of patients undergoing Transoral Endoscopic Thyroidectomy Vestibular Approach (TOETVA) and to evaluate the early outcomes of applying the Nerve Integrity Monitor (NIM) in this procedure at Hanoi Medical University Hospital.

II. PATIENTS AND METHODS

1. Patients

30 patients indicated for TOETVA with NIM application at the Oncology Center - Hanoi Medical University Hospital from September 2021 to September 2022.

Inclusion criteria:

- Patients diagnosed with benign thyroid tumors or differentiated thyroid carcinoma stage cT1N0M0, had indication for TOETVA for partial or total thyroidectomy.

- Tumor size on ultrasound ≤ 6cm.

- NIM system used for support during surgery.

- Patients had full medical records and agreed to participate in the study.

Exclusion criteria:

- Patients with contraindications for surgery or anesthesia: coagulation disorders, chronic systemic diseases, poor physical status, etc.

- Patients with a history of prior neck irradiation or open surgery.

- Patients with preoperative confirmed recurrent laryngeal nerve palsy.

- Cases requiring conversion to open surgery or NIM device technical failure resulting in no intraoperative signal.

2. Methods

Study design: This is a prospective observational study.

Procedure: Transoral Endoscopic Thyroidectomy Vestibular Approach (TOETVA) using Nerve Integrity Monitor (NIM):

- System setup and Patient preparation:

+ The power was turned on, the head and neck surgical region was selected, and the thyroid organ mode was selected.

+ NIM endotracheal tube placement: The anesthesiologist placed the endotracheal tube with electrodes ensuring contact between the vocal cords; no local anesthesia was used and the tube was secured firmly.

+ The ground electrode was placed at the sternal notch or left shoulder, the stimulation probes and interference cables were attached, and all components were attached to the interface connector.

+ Stimulation parameters were set at 1mA and 100µV.

+ The patient was placed in a neck extension position with a shoulder roll; antisepsis and draping were performed to begin surgery.

- Trocar placement and surgical space establishment

+ A 10mm transverse incision was made in the center of the oral vestibule at 2/3 of the distance between the vermilion border and the frenulum.

+ A small forceps was utilized to tunnel the submucosal layer along the mandible downwards without injuring the mentalis muscles.

+ A hydro-dissection solution comprising 1ml adrenaline mixed with 500ml normal saline mixture was injected into the sub-platysmal plane to dissect the surgical field by using a dedicated needle. Subsequently, a blunt dissector was used to create the central cavity and widen the surgical space.

+ A 10mm trocar was inserted through the incision with a 30° optic, and CO_2 insufflation was maintained at a pressure of 8 – 10mmHg with a flow rate of 3l/min.

+ Two 5mm trocars were placed bilaterally to the 10mm trocar through lateral incisions allowing the 3 trocars to converge at the midline. The 5mm trocar positions were lateral to the canines and above the lower lip to avoid mental nerve injury.

+ After trocar placement, monopolar cautery and an ultrasonic scalpel were used to dissect the skin flap deep to the platysma muscle and create the surgical space with the following landmarks: (1) inferiorly at the suprasternal notch, (2) laterally at the anterior border of the sternocleidomastoid muscles, and (3) superiorly at the thyroid cartilage. The midline was then opened to expose the thyroid isthmus. The strap muscles were dissected and suspended laterally using a Vicryl 3-0 suture.

- Thyroidectomy

+ The carotid sheath was exposed then the NIM probe stimulated the carotid sheath, recording the response signal of the Vagus nerve - V1 (µV).

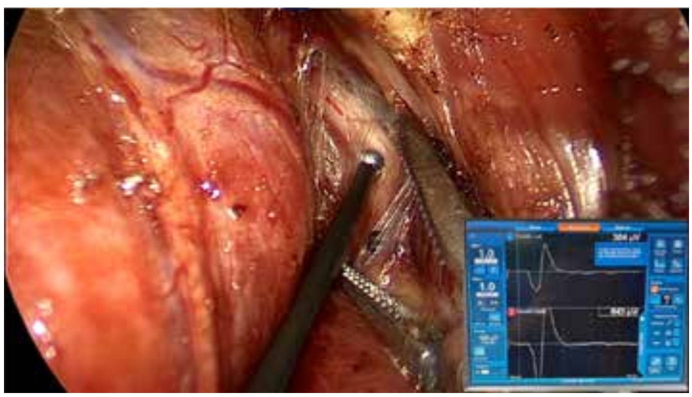

Figure 1. Intraoperative Vagus nerve stimulation using NIM probe

(Patient Tran Thi Khanh L.; File code: 2203120625)

+ The pyramidal lobe and thyroid isthmus were resected using the ultrasonic scalpel. The superior thyroid pedicle was then transected with the ultrasonic scalpel close to the gland to preserve the external branch of the superior laryngeal nerve and superior parathyroid gland; NIM was used to exclude the nerve before slicing.

+ After dissecting the upper pole, the thyroid lobe was retracted contralaterally using a grasper.

+ The NIM probe was used to locate the RLN near its entry point into the larynx, recording the amplitude of the RLN response signal as R1 (µV).

+ Kelly clamp was used to dissect and expose the RLN, using NIM during exposure to distinguish the nerve from other neurovascular structures.

+ The inferior thyroid pedicle was clamped, using NIM to distinguish it from the RLN before cutting.

+ Berry's ligament was cut, using NIM to distinguish the RLN before cutting.

+ The thyroid was resected close to the capsule and released from the tracheoesophageal groove. NIM was used to check nerve integrity after resection.

+ Central lymph node was dissected in cases of thyroid cancer. NIM was used to check after dissection.

+ The specimen was extracted by an endoscopic bag through the 10mm trocar port.

- Hemostasis and Closure:

+ Hemostasis and irrigation.

+ NIM was used to assess the integrity of the RLN via two stimulation sites: carotid sheath (V2) and RLN (R2).

+ The midline and intraoral incisions were closed.

Study Variables: Age, tumor characteristics on ultrasound (size, location, number), postoperative pathology results (histopathological type, T stage, number of metastatic lymph nodes), nerve integrity based on signal amplitudes V1, R1, R2, V2 (good response ≥100 μV / weak or lost signal <100 μV), postoperative complications (recurrent laryngeal nerve palsy, mental nerve palsy).

Data Analysis

Data were collected and processed using SPSS 20.0 software.

3. Ethics

Patients selected for the study sample participated voluntarily. The study aims solely to improve the quality of diagnosis and treatment. Patient confidentiality was strictly maintained.

III. RESULTS

Table 1. Characteristics of patients

Characteristics	Malignant (n=23)	Benign (n=7)	Total (n=30)
Age			
< 55 years old	23 (100%)	6 (85,7%)	29 (96,7%)
≥ 55 years old	0	1 (14,3%)	1 (3,3%)
Mean	40,2±7,1	38,0±10,4	39,7±7,9
(min - max)	(28-52)	(28-58)	(28-58)
Number of tumors			
1 tumor	17 (73,9%)	5 (71,4%)	22 (73,3%)
≥ 2 tumors	6 (26.1%)	2 (28,6%)	8 (26,7%)
Tumor location			
Right lobe	11 (47.9%)	5 (71,4%)	16 (53,4%)
Left lobe	10 (43,5%)	2 (28,6%)	12 (40%)
Isthmus	1 (4,3 %)	0	1 (3,3%)
Bilateral	1 (4,3%)	0	1 (3,3%)

Characteristics	Malignant (n=23)	Benign (n=7)	Total (n=30)
Tumor size			
≤10 mm	21 (91,3%)	0	21 (70%)
10-20mm	2 (8,7%)	0	2 (6,6%)
>20mm	0	7(100%)	7(23,3%)
Mean ± SD (mm)	7,2±2,9	28,9±5,8	12,3±10

In our study, 96.7% of patients were under 55 years old; only 1 case of benign tumor over 55 years old was recorded (3.3%). The mean age of the cancer group was 40.2 ± 7.1 years old, higher than the benign group (38.0 ± 10.4 years old); however, this difference was not statistically significant with p = 0.53.

Regarding tumor characteristics on ultrasound, the majority of patients had only one thyroid tumor; the rate of multinodularity in the cancer and benign groups was equivalent (26.1% and 28.6% respectively; the difference was not statistically significant with p = 0.321). Tumors were mainly localized in one thyroid lobe (93.4%), most commonly found in the right lobe (53.4%) and left lobe (40%); isthmus and bilateral locations were less common (both 3.3%). The most distinct difference lay in tumor size: the mean size in the cancer group was significantly smaller than in the benign group (7.2 ± 2.9 mm vs 28.9 ± 5.8 mm); this difference was statistically significant with p < 0.001.

Table 2. Anatomical Characteristics of the Recurrent Laryngeal Nerve (RLN)

Anatomical characteristics	Quantity (n)	Proportion (%)
Relation to inferior thyroid artery		
Posterior to artery	22	71,0%
Between branches	7	22,6%
Anterior to artery	2	6,4%
Relation to Berry's ligament		
Deep/ Lateral	24	77,4%
Penetrating ligament	7	22,6%
Relation to tracheoesophageal groove		
Within groove	26	80,6%
Lateral to groove	5	19,4%
RLN branching		
Non-branching	26	83,8%
Branching	5	16,1%

The majority of nerves passed posterior to the inferior thyroid artery (71%), ran deep to Berry's ligament (77.4%), and laid within the tracheoesophageal groove (80.6%). Additionally, approximately 22.6% of cases involved the nerve penetrating Berry's ligament, and 22.6% passed between arterial branches. Nerve branching was 16.1%.

Table 3. Signal response results

Parameter		Number of nerves	Proportion
V1 (μV)	>100	31	100%
	<100 or loss of biphasic waveform	0	0%
R1 (μV)	>100	31	100%
	<100 or loss of biphasic waveform	0	0%
R2 (μV)	>100	30	96,8%
	<100 or loss of biphasic waveform	1	3,2%
V2 (μV)	>100	30	96,8%
	<100 or loss of biphasic waveform	1	3,2%

** Total 31 nerves (including 1 patient with bilateral dissection)*

The study results indicate that the rate of successful stimulation and recording of the initial Vagus nerve response signal (V1) as well as the RLN localization signal (R1) reached an absolute 100%. However, during the phase of assessing nerve integrity after completing thyroidectomy, we recorded one case of complete signal loss at both check positions (loss of R2 and V2). After performing a comprehensive check procedure to rule out causes such as device error, electrode displacement, or interference factors, this case was determined to be a physical injury to the recurrent laryngeal nerve occurring during dissection.

Table 4. Postoperative complications

Complication	Frequency	Proportion
RLN Palsy (n=30)		
Temporary	1	3,3%
Permanent	0	0
Mental Nerve Palsy (n=30)		
Temporary	1	3,3%
Permanent	0	0

The overall complication rate in the study group was 6.7%. Specifically, we recorded 3.3% cases of temporary recurrent laryngeal nerve palsy and 3.3% cases of temporary mental nerve injury.

IV. DISCUSSION

This prospective study evaluated the outcomes of applying the Nerve Integrity Monitor (NIM) in transoral endoscopic thyroidectomy vestibular approach (TOETVA) at Hanoi Medical University Hospital. Our findings demonstrate that NIM is technically feasible in the transoral endoscopic setting, provides valuable intraoperative guidance for recurrent laryngeal nerve (RLN) identification, and contributes to favorable postoperative outcomes with a temporary RLN palsy rate of 3.3% and no permanent injury.

In our study, the mean age of patients was 39.7 ± 7.9 years old, with 96.7% of patients under 55 years of age. This demographic profile is notably younger than reported in traditional open thyroidectomy series (46.9 ± 12.5 years old) and accurately reflects the target population for TOETVA-patients with high aesthetic expectations who are motivated to avoid visible cervical scarring.[6] The female predominance in our study (93.3%) with a female-to-male ratio of 14:1 aligns with the well-established gender disparity in thyroid pathology and is consistent with other TOETVA series reporting ratios of 7.5:1 to 10:1.

Regarding tumor characteristics on ultrasound, the mean tumor size in the cancer group (7.2 ± 2.9 mm) was significantly smaller than in the benign group (28.9 ± 5.8 mm) ($p < 0.001$). This aligns with current TOETVA indications, which usually prioritize early-stage, small-sized cancerous tumors to ensure oncological safety, while benign tumors are usually only intervened upon when the size is large enough to cause compression or aesthetic impact. The 34.8% rate of occult central lymph node metastasis in our cancer patients, despite all being clinically node-negative preoperatively, aligns with international literature reporting rates of 30-60% for papillary microcarcinoma. This finding supports routine central compartment dissection in thyroid cancer surgery and highlights the importance of NIM in protecting the RLN during this additional dissection.

Our detailed intraoperative anatomical study of 31 RLNs revealed a 27.3% rate of anatomical variations, including 16.1% with extralaryngeal branching, 22.6% with nerves passing between branches of the inferior thyroid artery, and 22.6% with nerves penetrating through Berry's ligament. These findings are consistent with international literature but represent the first detailed report of RLN anatomical variations in a Vietnamese cohort undergoing TOETVA.[7,8]

The 22.6% of nerves passing between arterial branches represents a particularly high-risk configuration, as ligation of the inferior thyroid artery without clear visualization could easily result in injury. Similarly, the 22.6% penetration rate through Berry's ligament has significant clinical implications: when the nerve runs through the ligament, it is intimately associated with the thyroid gland and at high risk during final dissection. The single case of RLN injury in our series occurred precisely in such a patient, when ultrasonic shears activation near the ligament caused thermal injury to a nerve penetrating this structure. The 16.1% rate of extralaryngeal branching, while somewhat lower than the 20-40% reported in some anatomical studies, underscores the value of NIM in scanning the operative field to detect and preserve branches that might otherwise be overlooked.[9,10]

The NIM system demonstrated excellent performance with 100% successful signal detection for initial vagus (V1) and RLN (R1) stimulation. Mean setup times (1.7 ± 1.1 minutes for tube placement; 2.0 ± 0.7 minutes for system configuration) were comparable to open thyroidectomy, confirming that NIM integration does not significantly prolong operative time in the TOETVA setting.[11] Our study also recorded the rate of signal interference (46.5%) was higher than in open surgery (11.7%) and reflects the specific challenges of NIM use in endoscopic surgery.[12,13] The most common cause was endotracheal tube displacement (46.6%), occurring during patient repositioning and surgical manipulation. Patient awakening caused interference in 16.6% of cases. All episodes were successfully managed by tube repositioning or adjusting anesthetic depth, with no case requiring tube replacement. The interference rate decreased over the course of the study, from 60% in the first 10 cases to 35% in the last 10 cases, demonstrating a learning curve for interference management.

The temporary RLN palsy rate was 3.3% (1 patient), with no permanent injury. This compares favorably with reported rates for both TOETVA (2-8%) and open thyroidectomy (2-6%). Anuwong's initial series reported 3.3%, while Zhang et al. reported 6.4% temporary and 0.5% permanent palsy rates in 145 TOETVA patients.[2,14] The single injury occurred during dissection of Berry's ligament in a patient whose nerve penetrated this structure. Thermal injury from ultrasonic shears caused sustained loss of signal that did not recover by procedure end, and postoperative laryngoscopy confirmed ipsilateral vocal cord palsy. The patient recovered completely within 3 months, consistent with the expected time course for thermal injury. This case confirms that NIM accurately detects intraoperative nerve injury (100% positive predictive value) and provides valuable information for postoperative management. Importantly, no patient with stable intraoperative signals developed postoperative RLN palsy, giving NIM a 100% negative predictive value. This finding provides strong intraoperative reassurance and allows confident prediction of normal postoperative vocal cord function.

Transient mental nerve injury occurred in one patient (3.3%) and resolved completely within 1 month. This rate is comparable to Anuwong's later 200-case series had 1.5% after modifying trocar placement.[15] In our current practice, we use a blunt dissector to create the tract before trocar insertion and avoid electrocautery during placement to minimize this risk.

Our 3.3% temporary palsy rate compares favorably with TOETVA series that did not routinely use NIM. While our study was not designed to compare NIM versus no NIM, the device proved valuable for detecting anatomical variations, confirming nerve identity before vessel ligation, and providing immediate feedback during nerve stress. The two transient signal decreases during retraction that resolved after tension release-events that would not have been detected with intermittent monitoring alone-exemplify the potential of neuromonitoring to prevent injury.

For surgeons adopting TOETVA, NIM may serve as a valuable educational tool, particularly during the learning curve where 35-50 cases are required to achieve proficiency.The real-time feedback can help surgeons recognize safe limits of tis?. While this study provides valuable preliminary data on NIM application in TOETVA, several limitations warrant consideration.[11] The modest sample size of 30 patients limits the precision of our estimates and precludes definitive subgroup analyses. The single-arm descriptive design, lacking a control group, means we cannot definitively quantify the added benefit of NIM compared to TOETVA without monitoring. Additionally, the single-center nature and the fact that all procedures were performed by surgeons beyond their initial learning curve may limit generalizability to less experienced settings. Our three-month follow-up, while adequate for detecting temporary palsy, does not capture very late recoveries or subtle voice changes detectable only with objective acoustic analysis.

Future research should include larger multicenter prospective studies with control groups to definitively establish the magnitude of benefit conferred by NIM in TOETVA. Randomized controlled trials comparing NIM-assisted TOETVA with conventional TOETVA would provide the highest level of evidence. Studies specifically evaluating NIM's impact during the learning curve would offer valuable guidance for training programs. The incorporation of routine postoperative laryngoscopy and objective voice assessment tools would enhance detection of subclinical dysfunction. Finally, cost-effectiveness analyses are needed to guide resource allocation decisions, and emerging technologies such as continuous intraoperative neuromonitoring and machine learning-based signal analysis hold promise for further enhancing nerve protection in transoral endoscopic thyroid surgery. sue manipulation and adjust accordingly.

V. CONCLUSION

The application of the Nerve Integrity Monitor (NIM) in Transoral Endoscopic Thyroidectomy Vestibular Approach is feasible and safe. NIM facilitates the identification of complex anatomical variations of the recurrent laryngeal nerve under endoscopic visualization, enables early intraoperative detection of nerve injury, and supports nerve preservation, thereby potentially improving functional outcomes. .

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