Review Article

The application of intraoperative neuromonitoring in lateral neck dissections for thyroid cancers

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Abstract: Neck dissections play an essential role in the management of thyroid cancer, it involves resection of the metastatic lymph nodes from levels II to V and often relating to important anatomical structures such as the motor branch of the vagus nerve (VN), spinal accessory nerve (SAN), hypoglossal nerve (HN), mandibular marginal nerve (MMN), phrenic nerve (PN) and brachial plexus (BP). Intraoperative neuromonitoring (IONM) of these motor nerves is relatively rare, however, it offers a potential way of protecting nerve integrity and reducing surgical risks in difficult cases. This review article will introduce the recent progress of IONM of six vulnerable motor nerves in lateral neck dissections (LNDs) for thyroid cancers.

Keywords: Intraoperative nerve monitoring (IONM); neck dissection; vagus nerve (VN); spinal accessory nerve (SAN); hypoglossal nerve (HN); marginal mandibular nerve (MMN); brachial plexus (BP); phrenic nerve (PN)

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Introduction

Thyroid cancers frequently advance to cervical lymph nodes. There are specific criteria to indicate lateral neck dissection (LND) in levels II though V that are those more involved (1). Such lesions may endanger the important anatomical structures of the neck, such as the common carotid artery, internal jugular vein, and many motor nerves. Peripheral motor nerves are often vulnerable to injury during surgery, leading to significant pain, dysfunction, and reduced the quality of life for the patient. Several studies have looked at the morbidity of LNDs in thyroid cancers and yielded many nerve-related results. A recent large analysis of surgical morbidity in neck dissection for thyroid cancer over 25 years observed that after LND, the lesions of vagus nerve (VN) in 0.14%, of spinal accessory nerve (SAN), transient in 1.34% and permanent in 0.29%, of hypoglossal nerve (HN) in 0.29%, of facial nerve in 0.44%, of phrenic nerve (PN) in 0.14%, of cervical plexus in 0.29% (2).

Nowadays, many technical changes have been widely used in surgery in order to preserve loco-regional structures and its functions without reducing the therapeutic effect of the surgical procedure. Intraoperative neuromonitoring (IONM) based on electromyography (EMG) is a relatively recent advance for real-time identification and functional assessment of inferior laryngeal nerves during thyroid surgery (3). It is noteworthy that the IONM technology is also applicable to the functional protection and monitoring of the other motor nerves during the LND, such as the SAN, HN, facial nerve, PN, and brachial plexus (BP), although it has not received enough attention at present (4).

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VN

The VN, as the upstream nerve of inferior laryngeal nerves, has been routinely monitored based on the standardized procedure of IONM in thyroid surgery (3). VN monitoring tests the functional integrity of the neural circuit, thus facilitates the inferior laryngeal nerves dissection and avoids neglecting the downstream lesion of the stimulation point. Moreover, VN stimulation is helpful in predicting the non-recurrent laryngeal nerve (NRLN). One of the signs of NRLN is that a negative muscle response at the low VN stimulation point (near the inferior border of the fourth tracheal ring) and a positive muscle response at the high VN stimulation point (near the superior border of the thyroid cartilage). EMG signal shows shorter latency (generally defined as <3.5 ms) is another sign of NRLN, because it depends on the distance between the ipsilateral vocal cord and the stimulation point. Shorter and more direct NRLN pathways should elicit shorter latency values (5).

Recently, continuous intraoperative neuromonitoring (CIONM) via VN stimulation has been considered as an innovation in real-time monitoring the entire course of inferior laryngeal nerves. Several studies have reported the reliability, feasibility and safety of CIONM for RLN via an automated periodic stimulation (APS) electrode clipped onto the VN. CIONM can alert the surgeon to the impending risk of nerve injury in two ways: muscle response decreases in amplitude >50%, and increases in latency >10%, reversibility is proportional to duration and severity. CIONM provides comprehensive EMG documentation (more than intermitted IONM), detects and prevents imminent RLN failure, elucidates RLN stress mechanism, surgeons can synchronize his surgical maneuver to avoid permanent injuries; additionally, CIONM can determine EMG tube malposition identification (6-9). A safety analysis of 400 VN dissections and APS electrode placements of CIONM was reported to be safe (9). Besides, some studies have shown that CIONM has certain risks, such as bradycardia and hypotension by continues stimulation and trauma by electrode placement (7,10).

In addition, VN monitoring is also important for its own protection. VN injury in neck surgery is mainly caused by lymph node invasion, or transection while the internal jugular vein dividing. It may also occur in the surgery of carotid body tumors, glomus jugulare tumors, and vagal paraganglioma. Imperatori *et al.* reported one case of cervicomediastinal schwannoma of the VN resection under stimulating the VN proximally to the lesion; pre-resection VN signal reached 800 μV at 1.0 mA intensity (11). We also encountered a suspicious spindle mass in neck dissection, which was confirmed by IONM as vagal schwannoma rather than metastatic lymph nodes, thus avoiding the possible vagal nerve injury caused by resection of the mass.

SAN

The extracranial SAN travels behind the internal jugular vein, obliquely downwards into the sternocleidomastoid muscle and passes through the midpoint of its posterior margin, then runs through the posterior cervical triangle, downwards into trapezius muscle. It is usually described as a pure motor nerve that provides innervation to the sternocleidomastoid and the upper trapezius muscles (12). Injury of the SAN results in trapezius denervation and atrophy, leading to the 'neck-shoulder-arm syndrome' that consists of pain, weakness, deformity (winging scapula) and limited range of shoulder movement, all above can greatly affect the quality of life of patients.

Shoulder morbidity following neck dissections is addressed in various investigations, they generally showed a tendency to increase when more comprehensive neck dissection was performed, especially during level V and/or level IIB dissection (13,14). Prevalence of shoulder complaints ranges from 31% to 40% after selective neck dissection (SND), from 18% to 77% after modified radical neck dissection (MRND), and from 47% to 100% after radical neck dissection (RND) (15). The SAN travels relatively superficial in the fat and connective tissue above the paravertebral fascia through the posterior cervical triangle to the trapezius muscle and is closely related to the superficial cervical lymph nodes, which is one of the reasons for its vulnerability. However, most of the lymph nodes located in the occipital triangle are deep in the SAN, which makes it difficult to expose. In addition, the SAN is at risk of injury during the endoscopic thyroid surgery via dorsal approach. When dissecting the lymphatic tissue around the internal jugular vein, particularly in level IIB dissection, the more traction applied to the SAN and the sternocleidomastoid muscle is considered to be the main reason for the increased risk of neural dysfunction (14).

Evidence in the literature for the application of IONM during neck dissection in potentially reducing the SAN injury and predicting postoperative function is relatively minimal and contradictory. Lanišnik *et al.* performed a prospective randomized trial in which IONM was used on one side of the neck while the other side was operated

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without IONM during MRND. The results showed that patients had better EMG signals of the trapezius muscles at 6 weeks with smaller decrease of the Constant Shoulder Score and recuperated better on the IONM side than the non-IONM side of the neck (P=0.041) (16). Other studies have suggested similar results and have shown that postoperative shoulder morbidities were less with SAN monitoring when compared to non-IONM (17,18). Birinci *et al.* indicated that amplitude decrement ≥72% and threshold increment ≥0.25 mA were significant IONM alterations for predicting shoulder activity restriction and function deterioration scores (17). However, Witt *et al.* conducted two studies on IONM of SAN and concluded that SND patients had a smaller threshold change than MRND patients, but electrophysiological integrity of the SAN was not completely correlate with postoperative shoulder function. In these two studies, ≥0.4 mA was the cutoff value for defining the significance in threshold increase (19).

There is no clear consensus on the contribution of the cervical plexus to the innervation of the trapezius muscle. Some authors concluded that the innervation from the cervical nerves is exist but unpredictable; however, some authors suggested that nerves have purely proprioceptive effects. In recent years, several electrophysiological studies have demonstrated that the branches from cervical plexus are similar to the SAN at the neuromuscular level, and also innervate all parts of the trapezius muscle equally (12,20). Since the clearance the area surrounding the cervical plexus from lymphatics and adipose tissue is part of the routine neck dissection procedure, IONM can be used to identify these small motor nerve branches that are important to the trapezius muscle (20). The description of different types of trapezius branches patterns might help to its identification and protection during neck dissection (21).

The SAN can be intraoperative monitored by observing muscle movement and trapezius EMG. During thyroidectomy or neck dissection with laryngeal nerves IONM, using a nerve stimulator to stimulate SAN with supramaximal intensity (empirically use of 3.0 mA), the obvious shoulder muscle twitch can be observed. Moreover, for the operation with a high risk of SAN injury, EMG can be recorded with surface electrodes placed in the trapezius muscle, 5 and 7 cm lateral to the midline at the C7 level. Nerve monitoring is performed at 1.0 to 3.0 mA stimuli intensity with bipolar needle, bringing out the distinctive audio signal and the EMG wave could alert the surgeon when approaching or over-excessively manipulating with the SAN. In addition, it can avoid cutting off any motor branches originating from SAN and/or cervical plexus to the trapezius muscle.

HN

The extracranial HN travels downwards along the internal carotid artery and VN, runs medially through the superficial external carotid artery, travels behind the posterior belly of the digastric muscle to innervate all the intrinsic and extrinsic lingual muscles except palatoglossus. Hence, HN plays a vital role in swallowing, speaking, coordinated chewing and breathing (22). Injury to the HN can cause ipsilateral tongue paralysis, which leads to long-term dysphagia, dysarthria, tongue atrophy and deviation.

Iatrogenic HN injury is not uncommon. According to an investigation, in 26 years of experience, 5% of all HN injuries in a hospital were caused by neck surgery (23). In addition to the surgery in the carotid triangle, such as neck dissections, can endanger the HN; there are still cases of the HN injury following thyroidectomy (24,25). It might be related to the extension of tumor or metastatic lymph node to the upper pole near the hyoid bone level, where the HN travels closely, and the neck extension and superolateral strap muscles contraction might stretch the nerve on C1 transverse process excessively, making the nerve more vulnerable to injury. Moreover, several anesthetic oropharyngeal manipulation factors, including forced placement of laryngoscope at the base of the lateral tongue, hyperinflation of the laryngeal mask airway, and tight oropharyngeal packs, could contribute to HN palsy development. In addition, nerve anatomic variants, hypoglossal schwannoma, and ectopic thyroid gland are also the possible risk factors for HN injury in neck surgery (26,27).

IONM of the HN is commonly reported during carotid, skull base, and oral surgery; however, head and neck surgeons familiar with laryngeal nerve monitoring can also easily implement HN monitoring by following other surgery procedures using IONM. Duque *et al.* introduced the application of intraoperative HN monitoring in head and neck surgery with four complicated cases with lesions of the tongue and floor of the mouth. Intraoperative neuromonitoring is based on Nerve Integrity Monitor-Response system (Medtronic; Jacksonville, Florida, USA). Pairs of subdermal needle electrodes were placed on both side of the tongue, therefore the nasotracheal intubation or a tracheostomy was undertaken. A single stimulus at intensity ranges from 0.5 to 1.0 mA was applied with a hand-held monopolar stimulation probe; while in other articles, the current intensity is set to 1.0 to 2.0 mA

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(22,27). After tumor resection, stimulation of HN leads to ipsilateral EMG activity and corresponding contraction of the remaining tongue. Ishikawa *et al.* reported a case of hypoglossal schwannoma removed under intraoperative monitoring with the HN, VN and SAN by the EMG response from the tongue and from the vocal cords, as well as movement of the patient's shoulder.

MMN

The MMN is one of the main terminal branches of the facial nerve. It passes through the parenchyma of parotid gland and runs anteriorly towards and forwards the lower mandible angle and deep to the platysma, and then sends fibers to innervate the muscles of the lower lip and chin. Injury to the MMN can cause cosmetic and functional morbidity, leading to the ipsilateral lower lip unable to move downward and laterally, especially when the patient smiles or cries, that is called 'asymmetric crying facies' (28).

The MMN is vulnerable to damage during neck dissection in level IB or II due to the close anatomical relationship between the course of the long and thin MMN and lymph nodes in submandibular region, with a reported incidence rate ranging from 18% to 21% (29). Furthermore, when the neck is extended backward and upward during thyroidectomy to exposure the surgical field sufficiently, the MMN may in an inferior and anterior direction along the facial vein complex. Therefore, excessive separation of flaps during neck dissection also may lead to negligent injury of MMN, especially in elderly patients with lax and atrophic tissue.

Facial nerve monitoring has been widely used in parotid, neurotologic, otologic, and skull base surgery. Many electrophysiologic neuromonitoring systems are commercially available. Taking the NIM-Response 3.0 system as an example, needle electrodes are inserted subcutaneously in optimal locations to record response from the facial muscles, typically in the four areas supplied by the facial nerve: frontal (m. frontalis), zygomatic (m. orbicularis oculi), buccal (m. mentalis), and marginal mandibular (m. orbicularis oris). With regard to the protection of MMN in neck dissection, one recording electrode placed at the inferior margin of mandible is usually enough. An adjustable impulse stimulator for evoking EMG, such as a probe-tip is used for intermittent monitoring (30) and a burr (StimBurGrad) for continuous monitoring in otologic surgery (31). Typical system parameters are set as stimulus intensity, 0.5 to 1.0 mA; event threshold, 100 μV; duration, 100 ms; and rate 4 bursts/s. With facial nerve stimulation, the immediate EMG response with characteristic waveform is visible and audible (31,32).

However, the percutaneous electrodes in facial muscles seem more than what is due to cervical lymphadenectomy of thyroid cancer. Therefore, we can use another simple method of not placing an additional electrode, similar to monitoring the external branch of superior laryngeal nerves during thyroidectomy, that is, to observe the facial movements visually or tactually that evoked electrically with a stimulation current at 0.5 to 1.0 mA or evoked mechanically by electrosurgical instruments during dissection (32).

BP

The BP arises from spinal nerve roots C5-T1 and courses through the middle and anterior scalene muscles, travels behind and above the subclavian artery and enters the axilla through the clavicle posteriorly, before giving rise to the peripheral nerves of the upper extremities. The BP provides motor, sensory and sympathetic innervation to the shoulder and upper arm. Hence, the BP injury can lead to pain, paresthesia and movement limitation of the ipsilateral shoulder or upper extremity.

Brachial plexopathy secondary to neoplastic infiltration or compression is a relativity rare complication of thyroid malignancy, with <0.5% of cancer patients being affected (33,34). Iatrogenic injury in neck dissection is not common as well, but excessive separation or traction of deep cervical fascia and overuse of energy instruments are risk factors for nerve injury. Additionally, the incidence of brachial plexopathy can reach 0.1% to 8.0% during transaxillary robot-assisted thyroidectomy (RAT), due to the patient's unilateral arm is retracted overhead and maintained in a flexed position about 90 degree for a long time, the neural and vascular elements may be stretched or compressed (35,36).

Some studies described the incorporation of intraoperative BP monitoring with somatosensory evoked potentials (SSEPs) and transcranial motor evoked potentials (MEPs) in RAT to identify and prevent imminent position-related injury. Impending BP neuropathy was defined as a 50% decrease in amplitude or a 10% increase in latency of SSEP, and a 90% reduction in amplitude of MEP in the ipsilateral arm (37). Davis *et al.* reported of a case in which SSEPs amplitude was detected to decrease completely 30 minutes after the first incision, then after repositioning the arm, the amplitude restored to baseline within 1 minute (38). Luginbuhl *et al.* reported a case of unilateral amplitude

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loss in MEPs and SSEPs in an obese woman, which was attributed to positional damage of the BP during the early stages of RAT (39). None of these cases above had permanent neurological deficits.

Alkan *et al.* conducted a cohort study with 30 patients to investigate the cause of BP injury and compared shoulder morbidity with and without BP monitoring during RAT. In general, the IONM group had significantly better shoulder movement, less pain, lower rate of hypoesthesia and higher quality of life in the early postoperative period than the non-IONM group. Besides, three patients in the IONM group showed neurophysiological evidence of imminent BP injury (partial or complete reduction of SSEP and MEP amplitudes) during the first 20 to 40 minutes of surgery, and these cases were restored by adjusting the arm position or relaxing the extreme retraction of the flap. Particularly, in the second case, the signs alterations occurred during the process of creating working space, so the arm was repositioned only after tunneling was completed. When the arm was in neutral position, the amplitudes of MEP and SSEP were returned to baseline, but they decreased again every time the surgeon tried to reposition the arm in extension. And, in the third case, the reduction both in SSEPs, MEPs, as well as in the pulse oximeter readings, which was probably associated with the pressure exerted by the retractors, that might damage the blood supply of axillary artery (37).

In addition, according to the author's experience, in several neck dissection of giant thyroid tumor or metastatic lymph nodes in level IV and V, when the tumor penetrates above the thoracic entrance and compress the BP to make it difficult to separate, the application of the NIM-Response system that used in RLN EMG monitoring to detect the BP or its adjacent area with a stimulus range from 0.5 to 1.0 mA, can induce muscle contraction in the upper arm and forearm, thus assisting the surgeon in identifying the BP and its position, course and adjacent to the surrounding tissue.

PN

The PN originates from C3 to C5, passes vertically downward through the anterior of the scalenus anterior muscle, then posterior and deep into the internal jugular vein, and enters the thoracic cavity through the subclavian artery before innervating the diaphragm. The PN injury can result in paralysis of the diaphragm, and then the diaphragmatic muscle elevation can lead to pulmonary parenchyma compression, thus affecting the reduction in the respiratory space and a hypoxic restrictive syndrome, especially in elderly patients.

The most common cause of PN injury associated with thyroid diseases is the invasion of lymph nodes metastasis, followed by compression of cervico-mediastinal goitre, especially where the nerve behind the first rib, through the thoracic inlet, enters the mediastinum. The PN in that area is neither under direct vision nor is there an effective method for identifying and preserving the nerve. If the dissection is too deep, it may cause iatrogenic injury to the PN during surgical procedures (40,41).

Duque *et al.* first reported the application of intraoperative PN monitoring during neck dissection for thyroid cancer. Among a series of 400 patients who underwent neck and mediastinal dissection, nineteen had advanced metastatic thyroid cancer in close proximity to the anterior scalene muscle that places the PN at risk. Routinely, IONM was used to preserve the VN and the RLN during thyroidectomy. When neck dissection was performed in level IV and the PN is not clearly exposed, the surgeon used the stimulation probe to ensure and locate an intact PN (42). The intensity of nerve stimulator decreased to 0.5 mA or even 0.3 mA, which resulted in diaphragm contraction and chest wall visible elevation. The nerve beneath the tumor resection area was then stimulated. It is important to note that during both procedures, surgeons and/or assistants should place their hands on the patient's chest to detect the movement of the thoracic wall during nerve stimulation. In addition, the anesthesiologist might observe a minimal change in the patient's respiratory patterns.

However, PN stimulation produced a current delivery tone or brief tone, similar to the sound heard when the probe was placed on non-targeted nerve tissue or vessels. Because there were no recording electrodes placed in the diaphragm or the intercostal muscles to record such a movement. A quantitative and objective method of measuring the contraction of the diaphragm is to insert a recording electrode into the ipsilateral intercostal muscle or the lower part of the diaphragm (43). This will allow recording of the EMG signal changes including the amplitude or the latency of the nerve. However, such an invasive way carries a higher risk and cost to the patient.

Conclusions

In conclusion, the practice of LND has made great progress from radical to functional preservation surgery. In order to avoid the postoperative neck and shoulder morbidities, current neck dissection techniques tend to be more selective.

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Intraoperative nerve monitoring opens new possibilities in peripheral nerve protection. Although IONM of the VN, SAN, HN, MMN, BP and PN during lateral neck dissection is not a regular indication of this technique, and the standardized protocol and prognostic criteria on this issue are not yet clarified, surgeons should be aware that the potential unconventional applications of IONM can offer to challenging surgical cases under special conditions.

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Footnote

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