

The Effect of the Intraoperative Neuromonitoring to the External Branch of the Superior Laryngeal Nerve Identification and Contribution of the Nerve to the Motor Function of the Thyroaritenoid Muscle

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ABSTRACT:

The effect of the intraoperative neuromonitoring to the external branch of the superior laryngeal nerve identification and contribution of the nerve to the motor function of the thyroaritenoid muscle

Objective: Meticulous anatomical studies of cadaver larynges revealed terminal branches of the external branch of the superior laryngeal nerve (EBSLN) reaching the anterior thyroaritenoid muscle (TA) region and communicating with branches of the recurrent laryngeal nerve (RLN) in 41% to 85% of cases. This nerve is called "human communicating nerve". Although the visual identification of the RLN is accepted to be the gold standart to preserve the nerve, there is still not a standart technique to preserve the EBSLN. In this study; we aimed to evaluate the intraoperative neuromonitoring's (IONM) contribution to visual and functional identification of EBSLN, and the nerve's contribution to the TA muscle function electrophysiologically.

Material and Methods: The prospective data of 50 consecutive (42F, 8M) patients, who underwent thyroid surgery with IONM for the exploration of EBSLN, were evaluated. The surface endotracheal tube-based Medtronic NIM3 (Medtronic, Jacksonville, FL) IONM device was used. The function of EBSLN was evaluated by cricothyroid muscle twitch. Additionally, EBSLN's contribution to the vocal cord adduction was evaluated by the electromyographic records.

Results: Forty one patients were bilaterally and 9 were unilaterally intervened. Eighty four (92.3%) of 91 EBSLNs at risk (43 left, 48 right) were identified. Fourty four (52.4%) of 84 EBSLNs were identified visually, before being stimulated with the probe. Additionally, 18 (21.4%) EBSLNs were identified visually, after being identified with the probe. Although 22 (26.2%) EBSLNs were identified with the probe, they were not able to be visualized. The IONM provided significant contribution to visual ($p<0.05$) and functional ($p<0.001$) identification of EBSLN. Positive EMG responses were obtained from 44 (52.4%) of 84 identified EBSLNs.

Unilateral or bilateral positive EMG responses were achieved from the TA muscles in 29 (70.7%) out of bilaterally intervened 41 patients, with the stimulation of the EBSLNs. Positive EMG waveforms of TA muscles were detected in 13 (44.8%) patients bilaterally and 16 (55.2%) patients unilaterally.

Conclusion: IONM is superior to the only visual identification, because IONM improves the visual and functional identification rate of the EBSLN. We suggest that the IONM should be used to diminish the risk of EBSLN injury in the superior pole dissection routinely. Although the EBSLN's main function is to innervate the cricothyroid muscle, it also contributes to the vocal cord's adductor function unilaterally or bilaterally, in two third of the patients. This innervation may be related to the vocal cord's functional and positional variabilities in the patients with RLN paralyses after thyroidectomies.

Keywords: Cricothyroid muscle, human communicating nerve, intraoperative neuromonitoring, the external branch of the superior laryngeal nerve, thyroaritenoid muscle

ÖZET:

Süperior laringeal sinirin eksternal dalı'nın belirlenmesinde intraoperatif sinir monitorizasyonunun etkisi ve sinirin tiroaritenoid kasın motor fonksiyonuna katkısı

Amaç: Kadavra larinksleri üzerinde yapılan özenli çalışmalar; vakaların %41 ile %85'inde, superior laringeal sinirin eksternal dalının (SLSED) terminal dallarının tiroaritenoid kasın ön bölgesine erişerek rekürren laringeal sinirin (RLS) dalları ile birleştğini göstermiştir. Bu sinirin adı "insan birleştirici siniri" dir. RLS'nin gözle identifikasyonu sinirin korunması için altın standart olarak kabul edilmesine rağmen, henüz SLSED'yi korumak için standart bir teknik yoktur. Bu çalışmada, SLSED'nin görsel ve fonksiyonel identifikasyonuna intraoperatif sinir monitorizasyonunun (İÖSM)'nin katkısını ve SLSED'nin elektrofizyolojik olarak TA kas fonksiyonuna katkısını değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Superior laringeal sinirin eksternal dalının eksplorasyonu için İÖSM ile tiroid cerrahisi geçiren 50 (42 K, 8 E) ardışık hastanın prospektif verileri değerlendirildi. Yüze endotrakeal tüp bağlı Medtronic NIM3 (Medtronic, Jacksonville, FL) cihazı kullanıldı. SLSED'nin fonksiyonu krikotiroid kasın kasılması ile değerlendirildi. Ayrıca, SLSED'nin vokal kord addüksiyonuna katkısı elektromiyografik kayıtlarla değerlendirildi.

Bulgular: Kırk bir hastaya bilateral ve 9 hastaya unilateral olarak müdahale edildi. Risk altındaki 91 (43 sol, 48 sağ) SLSED'nin 84'ü (%92.3) identifiye edildi. Seksen dört SLSED'nin 44'ü (%52.4) prob ile uyarılmadan önce gözle identifiye edildi. Ek olarak, 18 (%21.4) SLSED proba identifiye edildikten sonra gözle görüldü. Yirmi iki (%26.2) SLSED proba identifiye edilmesine rağmen gözle görülemedi. Intraoperatif sinir monitorizasyonu SLSED'nin görsel ($p<0.05$) ve fonksiyonel ($p<0.001$) identifikasyonuna belirgin katkı sağladı. Identifiye edilen 84 SLSED'nin 44'ünden (%52.4) pozitif EMG cevapları alındı. Bilateral müdahale edilen 41 hastanın 29'unda (%70.7), SLSED uyarısıyla TA kaslardan unilateral ya da bilateral olarak pozitif EMG cevapları alındı. Tiroaritenoid kasların pozitif EMG dalgaları, 13 (%44.8) hastada bilateral ve 16 (%55.2) hastada unilateral olarak saptandı.

Sonuçlar: İÖSM sadece gözle identifikasyona göre üstündür, çünkü İÖSM SLSED'nin görsel ve fonksiyonel identifikasyon oranlarını artırır. Biz, İÖSM'nin SLSED'nin yaralanma riskini azaltmak için superior pol diseksiyonunda rutin olarak kullanılmasını öneriyoruz. SLSED'nin ana görevi krikotiroid kası innerve etmek olmasına rağmen, ayrıca hastaların 2/3'ünde vokal kordun addüktör fonksiyonuna unilateral ya da bilateral olarak katkı sağlar. Bu innervasyon, tiroidektomilerden sonra RLS paralizili hastalarda vokal kordun fonksiyonel ve pozisyonel değişiklikleri ile ilişkili olabilir.

Anahtar kelimeler: İnsan birleştirici siniri, intraoperatif sinir monitorizasyonu, krikotiroid kas, süperior laringeal sinirin eksternal dalı, tiroaritenoid kas

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INTRODUCTION

Altered phonation is a common problem after thyroid surgery, thus it is important to preserve the nerves and muscles that are fundamental to phonatory. The importance of the external branch of the superior laryngeal nerve (EBSLN) has been overshadowed by a focus on the recurrent laryngeal nerve (RLN) in the thyroid surgical and monitoring literature (1). The superior laryngeal nerve is among the first branches of the vagus nerve, after it exits the skull base. About 1.5 cm caudally, the superior laryngeal nerve divides into an internal and external branch. The EBSLN descends dorsally to the carotid sheath and then crosses medially, extending to the larynx. The EBSLN is superficial to the inferior pharyngeal constrictor muscle as it descends and travels medially to innervate the cricothyroid muscle (CTM) on the anterolateral aspect of the lower portion of the cricoid cartilage of the larynx (2). Primary function of the CTM is to increase the length and longitudinal tension of the vocal folds during pitch elevation. The CTM paralysis due to EBSLN injury during thyroid surgery often goes unrecognized, because of the absence of clear laryngoscopy findings and variable associated voice changes (1).

Meticulous anatomical studies of cadaver larynges revealed terminal branch of the EBSLN continues on after innervating the CTM, extending through the cricothyroid membrane to innervate the anterior thyroarytenoid muscle region and communicating with branches of the RLN in the larynx (3,4). This branch is called a "human communicating nerve" (5). This was confirmed by EMG recordings from thyroarytenoid muscle following the electrical stimulation applied to the EBSLN (6).

In up to 20% of cases, the EBSLN may not be able to be visualized due to subfacial course along the inferior constrictor muscle, which requires a micro-dissection for the identification of the nerve (7).

Intraoperative neuromonitoring (IONM) has gained widespread acceptance as an adjunct to the gold standard of visual identification of RLN during thyroid surgery (8). Although the use of IONM for the exploration of EBSLN is increasing day by day, it was reported to be used for the identification of the EBSLN

by only 26.3% of low-volume versus 68.4% of high-volume surgeons with known interest in thyroid surgery (9).

In this study; we aimed to evaluate the contribution of IONM to visual and functional identification of EBSLN, and the nerve's contribution to the thyroarytenoid muscle function electrophysiologically.

MATERIALS AND METHODS

We prospectively obtained the intraoperative electrophysiologic stimulation data of 50 consecutive patients undergoing thyroid surgery with IONM for the exploration of EBSLN, between January and September of 2013. Data was stored in a dedicated database at the end of each surgical procedure with approval from the Institutional Review Board of Sisli Etfal Training and Research Hospital. Each side of the neck was considered as a separate entity and 91 neck sides were assessed. The exclusion criteria were secondary thyroid procedures, cancer with massive extrathyroidal extension, intentional nerve transection because of cancer invasion, and failure to assess EBSLN function because of the technical issues.

IONM Technique: The NIM 3.0 Nerve Monitoring System (Medtronic Xomed, Jacksonville, FL, USA) and the reinforced endotracheal tube (size 6.0 , 7.0 or 8.0) with surface electrode was used to test the nerves intraoperatively. The patient was under general anesthesia with a low-dose short-acting neuromuscular blockade (rocuronium 0.3 mg/kg) and was intubated with Medtronic Xomed Nerve Integrity Monitor Standart Reinforced Electromyography Endotracheal Tube (size 6.0 , 7.0 or 8.0). A sterile, single-use, pulse-generated monopolar stimulator probe (Medtronic Xomed, Jacksonville, FL, USA) was used for nerve stimulation in the operative field with an interrupted stimulation technique in which the probe was set on a value of 1 mA, 100 μ s impulse duration at 4 Hz frequency and monitor was set for an event threshold at 100 μ V. The IONM setup, applications and data interpretation were in compliance with the International Neural Monitoring Guidelines (1,9). The amplitude of the

electromyographic (EMG) waveform defined the adductor motor function of the vocal cords. Standart IONM was performed as a 4-step procedure for RLN (V1, R1, R2, V2). The function of EBSLN was assessed by the cricothyroid muscle (CTM) twitch. An auditory signal and a clear glottis EMG waveform with EBSLN stimulation were obtained in some cases. The EMG responses were recorded. Positive stimulation was defined as both the audible alarm of the monitoring system and achievement of a recognizable EMG waveform amplitude that was $>100 \mu V$, for both RLN and EBSLN.

Surgical Technique: Thyroidectomy and/or central neck dissection was performed by 4-6 cm collar transverse incision. Subplatysmal flaps were raised, strap muscles were divided along the midline, the thyroid lobe was medialized and middle thyroid vein was divided.

All the patients underwent total extracapsular thyroidectomy in which the branches of the superior and inferior thyroid arteries were divided close to the thyroid capsule.

Superior Pole Dissection: Superior pole dissection was performed before or after lateral gland mobilization. The upper pole of the lobe was retracted laterally and caudally to expand the sternothyroid-laryngeal triangle (SLT). However, in cases of enlarged gland within the superior portion of the thyroid lobe or in a patient with a short neck, sternothyroid and sternohyoid muscles were transected with a ligasure thermal sealing system (Covidien, Mansfield, MA) by preserving the ansa servicalis (10). The avascular space between the superior pole and CTM was exposed with blunt dissection to create a clear surgical control and better exposure of SLT, where the EBSLN is located. EBSLN was tried to be identified visually, after dissection of SLT. When the presumed EBSLN was identified, it was confirmed to be the EBSLN with a concomitant CTM twitch in response to neural stimulation. If the auditory signal and the glottis evoked EMG response with EBSLN stimulation were obtained, the response amplitudes were recorded. If EBSLN was not able to be identified visually, it was searched with the monopolar stimulator probe. If EBSLN was not identified with the probe, the fibers of inferior pharyngeal constrictor

muscle were not attempted to be dissected to identify the nerve visually.

In management of the superior pole dissection, each portion of the pedicle tissue was stimulated with a probe to ensure that the EBSLN is not trapped during the maneuvers of clamping or cauterization. After individual ligation of the branches of the superior thyroid vessels, we stimulated the EBSLN with the probe at a point cranial to the ligation of the vessels to confirm the integrity of the EBSLN.

Lateral Dissection: Nervus vagus was routinely identified and stimulated before the identification of RLN (V1). The RLN was identified and stimulated by IONM at the level of the inferior thyroid artery (R1). The thyroid gland was meticulously dissected from the anterior and medial surface of the RLN up to the nerve's entry point (NEP) into the larynx, under the cricopharyngeus muscle (CPM). The RLN was stimulated on its proximal portion after the complete nerve dissection (R2). Nervus vagus stimulation was also performed after the complete hemostasis of the surgical field (V2).

Statistical Analyses

The incidence of nerve events was calculated based on the number of nerves at risk. Differences between continuous and categorical variables were assessed by the Mann-Whitney U test and Fisher's exact test or chi-square test, respectively. Spearman's correlation was used for the parameters that were not normally distributed. A value of $p < 0.05$ was considered statistically significant.

RESULTS

During the study period, 91 neck sides of 50 patients (42 F, 8 M) with a median age of 49 years (range, 20-75), were assessed. Indications for the operation were benign thyroid disorders ($n=34$; euthyroid=24; hyperthyroid=10), thyroid cancer ($n=9$), undetermined or suspicious cytology for malignancy after fine needle aspiration biopsy ($n=7$). Forty one total thyroidectomies (with central lymph node dissection in 7, and lateral lymph node dissection in 2 patients), and 9 lobectomies were performed.

Eighty four (92.3%) of 91 EBSLNs at risk (43 left, 48 right) were identified. Forty four (52.4%) of 84 EBSLNs were identified visually, before being stimulated with the probe. Additionally, 18 (21.4%) EBSLNs were identified visually, after being identified with the probe. Although 22 (26.2%) EBSLNs were identified with the probe, they were not able to be visualized. The IONM provided significant contribution to visual ($p<0.05$) and functional ($p<0.001$) identification of EBSLN.

Additionally, positive EMG responses were obtained from 44 (52.4%) of 84 identified EBSLNs. The EMG amplitudes achieved from the RLNs and EBSLNs were 928 ± 616 μ V (range, 336-2745) vs 181 ± 69 μ V (range, 100-345) respectively, with a significant difference when compared with each other ($p<0.0001$).

Unilateral or bilateral positive EMG responses were achieved from the thyroarytenoid (TA) muscles in 29 (70.7%) out of bilaterally intervened 41 patients, with the stimulation of the EBSLNs. Positive EMG waveforms of TA muscles were detected in 13 (44.8%) patients bilaterally and 16 (55.2%) patients unilaterally.

The positive CTM twitch were obtained from the proximal portions of 82 (97.6%) out of 84 EBSLNs, but no twitch were achieved from the rest 2 (2.4%) EBSLNs despite the presence of the nerve integrity at the end of the lobectomies.

The rate of temporary RLN palsy was 5.3% ($n=5$ RLNs), while that of permanent RLN palsy was 0.9% ($n=1$ RLN).

DISCUSSION

EBSLN is closely associated with the superior thyroid vasculature, causing it to be at risk during thyroid surgery. Adversely to routine dissection of RLN, many surgeons tend to avoid exposing and identifying the EBSLN routinely (1).

The preservation of the physical and functional integrity of the EBSLN is also important as much as that of RLN and parathyroid glands for a safe thyroid surgery. Although the visual identification of the RLN is accepted to be the gold standart to preserve the nerve, there is still not a standart technique to preserve

the EBSLN and no uniform consensus on the surgical protocol for the identification of it (11). Several techniques have been described to avoid injury to the EBSLN during superior thyroid vessels dissection and ligation: peripheral ligation of the individual branches of the superior thyroid vessels just on the thyroid capsule, identification of the nerve before ligation of the superior thyroid pole vessels (12), and the use of either a nerve stimulator or intraoperative neuromonitoring (1).

The reported prevalence of EBSLN injury in the literature varies widely from 0 to 58%. Therefore, EBSLN injury is believed to be the most commonly underestimated morbidity following thyroid surgery. (1,13,14). This wide range depends on the use of different post-operative assessment methods (clinically or through one of laryngoscopy, stroboscope, electromyography or voice analysis with one of these methods) to detect EBSLN injury. Jansson et al. (13) evaluated EMG responses of the CTMs in 26 patients after thyroidectomy, without EBSLN identification intraoperatively, and they found temporary EBSLN injury in 58% and permanent injury in 3.8% of the patients. Cernea et al. (14) found between 12% and 28% incidence of injury when the EBSLN was not identified intraoperatively, and some of these injuries were permanent as confirmed by longterm EMG evaluation. However, they detected no EBSLN injury in the patients whose EBSLNs were identified and confirmed with IONM, before dividing the superior thyroid vessels. On the other hand, Bellantone et al (12) found in a randomized study that accurate distal ligation of the branches of the superior thyroid artery without attempts to visually identify the nerve is a safe technique in expert hands with similar prevalence of EBSLN injury as routine nerve identification (0.5% vs 0.8% for temporary lesions) (12). Hortado Lopez et al. (15) evaluated the effect of IONM use on the risk of EBSLN injury in their prospective trial including 148 patients and detected no alterations in the postoperative laryngoscopy and subjective voice assessment. They concluded that the use of IONM diminishes the risk of EBSLN injury to 0%.

We detected loss of signal in only 2 (2.4%) of 84 identified EBSLNs with IONM, postoperatively. We

believe that this is an important finding supporting the IONM's significant contribution to avoid the injury to the EBSLN. Similar to our study, Dionigi et al. (16) found loss of signal in 9 (2.3%) of 400 identified EBSLNs with IONM, postoperatively.

A cardinal principle of any surgery is the identification of anatomical structures in order to preserve them. This strategy certainly applies to the identification of the EBSLN (17). Lenquist and Friedman reported that nearly 20% of EBSLNs couldn't be visually identified due to their subfasial/intramuscular course (7,18).

In the present study, 44 (52.8%) of 84 EBSLNs were visually identified without the use of IONM. Eighteen (21.4%) more EBSLNs of 84 were also able to be visualized with the help of IONM. IONM's contribution to the nerve's visual identification is significant and also it is important to confirm the visually identified structure as EBSLN with IONM during the superior pole dissection. Because, Selvan et al. (19) has shown that in many cases, non-neural fibers or tendinous fibers of regional musculature can be mistaken for the EBSLN. Although 22 (26.2%) of 84 EBSLNs were identified with IONM, they were not able to be visualized due to their subfasial/intramuscular course on the inferior pharyngeal constrictor muscle in this study. The functional identification rate of EBSLN with IONM is 92.3%, which is twofold of the visual identification rate in this study. The IONM provided significant contribution to visual ($p<0.05$) and functional ($p<0.001$) identification of EBSLN.

In a prospective study on video-assisted thyroidectomies, Dionigi et al. (20) randomized 72 patients to 2 groups and found that the identification rate of EBSLN in the group in which IONM was used was 84% compared to 42% in the non-IONM group. Barczynski et al. (21) in a prospective randomized controlled study of visualization versus EBSLN IONM, showed that EBSLN detection rate was superior via IONM (84% with IONM versus 34% without IONM). The functional identification rates ranging from 97 to 100% have been reported in the other studies (15,16,22,23). In addition to the observed cricothyroid twitch, several studies recently have found that EMG data could be obtained by

EBSLN stimulation with standard monitoring tubes in 70% to 80% of cases due to the presence of communicating nerves between the RLN and EBSLN and the mean amplitude of EBSLN stimulation was significantly lower than that of RLN (21,22). Darr et al. (2) could identify all the EBSLNs and observed quantifiable EMG responses in 100% of cases via the use of a novel endotracheal tube with its increased surface electrode, in their prospective study. Positive EMG responses were obtained from 44 (52.4%) of 84 identified EBSLNs in our study. The mean amplitude of EBSLN stimulation was $181 \pm 69 \mu V$ lower than that of RLN which is $928 \pm 616 \mu V$ ($p<0.0001$). It might be thought that the rate of positive EMG responses we obtained from our study are relatively lower than the rates of the literature. However, positive EMG signals were achieved from at least ipsilateral vocal cords in 29 (70.7%) of 41 bilaterally explored patients as this rate is similar to the literature. These EMG responses were detected bilaterally in 13 (44.8%) of 29 and unilaterally in 16 (55.2%) of 29 patients. In the autopsy studies, it is documented that the human communicating nerve provides connection to the vocal fold in 41% to 85% of cases, which is bilaterally in 44% and unilaterally in 41% (3-5). Marañillo et al. (4) found that the human communicating nerve was identified in 85% of cases, bilaterally in 44% and unilaterally in 41%. The variability of this neural connection, variability in recording the small and early glottic waveform associated with EBSLN stimulation, and variability in endotracheal tube position are all likely responsible for defined waveforms being recordable in <100% of patients during EBSLN stimulation with currently available monitoring technology (1).

The variabilities in the vocal cord function and position may be due to the innervation of the TA muscle by the EBSLN after the RLN paralyses. The unilateral innervation of TA with the EBSLN stimulation is not rare, therefore the position and function of the vocal cords may alter in the same patient who have right or left RLN paralyses.

As a conclusion; IONM is superior to the only visual identification alone, because IONM improves the visual and functional identification rate of the EBSLN. We suggest that the IONM should be used to

diminish the risk of EBSLN injury in the superior pole dissection routinely. Although the EBSLN's main function is to innervate the cricothyroid muscle, it also contributes to the vocal cord's adductor function

unilaterally or bilaterally, in two third of the patients. This innervation may be related to the vocal cord's functional and positional variabilities in the patients with RLN paralyses after thyroidectomies.

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