Effect of Intraoperative Neuromonitorization on Voice Quality in Total Thyroidectomy

Aim: Thyroid gland surgery has possible serious complications. Advancements in technology have led to improvements in complications but significant challenges in airway and voice security still remain. The purpose of this study was to evaluate the voice quality following total thyroidectomy under neuromonitorization and effect of intraoperative neuromonitorization (IONM) for identification of recurrent laryngeal nerve (RLN) and external branch of superior laryngeal nerve (EBSLN).

Methods: A total of 80 patients planned for total thyroidectomy between May 2015 and March 2016 were included into the study. All RLN and EBSLN were identified. Voice assessment included preoperative and postoperative fiberoptic laryngoscopy, analysis of Jitter, Shimmer, fundamental frequency and ratings of voice handicap index-10.

Results: Eighty patients were included in this study (71 females/9 males). The mean EMG initial and post-dissection amplitudes of both RLN and EBSLN were not significantly different. The rate of postoperative transient RLN palsy per nerve at risk was 4.375% (7/160) and null for permanent RLN palsy (0% 0/160).

Conclusion: Both subjective and objective assessment revealed the preservation of voice quality in patients after total thyroidectomy under neuromonitorization. IONM may be used effectively and safely in order to identify EBSLN during thyroid surgery.

Keywords: Neuromonitorization, thyroidectomy, voice quality

Amaç: Tiroit ameliyatının olası ciddi komplikasyonları vardır. Teknolojideki ilerlemeler komplikasyonların azalmasına neden olmuştur ama hava yolu ve sesle iliği önemli sorunlar halen devam etmektedir. Bu çalışmanın amacı, intraoperatif sinir monitörizasyonunun (İONM) rekürren larengeal sinirin (RLN) ve superior larengeal sinirin ekternal dalının (EBSLN) tanımmasıyla total tirotektomiyi takiben ses kalitesinin değerlendirilmesidir.


Bulgular: Seksen hasta (71 kadın/9 erkek) çalışma dahil edildi. Diseksiyon başlangıç ve sonrası RLN, EBSLN için ortalama EMG amplitüdünde anlamlı ölçüde fark yoktu. Postoperatif RLN transient palsy risk altındaki %4.375 (7/160) ve永久 RLN palsy oranı %0 (0/160) rastlanmadı.

Sonuç: Hem öznel, hem de nesnel değerlendirmelerde total tirotektomi esnasında sinir monitörizasyonu kullanıldığında, hastalarda ses kalitesinin korunduğu tespit edildi. İONM, tirotektomi sırasında EBSLN tespitinde etkili ve güvenli bir şekilde kullanılabilir.

Anahtar Sözcükler: Sinir monitörizasyonu, tirotektomi, ses kalitesi
**Introduction**

Thyroid gland surgery has possible serious complications due to the gland’s endocrine functions and close anatomic relations with critical structures. Complications of thyroid surgery may be classified as minor and major complications. Major complications include injury to recurrent laryngeal nerve (RLN) and superior laryngeal nerve (SLN), bleeding (hematoma), hypoparathyroidism (hypocalcemia) and thyroid storm. Minor complications include seroma, hypertrophic scar formation, wound infection and suture reaction. Advancements in hemostasis, anatomical knowledge, anesthetic and antiseptic strategies have led to improvements in the rates of complications in thyroid surgery. However, challenges with voice and respiratory outcomes still remain a significant area of concern for physicians and patients undergoing thyroid surgery.

We need intact laryngeal framework and intact laryngeal nerves for generation and consistency of voice. The incidence of recurrent laryngeal nerve (RLN) paralysis was reported in a wide range from 1 to 17% in literature (1-4). It is accepted as 1-2% for experienced surgeons. The incidence of external branch of superior laryngeal nerve (EBSLN) injury was reported in a wide range from 0 to 58% in literature and resulted in a vocal cord level difference due to weakening in vocal cord tension (5-7).

Total thyroidectomy has bilateral RLN injury risk, which is important for airway security. Nowadays, gold standard technique for avoidance of RLN injury is still identification and dissection of nerve (6,8). Due to anatomic variations such as non-recurrent nerve, extra laryngeal branching of RLN, excessive bleeding may result with iatrogenic nerve injury in case of experienced surgeons. Beside of these in case of all efforts, nerve conduction may be altered due to compression, strain, crushing, heat (bipolar or monopolar cauterization) or ischemic axonal injury (9). In order to identify and predict the function of nerve we may need new techniques such as intraoperative nerve monitoring (IONM). By the use of IONM we can get electromyography (EMG) responses and able to control the integrity of nerve. After getting positive EMG response, the possibility of normal laryngoscopic examination is very high. However if we did not get any EMG response there is still possibility of normal laryngoscopic examination. In addition of these there is also possibility of undetection of laryngeal injury. In case of IONM usage there is still incidence of temporary paralysis with 1.6% and permanent paralysis with 0.4% incidence (10).

The injury of EBSLN is usually underestimated in the case of RLN. But this may also results with serious morbidity especially in singers, speaker or teachers who are voice professionals. EBSLN innervates the cricothyroid muscle and has a close relation with superior thyroid artery. So this nerve is under risk during dissection and ligation of upper pole of thyroid. The incidence of EBSLN injury has a wide range in literature due to difficulties on evaluation (6). Injury of EBSLN results with easy fatigue and roughness on voice, addition to these symptoms aspiration and foreign body sensation in throat can be seen in patients. EBSLN integrity can be evaluated by the use of IONM.

In this study we aimed to investigate the postoperative voice quality for patients following total thyroidectomy with the diagnosis of multinoduler goiter or well differentiated thyroid cancer. Efficiency and safety of IONM will be investigated in identification of EBSLN in order to preserve the voice quality.

**Methods**

A total of 80 patients planned for primary total thyroidectomy between May 2015 and March 2016 with the multinoduler goiter and well differentiated thyroid cancer diagnosis in Sultangazi, Istanbul, Lütfiye Nuri Burat State Hospital were included into the study. This study was approved from local ethic committee (Haseki Research and Training Hospital/ 333-2015). Patients were informed with IONM and operation. All informed consents obtained from patients. For standardization, patients with lymph node in neck, planned for neck dissection and revision thyroid surgery cases were excluded from the study. All patients were examined preoperatively in otolaryngology department with fiberoptic flexible laryngoscopy. Children, pregnant, mental retarded patients and patients with prior laryngeal surgical history were excluded from the study. All patient’s operation and hospital records were examined. Patients’ age, sex, total operation time, comorbidities, ultrasonographic findings, thyroid specimen sizes were recorded. Preoperative and postoperative voice records were obtained for objective analysis. All patients were operated under neuromonitorization. Intraoperative EMG amplitudes and action potentials initial RLN and EBSLN identification and post-dissection were recorded twice as μV for each nerve. Patients were again examined postoperatively in otolaryngology department for vocal cord pathologies.

**Voice Analysis:** Preoperative and postoperative subjective and objective voice assessments were performed for each patient. Voice Handicap Index-10 (VHI-10) survey, which is translated in Turkish and studied for reliability in 2008, was applied preoperatively and postoperative 3rd week (between 14-21st days) for subjective analysis (11). Voice records of patients were obtained preoperatively and postoperative 3rd week for objective analysis. In order to minimize the effect of edema, pain and nerve fatigue on voice quality we prefer 3rd week control. All records were
obtained in a silent room with Trust mark microphone with headphone. Patients were asked to phonate vowel /a/ at comfortable habitus for at least 5 seconds. Voice samples were directly recorded to computer and middle 3-second part was edited. All records were sent to acoustic laboratory of Çukurova University, Department of Otolaryngology and analyzed with updated PRAAT software program. Acoustic measurements related with frequency and perturbation of voice were recorded and analyzed. Disturbance of voice signal in the manner of frequency and amplitude called as perturbation. Most popular acoustic measurements for perturbation are Jitter and Shimmer. Jitter describes short-term (cycle to cycle) variability in fundamental frequency (F0), Shimmer describes variability in amplitude and intensity of voice signal (12). Preoperative and postoperative Jitter percent(local %), Shimmer percent(local %), Shimmer in dB and fundamental frequency (F0) parameters were documented and compared in the study.

**Intraoperative Nerve Monitorization Technique**

All thyroid surgeries were performed under general anesthesia using short acting muscle relaxants with intraoperative neuromonitorization (IONM) using Nerve Integrity Monitor (DR.Langer,Germany) system. Endotracheal tube with integrated surface electrode was inserted between the vocal folds by an anesthesiologist under direct vision during intubation. Neuromonitorization starts after resolution of muscle relaxants effect. Repetitive stimulation of RLN and EBSLN with 1mA to 2 mA was performed with a standard monopolar or bipolar probe. Proper stimulation was defined with both audible alarm of the NIM system and observation of recognizable EMG waveform (>100 μV for RLN and >50 μV for EBSLN). RLN initial EMG amplitudes were recorded with identification of RLN and final amplitudes after resection of thyroid. EBSLN initial EMG amplitudes were recorded with prior to superior pole ligation and cricothyroid muscle twitch and final amplitudes were recorded after the resection of thyroid.

**Statistical Analysis**

Statistical analysis was performed by the SPSS software package for Windows (Statistical Package for Social Sciences, version 17.0, SPSS Inc., Chicago, Illinois, USA). Quantitative variables were expressed as mean±standard deviation (SD) or median (IQR), whereas categorical variables as number of patients and percentage. The normality of quantitative variables were analyzed by Kolmogorov-Smirnov test and normally distributed variables were compared with paired sample t test or compared with Wilcoxon Signed Ranks Test when they did not normally distributed. Categorical variables were compared by chi-square or Fisher’s exact test. P<0.05 was considered as statistically significant.

**Results**

A total of 80 patients (71 female and 9 male) who underwent to total thyroidectomy were included to study. The age range was 30 to 70 years with a mean of 47.8 years. Total operation time range was 60 to 170 minutes with a mean of 102.7 minutes. All 160 RLNs were identified visually and electrically but only 151 EBSLNs (94.375%, 151/160) could be identified electrically. Intraoperatively, we could achieve to identify EBSLNs at both sides in 72 patients, EBSLNs at only one side in 7 patients. We couldn’t find EBSLN in both sides for only 1 patient. A total of 151 EBSLNs could be electrically identified intraoperatively (94.375%, 151/160).

**EMG Quantitative Data**

The mean EMG amplitude obtained for initial (identification of nerve) right RLN was 827.79 μV (min:156 μV, max:1500 μV, SD ± 277.320) and mean final amplitude (post-dissection) was 840.83 μV (min: 635 μV, max: 1660 μV, SD ±288.085) with no significant difference (p=0.291). The mean EMG amplitude for initial left RLN and final amplitude were 667.96 μV (min:297 μV, max:1150 μV, SD ± 212.065) and 689.17 μV (min: 367 μV, max:1243 μV, SD ± 167.932) respectively, similarly with no significant difference (p=0.363). The mean EMG amplitude for initial right EBSLN (prior to ligation of superior pole) and final amplitude (post-dissection) were 149.46 μV (min:97 μV, max: 279 μV SD± 51.346) and 155.42 μV (min:113 μV, max:295 μV SD± 56.228) respectively, with no significant difference (p=0.220). The mean EMG amplitude initial left EBSLN and final amplitude were 149.96 μV (min:97 μV, max: 316 μV SD ± 47.991) and 154.29 μV (min: 89 μV, max:315 μV SD ± 689.17 μV, SD ±212.065) respectively, similarly with no significant difference (p=0.059) (Table 1). Proper stimulation was accepted through the observation of cricothyroid muscle twitch and recognizable EMG waveform.

**Voice Analysis**

The mean acoustic parameters of voice signals (Jitter percent (local %), Shimmer percent (local %), Shimmer in dB (dB) and Fundamental frequency (F0 median)) were preoperatively 0.572, 4.327, 0.474dB and 215.541. The mean of same acoustic parameters postoperatively were 0.652, 4.722, 0.456dB and 209.785 with no

<table>
<thead>
<tr>
<th>MinorComplications</th>
<th>MajorComplications</th>
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<tr>
<td>Seroma</td>
<td>Bleeding (hematoma)</td>
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<tr>
<td>Hypertrophic Scar Formation</td>
<td>Injury to RLN and SLN</td>
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<tr>
<td>Wound infection</td>
<td>Hypoparathyroism</td>
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<td>Suture reaction</td>
<td>Thyroid storm</td>
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During subjective analysis the mean of VHI-10 ratings preoperatively was 5.60/40 and was 8.50/40 postoperatively, without a significant difference (p=0.123).

Histopathological examination revealed malignancy (papillary carcinoma) for 12 patients; and benign nodular or multinodular disease for 68 patients. Management of 12 malignant cases was provided with cooperation of endocrinology and nuclear medicine departments. We did not observe clinical or radiological metastatic lymph nodes in neck, so none of the patients required neck dissection.

First day laryngoscopy examination revealed 7 vocal fold paralyses in 160 RLN under risk. Three of them recovered in first month control and four of them recovered in 3rd month control and all these paralyses were accepted as temporary paralysis. We did not observe bilateral vocal fold paralysis. Incidence of temporary vocal fold paralysis was 4.375% (7/160) and permanent vocal fold paralysis incidence was 9.0% (0/160).

We did not observe permanent hypocalcaemia; only 11 patients developed transient hypocalcaemia and easily recovered with calcium replacement. None of the patients developed hematoma or wound infection (Table 3).

### Table 2. Mean EMG amplitudes under neuromonitorization (μV)

<table>
<thead>
<tr>
<th></th>
<th>RLN pre</th>
<th>RLN post</th>
<th>p value</th>
<th>EBSLN pre</th>
<th>EBSLN post</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td>827.79 μV (±277.320)</td>
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</tr>
</tbody>
</table>

### Discussion

Neuromonitorization is one of the most important technologic advancement in modern thyroid surgery. It is accepted as a helpful technique for both airway security and vocal functions. In case of absence of accepted consensus for IONM usage, guideline of American Academy of Otolaryngology Head and Neck Surgery advise IONM usage during thyroid surgery for voice quality preservation (13). Both German Association of Endocrine Surgeons and International Neural Monitoring Study Group advise the usage of IONM in all thyroid surgeries, but American Head and Neck Society advise its usage only for patients with thyroid cancer (14,15).

Dysphonia related with thyroid surgery may result from neural etiologies and non-neural etiologies. Neural etiologies include RLN or EBSLN injury. Non-neural etiologies include cricothyroid muscle injury, strap muscles injury, local edema, hematoma and intubation trauma (16).

Subjective voice complaints without laryngeal nerve injury were reported in 30% to 87% in many studies (7,17-19). Previous similar studies including objective vocal assessment after thyroid surgery reported reduced fundamental frequency, diminished vocal range, decreased maximum sound pressure and increased vocal jitter (20-22). In this study, our patients described generally transient vocal changes during early recovery period but at 3rd week control we did not observe any significant difference between preoperative and postoperative subjective voice assessment. Also, according to objective voice assessment we did not find any significant difference in preoperative and postoperative acoustic parameters (Jitter, Shimmer and fundamental frequency). Muscle traumas related with intraoperative surgical manipulations may result with longlasting dysphagia and pain. Also transient myositis or direct injury of cricothyroid muscle is one of the important causes of non-neural etiologies of dysphonia (20). Preservation of objective voice quality in our study was thought to be related with identification and preservation of both RLN and EBSLN with IONM. EBSLN innervates cricothyroid muscle, causing vocal fold lengthening and tension. The paralysis of EBSLN causes inferior displacement of affected cord, resulting easy vocal fatigue and decreased pitch of voice. Direct visual identification of EBSLN is not possible for all cases but detection of recognizable EMG amplitude with help of IONM and observation of cricothyroid muscle twitch generally reveal valuable information for integrity of nerve.

In this study we did not observe significant difference between initial and final mean EMG amplitudes for both RLN and EBSLN. All RLNs were effectively detected with IONM and visual identification but only 151 EBSLNs could
be identified electrically (94.375%, 151/160). These results give us reliable data for prediction postoperative integrity of nerves.

Kandil et al reported lower significant mean EMG amplitudes for EBSLN comparing with RLN in their study at 2015 (23). Similarly, in our study we observed lower mean EMG amplitudes for EBLSN. This is thought to be related with smaller anatomic size of EBSLN comparing with RLN.

In general practice, direct visual identification of EBSLN is not possible for all patients because of subfascial (deep to inferior constrictor muscle fascia) placement of nerve (8). IONM help us to stimulate and identify the nerve even if subfascial located ones. Darr et al reported identification of EBSLN in 100% patients with IONM in their study (24). In their study they investigated 29 EBSLN in 22 patients; achieved positive EMG response and ipsilateral cricothyroid muscle twitch in all patients. They advocate the 100% possibility of EBSLN identification in all thyroid surgery. Hurtado- Lopez LM et al reported in another comparable prospective study that IONM was found significantly superior to direct visual identification of EBSLN. In their study IONM identified 234 of 240 EBSLN (97.5%) whereas 190 (79.1%) were identified visually (25). Similarly in our study we could identify EBSLN with a very high rate (94.375%, 151/160) by the help of IONM prior to superior pole ligation. Successful identification was defined with recognizable EMG amplitude and ipsilateral cricothyroid muscle twitch. Because of the difficult dissection and resulting minor problems, it is not strictly advised to look EBSLN during thyroid surgery as a routine by some authors. It is advised to preserve the nerve if it comes into view. Recent studies showed very high rate of EBSLN identification with help of IONM similar to our results. Because of the absence of control group in our study we therefore could not comment that EBSLN identification with IONM is the only factor for voice quality preservation. However we advise identification of both RLN and EBSLN in order to protect the voice quality.

Although we get EMG responses for all RLN, we experienced with 7 transient vocal cord paralyses. Early recoveries of paralysis make us to think the reasons may be related with excessive manipulation and multiple stimulation of nerve. Because of the final amplitudes were reliable predictors for intact vocal cord mobility; these final amplitudes relieve the surgeon’s mind for the function of vocal cord. Shindo M et al reported in a 2007 date study, RLN monotorization does not change the incidence of transient or permanent vocal cord paralysis (26). Similar to this results in another comparative comprehensive study Calo et al did not show a significant difference between the direct visualization and IONM usage for incidence of either transient or permanent vocal cord paralysis (27). Pisanu et al. investigated 20 studies comparing direct visualization and IONM in a meta analysis in 2014. Total 35513 nerves (24038 IONM, 11475 direct visualization) were included in to this meta analysis and the incidence of paralysis was 3.47% in IONM group and 3.67% in direct vision group with no significant difference (28). However Barczyński M et al showed decrement in transient paralysis with IONM usage especially in high-risk patients (29). Frattini F et al. reported decrement of incidence of both transient and permanent paralysis in their comparative study with thyroid cancer patients (76 IONM, 76 direct vision) (30). In case of absence of accepted consensus for IONM usage, different comparative studies reveal that the incidence of laryngeal nerve injuries may not be decreased with the use of IONM. But neuromonitorization is very effective and safe method for identification and preservation of both RLN and EBSLN. Identification of both RLN and EBSLN by the help of IONM ensures the surgeon for airway and voice security of patients. Beside all of these; legal problems may also be an important indication for neuromonitorization.

Conclusion

In this study we observed stable voice quality after total thyroidectomy under neuromonitorization according to objective and subjective voice assessment. Neuromonitorization is very effective and safe for identification of both RLN and EBSLN with very high rate of identification. In order to protect the quality of voice we advise to identify both RLN and EBSLN with the help of IONM. This study designed as a self-control study. Absence of the control group is the weak point of the study but both objective and subjective voice analysis of the patients and prospective design are the strong points of the study. New multicentric prospective randomized studies with control groups will provide more enlightening explanations and informations in this field.

Ethics

Ethics Committee Approval: The study protocol was approved by the local ethic committee (Haseki Research and Training Hospital/ 333-2015).

Peer Review: Internally peer-reviewed

Conflict of Interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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References


