https://doi.org/10.46629/JMS.2022.90

Prospective Comparison of Continuous and Intermittent Intraoperative Nerve Monitoring in Thyroid Surgery

Tiroid Cerrahisinde Sürekli ve Aralıklı İntraoperatif Sinir Monitorizasyonu Yöntemlerinin Prospektif Karşılaştırılması

Emre BOZDAG[1], Faruk Seckin YUCESOY[2], Nurcihan AYGUN[3], Mehmet ULUDAG[3]

EB: 0000-0002-2729-1667 FSY: 0000-0001-5977-9985 NA: 0000-0002-7353-8245 MU: 0000-0003-1826-1615

[1] Kanuni Sultan Süleyman Health Practice and Research Center, Department of General Surgery, Istanbul-Turkey
[2] Istanbul Sisli Hamidiye Etfal Health Practice and Research Center, Department of Anesthesiology and Reanimation, Istanbul-Turkey
[3] Istanbul Sisli Hamidiye Etfal Health Practice and Research Center, Department of General Surgery, Istanbul-Turkey

Abstract

Aim: As technology progresses further in medicine, intraoperative neuro-monitorization has become a powerful safety tool especially for thyroid surgeries. The effectiveness of intermittent or continuous intraoperative nerve monitorization (IONM) on reducing recurrent laryngeal nerve (RLN) palsy has been a highly debated issue to ensure that RLN does not get damaged regardless of the surgeon's experience level. In this prospective study we compared continuous intraoperative nerve monitoring (C-IONM) with intermittent intraoperative nerve monitoring (I-IONM) for prevention of iatrogenic RLN palsy due thyroidectomy.

Material and Methods: One hundred and nine patients aged between 18 and 75 were divided into 2 groups of 64 and 45, which received either I-IONM or C-IONM respectively. Patients were selected for minimally invasive surgery, and those RLN cannot be totally explored or resected on purpose due to tumor invasion are excluded.

Results: High risk intervention rate was 54% in group 2 and was significantly higher compared with group 1 (p=0.022). Temporary and permanent vocal cord paralysis in group 1 and 2 were 4,5% - 0,6% and 2,8% - 0% respectively. There were no significant differences between groups (p>0,05). Multi variant analysis showed that extra laryngeal branching is an independent risk factor for vocal cord palsy (p=0.21)

Discussion and Conclusion: C-IONM is a superior technique as it enables surgeon to detect and stop preventable RLN damage beforehand. In order to minimize the number of RLN palsy incidences and to avoid bilateral RLN paralysis, we believe IONM should be used as a standard approach during thyroid surgeries.

Keywords: Intermittent intraoperative neural monitorization, Continuous intraoperative neural monitorization, Recurrent Laryngeal Nerve palsy

Öz

Amaç: Tıpta teknoloji ilerledikçe intraoperatif sinir monitorizasyonu özellikle tiroid ameliyatları için güçlü bir güvenlik aracı haline gelmiştir. Aralıklı veya sürekli intraoperatif sinir monitörizasyonunun (IONM) rekürren laringeal sinir (RLN) felcini azaltmadaki etkinliği, cerrahın deneyim düzeyi ne olursa olsun RLS'nin hasar görmemesini sağlamak için oldukça tartışılan bir konu olmuştur. Bu prospektif çalışmada, tiroidektomiye bağlı iyatrojenik RLS felcinin önlenmesi için sürekli intraoperatif sinir monitörizasyonunu (C-IONM) aralıklı intraoperatif sinir monitörizasyonu (I-IONM) ile karşılaştırdık.

Gereç ve Yöntem: Yaşları 18 ile 75 arasında değişen 109 hasta, sırasıyla I-IONM veya C-IONM uygulanan 64 ve 45'er kişilik 2 gruba ayrıldı. Minimal invaziv cerrahi için seçilen hastalarda RLS'lerin tam eksplore edilememesi veya sinirde tümör invazyonu bulunması dışlama kriteri olarak kabul edildi.

Bulgular: Grup 2'deki hastaların sinirlerinin %54'ü yüksek risk altında olup, bu oran Grup 1'e göre anlamlı derecede yüksek bulundu (p=0.022). Grup 1 ve Grup 2'deki hastalarda kalıcı ve geçici vokal kord paralizlerinin oranları sırasıyla 4,5% - 0,6% ve 2,8% - 0% olarak saptandı. İstatiksel olarak bu oran anlamlı bulunmadı (p>0,05). Yapılan multivaryant analizde ekstra laryngeal sinir dallanmasının varlığının vokal kord paralizi için bağımsız bir risk faktörü olduğu görüldü (p=0.21).

Tartışma ve Sonuç: C-IONM, cerrahın önlenebilir RLS hasarını önceden tespit edip durdurmasını sağladığı için üstün bir tekniktir. RLS felci vakalarının sayısını en aza indirmek ve bilateral RLS paralizisini önlemek için tiroid ameliyatlarında İONM'nin standart bir yaklaşım olarak kullanılması gerektiğine inanıyoruz.

Anahtar kelimeler: Aralıklı intraoperatif sinir monitorizasyonu, Sürekli intraoperatif sinir monitorizasyonu, Rekürren laringeal sinir felci

Sorumlu Yazar / Corresponding Author:Emre BOZDAG
E-posta: emrebozdag1923@hotmail.com

Introduction

Thyroid surgery is one of the most common interventions in the cervical region. Permanent hypoparathyroidism and RLN palsy are the two most common long-term complications after total thyroidectomy. They can cause significant morbidity (1). Unilateral RLN palsy can cause hoarseness, dysphagia, and respiratory failure due to aspiration. Bilateral RLN palsy can lead to more severe complications such as acute respiratory failure and aphonia (2). It has been long known that the best cure for RLN palsy is its prevention. A manuscript published by Dr. Lahey (3) emphasized that visualizing the RLN during surgery decreased the RLN damage from 10% to 0.3%. Today, exploration of RLN visually and manually is the gold standard for routine thyroid surgery (4, 5). However, RLN being intact anatomically does not guarantee undisturbed motor functionality. In most RLN palsies, RLN is found to be anatomically intact (6, 7).

IONM is a unique technique that relies on the functional interpretation of the laryngeal nerve. IONM during thyroid and parathyroid surgery has gained widespread acceptance as an adjunct to the gold standard of visual nerve identification, adding a new functional dynamic during thyroid surgery. IONM is a supplementary technology used to identify the external branch of the superior laryngeal nerve (EBSLN) and assess nerve function during thyroid surgery (8).

IONM is more widely used every day for thyroid surgeries. There are still debates about the benefits of IONM use during thyroid surgeries because the possibility of RLN damage is considered to be already low with direct visual identification of RLN intra-operatively in experienced hands. Although some studies show no reasonable decline in RLN damage with the use of IONM, (9, 10) many studies are showing the benefits of IONM (4, 11). IONM is found to decrease the incidence of especially temporary RLN palsies (4, 11). During bilateral thyroid surgeries, once signal loss is detected in the cervical region, bilateral RLN palsy can be avoided by ceasing further manipulations in that region (12). IONM is helpful with localizing the RLN early, identifying variations, and finding the path of the nerve. It also prevents the false identification of RLN (13). To assure confidence in study results and conclusions regarding the benefits of IONM use, prospective studies are needed to be done with more than 7000 patients in case and control groups (4). IONM can be performed either intermittently (I-IONM) or continuously (C-IONM). Since the discovery of IONM, I-IONM has been widely used in operating theaters. One of the most prominent limitations of I-IONM utilization is that I-IONM stimulation only reveals information about the moment of stimulation of the distal segment of the nerve. The surgeon does not know about potential functional nerve injury until the subsequent stimulation (14). In order to overcome the limitations of I-IONM, C-IONM has been developed and recommended (15, 16). Similar to I-IONM, studies about the utility of C-IONM are limited. Recent data from the German Society of General and Visceral Surgery StudDoQ/Thyroid registry showed that only 17.4 percent of surgeons used C-IONM (17).

C-IONM shows that C-IONM use supports the surgeon with greater confidence than I-IONM use (18-20). In our institute, IONM has been used as a standard procedure since 2012. In this study effectiveness of the two intra operative neural monitorization methods (C-IONM vs. I-IONM) on decreasing vocal cord paralysis rates after thyroidectomy is evaluated in comparison to each other.

Material and Methods

Between January 2015 and December 2016, 106 patients who underwent thyroidectomy diagnosed with malignant or benign thyroid disease were evaluated intra-operatively by either I-IONM or C-IONM. Procedures have been carried out by the same surgical team under the supervision of trained surgeons with at least 500 I-IONM and more than 50 C-IONM experiences. Patients are prospectively randomized and divided into 2 groups; I-IONM and C-IONM and relatively risky thyroidectomy cases are involved in the C-IONM group.

This single-center randomized prospective cohort study is conducted at Sisli Etfal Training and Research Hospital. Ethical approval for the study was granted by the hospital in which the procedures were performed (IRB No: 2015.4.483). Written informed consent was obtained from all subjects before the study. The primary goal of the study was to compare the effects of two different IONM techniques on vocal cord paralysis and to assess the other risk factors which lead to paralysis even with IONM.

Exclusion Criteria:

The exclusion criteria for this study were the following:

Patient age younger than 18 years and older than 75 years

Minimal invasive surgery where RLN cannot be located at the laryngeal inlet

Patients whose RLN is resected on purpose due to tumor invasion

Patients on whom IONM cannot be applied due to technical problems

In an effort to predict which patients may experience RLN damage postoperatively, thyroid surgeries are categorized into 2 risk groups: low and high. For this evaluation, each cervical side is evaluated separately. High-risk RLN interventions comprise secondary interventions due to malignant or benign tumors, substernal goitre, Graves› disease, malignancy, lobe weight more than 50 grams, and central dissections.

IONM Technique:

All interventions were performed under general anesthesia, and IONM was done with a neural integrity monitor (NIM) Response 3.0 system (Medtronic, Jacksonville, FL, USA). Inductions of anesthesia were achieved with 0.3 mg/kg rocuronium. Patients were intubated with surface electromyographic sensor integrated endotracheal tubes (Medtronic Xomed NIM standard Reinforced Electromyography Endotracheal Tube, Medtronic, Jacksonville, FL, USA). During laryngoscopy, the proper position of the tube between vocal cords was verified, and the endotracheal tube was fixed. Sterile monopolar stimulating electrode (Stimulator probe, Medtronic Xomed, Jacksonville, FL, USA) was connected to the NIM 3.0 via a connection port. The stimulating potential is set to 1 mA. IONM setup and data collection were performed according to the international neural monitoring study group guidelines (8). Intraoperative neural monitoring was applied in 4 stages.

Starting I-IONM, initial vagus motor activity is recorded as V1 before dissection, RLN is recorded as R1. Post lobectomy RLN and post lobectomy vagus are recorded as R2 andV2, respectively. Electromyographic amplitudes over 100µV are accepted as positive. Less than 100µV amplitude is defined as signal loss (8). C-IONM technique comprised 10 pulses per minute with 1mA stimulation (100µS, 4 Hz). Electromyographic wave amplitude and latency were recorded. The monopolar probe was used along with V1 and V2 pulses during RLN dissection. In any case of amplitude drop to less than 50% and/or more than 10% latency delay, an auto signal is produced. Amplitudes less than 100µV were accepted as signal loss (Table-1). During C-IONM, both amplitude drop to less than 50% and latency delay of more than 10% is defined as the combined event (21). Whenever more than 50% amplitude drop or combined events are recorded, the operation was halted merely continued when amplitude rose over 50%. During C-IONM ipsilateral carotid sheath was longitudinally dissected and as well as vagus nerve and with a 1 cm diameter rounded 360° degree, vagus is stimulated by monopolar hand probe. 2 or 3 mm automated periodic stimulation (APS) probe is attached (Medtronic Xomed Jacksonville, FL, USA). At the end of each operation, V2 pulses are recorded after disconnection of the APS probe from the proximal and distal parts of the attached tissue.

Age, sex, preoperative vocal cord examination, diagnosis, operation type, specimen weight, operation length, disease relapse, thyroid location, vagus position in the carotid sheath, relative inferior thyroid artery location, RLS diameter, RLN branching were recorded. Monitorization data was recorded as a PDF file on the computer. All patients are examined for their vocal cords before and after surgery (within the first 48 hours) with fiberoptic laryngoscopy. Patients who are diagnosed with vocal cord paralysis are further examined on the 15th day, 1st, 2nd, 4th, and 6th months. Vocal cord paralysis that did not recover at the 6th month was accepted as permanent vocal cord paralysis.

Statistical Analysis

In this study, the patients who experienced RLN palsy postoperatively are compared through age, sex, monitorization type, hyperthyroid status, side of the neck surgery is performed, the relation of inferior thyroid artery to RLN, RLN diameter, RLN branching with multivariate analysis.

Patients were divided into 2 groups as I-IONM and C-IONM group. The IBM SPSS Static program for Windows version 22 was used for statistical analysis. Quantitative variables were described using the mean, standard deviation, and range. For qualitative variables, absolute and relative frequencies were obtained and expressed in percentages. For comparison of injury prevalence after neuromonitoring with I-IONM and C-IONM, matched groups are analyzed with T-test and Mann-Whitney U test, Pearson Chi-Square score, Fischer›s exact test Multinomial Logistic Regression analysis.

Results

One hundred nine patients (81 Female, 28 Male) with an age range of 18 to 75 years were included to receive IONM per operatively between January 2015 and December 2016. Patients were divided into two groups; group 1 as I-IONM and group 2 as C-IONM. One hundred ten procedures were performed on 106 patients, 103 being monitored with I-IONM and 74 with C-IONM in groups 1 and 2, respectively. Three patients who had interventions bilaterally were included in both groups as one side is monitored with I-IONM and the other with C-IONM. Four patients were re-operated on the single side and had total thyroidectomy after pathology report diagnosis of papillary carcinoma. Three patients were operated only on one side as there had been signal loss detected, and surgery was halted. Overall, we have compared 64 patients in group 1 and 45 patients in group 2. Groups were statistically similar in terms of age, sex, operation type, and specimen weight (Table 1). Group 1 consisted of 103 nerves under risk, and in group 2, 74 nerves, respectively. Operation side and inferior thyroid artery (ITA) – RLN position did not show significant relation to extra-thyroidal branching. There was no significant difference between the two groups in terms of initial and final vagus nerve amplitudes (V1, V2, RLS, R1, R2). Nervus vagus nerve amplitudes (V2) were significantly higher in Group 2 (p=0.021) (Table-2). There was no significant difference between the two groups in terms of total VCP, temporary VCP, and permanent VCP according to the number of nerves at risk (Table 1).

Age, sex, IONM type, hyperthyroid existence, high-

Table 1. Distribution of characteristics of the groups according to the number of patients

Variables			Group 1 (I-IONM) (n= 64)	Group 2 (C-IONM) (n=45)	p value
Age, years (mean ± SD)			45.9 ± 12.8	45.2 ± 14.3	0.737
Sex		Male	49 (76.6%)	32 (71.1%)	0.521
		Female	15 (23.4%)	13 (28.9%)	
Diagnosis		MNG	49 (75%)	28 (65%)	0.034
		Recurrence of MNG	3 (5%)	1 (2%)	
		Graves	6 (9%)	1 (2%)	
		Malignant	7 (11%)	14 (31%)	
		Hyperthyroidism	12 (18.5%)	5 (11.1%)	
Surgery*	One-sided	Lobectomy	28 (43.75%) **	16 (35.6%)	0.059
		CLND	-	2 (4.4%)	
	Two-sided	TT	32 (50%)	21 (46.7%)	
		TT+CLND	4 (6.25%)	2 (4.4%)	
		TT+CLND+LLND	-	4 (8.9%)	
Specimen weight, gr		Lobectomy	16.5 ± 9.8	21.1 ± 12.7	0.229
		TT	56.9 ± 59	60.2 ± 64.5	0.754
Duration of the surgery, min		One-sided	53.9 ± 12.7	74 ± 43.7	0.057
		Two-sided	89.1±24.5	114.4±46.7	0.037
RLN palsy		Transient	6	4	0.255
		Permanent	1	0	

*Preop vocal cord palsy (VCP) was detected in 1 patient and complementary thyroidectomy was performed in 4 patients.
**Subsequently, completion thyroidectomy was performed in 4 patients.

TT: Total thyroidectomy; **CLND:** Central lymph node dissection; **LLND:** Lateral lymph node dissection; **RLN:** Recurrent laryngeal nerve; **MNG:** Multinodular goiter

Table 2. Distribution characteristics of RLN at hazard

Number of Nerves		Group 1	Group 2	p value
Operation sides	Right	53 (52%)	41 (55%)	0.767
	Left	49 (48%)	34 (45%)	
Surgery Risk	Low Risk	66 (64%)	34 (46%)	0.022*
	High Risk	37 (36%)	40 (54%)	
RLN Extralaryngeal Branching	Presence	19 (18%)	17 (23%)	0.531
	Absence	45 (82%)	28 (67%)	
Vagus and RLN Amplitudes, mV	V1	747±650 (101-3366)	911 ±684 (143-2633)	0.116
	V2	729 ±607 (101-2829)	977 ±804 (178-3911)	0.021*
	R1	788 ±612 (101-2900)	974 ±645 (158-3502)	0.054
	R2	858 ±642 (108-3144)	1070 ±820 (147-4437)	0.137

Table 3. Evaluation of factors that could affect the improvement of vocal cord paralysis

Factors Affecting on VCP	HR	95% CI	p-value
Age	1.041	0.982-1.103	0.179
RLN Diameter, ≥1.8 mm	1.600	0.140-18.297	0.705
Sex, female	1.153	0.230-5.776	0.863
Side of surgery, right	1.569	0.323 - 7.616	0.577
Branching, absence	0.140	0.026-0.747	0.021

risk operation, ITA-RLN relationship, extra laryngeal branching are compared with multivariate analysis (Table 2). Extra laryngeal nerve branching alone has been found to be an independent risk factor for vocal cord paralysis (p=0,021) (Table 3).

Discussion

Modern thyroid surgeries aim to achieve the least amount of complications postoperatively. However, some complications are still inevitable despite modernized techniques (4, 22). RLN palsy is one major complication of thyroid surgery. The prevalence of RLN palsy is thought to be underestimated due to different postoperative evaluation strategies. RLN palsy has a spectrum of clinical results; methods of assessing symptoms and timing of assessment are important considerations, and counting only the most symptomatic patients may lead to underestimation of RLN palsy incidence (23). Centers where many thyroid surgeries are performed usually have a lower incidence of RLN palsy (24). A meta-analysis of 27 trials comprising more than 25000 thyroid surgery cases shows that RLN palsy rates range from 1,4 to 38,4%, with a mean value of 9,8%. Permanent RLN palsy rates are 0 to 18.6 %, with a mean value of 2,3%. These numbers reflect a substantially high incidence (23).

The gold standard approach to the preservation of RLN is shown to be the exploration of RLN intraoperatively (4). In most of the iatrogenic RLN palsies, nerve anatomy seems to be intact though it doesn›t guarantee proper functionality. IONM stands as a powerful technique for the monitorization of the functionality of

RLN per-operatively (25, 26). Between 7-16 % of RLN injuries can be noticed during dissection of the tissue (27).

I-IONM is used more often worldwide compared to C-IONM. The limitation of I-IONM is that there is no warning of signal loss or data about instant RLN damage during the intervention. The functionality of the nerve can only be tested intermittently (14). In order to overcome this limitation of I-IONM, the C-IONM technique has come forth (15, 16). C-IONM can warn the surgeon before starting a risky manipulation on RLN as it monitors RLN via the vagus nerve in real-time.

The main reason for RLN damage is traction trauma, unintentional suturing of the nerve, electro-cauterization, and thermal damage to the nerve (6, 7). RLN palsy is associated with signal loss, and the most common reason is traction trauma (6, 8). Traction damage does not occur suddenly. Wu et al. performed an experimental trial to detect traction trauma early with C-IONM. It is shown that the duration of the traction time and intensity of the traction force is directly proportional to the extent of RLN damage. It is also shown that if signal loss of 50% is detected and traction is finalized, there is more chance for the RLN to completely recover compared with the total signal loss. C-IONM has significant importance for the early detection of signal loss to preserve the RLN (28-31).

We compared 103 I-IONM with 75 C-IONM patients in preventing RLN palsy. The two groups were not significantly different in terms of demographics and co-morbidities. Although this study is prospective, it is not randomized, and patients with malignant thyroid masses received C-IONM more often. We have found vocal cord palsy rates to be 5.8% with I-IONM and 5.4% with C-IONM, permanent palsy rates were 1% and 0%, respectively. Two groups did not differ about vocal cord palsy. Both groups had lower permanent, and temporary VCP rates compared to metanalysis means. We only had one patient with permanent vocal cord palsy in the I-IONM group and none in the C-IONM group. In this study, risked RLNs were limited to a small number to evaluate a rare complication that may explain statistically similar results. The high-risk intervention was significantly higher (54.1%) in the C-IONM group compared with the I-IONM group (36.3%). Although high-risk cases were prominently more dense in the C-IONM group, it still enabled to perform thyroid surgery without increasing vocal cord palsy rates. Bilateral vocal cord palsy was not seen in this study which may be related to limited surgical intervention in 3 patients whose operation was ended abruptly due to signal loss. We have found extra laryngeal branching to be a single independent risk factor for vocal cord palsy due to multivariant analysis. There are also other studies stating that extra laryngeal branching increases the risk for vocal cord palsy (28-31). Sancho et al. (31) have reported to have found a doubled risk of vocal cord palsy with patients who have branching RLNs (15,8% vs. 8,1%, p=0,022). Casella et al. (30) have reported that branching nerves have a temporary unilateral palsy risk 7 times and permanent palsy risk 13 times more. Traction of RLN is related to a traction force of the thyroid lobe. Branched RLNs are more prone to get damaged from traction as they are thinner in diameter and their epineurium or fascia is more vulnerable (32). The same amount of force results in more shearing stress in a small diameter nerve compared with a thicker one. Calculated from the formula ; $s = F/d^2$ where s is the traction force on the nerve, F is the force, and d is the diameter (33). It means a nerve with a 1 mm diameter can lose signal with only a quarter of the force another nerve with a 2 mm diameter requires. Serpell et al. have reported that on single-sided interventions, left RLN gets paralyzed more often than the right RLN. Left RLN being thinner than the right RLN may be the main explanation for this finding (1,6 mm to 1,7mm p = 0,0012) (33).

While IONM usage during thyroidectomy for RLN preservation is still controversial, metaanalysis of 34 prospective randomised and non-randomised trials comprising 59380 nerves have shown that IONM is successful at decreasing total VCP (RR=0.68, %95Cl:0.55-0.83, p=0.0002),, temporary VCP (RR=0.71, %95Cl.0.57-0.88, p=0.0017) and permanent VCP (RD:-0.0026, %95Cl:-0.0039- -0012, p=0.0003) rates (34).

Barzcynski at al. (11) are the first group of people to conduct a prospective randomized study comparing IONM of RLN vs. RLN dissection without IONM. Each group consisted of 1000 RLNs at risk. IONM group was shown to have a lower RLN palsy rate (2,7%) compared to the RLN dissection group (5%) (p=0.007). The reduction in RLN palsy is significant in temporary palsies but not permanent RLN palsies. Temporary paralysis is reported to be 2,9 % more often in high-risk thyroid surgeries (malignancy, substernal goiter, thyroiditis, central node dissection) (p=0,011). However, In the low-risk RLN palsy group, there was no difference regarding RLN palsy between the two groups (%0.9;p=0.249). Especially secondary surgeries tend to have a higher risk of RLN damage due to scar tissue formation. Huge goiter, Grave›s disease, thyroidal adhesions increase the pressure on the RLN and lead to a more vulnerable nerve. Branched nerves are also more prone to injury (35). Studies regarding C-IONM have been increasing over time, although it is still less popular compared to I-IONM. Before cautions and limits for C-IONM were set, the first two studies showed that the temporary VCP rate was 1.6 % and the permanent VCP rate was 1.1% and 0.6% (36, 37).

Yu et al.'s study (38) compared C-IONM (106 patients, 173 NARs), with I-IONM (238 patients, 374 nerve at risk (NARs)) in high-risk surgeries, and their study showed that temporary and permanent RLN palsy rates were similar (temporary 1.2% and 1.9% respectively p=0.726 and permanent 0% vs. 0.8%, respectively, p=0.555). The ability of IONM to prevent RLN palsy has been found to be 5.2%. It has been mentioned that both IONMs are safe in high-risk thyroidectomies, and C-IONM is a real-time monitorization to minimize complications during critical maneuvers.

I-IONM and C-IONM have been compared by Sedlmaier et al. (39) on 613 nerves at risk (NAR) in 346 patients undergoing benign thyroid surgery. Early VCP rates have been shown to be significantly lower in both C-IONM techniques (%4.9 vs %10.5, p<0.05). They have not been able to show any significant difference on permanent VCP (%1 vs %1.5, p=0.619). Sedlmaier et al. have also evaluated C-IONM to be a superior approach and able to significantly lower early VCP while there seems to be no difference regarding permanent VCP, still counts the surgery as a low risk intervention.

Jonas and Boskovic have reviewed 458 I-IONM and 667 C-IONM patients. VCP rates were 3.3% and 2.8%, and permanent palsy rates were 0.7% and 0.08%, respectively, for the two groups. Although the rates of transient VCP were similar, the rate of permanent VCP (p=0.01) was significantly lower in the C-IONM group. In this study, the rate of recognizing the maneuver threatening the RLN was only 20.6% with I-IONM, while it increased to 67.7% with C-IONM (p<0.001) (18). Schneider et al. have reviewed prospective data of benign thyroid tumor operations. They reported vocal cord palsy rate to be 2,3% with I-IONM and 2.6% with C-IONM, permanent vocal cord palsy rate 0,4% and 0%, respectively (17). Similar to Jonas and Boskovic's study, although there was no difference between the two groups in terms of transient VCP, the rate of permanent VCP was statistically significantly lower in the C-IONM group. When the combined event with C-IONM occurred, 82% stated that it was reversible when the surgical procedure was terminated.

In patients who had C-IONM, there were 77 combined EMG events, of which 63 (82 percent) were reversible when the surgeon stopped the suspected causative maneuver.

The researchers stated that C-IONM is a safe and feasible method and a promising method to reduce the rates of permanent VCP after thyroid surgery. Within the limitations of this observational study, C-IONM is a feasible, safe, and promising method to reduce the rate of permanent palsy of the RLN after thyroid surgery.

Schneider et al. evaluated the data of patients who underwent I-IONM (2890 patients, 5024 nerves at risk) and C-IONM (3139 patients, 5208 nerves at risk) in their large series that included both malignant and benign thyroidectomies. In this study, both temporary VCP (2.5% vs. 4.3%, p<0.001, 1.7 times lower in C-IONM) and permanent VCP(0.003% vs. 1%, p<0.001, 33 times lower in C-IONM) has been shown to be lower with C-IONM compared to I-IONM (19).

According to last metaanalysis, compared to I-ONM, C-IONM subgroup exhibited higher sensitivity (0.9403 vs. 0.7589; p = 0.0126) and negative predictive value (0.9982 vs. 0.9920; p = 0.0213) (i.e., diagnostic odds ratio [DOR]), (633.1958 vs. 120.5936; p = 0.0232). There was no significant difference between two subgroups in specificity (0.9776 vs. 0.9787; p = 0.9431), positive predictive value (0.5830 vs. 0.5464; p = 0.8046). Therefore, C-IONM was diagnostically more powerful than I-IONM (40).

Schneider et al. (21) studied RLN palsy predictors in 32 patient groups of 52 NAR Decrease in amplitude (>50%) and increase in latency time (>10%) are called combined findings together. Only combined changes together are found to be meaningful for RLN palsy. Decreases in the amplitude of more than 50% and more than 10% increase in delay time are reported to be meaningful when found together. Another prospective study has reported that both combined findings and signal loss are related with vocal cord palsy. More than 7 combined findings are reported to have a specificity of 91.7% (41).

The main limitations of our study were the limited number of cases and that it is a non-randomized study despite being a prospective study. We did not perform randomization in these patients, as we thought that it would be more appropriate to use C-IONM instead of randomization, especially in patients known to be preoperatively at high risk.

There are still controversies about IONM usage to this day, but we know that during high-risk interventions, patients may benefit from IONM. Our study highlighted an independent risk factor, extra laryngeal we have hing, which is encountered often. This kind of anatomical variation cannot possibly be foreseen. Therefore, we agree as a team that in order to minimize RLN palsy risk, IONM should be a standard approach for thyroid surgery. C-IONM is also an advanced technique because it gives the surgeon a chance to notice the high-risk intervention beforehand and protect the nerve. It can help surgeons manage high-risk operations without increasing the RLN palsy rate. More prospective studies are needed that evaluate the results of both I-IONM and C-IONM approaches, as well as their short-term benefits and long-range results.

Conclusion

Extra laryngeal branching was a independent risk factor for vocal cord palsy. C-IONM has a valuable place in high risk thyroid surgeries and is a comfort both for the surgeon and patients. There still needs to be more studies to investigate the benefits and the optimum usage standardisation of IONM.

Ethics Approval Ethical approval for the study was granted by the hospital in which the procedures were performed (IRB No: 2015.4.483).

Received Date/Geliş Tarihi: 26.04.2022
Accepted Date/Kabul Tarihi: 08.06.2022

References

1. Rosato L, Avenia N, Bernante P, De Palma M, Gulino G, Nasi PG, et al. Complications of thyroid surgery: analysis of a multicentric study on 14,934 patients operated on in Italy over 5 years. World journal of surgery. 2004;28(3):271-6.
2. Rahim AAA, Ahmed ME, Hassan MA. Respiratory complications after thyroidectomy and the need for tracheostomy in patients with a large goitre. Journal of British Surgery. 1999;86(1):88-90.
3. Lahey RF. Routine dissection and demonstration of the recurrent laryngeal nerve in subtotal thyroidectomy. Surg Gynecol Obstet. 1938;66:775-7.
4. Dralle H, Sekulla C, Haerting J, Timmermann W, Neumann HJ, Kruse E, et al. Risk factors of paralysis and functional outcome after recurrent laryngeal nerve monitoring in thyroid surgery. Surgery. 2004;136(6):1310-22.
5. Hermann M, Alk G, Roka R, Glaser K, Freissmuth M. Laryngeal recurrent nerve injury in surgery for benign thyroid diseases: effect of nerve dissection and impact of individual surgeon in more than 27,000 nerves at risk. Annals of surgery. 2002;235(2):261.
6. Chiang F-Y, Lu IC, Kuo W-R, Lee K-W, Chang N-C, Wu C-W. The mechanism of recurrent laryngeal nerve injury during thyroid surgery—the application of intraoperative neuromonitoring. Surgery. 2008;143(6):743-9.
7. Snyder SK, Lairmore TC, Hendricks JC, Roberts JW. Elucidating mechanisms of recurrent laryngeal nerve injury during thyroidectomy and parathyroidectomy. Journal of the American College of Surgeons. 2008;206(1):123-30.
8. Randolph GW, Dralle H, with the International Intraoperative Monitoring Study G, Abdullah H, Barczynski M, Bellantone R, et al. Electrophysiologic recurrent laryngeal nerve monitoring during thyroid and parathyroid surgery: international standards guideline statement. The Laryngoscope. 2011;121(S1):S1-S16.
9. Calo PG, Medas F, Erdas E, Pittau MR, Demontis R, Pisano G, et al. Role of intraoperative neuromonitoring of recurrent laryngeal nerves in the outcomes of surgery for thyroid cancer. International Journal of Surgery. 2014;12:S213-S7.
10. Calò PG, Medas F, Gordini L, Podda F, Erdas E, Pisano G, et al. Interpretation of intraoperative recurrent laryngeal nerve monitoring signals: the importance of a correct standardization. International Journal of Surgery. 2016;28:S54-S8.
11. Barczyński M, Konturek A, Cichoń S. Randomized clinical trial of visualization versus neuromonitoring of recurrent laryngeal nerves during thyroidectomy. Journal of British Surgery. 2009;96(3):240-6.
12. Goretzki PE, Schwarz K, Brinkmann J, Wirowski D, Lammers BJ. The impact of intraoperative neuromonitoring (IONM) on surgical strategy in bilateral thyroid diseases: is it worth the effort? World journal of surgery. 2010;34(6):1274-84.
13. Chiang F-Y, Lee K-W, Chen H-C, Chen H-Y, Lu IC, Kuo W-R, et al. Standardization of intraoperative neuromonitoring of recurrent laryngeal nerve in thyroid operation. World journal of surgery. 2010;34(2):223-9.
14. Dionigi G, Donatini G, Boni L, Rausei S, Rovera F, Tanda ML, et al. Continuous monitoring of the recurrent laryngeal nerve in thyroid surgery: a critical appraisal. International Journal of Surgery. 2013;11:S44-S6.
15. Schneider R, Przybyl J, Pliquett U, Hermann M, Wehner M, Pietsch U-C, et al. A new vagal anchor electrode for real-time monitoring of the recurrent laryngeal nerve. The American Journal of Surgery. 2010;199(4):507-14.
16. Ulmer C, Koch KP, Seimer A, Molnar V, Meyding-Lamadé U, Thon K-P, et al. Real-time monitoring of the recurrent laryngeal nerve: an observational clinical trial. Surgery. 2008;143(3):359-65.
17. Bartsch DK, Dotzenrath C, Vorländer C, Zielke A, Weber T, Buhr HJ, et al. Current practice of surgery for benign goitre—an analysis of the prospective DGAV StuDoQ| Thyroid Registry. Journal of clinical medicine. 2019;8(4):477.
18. Jonas J, Boskovic A. Intraoperative neuromonitoring (IONM) for recurrent la-

ryngeal nerve protection: comparison of intermittent and continuous nerve stimulation. Surgical Technology International. 2014;24:133-8.

19. Schneider R, Machens A, Sekulla C, Lorenz K, Elwerr M, Dralle H. Superiority of continuous over intermittent intraoperative nerve monitoring in preventing vocal cord palsy. British Journal of Surgery. 2021;108(5):566-73.

20. Schneider R, Sekulla C, Machens A, Lorenz K, Nguyen Thanh P, Dralle H. Postoperative vocal fold palsy in patients undergoing thyroid surgery with continuous or intermittent nerve monitoring. Journal of British Surgery. 2015;102(11):1380-7.

21. Schneider R, Randolph GW, Sekulla C, Phelan E, Thanh PN, Bucher M, et al. Continuous intraoperative vagus nerve stimulation for identification of imminent recurrent laryngeal nerve injury. Head & neck. 2013;35(11):1591-8.

22. Papavramidis TS, Sapalidis K, Michalopoulos N, Triantafillopoulou K, Gkoutzamanis G, Kesisoglou I, et al. UltraCision harmonic scalpel versus clamp-and-tie total thyroidectomy: A clinical trial. Head & Neck: Journal for the Sciences and Specialties of the Head and Neck. 2010;32(6):723-7.

23. Jeannon JP, Orabi AA, Bruch GA, Abdalsalam HA, Simo R. Diagnosis of recurrent laryngeal nerve palsy after thyroidectomy: a systematic review. International journal of clinical practice. 2009;63(4):624-9.

24. Kandil E, Noureldine SI, Abbas A, Tufano RP. The impact of surgical volume on patient outcomes following thyroid surgery. Surgery. 2013;154(6):1346-53.

25. Dralle H, Sekulla C, Lorenz K, Thanh PN, Schneider R, Machens A. Loss of the nerve monitoring signal during bilateral thyroid surgery. Journal of British Surgery. 2012;99(8):1089-95.

26. Ho Y, Carr MM, Goldenberg D. Trends in intraoperative neural monitoring for thyroid and parathyroid surgery amongst otolaryngologists and general surgeons. European Archives of Oto-Rhino-Laryngology. 2013;270(9):2525-30.

27. Bergenfelz A, Jansson S, Kristoffersson A, Mårtensson H, Reihnér E, Wallin G, et al. Complications to thyroid surgery: results as reported in a database from a multicenter audit comprising 3,660 patients. Langenbeck's Archives of Surgery. 2008;393(5):667-73.

28. Wu C-W, Dionigi G, Sun H, Liu X, Kim HY, Hsiao P-J, et al. Intraoperative neuromonitoring for the early detection and prevention of RLN traction injury in thyroid surgery: a porcine model. Surgery. 2014;155(2):329-39.

29. Barczyński M, Stopa M, Konturek A, Nowak W. The overwhelming majority but not all motor fibers of the bifid recurrent laryngeal nerve are located in the anterior extralaryngeal branch. World journal of surgery. 2016;40(3):629-35.

30. Casella C, Pata G, Nascimbeni R, Mittempergher F, Salerni B. Does extralaryngeal branching have an impact on the rate of postoperative transient or permanent recurrent laryngeal nerve palsy? World journal of surgery. 2009;33(2):261-5.

31. Sancho JJ, Pascual-Damieta M, Pereira JA, Carrera MJ, Fontané J, Sitges-Serra A. Risk factors for transient vocal cord palsy after thyroidectomy. Journal of British Surgery. 2008;95(8):961-7.

32. Fontenot TE, Randolph GW, Friedlander PL, Masoodi H, Yola IM, Kandil E. Gender, race, and electrophysiologic characteristics of the branched recurrent laryngeal nerve. The Laryngoscope. 2014;124(10):2433-7.

33. Lee HY, Cho YG, You JY, Choi BH, Kim JY, Wu CW, et al. Traction injury of the recurrent laryngeal nerve: Results of continuous intraoperative neuromonitoring in a swine model. Head & Neck. 2016;38(4):582-8.

34. Bai B, Chen W. Protective effects of intraoperative nerve monitoring (IONM) for recurrent laryngeal nerve injury in thyroidectomy: meta-analysis. Scientific reports. 2018;8(1):1-11.

35. Deniwar A, Kandil E, Randolph G. Electrophysiological neural monitoring of the laryngeal nerves in thyroid surgery: review of the current literature. Gland surgery. 2015;4(5):368.

36. Jonas J. Continuous vagal nerve stimulation for recurrent laryngeal nerve protection in thyroid surgery. European Surgical Research. 2010;44(3-4):185-91.

37. Van Slycke S, Gillardin J-P, Brusselaers N, Vermeersch H. Initial experience with S-shaped electrode for continuous vagal nerve stimulation in thyroid surgery. Langenbeck's archives of surgery. 2013;398(5):717-22.

38. Yu Q, Liu K, Zhang S, Li H, Xie C, Wu Y, et al. Application of continuous and intermittent intraoperative nerve monitoring in thyroid surgery. Journal of Surgical Research. 2019;243:325-31.

39. Sedlmaier A, Steinmüller T, Hermanns M, Nawka T, Weikert S, Sedlmaier B, et al. Continuous versus intermittent intraoperative neuromonitoring in complex benign thyroid surgery: a retrospective analysis and prospective follow-up. Clinical Otolaryngology. 2019;44(6):1071-9.

40. Kim SW, Hwang SH. Intraoperative neural monitoring for early vocal cord function assessment after thyroid surgery: a systematic review and meta-analysis. World journal of surgery. 2021:1-8.

41. Phelan E, Schneider R, Lorenz K, Dralle H, Kamani D, Potenza A, et al. Continuous vagal IONM prevents recurrent laryngeal nerve paralysis by revealing initial EMG changes of impending neuropraxic injury: a prospective, multicenter study. The Laryngoscope. 2014;124(6):1498-505.