Review paper

Neuromonitoring – still highly controversial

Neuromonitoring – wciąż wiele kontrowersji

Piotr Bryk[1,2], Stanisław Głuszek[1,2]

[1]Clinic of General, Oncological and Endocrynological Surgery of Provincial Polyclinic Hospital, Kielce, Poland
Head of the Clinic: Jacek Bicki MD, PhD
[2]Department of Surgical Medicine with Laboratory of Medical Genetics, Institute of Medical Sciences, *Collegium Medicum*, Jan Kochanowski University, Kielce, Poland
Head of the Department: Prof. Stanisław Głuszek MD, PhD

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Słowa kluczowe: śródoperacyjny neuromonitoring, ciągły neuromonitoring, tyreoidektomia, stymulacja nerwu błędnego, nerw krtaniowy wsteczny.

Abstract

Recurrent laryngeal nerve (RLN) paralysis, although rare, is among the most serious complications of thyroid gland surgery. It effects the quality of life of the patient, increases the costs of hospitalization, and can be the cause of legal proceedings. Therefore, it is not surprising that for a long time, devices have been sought that minimize the risk of injury to the nerves. One of them is intraoperative neuromonitoring (IONM). Despite several decades of using neuromonitoring during thyroid gland surgeries, there is still much controversy concerning its effectiveness. The divergent results of various meta-analyses are probably associated with the lack of standardization and inappropriate use of the method. Indisputable benefits from the use of IONM were proven in high-risk surgeries, such as malignant cancer, overactive thyroid gland, recurrent goitre, or retrosternal goitre. Nerve monitoring can be carried out by intermittent (I-IONM) or continuous (C-IONM) stimulation. At present, increasing importance is attached to continuous monitoring, because it protects the nerve against injury in real time, and the surgeon is warned against performance of a dangerous manoeuvre. Neuromonitoring is safe and does not show undesirable effects. Even though its use increases the costs of surgery and hospitalization, it improves the quality of the procedure and ensures the safety of the patient and the surgeon.

Streszczenie

Porażenie nerwu krtaniowego wstecznego (RLN), choć nie zdarza się często, jest jednym z najgorszych powikłań zabiegów chirurgicznych gruczołu tarczowego. Wpływa na jakość życia pacjenta, zwiększa koszty hospitalizacji oraz może być przyczyną postępowania sądowego. Nie dziwi fakt, że od dawna poszukuje się urządzeń, które zminimalizują ryzyko uszkodzenia nerwów. Jednym z nich jest śródoperacyjny neuromonitoring (IONM). Pomimo kilkudziesięcioletniego okresu stosowania neuromonitoringu podczas zabiegów chirurgicznych tarczycy, wciąż istnieje wiele kontrowersji dotyczących jego skuteczności. Rozbieżne wyniki różnych metaanaliz mają związek z brakiem standaryzacji i niewłaściwym stosowaniem metody. Bezsprzeczne korzyści ze stosowania IONM udowodniono w operacjach wysokiego ryzyka, takich jak nowotwory złośliwe, wola nadczynne, wola nawrotowe czy wola zamostkowe. Monitorowanie nerwów można prowadzić za pomocą przerywanej (I-IONM) i ciągłej stymulacji (C-IONM). Obecnie coraz większą wagę przykłada się do ciągłego monitorowania jako metody, która jest krokiem milowym, gdyż chroni nerw przed urazem w czasie rzeczywistym i pozwala ostrzec chirurga przed wykonaniem niebezpiecznego manewru. Neuromonitoring jest bezpieczny i nie ma działań niepożądanych. Pomimo że jego stosowanie zwiększa koszty operacji i hospitalizacji, poprawia jakość zabiegu oraz zapewnia bezpieczeństwo pacjenta i chirurga.

Introduction

Thyroid gland surgeries have evolved over the years to become one of the safest types of procedure, with a low risk of complication. Nevertheless, the occurrence of undesirable effects may not only result in the deterioration of the patient's quality of life but also could be life threatening [1]. An appropriate surgical technique to ensure correct identification of all anatomical structures, precise dissection, and appropriate haemostasis are of key importance; however, this does not guarantee an absence of complications [2].

Therefore, modern technologies are sought and are being brought into use for increasingly safe performance of the surgery. One of them is intraoperative neurophysiological monitoring (IONM). This device facilitates the identification of nerves in the operative field, and thus it is supposed to reduce the risk of damaging these structures. Injury to the recurrent laryngeal nerves (RLN) is among the most serious complications during thyroid gland surgical procedures [3]. This complication may result in transient or permanent vocal cord paralysis [4]. Unilateral vocal cord paralysis may lead to hoarseness of the voice, respiratory complications related with aspiration, and dysphagia, whereas bilateral injury to the recurrent laryngeal nerves may cause severe life-threatening shortness of breath requiring tracheotomy [5].

The frequency of damage to the laryngeal nerves differs according to the results presented by different researchers, being from 0.3% to 13% in the case of unilateral injury, and up to 1% for bilateral injuries. Paralysis is considerably more often of a transient rather than persistent character [6, 7]. According to different researchers, the time after which the recurrent laryngeal nerve paralysis should be considered as permanent and irreversible is from 6 to 12 months [8]. The recurrent laryngeal nerve is more frequently damaged during procedures performed by insufficiently experienced surgeons [9]. Also, special situations predispose to injury of this nerve, such as surgery for recurrent goitre, giant goitre, retrosternal goitre, thyroid cancer, or surgeries performed in patients after neck radiation therapy [10, 11].

At present, there is still an ongoing discussion concerning the effect of the use of neuromonitoring on the reduction of the number of injuries to the recurrent laryngeal nerve during thyroid surgery. It is therefore worth taking a closer look at the application technique, effectiveness, and safety as well as disadvantages and advantages of the above-mentioned method.

Neuromonitoring

A neuromonitoring system is a device the operation of which is based on electromyographic response, which is a sensitive measure of damage to the peripheral nerves. The peripheral nerve is stimulated by using a probe sending electrical impulses causing the corresponding muscle to contract, the vibrations of which are registered by the receiving electrode. The first attempts to apply intraoperative identification of the laryngeal nerves were initially made on animals, whereas those undertaken in humans were first described by Donald Sheed and Cristopher Durham in 1966 [12]. Delgado *et al.* for the first time applied intraoperative monitoring of the facial nerve in 1979 [13]. Initially, the needle electrodes were applied inserted directly to the vocal muscles through the cricothyroid ligament of the larynx [14]. Currently, surface electrodes are used implanted in the endotracheal tube. The use of surface electrodes considerably increases the cost of the procedure; however, this method of signal acquisition is safer due to its being less invasive than needle electrodes. One of the described methods for identification of the laryngeal nerves without the necessity to use receiving electrodes is examination of laryngospasm. The operator places a finger backwards over the cricoid cartilage; subsequently, after stimulation of the recurrent laryngeal nerves and the vagus nerve with a current of 1–2 mA, the surgeon senses the contraction of the laryngeal muscles. Palpation examination of laryngospasm may be considered as a quick and easily available technique [15]. It should be emphasized that the methods of identification of the nerves based on electromyography are not techniques for imaging the course of the nerve, but only its functional activity. Based on the signal received from neuromonitoring it is not possible to foresee the course of the nerve; hence, new methods of nerve identification are being developed, based on attempts to visualize their course.

Techniques of using intraoperative neuromonitoring (IONM)

The technique of intraoperative neuromonitoring (IONM) has been described in detail in the international guidelines developed by the International Neural Monitoring Study Group [16]. These guidelines are aimed at improvement of the quality and safety of monitoring, and presentation of the correct identification of the recurrent laryngeal nerves, as well as superior laryngeal nerves. The principles of the correct use of the system require the engagement of the whole surgical team and include properly performed anaesthesia and the correct use of the system during surgery. The conditions for proper anaesthesia are based on the use of an endotracheal tube of the largest possible diameter so that the surface electrodes applied come into direct contact with the vocal folds. In addition, it is recommended that short-acting drugs are applied, e.g. succinylcholine. However, considering the large number of side effects of succinylcholine, i.e. cardiac arrhythmia, hyperkalaemia, and malignant hyperthermia, non-depolarizing muscle relaxants are more frequently applied. Most often it is recommended that a single dose of rocuronium be administered (0.3 kg/kg b.w.). Anaesthesia is maintained using nitrous oxide or a combination of remifentanil and propofol, the above-mentioned agents have no effect on the electromyographic signal. The authors of the guidelines encourage the dissection of the vagus nerve each time by incision of the carotid sheath and direct exposure of the vagus nerve along the length of about 10–15 mm. Subsequently, the vagus nerve is directly stimulated with a current of 1 mA, obtaining both a graphic and an acoustic signal from the neuromonitoring system. In the case of a lack of signal, stimulation of the vagus nerve should be performed above the upper pole of the thyroid gland. If the signal is positive, this may indicate the presence of the non-recurrent laryngeal nerve at this side. If the signal is negative, the stimulation of the vagus nerve should be performed on the opposite side, in order to exclude other causes of a false negative result, for instance based on the malfunction of the system itself. The above-described open technique is indispensable in the case of continuous intraoperative nerve monitoring (C-IONM), where a special probe is attached to the dissected segment of the nerve. It is also possible to use the closed technique described by Wu *et al.*, which consists of stimulation of the vagus nerve through the carotid sheath with a current of 2–3 mA. The closed method is safer and reduces risk of injury not only to the vagus nerve itself but also to the jugular vessels [17]. Based on the literature there is strong evidence that stimulation of the nerves is safe, and does not cause injuries to the nerves or the adjacent tissues.

Strict standardization becomes necessary for the correct use of new technologies, verification of their safety, and obtaining better outcomes of treatment. In the case of neuromonitoring this is the application of a protocol consisting of the following stages [18]:
- L1 – assessment of vocal fold mobility by laryngological examination performed before the surgery,
- V1 – stimulation of the vagus nerve before dissection of the thyroid lobe,
- R1 – stimulation of the recurrent laryngeal nerve before dissection of the thyroid lobe,
- R2 – stimulation of the recurrent laryngeal nerve after dissection of the thyroid lobe,
- V2 – stimulation of the vagus nerve after dissection of the thyroid lobe,
- L2 – assessment of vocal fold mobility by laryngological examination after performing surgical procedure,

It should be emphasized that only strict adhesion and compliance to the standardized technique of intraoperative monitoring allows the preservation of correct results, quality, and safety.

During the surgery loss of the electromyographic signal after the use of properly working before neuromonitoring may occur, or a decrease in the value of the EMG amplitude below 100 μV. These events are defined as intraoperative loss of signal (LOS). In such a case, laryngospasm after stimulation of the vagus nerve on the examined side should be checked first. If laryngospasm is present, the causes of the loss of signal should be sought in the receiving part of neuromonitoring. Usually it is sufficient to perform tracheal tube repositioning to re-attach the receiving electrode on the level of the vocal folds. More rarely, this problem concerns the grounding electrode, which should also be checked. A useful manoeuvre is contralateral vagus nerve stimulation. A signal obtained from neuromonitoring in this situation indicates a problem with the stimulatory part of neuromonitoring on the signal loss side. Similarly, in the situation of the absence of laryngospasm after performing stimulation of the vagus nerve the stimulation parameters should be checked, proper stimulation conditions provided in the form of a dry surgical field, and the stimulation probe should be checked, which, after attachment to the muscle, should cause its vibration. Obviously, each time it should be ascertained whether the stimulated structure is the nerve. It is also necessary to obtain information concerning the possible use of neuromuscular blocking agents. After checking all the above possibilities, the surgeon must consider the occurrence of the complication in the form of injury to the recurrent laryngeal nerve. In this situation, an attempt should be undertaken to find the site of the lesion from the most distal portion of the recurrent laryngeal nerve in the proximal direction. Identification of the site of injury allows determination of the type of damage. Two types of nerve injuries are distinguished. The first of these is segmental injury (type 1), concerning the short section of the nerve. In this situation the injury may be corrected by removal of the clip or garter. The second type is global injury (type 2) concerning the lack of conductivity in the entire section of the recurrent laryngeal nerve available for examination, most often caused by traction. The prognosis in type 2 injuries is better than in type 1 injuries [19]. If there is LOS, the surgeon must consider at least transient recurrent laryngeal nerve paralysis and postpone contralateral flap resection to protect against bilateral nerve paralysis. Goretzki *et al.* reported that the rate of bilateral vocal fold paralysis was 17% in the case of ignoring LOS. In the case of withdrawal from resection of the second lobe after the occurrence of LOS, no events of bilateral vocal fold paralysis were noted [20]. Similar results were obtained by Melin *et al.* – 16% of cases of bilateral paralysis [21]. It seems that stress, which impairs the performance of the surgeon, exerts an effect on such a large number of vocal fold paralyses in the case of the occurrence of LOS. According to the literature, the optimum time of repeated surgery is less than 3 days or more than 3 months. For thyroid cancer the time of repeated surgery should be less than 6 months [22]. Use of the method of electromyographic analysis of the obtained signal provides more information than the sole method for identification of the nerve based on acoustic registration of the electrostimulation signal. Analysis of the IONM signal takes place by means of peak-to-peak amplitude and latency. The amplitude measure is correlated with the number of muscle fibres, which are polarized by EMG. The peak-to-peak amplitude is the difference between the maximum positive and the maximum negative amplitudes of a waveform. The differences in peak-to-peak amplitude between patients may result from contamination of the operative field with fluid or blood, different degree of probe-nerve contact, different degree of adhesion of the receiving electrode to the vocal fold, or changes of temperature in the vicinity of the nerve after application of fluids. Latency is related with the rate or ease of stimulation-induced depolarization, and it depends on the distance between the stimulation site and the vocal cord. Taking into account the course of nerves, the delay is considerably longer on the left side. The application of the proper procedure of the use of intraoperative monitoring reduced the number of technical mistakes, facilitated nerve mapping, and enabled possible location of the site of injury to the recurrent laryngeal nerves.

I-IONM versus C-IONM

At present, intraoperative neuromonitoring may be carried out using 2 techniques. The technique of intermittent nerve monitoring (I-IONM) enables the surgeon periodical stimulation and assessment of the function of the recurrent laryngeal nerve. Although this is very useful, such a format of monitoring of intermittent stimulation potentially creates the risk of injury of the nerve during the time between stimulations. C-IONM is a technique consisting of continuous monitoring of the potential, indicating the integrity of the recurrent laryngeal nerve in real time throughout the entire surgical procedure. C-IONM offers continuous monitoring of the laryngeal nerve, thus enabling recognition of the upcoming damage to the nerve, which facilitates early corrective action. A drop in amplitude of the signal with respect to the output signal amplitude by 50% and extending signal latency by more than 10% imposes the necessity to immediately discontinue the surgical manoeuvre, assuming that this combination of EMG changes can lead to vocal fold paralysis [22].

In the method of intermittent nerve monitoring, functional impairment of the nerve is most often detected after its lesion, in contrast to continuous neuromonitoring, which provides constant information about the functional and morphological state of the nerve. Both techniques of intermittent and continuous neuromonitoring are safe for patients and do not show adverse effects on the part of the nervous, cardiovascular, respiratory, or gastrointestinal systems [23].

Effectiveness of IONM

The available literature and meta-analyses comparing IONM with sole macroscopic identification of the recurrent laryngeal nerves present conflicting conclusions [24–32]. There is evidence suggesting that the use of IONM reduces the number of complications in the form of both transient and persistent paralysis of the recurrent laryngeal nerves [32], only transient [31], and only persistent injuries of the recurrent laryngeal nerves [30]. Other researchers obtained contrasting results and did not observe a reduction in the number of persistent [26] or transient and persistent damage to the recurrent laryngeal nerves [27, 28]. These heterogeneous results may be due to the gradual advancement of IONM technology and the importance of the standardization method.

Based on the review of literature, neuromonitoring is characterized by the following sensitivity: 63.0–91.3% for I-IONM and 90.9–100% for C-IONM, as well as specificity: 97.1–99.5% for I-IONM and 90.2–99.7% for C-IONM. The positive predictive value (PPV) is 37.8–80.5% for I-IONM and 47.6–88.2% for C-IONM, whereas the negative predictive value (NPV) is 97.3–99.8% for I-IONM and 99.8–100% for C-IONM.

Table 1 presents the usefulness of individual methods: macroscopic visualization of nerves compared to I-IONM and C-IONM [33].

Undoubtedly, the most important advantage of C-IONM, compared to I-IONM, is the possibility of monitoring the functional integrity of the nerve in real time and the detection of the moment of upcoming potential injury to the recurrent laryngeal nerve [34].

Neuromonitoring is extremely useful in high-risk surgical procedures, including recurrent goitre, toxic goitre, retrosternal goitre, malignant cancer, Hashimo-

Table 1. Comparison of different methods of RLN identification

Parameters	Macroscopic visualization	I-IONM	C-IONM
Identification of LOS	–	+	+
Avoidance of bilateral vocal fold paralysis	–	+	+
Identification of intraoperative recovery of RLN function	–	(+)	+
Minimization of RLN injuries caused by traction	–	–	+
Avoidance of thermal injuries to RLN	–	–	(+)
Functional monitoring in real time throughout RLN	–	–	+
Detailed EMG documentation	–	–	+

+ – appropriate, (+) – limited, – – inappropriate, EMG – electromyogram, I-IONM – intermittent intraoperative nerve monitoring, C-IONM – continuous intraoperative nerve monitoring, LOS – loss of signal, RLN – recurrent laryngeal nerve.

to's disease, and Graves' disease. In re-operations of the thyroid gland the presence of a scar and altered anatomy hinder dissection and identification of the nerves. The risk of vocal fold paralysis during re-operation is 4.6–10.4 times higher than during the first surgery [35]. In the case of surgery for malignant tumours of the thyroid gland, injuries of the nerves more often occur while performing cervical lymphadenectomy [36].

Frequency of use

In 2019, in a questionnaire distributed to 1015 surgeons registered in the American Academy of Otolaryngology – Head and Neck Surgery, the International Association of Endocrine Surgeons, and the American Head and Neck Society, 83% of respondents admitted that they used IONM, of whom 65% used it routinely, while 18% selectively [37]. In turn, 3 years earlier, in a similar study conducted among 56 endocrine surgeons and head and neck surgeons who had completed internships accredited by the American Association of Endocrine Surgeons or the American Head and Neck Society, 95% of respondents reported the use of IONM, of whom 60% used it routinely, and 35% selectively. The most frequent reasons for the use of this method were increasing self-confidence (55%) and an improvement of safety (54%) [38]. In Germany, as many as 98% of thyroid surgeries are performed using IONM, of which 17.4% are performed with continuous monitoring [39].

Costs

Although the use of IONM is gaining increasing popularity and is considered as a standard of care, the profitability of this technology remains controversial [24]. The price of devices for neuromonitoring range, according to the country, between 5000 and 40000 US dollars, and that of disposable items used during the surgery – from 72 to 500 US dollars [33]. IONM constitutes approximately 5–7% of the cost of hospitalization of a patient who undergoes surgical removal of the thyroid gland [40]. Wang *et al.* indicated that IONM is unprofitable because the frequency of transient vocal fold paralysis is as high as 38.5%. The procedure is financially advantageous when the rate of paralysis of the vocal folds is 33.6% after 1 month, 22.9% after 2 months, 9.8% after 6 months, and 3.8% after 12 months [41]. Considering the rare occurrence of complications of these surgeries, some researchers questioned the profitability of the routine use of IONM [42]. Undeniably, the savings potential, and therefore the profitability of IONM, grows with increased risk of operative complications.

Legal aspects

Complications of thyroid gland surgery, bringing about the risk of injury to the recurrent laryngeal nerve, may give rise to legal claims. Although they are not frequent, lost lawsuits may concern abandonment of RLN identification, in which the application of IONM is undoubtedly useful, as well as the use of IONM itself, without maintaining proper standards – among others, resigning from the LOS procedure [43]. There is no doubt that medical records, which are the protocol of correctly performed intraoperative monitoring, are a strong line of defence against unjustified claims.

Conclusions

Despite the fact that intraoperative neuromonitoring during thyroid gland surgeries has been used for many years, contradictory results of research pertaining to its effectiveness still occur. The available literature and meta-analyses published comparing IONM with the sole macroscopic identification of the recurrent laryngeal nerves present different results. This is most probably associated with the lack of standardization and inappropriate use of the method. Macroscopic visualization of recurrent laryngeal nerves remains a gold standard. Undoubtedly, constant electrophysiological feedback information concerning the functional status of the nerve reduces stress and gives the surgical team peace of mind. It allows less experienced surgeons to master practical skills in the safer performance of the surgery. Considering the low positive predictive value of the method and the high number of false positive results, as well as the additional costs of the procedure, IONM is still not recommended as the standard instrumentarium in thyroid surgery. It seems that C-IONM is a more promising method than I-IONM because it protects the nerve against injury in real time. However, this thesis requires confirmation by scientific research. To date, no side effects associated with the use of IONM have been reported. Despite the fact that its use increases the costs of surgery and hospitalization, it improves the quality of the procedure and ensures the safety of the patient and the surgeon.

Conflict of interest

The authors declare no conflict of interest.

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Address for correspondence:

Piotr Bryk MD, PhD
Clinic of General, Oncological and Endocrynological Surgery
Provincial Polyclinic Hospital
ul. Grunwaldzka 45, 25-736 Kielce, Poland
Phone: +48 508 330 727
E-mail: bryk.piotr@gmail.com