The Effect of Intraoperative Neuromonitoring on Damage to the Laryngeal Nerves in Patients Undergoing Total Thyroidectomy.

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Research

Keywords: thyroid, neuromonitoring, recurrent laryngeal nerve, nodular goiter

DOI: https://doi.org/10.21203/rs.3.rs-150292/v1

Abstract

Background: Assessment of intraoperative neuromonitoring in the prevention of damage to the recurrent laryngeal nerve during total thyroidectomy.

Material and methods: A group of 367 patients qualified for the study, including 312 women (85.01%) and 55 (14.99%) men, aged 18-79, having undergone total thyroidectomy due to a neutral nodular goiter. The patients were operated on by one surgeon. The study group consisted of 205 patients, including 173 (84.39%) women and 32 (15.61%) men, aged 19-79, who were operated on with the use of intraoperative neuromonitoring. The control group consisted of 162 patients, including 139 (85.80%) women and 23 (14.20%) men, aged 18-77 years, who had undergone surgery only with macroscopic visualization of the recurrent laryngeal nerve without the application of intraoperative neuromonitoring. Then, in the period from 2 to 10 years after the surgery, follow-up examinations were performed, which included 153 patients from the control group (74.6% [153/205]) and 122 patients from the study group (75.3% [122 / 162]

Results: The frequency of vocal fold palsy did not differ significantly statistically in the study group and the control group (study group: 4.9% [10/205], control group: 4.9% [8/162]; p = 0.979). In the follow-up study, the incidence of laryngeal fold palsy did not show statistically significant differences between the study and control groups. Most of the damage to the recurrent laryngeal nerves was persistent.

Conclusions: Neuromonitoring did not reduce the number of recurrent laryngeal nerve injuries in relation to the nerve visualization alone in noncapsular total thyroidectomy for benign nodular goiter, performed by the same experienced surgeon.

Introduction

Thyroid surgery has evolved over the years from one of the most dangerous procedures to operations that are not only safe, but also well-tolerated and complication rates are low. These complications, however, may not only reduce the quality of life, as in the case of hypoparathyroidism or vocal fold palsy, but may also be life threatening in the case of a rapidly developing hematoma in the resection cavity. Damage to the recurrent laryngeal nerves, despite the fact that it does not occur frequently, is a significant clinical problem causing deterioration in the quality of life of patients and is often the cause of surgical claims. The most important factors reducing the incidence of these types of adverse events are the experience of the surgeon and routine macroscopic visualization of the recurrent laryngeal nerves. It is assumed that neuromonitoring, a tool for the intraoperative identification of the recurrent laryngeal nerves, enables safe movement within the operating site and thus reducing the number of life threatening events and health complications caused by thyroidectomy.

Aim Of The Study

The aim of the study was to evaluate the intraoperative neuromonitoring in the prevention of damage to the recurrent laryngeal nerves in total thyroidectomy. The material analysis took into account both the immediate postoperative period in which the clinical voice assessment and indirect laryngoscopy were performed, as well as the current health status of the patient with an assessment of the mobility of the vocal folds in laryngoscopic examination.

Material And Methods

A group of 367 patients was enrolled in the study, including 312 women (85.01%) and 55 (14.99%) men, aged 18–79 (median: 53), who had undergone total thyroidectomy due to neutral nodular goiter. The patients were operated on by the same surgeon. In an indirect laryngoscopic examination performed by a laryngologist before the surgery, no disturbances in the mobility of the vocal folds were found, and no other voice disorders unrelated to thyroid diseases in the form of hoarseness, aphonia, dyspnea or laryngeal wheezing were found. The study excluded patients who had undergone partial thyroidectomy, patients who had been operated on with minimally invasive techniques, patients operated on for an overactive nodular goiter, recurrent goiter, cancer or suspected thyroid cancer, patients with clinical signs of vocal fold palsy before surgery, and patients with diseases of the central or peripheral nervous system that may cause damage to the motor system or neuron of the motor system.

The study group consisted of 205 patients, including 174 (84.9%) women and 31 (15.1%) men, aged 18–79 (mean 52.2; median 53), operated on with intraoperative neuromonitoring used in accordance with the guidelines of the International Research Group on Neuromonitoring. Patients constituting this group underwent surgery during which macroscopic visualization of the recurrent laryngeal nerves was performed, then nerve identification was confirmed by intraoperative neuromonitoring.

The control group consisted of 162 patients, including 139 (85.8%) women and 23 (14.2%) men, aged 18–77 (mean 51.6; median 54). Patients from this group underwent surgery only with macroscopic visualization of the recurrent laryngeal nerves, without the use of intraoperative neuromonitoring.

All surgical procedures were performed from the anterior jugular access site. It should be emphasized that the superior laryngeal nerve was not routinely identified, while, at the same time, the focus was on preventing its damage. In each case, however, the recurrent laryngeal nerve was identified along its course.

All patients on the first or second day after the surgery underwent indirect laryngoscopy.

A follow-up study conducted between 2 and 10 years (median: 6) after surgery, included 153 patients in the control group (74.6% [153/205]) and 122 patients in the study group (75.3% [122 / 162]). Each patient reporting for the examination underwent indirect laryngoscopy.

In indirect laryngoscopy, both in the immediate postoperative period and in the follow-up examination, the mobility of the vocal folds was assessed.

The end points were:

• vocal fold palsy, vocal fold position:

- paramedian,
- intermediary,
- lateral,

• correct mobility of the vocal fold.

Statistical analysis

In the statistical description of quantitative characteristics arithmetic mean, standard deviation (sd), median, lower quartile (Q1), upper quartile (Q3) and a value range (minimum and maximum) were used. Distributions of qualitative characteristics were presented with frequencies and percentages. Normality of distributions was checked with the use of the Shapiro-Wilk Test. Because the analyzed distributions were not normal, the U Mann-Whitney test was used for comparison of continuous variables distributions in the groups subjected to analysis.

Frequencies in unrelated groups were compared with the Chi-square test (if the criteria for expected frequencies were met) or the Fisher’s exact test (in the case of not meeting the criteria for expected frequencies). The McNemar test was used to evaluate frequency changes in related groups (this concerned the assessment of the occurrence of laryngeal nerve palsy in the early postoperative period, and then reassessment of the occurrence of this palsy in a follow-up study).

The diagnostic value of neuromonitoring in the prediction of laryngeal nerve palsy during surgery, was assessed by the sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV).

All performed statistical tests were two-sided. The p-value < 0.05 was adopted as the criterion of statistical significance. Calculations were made in the R program (version 3.6.0; R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org /). The test results are presented in the next section.

Results

205 patients qualified for the study group, including 174 (84.9%) women and 31 (15.1%) men. The control group consisted of 162 patients, including 139 (85.8%) women and 23 (14.2%) men.

Table 1
Basic demographic and clinical characteristics, duration of the surgery, duration of hospitalization and postoperative parameters in the study and control groups.

	Study group (N = 205)	**Control group (N = 162)**	**p (value)**
Age (years)			0.567
Mean (sd)	52.2 (13.1)	51.6 (13.2)	
Median (Q1, Q3)	54.0 (43.0, 63.0)	54.0 (42.0, 61.0)	
Range	18.0–79.0	18.0–77.0	
Study subjects			0.804
Women	174 (84.9%)	139 (85.8%)	
Men	31 (15.1%)	23 (14.2%)	
Duration of surgery (minutes)			**< 0.001**
Mean (sd)	96.5 (28.8)	83.2 (18.6)	
Median (Q1, Q2)	90.0 (75.0, 105.0)	80.0 (70.0, 90.0)	
Range	60.0–275.0	50.0–165.0	
Hospitalization (days)			0.771
Mean (sd)	4.2 (0.6)	4.2 (0.7)	
Median (Q1, Q3)	4.0 (4.0, 4.0)	4.0 (4.0, 4.0)	
Range	3.0–8.0	3.0–7.0	
Calcium concentration after surgery (mEq/ml)			**< 0.001**
Mean (sd)	4.3 (0.4)	4.4 (0.7)	
Median (Q1, Q3)	4.4 (4.1, 4.6)	4.6 (4.3, 4.7)	
Range	2.4–5.0	2.2–5.4	
Calcium concentration after surgery (mEq/ml)			**< 0.001**
Below 4.50	128 (62.4%)	52 (32.1%)	
From 4.50 to 5.50	77 (37.6%)	110 (67.9%)	
Parathyroid levels after surgery (pg/ml)			0.791
Mean (sd)	23.4 (12.5)	26.0 (18.2)	
Median (Q1, Q3)	25.0 (14.0, 34.0)	22.0 (13.9, 37.0)	

	Study group (N = 205)	Control group (N = 162)	p (value)
Range	2.0–52.0	1.0–78.0	
Parathyroid levels after surgery (pg/ml)			0.056
Below 15	33 (25.6%)	10 (28.6%)	
From 15 to 65	96 (74.4%)	23 (65.7%)	
Over 65	0 (0.0%)	2 (5.7%)	

The duration of the surgery was significantly longer in the study group ($p < 0.001$), but there were no significant differences between the groups in terms of the period of hospitalization. Longer surgery time was associated with the use of neuromonitoring and the procedure of recording individual stimulations (V1, R1, R2, V2). The overall hospitalization period in both groups was similar and averaged 4 days.

In the period immediately after the operation, the study group and the control group differed significantly in calcium concentration ($p < 0.001$). Postoperative hypocalcaemia was more common in patients operated on with intraoperative neuromonitoring (62.4% vs 32.1%), which could be related to more careful preparations and thus a greater risk of transient ischemia of the parathyroid glands.

Assessment of recurrent laryngeal nerve damage in the early postoperative period in both groups

The incidence of at least 1 vocal fold palsy was not statistically significantly different in the study and control groups (study group: 4.9% [10/205], control group: 4.9% [8/162]; $p = 0.979$). There were no statistically significant differences between the study group and the control group in the frequency of palsy of either fold in any of their positions (paramedian, intermediary, lateral).

Palsy of both vocal folds was found in only one patient (0.5%) from the study group.

In the case of the right vocal fold, palsy was not observed in the medial position, and in the case of the left vocal fold, palsy occurred only in the intermediary position.

Table 2
Detailed characteristics of vocal fold palsy in the early postoperative period.

	Study group (N = 205)	Control group (N = 162)	p (value)
Right fold palsy in intermediary position	6 (2.9%)	4 (2.5%)	1
Right fold palsy in lateral position	0 (0.0%)	1 (0.6%)	0.441
Left fold palsy in intermediary position	5 (2.4%)	3 (1.9%)	1
Right fold palsy	6 (2.9%)	5 (3.1%)	1
Left fold palsy	5 (2.4%)	3 (1.9%)	1
Palsy of at least one fold	10 (4.9%)	8 (4.9%)	0.979
Number of paralyzed folds			0.893
0	195 (95.1%)	154 (95.1%)	
1	9 (4.4%)	8 (4.9%)	
2	1 (0.5%)	0 (0.0%)	

Analysis of data from neuromonitoring

The use of intraoperative neuromonitoring (IONM) using the C2-NerveMonitor provided by the INOMED company was in accordance with the guidelines of the International Neural Monitoring Study Group.

Stimulation was performed with the use of a manual bipolar probe which generated an electric impulse of 5 Hz with a rectangular impulse of 200 μs, and amperage of 5 mA in the case of the stimulation of the vagus nerve (V1, V2) and 2.5 mA in the case of the recurrent laryngeal nerve (R1, R2). Due to the fact that the receiving electrode was placed on the tracheal tube at the level of the vocal folds, the device recorded the highest peak-to-peak amplitude Vpp (mV) for each of the individual stimulations on both sides (V1, R1, R2, V2). Data obtained from neuromonitoring were saved in the device memory.

The signal from stimulation of the left vagus nerve before resection of the thyroid lobe (V1L) was obtained in 199 patients (97.1%), while after lobe resection (V2L), in 197 patients (96.1%). The signal from the stimulation of the left recurrent laryngeal nerve before lobe resection (R1L) was obtained in 198 patients (96.6%), whilst after lobe resection (R2L), in 196 patients (95.6%). On the right side, the signal from stimulation of the vagus nerve (V1P) was obtained in 200 cases (97.6%), and after lobe resection (V2P), in 197 cases (96.1%). The stimulation signal from the right recurrent laryngeal nerve was present in 200 patients (97.6%) before the lobe resection (R1P), and in 197 patients (96.1%) after the lobe resection (R2P).

The mean peak-to-peak amplitude obtained after stimulation of the left vagus nerve before lobe resection was 0.729 mV (maximum: 2.340 mV), and 0.631 mV after lobe resection (maximum: 2.010 mV). For the left recurrent laryngeal nerve before lobe resection, the mean value was 1.059 mV (maximum: 2.630 mV), and 0.960 mV after lobe resection (maximum: 2.450 mV).

On the right side, the mean peak-to-peak amplitude after vagus nerve stimulation, before lobe resection, was 0.709 mV (maximum: 2.010 mV), and 0.510 mV after lobe resection (maximum: 1.860 mV). For the recurrent laryngeal nerve, the mean value was 1.027 mV (maximum: 2.870 mV) before lobe resection, and 0.919 mV after lobe resection (maximum: 2.870 mV).

Based on the obtained results, it can be concluded that the mean peak-to-peak amplitude values for both the left vagus nerve and the left recurrent laryngeal nerve were higher than the values for the same nerves on the right side.

In addition, mean peak-to-peak amplitude values before lobe resection were higher than after resection for both vagus and recurrent laryngeal nerves. This association occurred bilaterally.

Mean peak-to-peak amplitude values were higher on both sides for the recurrent laryngeal nerves, compared to the vagus nerves, both before and after resection of the thyroid lobes.

Intraoperative loss of neuromonitoring signal (positive test result) was found in 13 cases, of which in 6 cases it was true and corresponded with paresis of the vocal fold, and in 7 cases it was false, because the mobility of the vocal fold was preserved. Among 192 cases of the preserved neuromonitoring signal after thyroid lobe resection, 188 cases of vocal fold mobility were normal (true negative result), and in 4 cases vocal fold paresis was found (false negative result). Hence, the negative predictive value of the neuromonitoring method was 97.9 and the positive value 46.2.

Thus, neuromonitoring has a high specificity, but low sensitivity.

Table 3
Sensitivity, specificity, accuracy, positive and negative predictive values of neuromonitoring.

TP (true positive results)	**n = 6**
TN (true negative results)	n = 188
FP (false positive results)	n = 7
FN (false negative results)	n = 4
Sensitivity	60.0%
Specificity	96.4%
Accuracy	94.6%
PPV	46.2%
NPV	97.9%

Follow-up examination

153 patients from the study group (74.6% [153/205]) and 122 patients from the control group (75.3% [122/162]) reported for the follow-up examination.

All patients from the study and control groups who had vocal fold palsy in the early postoperative period (n = 18 patients, including 10 from the study group and 8 from the control group), reported for the follow-up examination.

Assessment of the recurrent laryngeal nerve damage in the early postoperative period in both groups

The characteristics of vocal fold palsy in the early postoperative period among patients who reported for the follow-up examination is presented in Table 4.

Table 4
Detailed characteristics of vocal fold palsy assessed in the follow-up examination.

Follow-up assessment	Study group (N = 153)	Control group (N = 122)	p (value)
Right fold palsy in intermediary position	5 (3.3%)	4 (3.3%)	1
Right fold palsy in lateral position	0 (0.0%)	1 (0.8%)	0.440
Left fold palsy in intermediary position	3 (2.0%)	3 (2.5%)	1
Right fold palsy	5 (3.3%)	5 (4.1%)	0.755
Left fold palsy	3 (2.0%)	3 (2.5%)	1

In the study group, the palsy regressed in two patients, including one with palsy of both folds (in the follow-up examination of this patient, no signs of palsy in neither the left nor in the right folds were found).

In the case of the right laryngeal fold in the study group, the frequency of palsy did not change in a statistically significant manner. 3.9% [6/153] of patients with right fold palsy in the early postoperative period vs. 3.3% [5/153] of patients with right fold paralysis in the follow-up study; p-value = 1).

In the case of the left laryngeal fold in the study group, the frequency of palsy did not change in a statistically significant manner. 3.3% [5/153] of patients with left fold palsy in the early postoperative period vs. 2.0% [3/153] of patients with left fold paralysis in the early postoperative period. follow-up; p-value = 0.48).

In the control group, there were no changes in vocal cord palsy (the follow-up examination revealed vocal cord palsy in the same patients as in the early postoperative study).

In the follow-up study, the incidence of laryngeal fold palsy did not show statistically significant differences between the study and control groups.

Assessment of the ratio of early to persistent damage indicators

In the case of the left or right laryngeal fold in the study group (i.e. the assessment of palsy regardless of which side it occurs on), the frequency of palsy did not change statistically significantly. 6.5% [10/153] in patients with left or right fold palsy in the early postoperative period vs. 5.2% [8/153] of patients with left or right fold palsy in the follow-up examination (p-value = 0.48) In the study group, persistent palsy occurred in 8 patients, and in 2 patients transient paralysis occurred.

Table 5
Vocal cord palsy in the control group during follow-up examination

Left or right laryngeal fold in the study group		**Follow-up examination**		**Total**
		No palsy	**Palsy**	
Early post- operative period	No palsy	143	0	143
	Palsy	2	8	10
Total		145	8	153

There were no changes in vocal fold palsy in the control group (the follow-up examination revealed vocal cord palsy in the same patients as in the early postoperative examination). All damage to the recurrent laryngeal nerves in the control group were considered to be persistent.

Table 6
Vocal folds palsy in the control group in the follow-up examination.

Left or right laryngeal fold in the control group		**Follow-up examination**		**Total**
		No palsy	**Palsy**	
Early postoperative period	No palsy	114	0	114
	Palsy	0	8	8
Total		114	8	122

Discussion

Due to enormous progress in surgical techniques, despite the increase in the scope of resection from subtotal resection to total extracapsular excision of the thyroid gland, it was possible to significantly reduce the number of intraoperative lesions of the recurrent laryngeal nerves, mainly due to their routine visualization. However, it is still not possible to completely eliminate this postoperative complication. In 1938, Lahey observed that careful preparation and visualization of the recurrent laryngeal nerves dramatically reduced the amount of damage[1]. In the following years, these findings were confirmed by several other scientists, including Riddell[2]. Despite the surgical technique described above, there are certain circumstances in which nerve damage may occur. Thomusch et al. showed that routine identification may be an independent, significant risk factor for damage of laryngeal nerve[3]. However, most researchers have demonstrated a significant reduction in the risk of injuries to the nerve structures after visualization[4–6], hence the intraoperative visualization of the recurrent laryngeal nerves has become the gold standard in thyroid gland surgery. There are many risk factors for damage to the recurrent laryngeal nerves, such as the experience of the medical facility, being of female sex, a recurrent goiter, a retrosternal goiter and neoplastic diseases [7].

The mechanisms of nerve damage include partial or total transection, traction, compression, contusion, burn, clipping and ischemia[8]. Persistent palsy lasting more than 6–12 months is caused by cutting, ligation or cauterization of the nerve[9].

In this study, the percentage of postoperative complications in the form of recurrent laryngeal nerve palsy was (4.9% vs 4,9%) for unilateral damage, as well as for bilateral damage (0.27% vs 0%) in the study and control groups, respectively. Most of the palsy incidents were persistent (3.9% vs. 4.9%). It should be emphasized that the study involved patients who had undergone total thyroidectomy due to a benign nodular goiter, hence the percentage of nerve damage is greater than in the case of less invasive surgeries, e.g. lobectomy or subtotal resection and lower than in the case of surgery due to recurrent, a retrosternal goiter or neoplastic diseases. In the literature, the frequency of transient recurrent laryngeal nerve palsy is 4.1% – 13.6%, whilst for persistent, 2.3% – 9% [10–12].

In unilateral tense palsy, the patient may experience only inspiratory dyspnea, and the patient's voice may remain voiced. In flaccid palsy, dyspnea is exercise-induced and the voice becomes aphonic. The most dangerous is bilateral palsy of the vocal folds, which may cause obstruction of the upper respiratory tract, requiring tracheostomy if the vocal folds are in the paramedian position. Occasionally, unilateral vocal fold palsy may be clinically silent and the only examination to determine the complication is indirect laryngoscopy. All patients operated on at the Clinic of General, Oncological and Endocrinological Surgery of Provincial Polyclinic Hospital in Kielce are routinely subjected to laryngoscopic examinations on the first or second day after surgery. In the event of a vocal fold palsy, it may remain in a paramedian, intermediary or lateral position.

In the studied group of patients, the palsy of the recurrent laryngeal nerve occurred in 10 patients (4.9%), including 9 patients (4.4%) unilaterally and 1 patient (0.5%) bilaterally. The right vocal fold was paralyzed in 6 cases (2.9%), and the left vocal fold in 5 cases (2.4%). All paralyzed vocal folds were in the intermediary position.

In the control group, the palsy of the recurrent laryngeal nerve occurred in 8 patients (4.9%) and it was unilateral in each case. The right vocal fold was paralyzed in 5 cases (3.1%), and the left vocal fold in 3 cases (1.9%). The paralyzed right vocal fold in 4 patients (2.5%) was in the intermediary position and in 1 patient (0.6%) in the lateral position. The paralyzed left vocal fold was in the intermediary position in each case.

A follow-up study performed 2 to 10 years after the surgery of total thyroidectomy included 153 patients from the study group (74.6%) and 122 (75.3%) patients from the control group. All patients who had vocal fold palsy in the postoperative examination reported for a follow-up examination.

In the follow-up laryngoscopic examination in the study group, the symptoms of vocal fold paralysis were found in 2 patients (0.99%), including one with bilateral paralysis of the vocal folds. Thus, persistent paralysis occurred in 8 (3.9%) patients from the study group.

In the control group, in all 8 patients (4.9%), the palsy became persistent.

In this study, the high level of patients with postoperative hypocalcemia, statistically significantly higher in the study group (62.4% vs. 32.1%), also draws attention. The decreased level of parathyroid hormone (PTH < 15 pg / ml) in the postoperative period occurred in 25.6% of patients in the study group and 28.6% in the control group. There was no significant difference in this aspect. This percentage is similar to the results presented by other authors[13,14]. Low serum PTH levels are common after total thyroidectomy, but the vast majority of patients will experience recovery of parathyroid function within 2 months after surgery. Only some patients undergoing total thyroidectomy develop permanent hypoparathyroidism, determined by serum PTH levels < 10 pg / ml or the need to continue supplementation with calcium or calcitriol to prevent symptoms of hypocalcemia one year after surgery[13]. It should be emphasized that no histopathological specimens showed an accidental removal of parathyroid glands.

Injury to the recurrent laryngeal nerves is undoubtedly the most serious complication of thyroidectomy. It reduces the quality of life, but can also be a direct threat to it. Due to this threat, a way to avoid this complication has been sought for years. Feinstein first mentioned the use of electromyography in diagnosing disorders of the laryngeal nerves in 1946. At the end of the 1960s, Shedd and Durham made the first attempts to use an electric neurostimulator in humans to identify the recurrent laryngeal nerves. Therefore, in addition to the routine visualization of nerves and the appropriate knowledge of anatomy and surgical technique, for several decades we have had a new technique for intraoperative nerve monitoring. In recent years, this technique has been refined and the method has been standardized by the International Research Group on Neuromonitoring in Thyroid and Parathyroid Surgery[15]. Neuromonitoring has been used in the Clinic of General, Oncological and Endocrinological Surgery of Provincial Polyclinic Hospital in Kielce since 2011. Since 2017, all thyroid surgeries performed at this Clinic have been performed with the use of IONM.

This study compares the group of patients undergoing surgery of total thyroidectomy due to a nodular goiter with the use of intermittent intraoperative neuromonitoring, with the group of patients operated on for the same reason, only with macroscopic visualization of nerves, without the use of intraoperative neuromonitoring. Surgical procedures in all patients were performed by one very experienced surgeon with over 30 years of work experience, a specialist in general and oncological surgery. All patients were euthyroid, and did not have any disorders in the mobility of the vocal folds in the preoperative laryngoscopic examination.

There was no statistically significant difference p = 0.979 between the study group and the control group in the incidence of recurrent laryngeal nerve damage (4.9% [10/205] vs 4.9% [8/162]). It is worth noting that according to the research conducted by Dralle, neuromonitoring does not reduce the amount of damage to the laryngeal nerves in surgical procedures performed by an experienced surgeon, which is in accordance with the findings of this research study[16].

The results of the research are consistent with the results presented in the literature. Higgins et al., in a meta-analysis evaluating 64,699 recurrent laryngeal nerves, showed no statistically significant difference in the frequency of vocal fold palsy after intraoperative neuromonitoring (3.52% [IONM] vs. 3.12%)[17]. Pisanu et al. analyzed 23,512 patients with a total of 35,513 recurrent laryngeal nerves, obtaining a score of 3.47% of recurrent laryngeal nerve injuries in the group with IONM, compared to 3.67% in the group with macroscopic visualization, which did not show a significant difference[18]. Zheng et al. analyzed 36,487 recurrent laryngeal nerves. In their study, the frequency of vocal fold palsy in patients operated with neuromonitoring was 3.37%, and in patients without IONM, it was 3.76% [19]. Another meta-analysis conducted by Lombardi included 38,820 nerves, and the frequency of vocal fold palsy was 0.73% for the IONM group and 0.89% for the non-IONM20 group, respectively. Similar results, showing no statistically significant difference in the prevention of laryngeal nerve damage in the case of intraoperative neuromonitoring, were obtained in meta-analyzes by other authors, e.g. Sanabria and Malik[21,22].

Contradictory results, showing a significant benefit from the use of intraoperative neuromonitoring were presented by Wong et al. They analyzed only the surgical procedures of a recurrent goiter, retrosternal goiter and thyroid malignant neoplasms[23]. Yang and Bergenfelz, in independent studies, showed a statistically significant difference in the use of IONM to prevent transient vocal fold palsy. They did not observe similar results for persistent palsy[24,25]. Barczyński et al. demonstrated that the use of intraoperative neuromonitoring not only reduces the amount of damage to the recurrent laryngeal nerves, but also reduces the amount of residual gland tissue left, which is of particular importance in the case of neoplastic diseases[26].

Currently, it is recommended to use intraoperative neuromonitoring in high-risk surgical procedures, including a recurrent goiter, toxic goiter, retrosternal goiter, malignant neoplasms, Hashimoto's disease and Graves' disease. In thyroid gland reoperations, the presence of scar tissue and altered anatomy make preparation and nerves identification difficult. The risk of palsy of the vocal folds in reoperation is even 4.6–10.4 times higher than in the case of primary surgery [27]. In the case of surgeries of malignant thyroid neoplasms, nerve damage is more common during cervical lymphadenectomy[28]. In this case, the risk increases even 5 times[27]. Studies by some authors indicate a reduction in the number of RLN palsy after IONM application in high-risk surgical procedures[29–31]. Other authors have not shown such dependencies [32–34].

In this study, the use of intraoperative neuromonitoring (IONM) was carried out in accordance with the guidelines of the International Research Group on Neuromonitoring. The C2-Nerve Monitor by INOMED was used. The highest obtained peak-to-peak amplitude Vpp (mV) in a given stimulation was assessed. Intraoperative loss of neuromonitoring signal was defined as: no EMG signal after stimulation of the recurrent laryngeal nerve and vagus nerve, EMG signal amplitude below 100 μV after stimulation with 2.5 mA for the recurrent laryngeal nerve and 5 mA for the vagus nerve.

Intraoperative loss of neuromonitoring signal was found in 13 cases, out of which in 6 cases it was true and corresponded to paresis of the vocal fold, and in 7 cases it was false, as the mobility of the vocal fold was preserved. Among 192 cases of preserved neuromonitoring signal after thyroid lobe excision, in 188 cases the mobility of the vocal folds was normal, and in 4 cases paresis of the vocal fold was found. Hence, the negative predictive value of the neuromonitoring method was 97.9 and the positive 46.2. Thus, neuromonitoring was characterized by high specificity, but low sensitivity. This is consistent with the results of studies available in the literature[16,32].

It is worth noting that the absent IONM signal did not always correlate with postoperative vocal fold paresis. This was the case in 7 cases (3.41%). In the case of a false positive, the problems with the device on both the stimulating and receiving sides, the lack of a dry operating site and the use of neuromuscular blocking agents should be considered. All situations related to the lack or loss of the signal were checked for the correct placement of the receiving electrode on the tracheal tube in relation to the vocal folds, the correct operation of the device and appropriate stimulation conditions in the operating site.

The most threatening situation is obtaining the correct signal from neuromonitoring with clinical palsy of the vocal folds in the postoperative period. Such false negative results were obtained in 4 cases (1.95%). This situation may occur in the case of stimulation distal from the site of the lesion of the recurrent laryngeal nerve, damage that occurs after the last stimulation, and delayed neuropraxia caused most often by edema [15].

In this study, the analysis of the intraoperative neuromonitoring signal was based on the values of the peak-to-peak amplitude. The mean value of this amplitude obtained after stimulation of the left vagus nerve before lobe resection (0.729 mV) was higher than after lobe resection (0.631 mV). For the left recurrent laryngeal nerve before the lobe resection, the mean values (1.059 mV) were higher than those obtained after the lobe resection (0.960 mV). On the right side, the mean value of the peak-to-peak amplitude of the vagus nerve before lobe resection was higher (0.709 mV) than that obtained after lobe resection (0.510 mV). For the right recurrent laryngeal nerve before the lobe resection, the mean value (1.027 mV) was higher than that obtained after the lobe resection (0.919 mV). The mean peak-to-peak amplitude values were higher for recurrent laryngeal nerves on both sides, and higher for the left vagus and laryngeal nerves. Other research results were presented by Lorenz et al. [35]. They obtained higher peak-to-peak amplitude values for the vagus nerves and higher values for both the vagus and the reccurent laryngeal nerve on the right side[35]. Ozemir et al. obtained lower peak-to-peak amplitude values in diabetic patients, which may indicate the development of diabetic neuropathy in recurrent laryngeal nerves, similar to other peripheral nerves [36].

The differences in peak-to-peak amplitude values among patients may be due to contamination of the operating site, varying degrees of probe-nerve pressure, the presence of surrounding tissues, a different degree of adhesion of the receiving electrode to the vocal folds, or changes in the temperature of the surrounding of the nerve itself after fluid application.

In this study, the duration of the surgery with the use of neuromonitoring was significantly ($p < 0.001$) longer in the study group, and amounted to an average of 96.5 minutes, and 83.2 minutes in the control group. It was connected with the necessity to visualize the vagus nerve running in the sheath of the jugular vessels. Moreover, the time of the procedure was extended by the very use of neuromonitoring (nerve stimulation and the need to record it each time by using the appropriate buttons on the device). The record was taken by an OR nurse, who did not have contact with the patient and was not always in the operating room at that moment. Other authors similarly showed in their research a longer duration of surgery associated with the use of IONM. e. g. Gremillion.[37]. There were no significant differences ($p = 0.771$) in the total hospitalization time of the patients, which was 4.2 days on average. The use of IONM undoubtedly increases the costs of surgery [37,38].

In view of such ambiguous results of research on the improvement of the results of vocal fold palsy surgery with the use of intraoperative neuromonitoring, the study by Chan et al. seems interesting [39] . They noted that the main reason members of the American Society of Endocrine Surgeons use IONM was to protect themselves from legal liability [39] . 150,000 thyroid surgeries are performed annually in the United States of America. In the years 1995–2015, the number of court cases concerning thyroid gland surgery amounted to 128 cases. More than half of the lawsuits were related to a postoperative complication in the form of damage to the recurrent laryngeal nerve. The total cost of hearings and compensation payments amounted to over US $ 30 million. When analyzing the expert opinions, it should be emphasized that the consent obtained from the patient for the surgery must contain information about possible complications in the form of unilateral or bilateral damage to the recurrent laryngeal nerves. It is also necessary to include information on the visualization of the laryngeal nerves in the postoperative report. The issues of the lack of use of intraoperative neuromonitoring were raised, although in the United States of America, as in Poland, it is not a routine procedure used in thyroid surgery [40] .

Summarizing the results of the study, it should be stated that the use of intraoperative neuromonitoring did not reduce the frequency of recurrent laryngeal nerve injuries, compared to macroscopic visualization. For these reasons, it is understandable that IONM is not required to be included in standard medical care and that surgical departments are not required to be equipped with this device. The recent introduction of continuous neuromonitoring may be a significant step forward as it allows the surgeon to react before irreversible nerve damage occurs[41], contrary to intermittent neuromonitoring, which informs us about impaired nerve function, usually after the damage [42]. However, intermittent neuromonitoring, which has been in use for years, has made it possible for medical personnel to prepare for a new method of continuous monitoring of the recurrent laryngeal nerves.

Conclusions

1. Neuromonitoring did not reduce the number of recurrent laryngeal nerve injuries in relation to nerve visualization alone in noncapsular total thyroidectomy for benign nodular goiter performed by the same experienced surgeon.

2. Most of the damage to the recurrent laryngeal nerves is of a persistent nature.

3. Postoperative hypocalcaemia was more frequent in patients operated on with intraoperative neuromonitoring (62.4%), compared to the control group (32.1%).

4. The mean time of the surgical procedure with the use of intraoperative neuromonitoring was on average 96.5 minutes, and was longer than the time of the surgical procedure with only nerve visualization – 83.2 minutes.

5. The mean period of hospitalization of patients undergoing surgery with the use of intraoperative neuromonitoring is similar to the hospitalization of patients operated on without the use of neuromonitoring, averaging 4.2 days.

6. Neuromonitoring is characterized by high specificity (96.4%) and low sensitivity (60%), hence its negative predictive value (97.9%) and low positive value(46.2%).

Declarations

The project was supported under the program of the Minister of Science and Higher Education under the name “Regional Initiative of Excellence” in 2019–2022, project number: 024/RID/2018/19, financing amount: 11.999.000,00 PLN.

Ethics approval and consent to participate

The consent of the Bioethical Committee at the Jan Kochanowski University in Kielce on 22 January 2019 was obtained. (Resolution of the Bioethical Committee No. 12/2019)

Consent for publication

– not applicable

Availability of data materials

– not applicable

Competing interests

– not applicable

Funding

– not applicable

Author’s contributions

– not applicable

Acknowledgements

– not applicable

Author’s information Ethics approval and consent to participate

– not applicable

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Figures

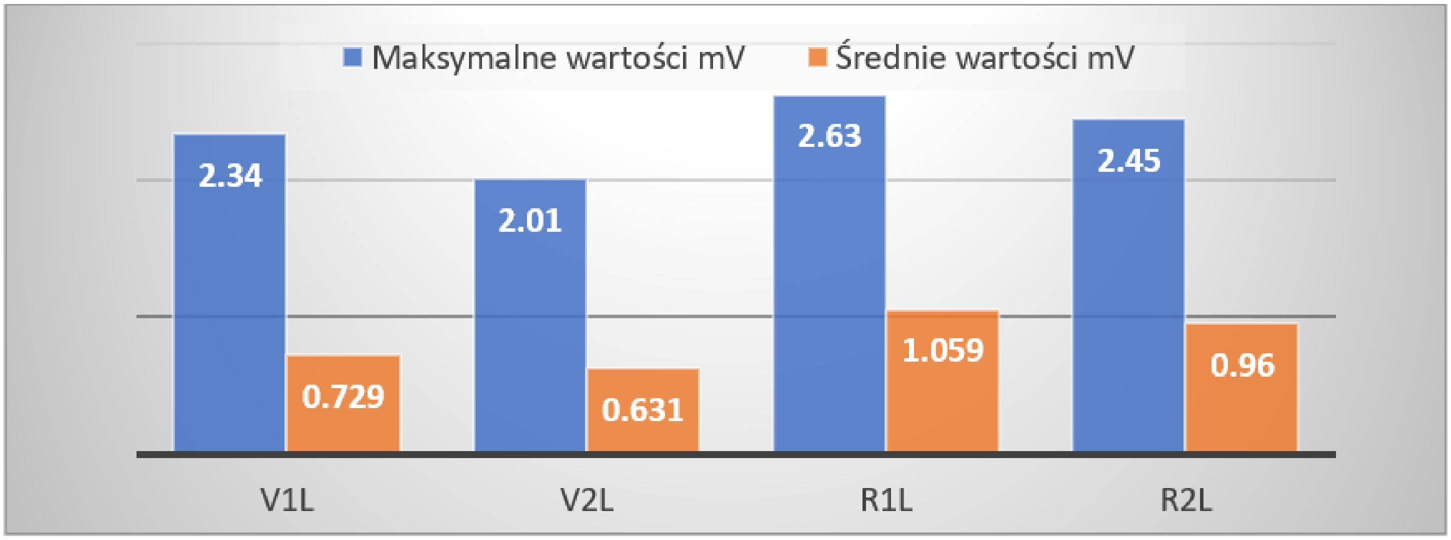

Figure 1

Peak-to-peak amplitude (mV) values for vagus and recurrent laryngeal nerves on the left side.

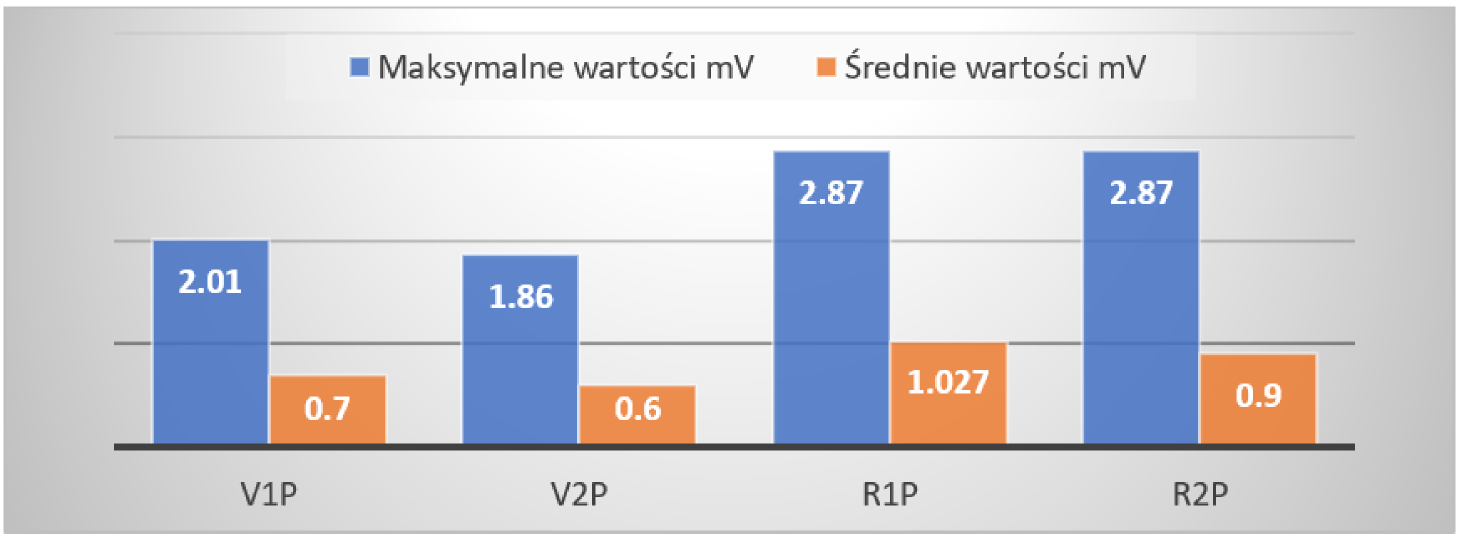

Figure 2

Peak-to-peak amplitude (mV) values for vagus and recurrent laryngeal nerves on the right side.

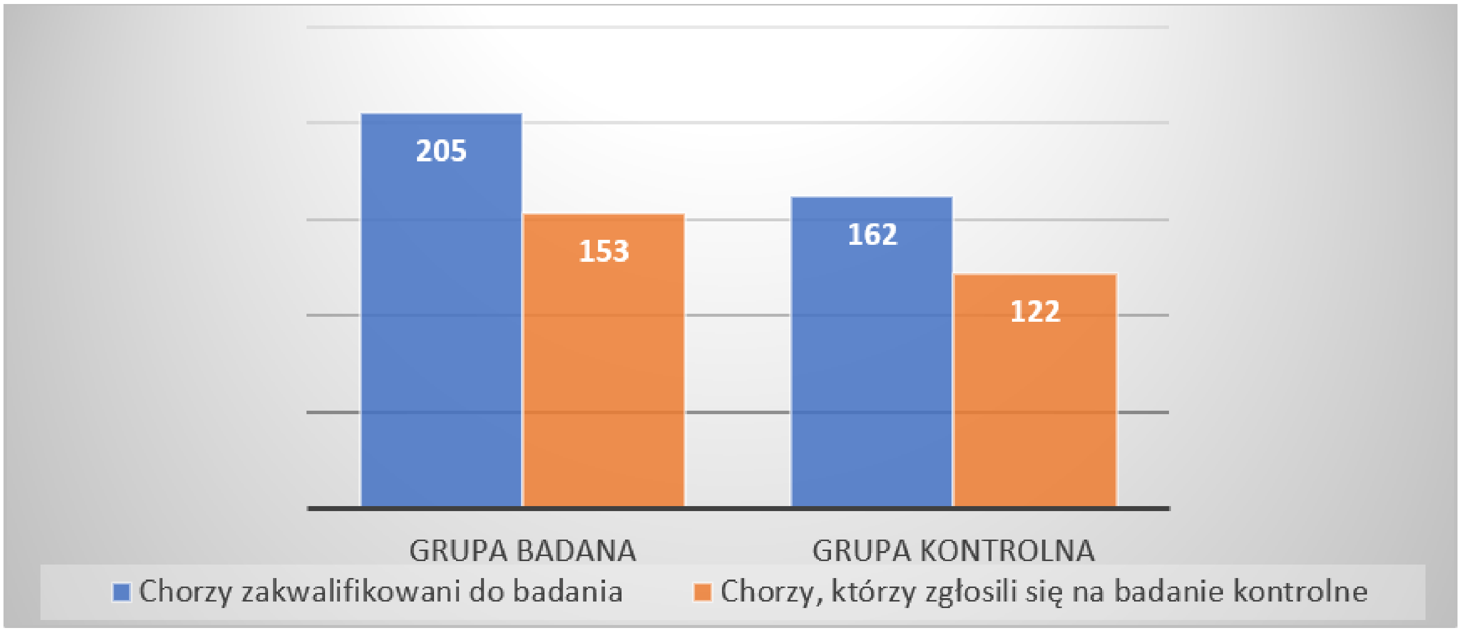

Figure 3

Patients participating in the follow-up examination.