VILNIUS UNIVERSITY

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The Role of Intraoperative Neurostimulation using Laryngeal Palpation and Intraoperative Laryngeal Ultrasound in Optimizing the Safety of Thyroidectomy

SUMMARY OF DOCTORAL DISSERTATION

Biomedical Sciences,
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VILNIAUS UNIVERSITETAS

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Intraoperacinės palpacinės neurostimuliacijos ir intraoperacinės gerklų sonoskopijos reikšmė optimizuojant tiroidektomijos saugumą

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Abbreviations

AR – autoregression
IONM – intraoperative neuromonitoring
LP – laryngeal palpation
LU – laryngeal ultrasound
RLN – recurrent laryngeal nerve
VC – vocal cord

Introduction

According to Loyo et al., the number of thyroid surgical cases in the US is steadily increasing [1]. The annual average of thyroid operations performed in Lithuania is 1500 [2]. Recurrent laryngeal nerve (RLN) palsy is a widely acknowledged complication in thyroid surgery. Incidence rates vary significantly in published literature and are generally accepted as underreported. The reason for this disparity could be attributed to the fact that many studies do not incorporate pre- and postoperative laryngeal examinations in their patient assessments and rely only on voice changes. According to a systematic review published in 2009 by Jeanon et al., which included 27 articles and 25 000 patients, the average incidence of temporary RLN palsy was 9.8% and ranged from 1.4% to 38.4%, whilst the incidence of a permanent RLN palsy ranged from 0% to 18.6% with an average value of 2.3% [3]. Another, more recent French study, published in 2017 by Lifante et al., included 3605 patients and 22 surgeons and showed similar results. The immediate RLN palsy rate demonstrated in this study was 9.3% (ranging from 3.8% to 21.8%), and the permanent RLN palsy rate was 3.1% (ranging from 0% to 9.1%) [4]. Though voice and speech have significant roles in human social life and professional performance, bilateral RLN injury is a particularly pressing concern for a surgeon, as it can inflict such serious ill effects as breathing difficulties, reintubation, tracheostomy or even death. In the case of bilateral RLN injury after thyroid surgery, symptoms can be acute with a need for critical airway management or may worsen after several weeks due to synkinesis caused by aberrant reinnervation [5]. Tracheostomy, as a common procedure in bilateral RLN palsy cases, diminishes the quality of life and even after the removal of a tracheostomy tube – only an incomplete psychosocial recovery is observed [6]. According to the Scandinavian Quality Registry, 0.36% of patients with bilateral thyroid surgery experienced bilateral RLN palsy [7]. A systematic review and meta-analysis published in 2016 by Pardal-Refoyo et al., which included 30 922 patients, demonstrated an incidence of bilateral RLN palsy in the series with neuromonitoring (IONM) to be 0.243% (0.155–0.35%) and without IONM to be 0.518% (0.253–0.87%) [8]. Most surgeons agree that an RLN should be identified in all cases. The superiority of this approach, introduced by Bier from Berlin in 1911 [9], Lahey from Boston in 1938 [10] and Riddell from London in 1956 [11], has been proven by many studies [12-14]. Identifying the functional status of an RLN during thyroidectomy is of a paramount significance, as in most cases, an injured nerve seems visually intact at surgery. Two-staged thyroidectomy remains a topic under discussion, and according to a survey of the French Association of Endocrine Surgeons (AFCE), the majority of surgeons continued the operation on the second side despite a loss of an intraoperative IONM signal [15]. Nevertheless, the majority of authors suggest that according to the IONM results, the surgical strategy should be reconsidered in patients with loss of signal: the operation on the second side can be cancelled, and bilateral nerve injury, with its devastating consequences, avoided [16-22]. Several different techniques, such as finger palpation of the cricoarytenoid muscle or the so-called laryngeal palpation (LP) [23-29], rigid or flexible fiberoptic laryngoscopy [30, 31], intramuscular vocal cord (VC) electrodes and others were used to confirm the response of the RLN to low-voltage stimulation [32, 33]. Electromyographic methods, brought into practice by Flisberg and Lindholm in 1970 [33], are adopted in modern thyroid surgery. IONM has gained general acceptance among thyroid surgeons, with the most common method in use to be a special endotracheal tube with embedded electrodes for electromyographic recordings. Despite the widespread popularity of this technique, disadvantages, such as increased cost, additional setup time, equipment dysfunctions and low sensitivity, as well as positive predictive value, are repeatedly mentioned; also, the possibility of a reliable intraoperative prediction of the RLN functional status or of reducing the RLN injury rate are sometimes seriously doubted [34-36]. A variety of different techniques without electromyographic documentation are less popular. A particular method – VC visualization using laryngeal mask anesthesia with flexible fiberoptic laryngoscopy – causes concern because of the potential loss of control of the airway [30, 31]. An alternative, simple and inexpensive technique of VC mobility evaluation is previously mentioned as the LP method. According to published data, the LP method's sensitivity and specificity for nerve injury detection varies between 33–100% and 92–100%, respectively [23-29], and are comparable to the values of IONM. According to Cavicchi et al., this method has very similar predictive values to IONM [26]. Cha et al. conclude that the LP method might be used to predict VC mobility when IONM is unavailable [29]. Most authors recommend this method for clinical use (Table 1).

The LP method is recommended by the International Neural Monitoring Study Group in the case of EMG activity being either not present or at an unusually low amplitude when using IONM systems [37]. However, it is not still clear if this method is specific and sensitive enough.

Another simple, inexpensive and noninvasive technique of VC mobility evaluation gaining popularity in the perioperative setting is the laryngeal ultrasound (LU) [38-48]. This method was proven as practical and accurate in preoperative and postoperative patient evaluation, but to our knowledge, there was no attempt to assess the feasibility of LU as an intraoperative technique. Keeping in mind such important points as its short learning curve [43], as well as the less invasive and more objective character of the intraoperative LU technique, it could be considered as a good alternative to the LP method. The sensitivity of LU in demonstrating VC palsy ranges from 62% to 93.3%, and specificity – from 97% to 97.8% [39, 44, 45]. Our study was designed to clarify the relationship between real-time VC mobility demonstrated by LU during intraoperative electrical stimulation of the RLN and vagal nerve and postoperative laryngoscopy. We hypothesized that nerve fibers capable of conducting a signal and producing visible muscle contraction on intraoperative LU at the suprathreshold stimulation of the RLN are sufficient for generating volitional VC movement postoperatively. The main disadvantage of LU method is a VC visualization rate. According to recently published data, VC cannot be assessed perioperatively by LU in approximately 20% of cases in general and less so in males

Table 1. The sensitivity and specificity of the LP method.

Publication year	Authors	Country of the study's origin	Study type	Number of patients	Sensitivity	Specificity	Recommendations for application to clinical practice
2018	Cavicchi et al.	Italy	Retrospective cohort	716	90%	99.1%	Recommended
2016	Cha et al.	South Korea	Prospective cohort	293	81.82%	100%	Recommended
2012	Cavicchi et al.	Italy	Prospective double blind RCT	250	33.4%	97.5%	Recommended
2009	Cavicchi et al.	Italy	Retrospective case – control	993	55.3%	95.2%	Recommended
2006	Tomoda et al.	Japan	Prospective cohort	1376	69.3%	99.7%	Questionable
2004	Randolph et al.	USA	Prospective cohort	449	100%	100%	Recommended
2002	Otto et al.	USA	Retrospective cohort	55	75%	92.2%	Recommended

[39, 40, 42, 48-50]. Different solutions are proposed to improve the rate of visualization. Woo et al. introduced a lateral approach [41]. A lateral vertical approach was suggested by Fukuhara et al. [47]. According to data published by Wong et al., the identification of all three sonographic landmarks (true cords, false cords and arytenoids) is not mandatory, as the visualization of normal movement in one of the sonographic landmarks is sufficient to exclude VC palsy [38]. Another objective of this study was to compare the predictive values of the intraoperative LU and LP methods. In both methods, responses can be elicited using a nerve stimulator, avoiding the costs of the disposable special endotracheal tubes used as a recording part of IONM systems.

Different factors for the increased VC palsy rate, such as malignancy, thyroiditis, recurrent disease, RLN identification and the extent of surgery are frequently suggested [14, 51-53]. Another goal of our study was to evaluate such factors as gender, age under or over 55 years, malignant histology, thyroiditis, the weight of a thyroid lobe under or over 100g and dysphonia as predictors for VC palsy.

Acoustic Speech Analysis for Voice Disorders

The literature shows that an altered voice is a common problem after thyroid surgery. The voice changes were reported in 25% to almost 90% of patients within the first few weeks after thyroidectomy [54-58]. It is very important to realize that VC palsy may occur without any voice changes [59, 60]. The majority of endocrine surgeons agree that pre- and particularly postoperative laryngoscopies should be mandatory in all patients undergoing thyroid surgery, as it is the most trustworthy method for determining VC palsy. Despite the reliability of this method, it could be uncomfortable and unpleasant for the patient, adds extra costs, needs special instruments and trained personnel, causes logistic problems [61]. As an alternative to invasive techniques, acoustic signal analysis-based non-invasive techniques were being explored extensively during the last two decades. The idea of applying an acoustical analysis of speech for voice disorder detection and evaluation is not new. Similar ideas were proposed

50–60 years ago [62, 63]. Various acoustic parameters were proposed and employed for this purpose[64]. These include, but are not limited to, the perturbations of fundamental tone [65], various noise estimation techniques [66], cepstral features [67, 68] and others. During the last decade, the task of acoustic signal analysis-based detection and the evaluation of pathological voices was studied intensively. A vast majority of studies focus on combining various features without any physiological reasoning.

The speech signal is generated in two stages. First, the so-called source signal is induced. The air flow generated by the lung causes the vibration of the VC. This vibration is known as the phonation process, and the fundamental frequency value describes its intensity. In the next step, the glottal flow is modulated by the voice tract. The result of this modulation is the speech signal, transmitting information of both the VC and the voice tract resonant properties. The disorders of VC (palsy among them) affect the speech inevitably. The effect depends on the dysfunction degree of the VC and can vary from inaudible changes up to severe changes of voice – for example, it becomes breathy, harsh, and weak. An acoustical analysis of the speech signal is considered to be an objective evaluation of the vocal tract's functionality rather than a perceptual analysis of the speech. Acoustic parameters represent the generative and articulatory properties of the voice and thus could be applied for detecting and evaluating pathologies. Different acoustic parameters describe different stages of the speech signal's production, thus should be chosen reasonably. To estimate the functionality (or immobility) of VC, we have to analyze the glottal flow.

Inverse Filtering Technique

The most common technique for estimating the glottal flow is to employ a source-filter production model. This model describes the speech signal as the convolution of the source signal (glottal flow) and a filter (vocal tract). Both the source signal and the vocal tract can be modelled using various joint estimation models, or separately, by ignoring or considering the close phase of the glottal cycle [69]. If we consider the glottal flow and the vocal tract as independent, the glottal flow can be extracted with an inverse filtering of the speech signal [68, 69]. The inverse filter eliminates the effect of the vocal tract, thus giving the estimate of the glottal flow. The process of inverse filtering can be simplified using linear modelling of the vocal tract. In this study, we applied the autoregression (AR) model for modelling the vocal tract. The choice was due to the following reasons: (1) the AR model (also known as the Linear Predictive Coding model) is an all-pole filter and had great success in speech applications [68, 70, 71]; (2) the linearity of the filter enables us to obtain an inverse version of the filter very easy; (3) the chosen parameter estimation technique enables us to obtain a variable model order, which is adequate to the individual characteristics of human vocal properties. Therefore, we can expect a more accurate estimation of the glottal flow.

Aim of the Study

The main objective of the prospective cohort study *The Role of Intraoperative Neurostimulation using Laryngeal Palpation and Intraoperative Laryngeal Ultrasound in Optimizing the Safety of Thyroidectomy* was to determine the reliability of LP and intraoperative LU methods for evaluating the RLN functional status during thyroid surgery.

The Goals of the Prospective Cohort Study

1. To determine the sensitivity, specificity, accuracy, positive predictive and negative predictive value of the LP method;
2. To assess the validity of the intraoperative LU method; determine the visualization rate, sensitivity, specificity, accuracy, positive predictive and negative predictive value of the intraoperative LU method;
3. To compare the prognostic values of the LP method with the intraoperative LU method;
4. To determine the influence of such factors as gender, age under or over 55 years, malignant histology, the weight of a thyroid lobe

under or over 100g and thyroiditis for VC palsy after thyroidectomy. To determine the significance of dysphonia as a predictor of VC palsy after thyroidectomy;

5. To apply acoustic speech analysis based on the inverse filtering technique to determine the prediction error-based glottal flow assessment criteria for detecting VC palsy.

Novelty of the Study

1. The LU method has never been tested in the intraoperative setting, and the validity of the method was not documented before our study was conducted;
2. As the acoustic speech analysis was applied for the same patients before and after thyroid surgery, in contrast to other studies, the same voices with and without VC palsies were evaluated. The autoregressive, model-based digital inverse filtering technique is presented for the estimation of the glottal flow. The novelty of the proposed method is the objective and adequate selection of a variable model order, which enables us to obtain a more accurate evaluation of individual articulation properties than a fixed-order modelling. This postulates the more accurate estimation of the glottal flow, disturbances of which are direct evidence of VC palsy.

Application in Clinical Practice

Nerve identification alone is insufficient as visual integrity does not guarantee a normal RLN functional status. One of the most significant attributes of neural testing is a prognostication of the postoperative neural function of RLN and its impact on surgical strategy in bilateral thyroid disease. An accurate identification of a unilateral RLN injury might postpone the second lobe surgery, and a bilateral nerve injury can be avoided. We designed this study to evaluate the efficacy of LP and intraoperative LU for the verification of the RLN functional status.

As an alternative to the invasive technique of laryngoscopy, non-invasive, acoustic signal analysis-based techniques were assessed to diagnose postoperative VC palsy.

Statements to be Defended

The following statements stand as those to be defended by this study:

1. LP is an accurate method for evaluating the intraoperative RLN functional status;
2. Intraoperative LU is a feasible and accurate method for evaluating the intraoperative RLN functional status;
3. There is no statistically significant difference between the results obtained by the LP method and the results obtained by the intraoperative LU method;
4. Such factors as gender, age under or over 55 years, malignant histology, the weight of a thyroid lobe under or over 100g and thyroiditis have no statistically proven predictive value for postoperative VC palsy. Postoperative dysphonia is not an accurate predictor of postoperative VC palsy;
5. Prediction error-based glottal flow assessment criteria, developed applying acoustic speech analysis based on the inverse filtering technique, could be used to detect pathological voices in the VC palsy group.

Methods

Patient selection

All patients who underwent thyroid surgery between March 2016 and December 2017 in Vilnius University Hospital Santaros Klinikos were screened for inclusion in this prospective cohort study. The protocol of the study was approved by the Vilnius Regional Bioethics Committee. All patients aged 18 years or older who had had thyroid pathologies and were scheduled for thyroid surgery were eligible. Exclusion criteria were as follows: pregnancy, refusal to participate in the study or a presence of RLN palsy before the surgery.

Study Protocol

All patients before the inclusion into the study underwent preoperative laryngeal examination by indirect or fiberoptic laryngoscopy for VC mobility evaluation. Those patients who had no evidence of RLN palsy were enrolled in the study and underwent thyroid surgery. In all cases, surgeries and all intraoperative tests for RLN functional status evaluation were performed by a single surgeon (A.R.). In order to reduce errors in LU interpretation, the surgeon was additionally trained in the Instructional Course of Transcutaneous Laryngeal Ultrasonography at the first World Congress of Neural Monitoring in Thyroid and Parathyroid Surgery (September 2015, Kraków) held by the International Neural Monitoring Study Group. Intraoperative LP and LU were performed as described below. A voice recording was performed a day before surgery and on the first postoperative day. Laryngoscopy was performed in all patients on the first postoperative day. Follow-up laryngoscopy was reserved for those patients who were diagnosed with VC palsy on the first postoperative laryngeal examination. Follow-up checkups were performed once in every 3 months during the first year after the surgery. If VC palsy was present for more than 1 year, it was considered as permanent RLN palsy.

RLN and Vagus Nerve Stimulation

Both the vagus nerve and RLN were stimulated during LP and LU at the end of the surgery of each side. The nerve stimulator Stimuplex HNS 12 (BBraun, Melsungen, Germany) was used for stimulation with a stimulation current 1mA as suggested by Phelan et al. [72] and a stimulus frequency of 2Hz. No neuromuscular blocking agents were used after the induction of anesthesia. The proper functioning of the neural stimulator was tested in each case on the muscular tissue of the surgical field before direct nerve stimulation. As the international neural monitoring study group has emphasized the importance of vagal nerve stimulation for accurate nerve prognostication, the vagus nerve was dissected and visually identified in all cases [37].

Laryngeal Palpation Technique

For laryngeal palpation, intraoperative neurostimulation was performed as described above, and the functional status of RLN was assessed by palpating the postcricoid region of the larynx, as well as sensing posterior cricoarytenoid muscle contraction, the so-called "laryngeal twitch response" [23] (Fig. 1).

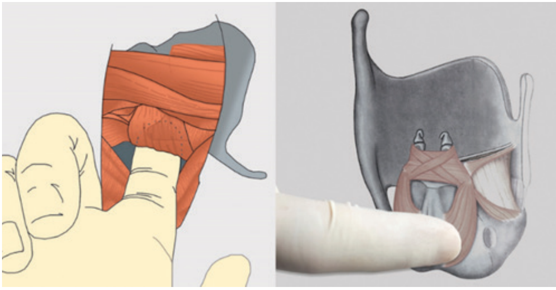


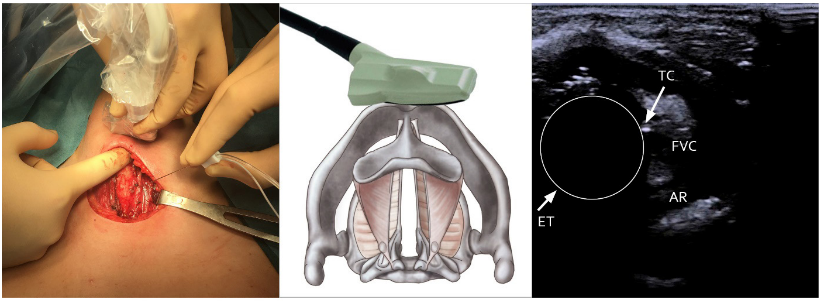
Figure 1. Laryngeal palpation technique.

Laryngeal Ultrasound Technique

Ultrasound system BK Flex Focus 800 8815, 4–10 MHz was used for ultrasound evaluation. The transcutaneous laryngeal ultrasonography technique was adopted for intraoperative use, applying acoustic gel and covering the probe with a sterile sleeve. To improve surface contact, warm, sterile saline was used on the outer surface of the probe cover. Anterior-approach and lateral approach LU were used to increase the assessability rate of VC. The techniques were performed as described elsewhere [40, 41]. Using the anterior-approach, a transducer was placed on the skin above the surgical wound at the middle of the thyroid cartilage (Fig. 2).

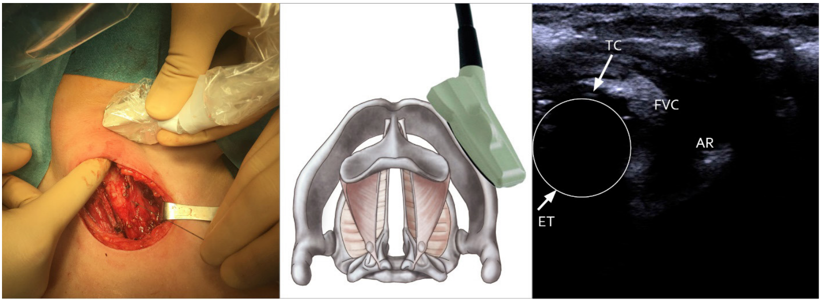
In the case of a lateral-approach, the transducer was placed on the lateral surface of the thyroid cartilage lamina (Fig. 3).

The three most commonly described sonographic landmarks were chosen for ultrasonographic visualization: false cords, true cords, and arytenoids (Fig. 2, Fig. 3). An intraoperative LU examination was defined as assessable if 1 or more landmarks were identified.



AR, Arytenoids; *FC*, false vocal cord;
TC, true vocal cord; *ET*, Endotracheal tube.

Figure 2. Anterior approach laryngeal ultrasound.



AR, Arytenoids; *FC*, false vocal cord;
TC, true vocal cord; *ET*, Endotracheal tube.

Figure 3. Lateral approach laryngeal ultrasound.

The anterior-approach LU was performed first, whereas the lateral-approach LU was performed only when a visualization using anterior-approach technique proved unsuccessful. The observed movement in any of 3 landmarks was considered as sufficient proof of a normal RLN function [38].

Voice Recording and Acoustic Signal Analysis

All the patient voices were recorded using a headset microphone in a quiet clinician's room environment. There were two recording sessions organized: one day before surgery and one day after surgery. The control group consisted of healthy people with no voice complaints.

The voices of ten female and ten male speakers were recorded using the voice recorder with an external microphone in a quiet room environment. The control group voice recordings were used in previous studies of healthy voice analysis. All the recorded persons were asked to pronounce the vowels Y, A, O and U in a sustained manner for 3–4 seconds and cough for three times. The vowel A was chosen for voice acoustic signal analysis, as this vowel is characterized by a minimal lip restriction during the radiation phase and a fully expressed phonation level. Besides, the vowel A is typical for most languages, what makes it universal for comparison purposes. The estimated signal of glottal flow and its spectral density function were analyzed to estimate the qualities of the pathological and healthy voices. The glottal flow was obtained from the voiced speech segments. Considering the source filter approach, the speech signal $s(t)$ was expressed as the convolution of the glottal flow $g(t)$ and the vocal tract filter $h(t)$

$$s(t) = g(t) * h(t).$$

Here, the lip radiation effect (modelled as a first-order differentiating filter) was included in the vocal tract processing and was not considered separately. We obtained an estimate of the inverse vocal tract filter $\hat{h}^{-1}(t)$ and applied it to the analyzed speech signal $s(t)$; in this way, we eliminated the effect of the vocal tract and thus obtained the estimate of the glottal flow.

$$\hat{g}(t) = s(t) * \hat{h}^{-1}(t)$$

In this study, we applied the AR model for the modelling of the vocal tract.

The quality of the estimated glottal flow was assessed on the basis of the ratio of estimated squared prediction error and estimated signal variance $\hat{b}^2/\hat{D}$. The value of $\hat{b}^2/\hat{D}$ indicates the relative part of the unmodelled signal: the higher ratio value we obtain, the higher signal prediction error is. Therefore, we can expect a low $\hat{b}^2/\hat{D}$ value for normal glottal flow and high values for pathological voices (with VC palsy). In this study, we expressed this ratio in percentages and called it the estimated error of glottal flow. For healthy and normal voices, this ratio would approach toward the level of zero, and for pathological voices, it would converge to 100% (in case of the paralysis of VC).

Definitions and Statistical Analysis

The study enrolled 112 patients and 200 nerves at risk.

If both the LU and postoperative laryngoscopy confirmed VC palsy, the case was defined as a true-positive. If both tests refuted VC palsy, the case was defined as a true negative. If movement was observed in any of the three chosen sonographic landmarks on intraoperative LU, but postoperative laryngoscopy had revealed a VC palsy, the case was interpreted as a false negative, and vice versa – if no movement was observed on intraoperative LU, but if postoperative laryngoscopy demonstrated a normal movement of the VC, the case was attributed to the false-positive category. The same principles were equally applied for the LP method interpretation.

Statistical analysis was performed using SPSS v.23 For Windows (SPSS 23, IBM, Armonk, NY, United States of America). The RLN injury incidence calculations were based on the number of the nerves at risk and per patient. The McNemar's test was applied to compare tests sensitivity and specificity. P values indicated the levels of significance. All p values of less than 0.05 were considered to indicate statistical significance. Sensitivity, specificity, positive and negative predictive values, and accuracy were calculated for LU, LP for vagal and RLN stimulation, considering VC palsy diagnosed postoperatively as the target outcome. Predictive values of both methods were calculated based on nerves at risk.

For comparing the difference in the sensitivity and specificity of the LU and LP examinations with postoperative laryngoscopy, the McNemar test was used. The McNemar test is the best test for dichotomous variables with two dependent sample studies. In our case, the McNemar test evaluates the probability that the nerves, damaged during surgery, will be recognized as damaged nerves and normal nerves will be recognized as the normal nerves. To more accurately evaluate the ability of the LU and LP methods to correctly diagnose the state of RLN, we calculated the degrees of association between the real state of the nerves (determined by laryngoscopy) and the results of the state of nerves, obtained using the appropriate techniques of LU and LP, respectively (the value equal to zero corresponds to the complete independence of the variables, and the value equal to one – to maximum association).

The degrees of associations were determined by Cramer's V and Cohen's kappa. Cohen's kappa (calculated on the basis of $\chi 2$) is used to determine the compatibility of the two methods that evaluate the same object or phenomenon. The Cohen's kappa value 1 indicates a complete overlap between the method estimates. The Cohen's kappa applies only if both variables have the same category values and the same number of categories.

To establish the influence of different factors for VC palsy after thyroidectomy, a statistically significant relationship between the related variables was determined using Fisher's Exact Test. The degree of association of variables for the nominal variables was determined using Cramer's V, the Contingency Coefficient and Spearman's rho. All p values of less than 0.05 were considered to indicate statistical significance. The confidence interval (CI) was calculated for a 95% confidence level.

Results

Clinicopathological characteristics

During the research period, we prospectively studied 112 patients with 200 nerves at risk. The statistical used tests confirmed that there were no missing values and all 200 nerves at risk were analyzed. Gender distribution was 20 (18%)/92 (82%), with the male to female ratio being 1:4.6. The age median was 58 years, with a range of 21–81 years and the mean 56.22 years and a standard deviation of 13.57 years. The two most common indications for surgery were suspected malignancy and goiter with compressive symptoms, both of them making up equally 39 cases (35%). Proven malignancy made up 14 cases (12%) (Fig. 4).

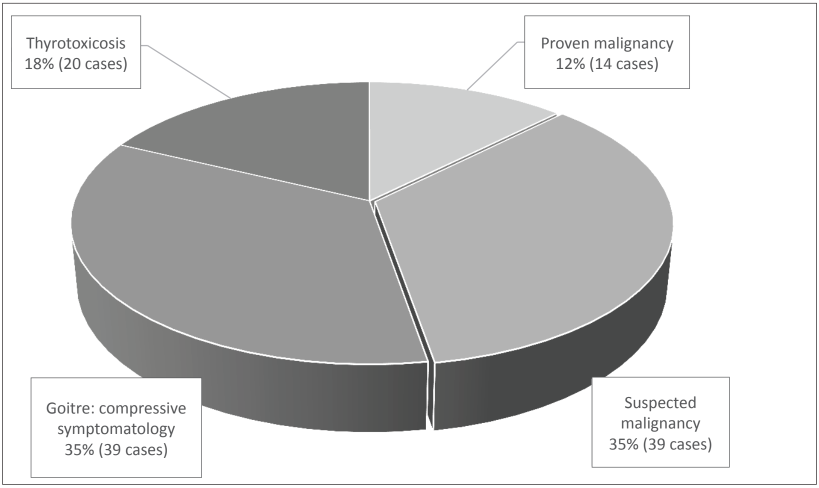


Fig. 4. Indications for surgery.

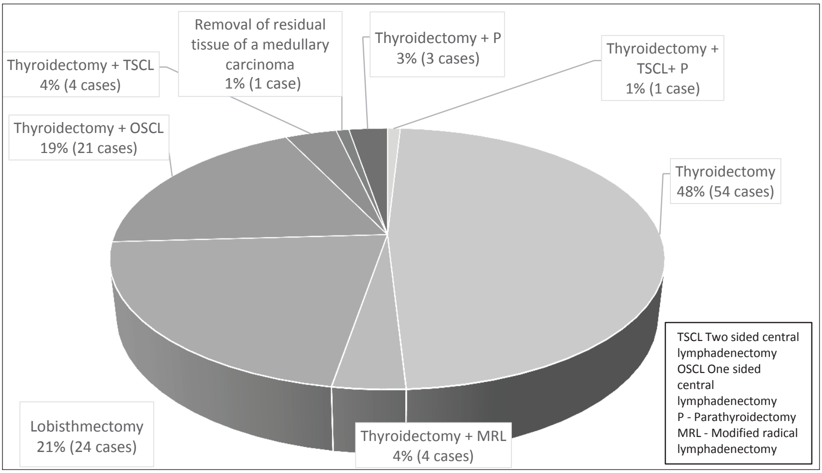


Fig. 5. Types of surgery performed.

The most common operation was a total thyroidectomy, which made up 54 cases (48%); lobisthmectomies made 24 cases (21%) (Fig. 5). There were no subtotal thyroidectomies which could underestimate the RLN palsy rate. Only two operations were reoperative cases, with a removal of residual medullar cancer tissue from the RLN in one of them.

The maximal weight for the right lobe was 371.21g and for the left lobe 409.91 g. Postoperative histological specimen evaluation revealed that 72 (64%) cases were benign and 40 (36%) malignant, and a papillary carcinoma accounted for 32 (29%) cases (Fig. 6).

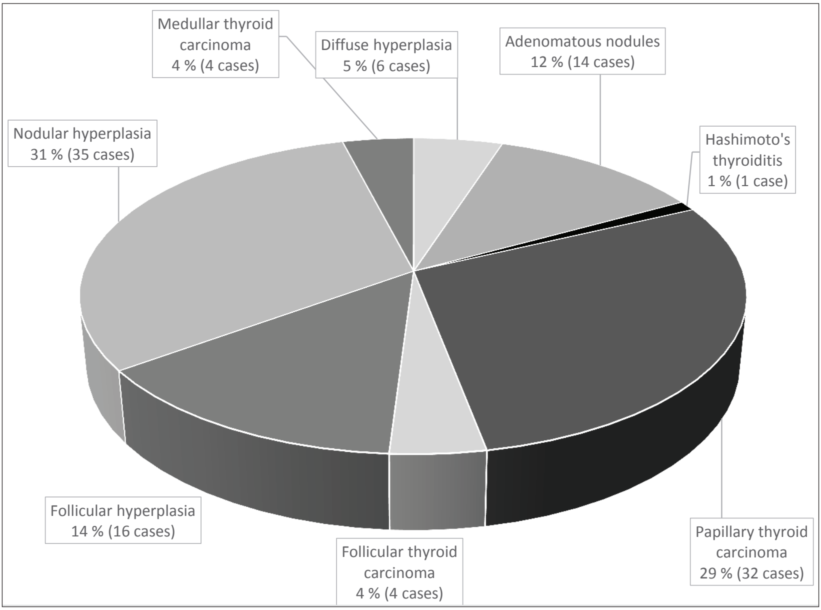


Fig. 6. Pathological diagnosis.

RLN Functional Status Assessment

The RLN and the vagal nerve were successfully dissected and visualized in all cases. Also, in all cases, the RLN and vagal nerve stimulation resulted in the same response. A visualization of at least one of the laryngeal sonographic landmarks by one of the two intraoperative LU techniques was successful in all cases (200 nerves at risk).

In order to meet entry criteria, VC palsy before enrollment into the study was excluded in all 112 patients. A high rate of compliance with the protocol for postoperative laryngoscopy was observed. Day 1 laryngoscopy was performed and documented in all 112 cases (100%). The measurement of the RLN palsy rate based on the number of nerves at risk was 3% and based on the number of patients was 5.4%. (6 cases). Based on consecutive documented laryngoscopic examinations, all 6 VCP patients recovered in 2–9 months during the follow-up period. None of the patients were lost to follow-up.

Using the LP method, the following results were obtained:

- The 6 out of 6 RLN damaged during the surgery were diagnosed correctly;
- The 6 normal RLN were classified as damaged;
- There were no damaged RLN attributed to the normal nerve category.

Using the LU method, the following results were obtained:

- The 5 out of 6 RLN damaged during the surgery were diagnosed correctly;
- The 3 normal RLN were classified as damaged;
- The 1 damaged RLN was attributed to the normal nerve category.

The LP method's sensitivity counted per nerve at risk both in the vagus nerve and the RLN group was 100%, specificity – 96.9%, accuracy – 97%, positive predictive value – 50% and negative predictive value – 100%.

LU method sensitivity counted per nerve at risk both in the vagus nerve and the RLN group was 83.3%, specificity – 98.5%, accuracy – 98%, positive predictive value – 62.5%, negative predictive value – 99.5%.

In the case of LP, the McNemar test showed a statistically significant difference between the quantity of the nerves actually damaged during thyroid surgery and the result obtained using the LP method ($p = 0.031$). There is a significant discrepancy between the two proportions. In other words, there is a large discrepancy between the real number of actually normal and damaged nerves and the number obtained by the LP method. Nevertheless, both the Cramer's V (association coefficient = 0.669) and Cohen's kappa (extent of agreement = 0.653) indicate a strong association between the actual functional state of the nerves and their estimation with the LP method. In both cases, the relationship shown is statistically significant, since the significance level is $p = 0.000$ ($p < 0.05$) (Table 2).

In the case of LU, the McNemar test showed that there was no statistically significant difference between the number of normal and damaged RLN (identified during postoperative laryngoscopic examination) and the normal and damaged nerves determined using intraoperative LU ($p = 0.625$) (there is no significant discrepancy between the two proportions). In other words, the LU method recognizes both damaged and normal nerves reasonably well. Both the Cramer's V (association coefficient = 0.712) and Cohen's kappa (extent of agreement = 0.704) indicate a strong association between the number of actually normal and damaged nerves and the normal and damaged nerves identified by LU method. In both cases, the shown relationship is statistically significant, since the significance level is $p = 0.000$ ($p < 0.05$) (Table 2).

Comparing both the LU and the LP methods, the McNemar test showed that there is no statistically significant difference between the result obtained using the LU method and the result obtained using the LP method ($p = 0.289$). In other words, the results obtained using the LU method are statistically not different from the results obtained using the LP method. However, both the Cramer's V (association coefficient = 0.593) and the Cohen's kappa (extent of agreement = 0.580) shows only the mean association between the results obtained using the LU method and the results obtained using the LP method. In both cases, the relationship shown is statistically significant, since the significance level is $p = 0.000$ ($p < 0.05$) (Table 3).

Table 2. The predictive values of the LP and LU methods.

	McNemar						Cramer's V		Cohen's kappa	
Methods	**p-value (2-sided)**	**Sensitivity**	**Specificity**	**Accuracy**	**Positive predictive value**	**Negative predictive value**	**Value**	**p-value**	**Value**	**p-value**
LU method, RLN stimulation	0.625	83.3%	98.5%	98%	62.5%	99.5%	0.712	0.00	0.704	0.00
LU method, Vagal stimulation	0.625	83.3%	98.5%	98%	62.5%	99.5%	0.712	0.00	0.704	0.00
LP method, RLN stimulation	0.031	100%	96.9%	97%	50%	100%	0.696	0.00	0.653	0.00
LP method, Vagal stimulation	0.031	100%	96.9%	97%	50%	100%	0.696	0.00	0.653	0.00

Table 3. A comparison of the LU and LP methods.

	McNemar	Cramer's V		Cohen's kappa	
Methods	**p-value (2-sided)**	**Value**	**p-value**	**Value**	**p-value**
LU method VS. LP method	0.289	0.593	0.00	0.580	0.00

Such factors as gender, age under or over 55 years, malignant histology, the weight of a thyroid lobe under or over 100g and thyroiditis had no statistically proven predictive value for the VC palsy. The statistically significant dependence was detected only in the analysis of the dependence of the VC palsy from the dysphonia on the first postoperative day ($p = 0.004 < 0.05$). However, association, as shown in association coefficients, is weak. The Cramer's V, is equal to 0.211, $p = 0.003$ (Table 4). Similar coefficients of symmetric dependence are captured and by other variables dependency criteria: Contingency Coefficient = 0.206, $p = 0.003$. Spearman's rho = 0.211, $p = 0.003$.

An odds ratio is calculated for the cohort "Dysphonia = VC palsy." It is equal to 0.392. This shows that when having a dysphonia, the risk to have a VC palsy is 39.2% higher than in the absence of a dysphonia (Table 4).

Voice acoustic signal analysis

Case Analysis

For the analysis of pathological and healthy voices, we have selected two voices for the inverse filtering procedure and the estimation of glottal flow. The estimated signal of glottal flow and its spectral density function were analyzed to estimate the qualities of the pathological and healthy voices. Figure 7 presents the results obtained for the healthy female's voice. The estimated order of the vocal tract filter was 11 (i.e., the vocal tract had 6 resonant frequency values). The estimated glottal flow can be evaluated as periodic and normal

Table 4. The association of different factors with postoperative VC palsy.

Factors	**VC palsy Yes (Cases, %)** ***N=6 (3.0%)***	**VC palsy No (Cases, %)** ***N=194 (97.0%)***	**P – value, two-tailed**	**Association coefficient**	**Odds Ratio**	**Confidence interval 95% Lower; Upper**
Dysphonia: *Yes* *No*	6 (7.3%) 0 (0.0%)	76 (92.7%) 118 (100.0%)	0.004 (Fisher's Exact test)	0.211 (Cramer's V)	0.392	0.329; 0.467
Gender: *Male* *Female*			1.00 (Fisher's Exact test)	0.002 (Cramer's V)	$p \geq 0.05$. There is no statistically significant dependence	
Age group: *<55 years* *≥55 years*			0.697 (Fisher's Exact test)	0.029 (Cramer's V)	$p \geq 0.05$. There is no statistically significant dependence	
Weight of a lobe: *<100 g* *≥100 g*			0.459 (Fisher's Exact test)	0.042 (Cramer's V)	$p \geq 0.05$. There is no statistically significant dependence	
Thyroiditis: *Yes* *No*			0.297 (Fisher's Exact test)	0.070 (Cramer's V)	$p \geq 0.05$. There is no statistically significant dependence	
Cancer: *Yes* *No*			0.408 (Fisher's Exact test)	0.080 (Cramer's V)	$p \geq 0.05$. There is no statistically significant dependence	

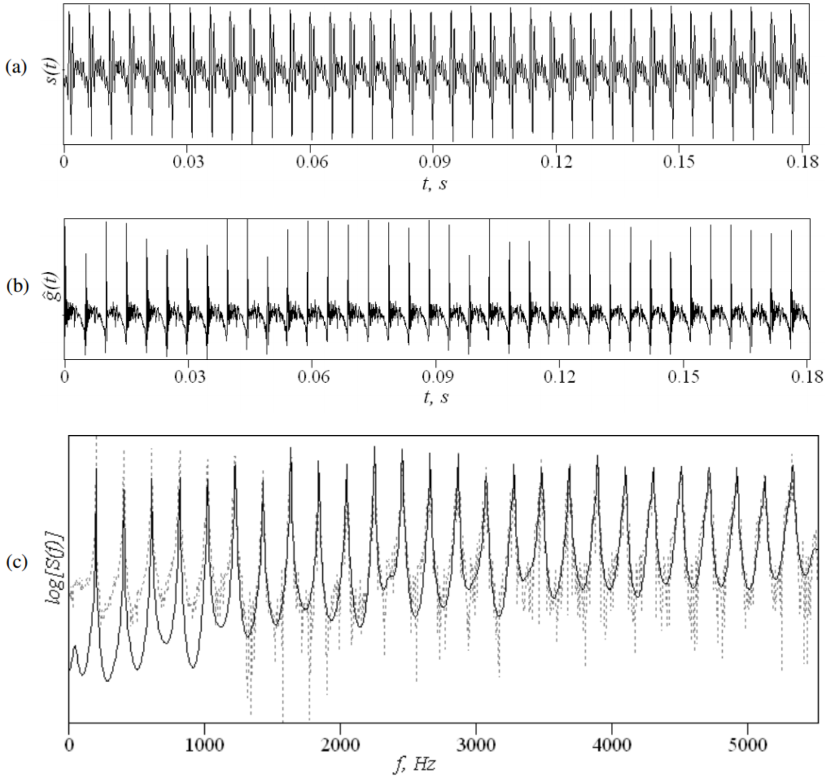


Fig. 7. The healthy voice: (a) the waveform of the vowel A; (b) the estimated glottal flow; (c) the spectral density of the glottal flow (an AR model-based spectral density is given in a solid line, a Fourier transform-based spectral density is given in a dotted line).

(Fig. 7(b)). Spectral density function (Fig. 7(c)) is also periodic, and the harmonic components are vivid through the entire frequency range of the signal. The results of pathological male voice analysis are given in Fig. 8. Here, we can see the distorted waveform of the utterance (Fig. 8(a)). The vocal tract was modelled by the 20th order model, which means ten resonant frequencies of the tract. The estimated glottal (Fig. 8(b)) flow is noisy with no sign of periodicity (what is characteristic for the vocalized vowel). The spectral density (Fig. 8(c)) of the flow

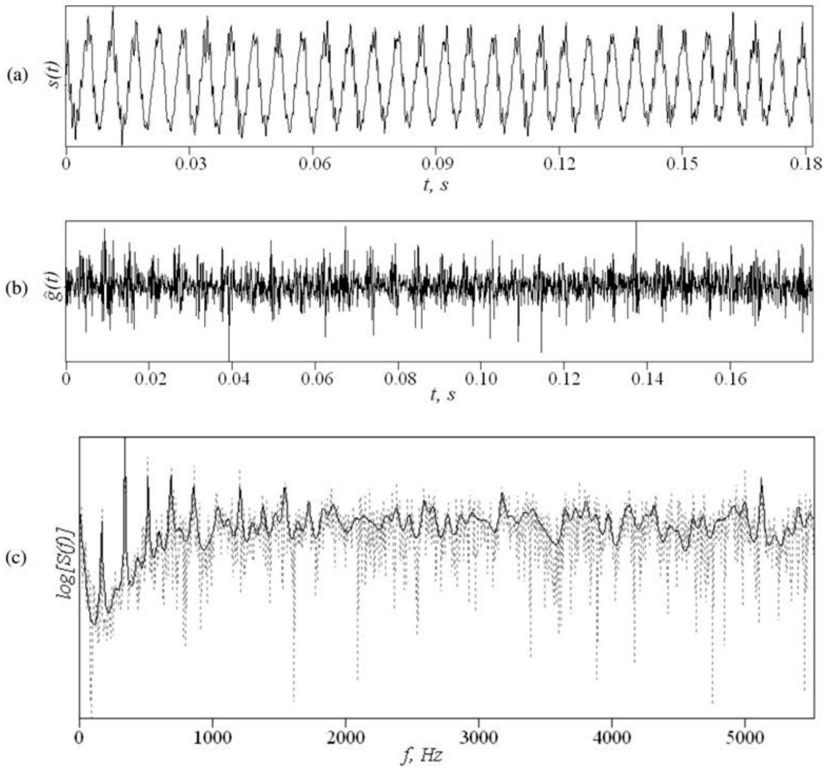


Fig. 8. The pathological voice: (a) the waveform of the vowel A; (b) the estimated glottal flow; (c) the spectral density of the glottal flow (the AR model-based spectral density is given in solid line, Fourier transform-based spectral density is given in dotted line).

is noise-like; here, we can see only 4–5 harmonic components. This is the evidence of VC immobility, which can be the result of the VC palsy. Similar results were obtained for all pathological voices: non-periodicity of the estimated glottal flow, noise-like spectral density function. The degree of non-periodicity was different for the individual voices. This difference may be an individual characteristic of the voices and require a more detailed study with larger datasets.

We evaluated the error level of glottal flow for healthy and pathological voices. The averaged results are given in Fig. 9. We can see the clear difference between healthy and pathological voices. The patients' voices (even before thyroidectomy) have, on average, a 21.7% higher error level than the healthy ones.

The thyroidectomy procedure with the output of the immobility of the VC increased the error level in the same patient on average by 13.5% and by 35.2% in comparison with the control group of normal voices. In the case of the VC palsy in the male patient (1 case assessed in our study), the error level in comparison to preoperative estimate increased by 43.9%. Therefore, the prediction error level of the glottal flow enables us to identify the case of VC palsy.

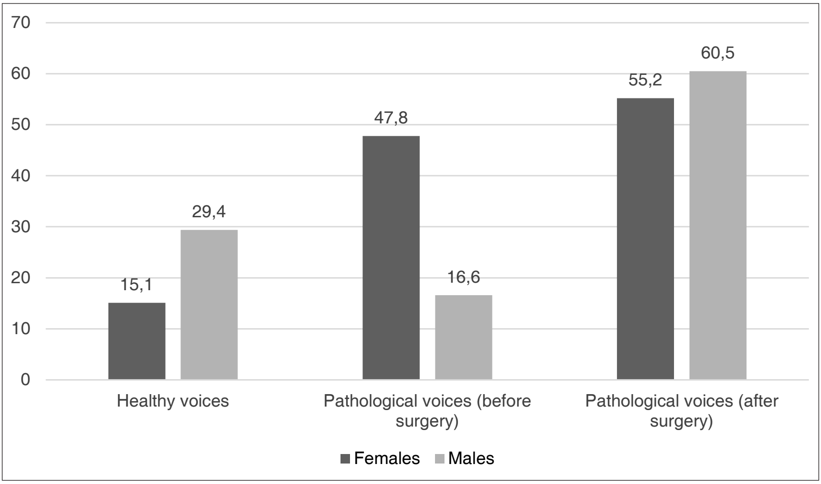


Figure 9. The averaged results for the evaluated error level of glottal flow for healthy and pathological voices.

The individual error levels of glottal flow are given in Table 5.

Table 5. Individual levels of glottal flow.

Patient	Error levels of glottal flow before operation %	Error levels of glottal flow after operation %
Pathological (parethic) voices		
Female 1	38.1	15.6
Female 2	25.7	42.1
Female 3	41.2	60.1
Female 4	69.2	82.1
Female 5	64.8	76.2
Male 1	16.6	60.5
Males (average)	16.6	60.5
Females (average)	47.8	55.2
All (average)	42.6	56.1
Healthy voices		
Males (average)	29.4	-
Females (average)	15.1	-
All (average)	20.9	-

Discussion

Our study demonstrated that LP, as well as the new method – LU, are both effective for evaluating the intraoperative RLN functional status. Nerve identification alone is insufficient because visual integrity does not guarantee a normal RLN functional status [7, 73]. Even when the nerve is visually intact, as few as 11 (3%) of unilaterally and 16 (7%) bilaterally damaged nerves are recognized intraoperatively [7]. In our study, in all 6 cases of VC palsy, RLN seemed visually intact during an operation. In general, only some kind of intraoperative neural testing can be relied on to indicate the function of the RLN, as information on neuropraxic nerve injury is missing through visual assessment alone. Despite different categories of benefit such as RLN identification, tracing the nerve and its branches in a surgical field and even nerve preservation are referred to in the growing body of literature; probably the most significant attribute of neural testing is a prognostication of postoperative neural function and its impact on surgical strategy in bilateral thyroid disease [17-19, 28]. An accurate identification of unilateral RLN injury might prevent second lobe surgery and bilateral nerve injury. Currently, IONM has received considerable attention and has gained popularity, but controversy remains as to whether electromyographic monitoring has any clear advantage in preventing nerve injury and whether it precisely predicts VC function postoperatively [32, 34, 36, 74]. Also, it is clear that the need for specialized neural monitoring equipment increases the surgery costs, and IONM is not used for this reason in some centers [32, 75, 76]. While the LP and LU methods require only a fixed cost of a neural stimulator and an ultrasound machine, electromyography demands additional costs associated with specialized endotracheal tubes. According to Gremillion et al., the use of IONM increases the cost of each surgery by $387 [75]. A cost-utility analysis performed by Rocke et al. suggests that only visual RLN identification in comparison to universal IONM application, can save $683 per patient [76]. Data provided by Dionigi et al. suggest that costs are 5–7% higher using IONM in comparison to traditional thyroidectomy [77]. The precise placement of the endotracheal tube electrodes over the VC requires fiberoptic laryngoscopy. That may add costs of equipment and increase operating time. The application of LP and LU methods adds no extra costs in our experience. According to a systematic appraisal of the literature presented by Dralle et al., the reported sensitivity of IONM for RLN injury is very variable and ranges from 23.5% to 100%. The revealed values of specificity ranged from 94% to 99.7% [78]. More recent data published by Mirallie et al. demonstrated low IONM sensitivity (29%) and high specificity (98%) values for detecting postoperative VC palsy [79]. Randolph et al. presented similar data: the sensitivity of IONM's loss of signal for postoperative VC palsy detection was 33%, and specificity was 99.9% [80]. The results published by Calo et al., on the contrary, showed very high predictive values of IONM: sensitivity was 93.6%, and specificity was 99.4% [22]. In general, the predictive values of IONM are comparable to the same values of the LP method with similar inconsistency in sensitivity. Our study demonstrated high sensitivity values of the LP method. This could be partially explained by the fact of the previous experience of LP method application. Some studies indicate that the LP method is as reliable and sensitive as IONM in predicting RLN functional status or can be used when IONM is unavailable [26, 27, 29]. Dionigi et al. assessed the learning curve of standardized IONM and determined that a safe application of the technique requires the surgeon to perform 50 cases [81]. Pragacz et al. suggest the same number of procedures to achieve comparable outcomes published by referral centers [82]. According to Jonas et al., the learning curve of IONM can last several years [83]. Recent studies described a new technique – the LU – to assess VC mobility and RLN functional status in a preoperative and postoperative setting [38-42, 49, 50]. The learning curve of the transcutaneous laryngeal ultrasound is shorter in comparison to IONM. According to data published by Wong et al., surgeons could master the skill in transcutaneous laryngeal ultrasound after seven examinations and assess VC function consistently and accurately after 40 procedures [43]. With regard to advantages as simplicity, the possibility of use in combination with minimally invasive surgery and the documentation of the real-time VC mobility, we considered that application of LU as an intraoperative technique would be valuable in improving thyroid surgery quality. However, it was never tested in the intraoperative setting, and the validity of the method was not documented before our study was conducted. The results of our study confirmed that intraoperative LU could be used for the intraoperative functional status assessment of RLN with a slightly higher accuracy than the technique of LP. Moreover, intraoperative LU can be a good alternative to LP in confined surgical fields, such as mini-invasive thyroidectomy or parathyroidectomy, when LP is complicated and probably dangerous [26]. The main disadvantage of LU may be the poor VC visualization rate. According to recently published studies, in a perioperative setting, VC cannot be visualized and assessed in approximately 20% of cases [40, 42, 48, 49]. However, we did not face this problem in our study, where the visualization rate was 100%. To increase the VC visualization rate, we used a modified LU technique – a combination of the traditional anterior-approach and the novel lateral approach LU as described by Woo et al. [41]. To achieve further increase in VC visualization rate, the LU examination was defined as assessable even if one out of the three laryngeal sonographic landmarks were identified, as was suggested by Wong et al. [38] Another potential limitation of the new intraoperative LU method is the distortion of normal laryngeal anatomy due to an endotracheal tube position, but our study achieved a 100% visualization rate. Our experience showed that in one case, there was no sensible contraction of the cricoarytenoid muscle, despite this a weak movement was observed on intraoperative LU. We can speculate that remaining nerve fibers after RLN damage would produce only muscular movement on suprathreshold stimulation, and too few of them have been left intact to produce volitional movement on postoperative laryngeal examination. We can presume that any movement observed on intraoperative LU could be a reliable prognostic factor for temporary palsy with a reasonable prospect of recovery. A single surgeon performed all operations in our study, and this fact gives rise to uncertainty as to whether the same results can be reproduced in other studies.

Our study established the association of the VC palsy with the dysphonia on the first postoperative day ($p = 0.004$); however, association, as shown in association coefficients, is weak. We conclude, in agreement with published data, that dysphonia is not a reliable predictor of VC palsy [60, 84].

It is difficult to draw conclusions when dealing with small numbers, and the low rates of RLN palsy may preclude the achievement of the most reliable evidence of LU predictive values.

Prediction error-based global and universal glottal flow assessment criteria for palsy detection cannot be formulated so far. The voice production system is very specific to each speaker, the impact of the surgery is also very specific. Thus, VC mobility should be estimated individually, taking into account individual qualities, comparing preoperative and postoperative voice qualities. The employed AR model parameter estimation technique is capable of describing these individual properties and using a prediction error to monitor the dynamics of VC functionality before and after thyroidectomy; however, the limited case number warrants a more comprehensive study to confirm these findings.

Conclusions

1. The LP method is an accurate method for evaluating the intraoperative RLN functional status. The LP method sensitivity is 100%, specificity – 96.9%, accuracy – 97%, positive predictive value – 50% and negative predictive value – 100%;
2. The intraoperative LU is a feasible and accurate method for evaluating the intraoperative RLN functional status. The visualization rate of the intraoperative LU method is 100%, sensitivity – 83.3%, specificity – 98.5%, accuracy – 98%, positive predictive value – 62.5%, and negative predictive value – 99.5%;
3. Comparing both the LU and the LP methods, the McNemar test showed that there is no statistically significant difference between the results obtained by the LU method and the results obtained by the LP method ($p = 0.289$);
4. Such factors as gender, age under or over 55 years, malignant histology, the weight of a thyroid lobe under or over 100g and thyroiditis had no statistically proven predictive value for VC palsy. The only significant predictor was dysphonia ($p = 0.004$) present on the first postoperative day; however, association, as shown by the association coefficients, is weak (Cramer's V – 0.211, $p = 0.003$).
5. The prediction error level of the glottal flow increased, on average, by 13.5% and up to 43.9% in the case of VC palsy; therefore, the prediction error level of the glottal flow enables us to identify the case of VC palsy. Further comprehensive research is needed to confirm prediction error-based glottal flow assessment criteria.

Practical recommendations

1. Intraoperative neurostimulation should be performed in all bilateral cases;
2. Only after the confirmation of the RLN functional integrity by the presence of muscle response to the nerve stimulation on the first side, an operation should be continued contralaterally;
3. Both the LP and intraoperative LU methods can be used based on the individual preference when IONM is unavailable. In regard to the higher sensitivity of the LP method despite its lower accuracy, LP could be the method of first choice.

Presentations

1. G. Tamulevičius, J. Kaukėnas, A. Rybakovas, "The Evaluation of a Speaker's Individual Qualities Using a High Order Autoregressive Model," Data Analysis Methods for Software Systems, Druskininkai, Lithuania, December 1–3, 2016.
2. A. Rybakovas, V. Beiša, G. Žaldokas, K. Strupas, „Could the Safety of Thyroid Operations be Improved? Assessing the Feasibility of Intraoperative Vocal Cord Ultrasonography in Identifying Vocal Cords Movement and Reducing the Risk of Bilateral Palsy. Data from a Prospective Trial," The 9th Congress of Baltic Association of Surgeons, Klaipėda, Lithuania, May 10–12, 2018.
3. G. Žaldokas, A. Rybakovas, E. Lesinskas, K. Strupas, "The Effectivness of Intraoperative Recurrent Laryngeal Nerve Neurostimulation with Laryngeal Palpation and Vocal Cord Ultrasonography for Predicting Vocal Cord Palsy after Thyroid Surgery," The 7th Baltic Otorhinolaryngology Congress, Riga, Latvia, June 7–9, 2018.

4. A. Rybakovas, V. Beiša, G. Tamulevičius K. Strupas, "Could We Use Intraoperative Vocal Cord Ultrasonography in Identifying Vocal Cord Movements and Reducing the Risk of Bilateral Palsy? Prospective Trial Data," Evoliucinė medicina: sveikata ir ligos besikeičiančioje aplinkoje, Vilnius, Lithuania, June 5–10, 2018.

Publications

1. Andrius Rybakovas, Augustinas Bausys, Andrius Matulevicius, Gytis Zaldokas, Mindaugas Kvietkauskas, Gintautas Tamulevicius, Virgilijus Beisa, Kestutis Strupas. Recurrent laryngeal nerve injury assessment by intraoperative laryngeal ultrasonography: a prospective diagnostic test accuracy study. *Videosurgery and Other Miniinvasive Techniques*, 2018/12/10. DOI: https://doi.org/10.5114/wiitm.2018.80066.

2. Andrius Rybakovas, Virgilijus Beiša, Kestutis Strupas, Jonas Kaukėnas, Gintautas Tamulevičius. Inverse Filtering of Speech Signal for Detection of Vocal Fold Paralysis After Thyroidectomy. *INFORMATICA*, 2018, Vol. 29, No. 1, 91–105. DOI: http://dx.doi.org/10.15388/Informatica.2018.159.

3. Andrius Rybakovas, Andrius Matulevičius, Viktorija Belogorceva, Virgilijus Beiša, Kęstutis Strupas. Laringinė palpacija skydliaukės chirurgijoje: praktinės rekomendacijos, remiantis išsamia literatūros apžvalga ir perspektyviojo kohortinio tyrimo rezultatais (Laryngeal palpation in thyroid surgery: practical recommendations for method integration into daily clinical practice according to a comprehensive literature review and prospective cohort study results). *Lietuvos chirurgija*, Vol. 17 No. 3–4 (2018).

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Qualifications:
Qualification of a Medical Doctor, June 23, 1998.
Qualification of a General Surgeon, June 17, 2002.
Qualification of an Abdominal Surgeon, June 23, 2003.
Certificate of an Endoscopist, July 1, 2003.

Postgraduate Education:
Internship in Medicine at Vilnius University 1997–1998.
Resident in General Surgery at Vilnius University 1998–2002.
Resident of Abdominal Surgery at Vilnius University 2002–2003.
Doctoral (PhD) studies at the Faculty of Medicine of Vilnius University 2014–2018

Work Experience:
Abdominal surgeon, Vilnius University Hospital Santaros Klinikos, Center of Abdominal Surgery, since March, 2013 until the present.

Abdominal surgeon, Department of Abdominal Surgery, Vilnius University Hospital Santariškių klinikos, Central branch (formely Red Cross Hospital) July 1, 2003 – February 28, 2013

Endoscopist, Department of Gastrointestinal Endoscopy, Vilnius University Hospital Santariškių Klinikos Central Branch (formely Red Cross Hospital) July 1, 2003 – February 28, 2013

Physician assistent at Vilnius University Hospital Santariškių Klinikos

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Physician assistent at Department of Gastrointestinal Endoscopy, Vilnius University Hospital Santariškių Klinikos, Central subsidiary (formely Red Cross Hospital) November 2002 – June 2003

Physician assistent at Department of Neurosurgery, St. Jacobs Hospital, Vilnius 1997-2002

Other Clinical Experience in Healthcare:

Nurse, Department of Neurosurgery, St. Jacobs Hospital, Vilnius 1993-1997

Nurse assistant, Vilnius Center of Mental Health, Vilnius 1991-1992

Courses and Clinical attachments:

- 1st World Congress of Neural Monitoring in Thyroid and Parathyroid Surgery and Instructional Courses Kraków, Poland, October17-19, 2015.
- 4th international course of endocrine surgery, intraoperative monitoring of laryngeal nerves in thyroid surgery, Stresa, Italy, July 27 2014..
- Laparoscopic Bariatric surgery course Kaunas, Lithuania April11-12, 2013.
- Laparoscopic Bariatric surgery course Goteborg, Sweden March 14-15, 2013.
- Honorary Observer as Visiting Doctor in Gastrointestinal Surgery, Southapton University Hospital, UK from 4 May until 30 May 2011.
- Laparoscopic Lower GI Surgery Course Cuschieri Skills Centre University of Dundee, UK May 24-27, 2010
- ATLS Courses Vilnius, Lithuania October 8-9, 2010.
- Laparoscopic Upper GI Surgery Course Cuschieri Skills Centre University of Dundee, UK September 22-25 2009

- Honorary Observer as Visiting Doctor in Gastrointestinal Surgery, Southapton University Hospital, UK from 29 April 2008 until 23 May 2008
- European Digestive Surgery Postgraduate Course – Contemporary Surgery of Alimentary Tract (Prof Helmut Friess, Secretary European Digestive Surgery) Kaunas, Lithuania November 9-10, 2007
- Falk Symposium Endoscopy 2006 Update and live demonstration Berlin, Germany May 4-5, 2006
- Gastrointestinal Endoscopy, Vilnius University Hospital Santariškių Klinikos February 24, 2003 – March 8, 2003 and May 5, 2003 - May 17, 2003
- Abdominal Ultrasound, Vilnius University Hospital Santariškių Klinikos February 25, 2002 – February 7, 2002
- Honorary Observer as a Visiting Doctor in Neurosurgery Southampton University Hospital, Wessex Neurological Centre, Department of Neurosurgery, UK August 7, 2000 –August 28, 2000.

Publications:

1. Samalavičius NE, Zdanytė E, Stanaitis J, Radžiūnas G, Rybakovas A, Kairevičiūtė D, Civilka R. Familial adenomatous polyposis in Lithuania : an update. 2-nd Baltic congress of oncology and radiology . 10-12 September, 1998, Riga, Latvia. Abstract book, p. 93.
2. Andrius Rybakovas, Augustinas Bausys, Andrius Matulevicius, Gytis Zaldokas, Mindaugas Kvietkauskas, Gintautas Tamulevicius, Virgilijus Beisa, Kestutis Strupas. Recurrent laryngeal nerve injury assessment by intraoperative laryngeal ultrasonography: a prospective diagnostic test accuracy study. Videosurgery and Other Miniinvasive Techniques, 2018/12/10. DOI: https://doi.org/10.5114/wiitm.2018.80066.

3. Andrius Rybakovas, Virgilijus Beiša, Kestutis Strupas, Jonas Kaukėnas, Gintautas Tamulevičius. Inverse Filtering of Speech Signal for Detection of Vocal Fold Paralysis After Thyroidectomy. INFORMATICA, 2018, Vol. 29, No. 1, 91–105. DOI: http://dx.doi.org/10.15388/Informatica.2018.159.
4. Andrius Rybakovas, Andrius Matulevičius, Viktorija Belogorceva, Virgilijus Beiša, Kęstutis Strupas. Laringinė palpacija skydliaukės chirurgijoje: praktinės rekomendacijos, remiantis išsamia literatūros apžvalga ir perspektyviojo kohortinio tyrimo rezultatais (Laryngeal palpation in thyroid surgery: practical recommendations for method integration into daily clinical practice according to a comprehensive literature review and prospective cohort study results). Lietuvos chirurgija, Vol. 17 No. 3–4 (2018).

Presentations in International Conferences:

1. G. Tamulevičius, J. Kaukėnas, A. Rybakovas, "The Evaluation of a Speaker's Individual Qualities Using a High Order Autoregressive Model," Data Analysis Methods for Software Systems, Druskininkai, Lithuania, December 1–3, 2016.
2. A. Rybakovas, V. Beiša, G. Žaldokas, K. Strupas, „Could the Safety of Thyroid Operations be Improved? Assessing the Feasibility of Intraoperative Vocal Cord Ultrasonography in Identifying Vocal Cords Movement and Reducing the Risk of Bilateral Palsy. Data from a Prospective Trial," The 9th Congress of Baltic Association of Surgeons, Klaipėda, Lithuania, May 10–12, 2018.
3. G. Žaldokas, A. Rybakovas, E. Lesinskas, K. Strupas, "The Effectivness of Intraoperative Recurrent Laryngeal Nerve Neurostimulation with Laryngeal Palpation and Vocal Cord Ultrasonography for Predicting Vocal Cord Palsy after Thyroid Surgery," The 7th Baltic Otorhinolaryngology Congress, Riga, Latvia, June 7–9, 2018.
4. A. Rybakovas, V. Beiša, G. Tamulevičius K. Strupas, "Could We Use Intraoperative Vocal Cord Ultrasonography in Identifying

Vocal Cord Movements and Reducing the Risk of Bilateral Palsy? Prospective Trial Data," Evoliucinė medicina: sveikata ir ligos besikeičiančioje aplinkoje, Vilnius, Lithuania, June 5–10, 2018.

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