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# **Self-assessment of voice outcomes after total thyroidectomy using the Voice Handicap Index questionnaire: results of a prospective multicenter study.**

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## **Abstract**

**Background.** Voice disorders are frequent after thyroidectomy. We report the long-term voice quality outcomes after thyroidectomy using the voice handicap index (VHI) self-questionnaire.

**Methods.** Eight hundred patients who underwent total thyroidectomy between 2014 and 2017 in seven French hospitals were prospectively included. All patients filled in VHI questionnaires, preoperatively and 2 and 6 months after surgery.

**Results.** Median [range] VHI scores were significantly increased at month-2 (4 [0; 108]) compared to preoperative values (2 [0;76]), and were unchanged at month-6 (2 [2;92]). Clinically significant voice impairment (VHI score difference  $\geq 18$  points) was reported in 19.7% at month-2 and 13% at month-6. Thirty-seven (4.6%) had postoperative vocal cord palsy (VCP). In patients with VCP compared to those without, median VHI scores were increased at month-2 (14 [0;107] versus 4 [0;108];  $p=0.0039$ ) but not at month-6 (5 [0;92] versus 2 [0;87];  $p=0.0702$ ). Clinically significant impairment was reported in 38% vs. 19% at month-2 ( $p=0.010$ ), and in 19% vs. 13% at month-6 ( $p=0.310$ ). Thyroid weight, postoperative hypocalcemia, VCP, and absence of intraoperative neuromonitoring utilization were associated with an increased risk of clinically significant self-perceived voice impairment at month-2.

**Conclusion.** Thyroidectomy impairs patients' voice quality perception in patients with and without VCP.

## **Introduction**

Hypoparathyroidism, vocal changes and swallowing impairment are the most frequent and dreaded sequelae after thyroidectomy. As thyroidectomy is the most frequent surgical endocrine procedure performed worldwide, these potential complications may concern a large population of patients<sup>1</sup>. There are many causes of post-thyroidectomy related voice changes. The most common are injuries of the recurrent laryngeal nerve (RLN) or the external branch of the superior laryngeal nerve (EBSLN). Postoperative vocal cord palsy (VCP) rate varies from 0.5% to 20%<sup>2-4</sup>. Damage to the EBSLN may reduce the ability to produce high frequency tones and may induce a hoarse voice<sup>5</sup>. EBSLN injury affects up to 28% of patients after total thyroidectomy <sup>6</sup>. Vocal disturbances may impair quality of life (not only in professional voice users). Consequently, thyroid surgeons know that identification and preservation of both RLN and EBSLN are crucial steps during thyroidectomy.

However, postoperative voice problems are not always nerve damage-related<sup>1,7-9</sup>. Many studies have shown that 25% to 87% of patients complain about voice impairment after thyroidectomy, making post-thyroidectomy voice disorders the most frequent complication following thyroidectomy<sup>1,7,8,10,11</sup>. The rate of post-thyroidectomy voice disorders depends on the time between thyroidectomy and evaluation, the methods used for voice evaluation (patient-reported or objective), and the extent of surgery (lobectomy versus total thyroidectomy)<sup>11,12</sup>. The most often reported symptoms are vocal fatigue and difficulty in high pitch generation particularly during singing <sup>10</sup>. Multiple causes have been mentioned to explain these disorders, such as pain, laryngeal edema, strap muscles division, laryngotracheal fixation, cricothyroid or cricoarytenoid traumas, neural plexus lesions, mucosal changes due to modification in vascularization

or lymphatic drainage of larynx, psychologic postoperative reaction, swelling of the RLN, or endotracheal intubation<sup>1,9,10,13</sup>.

The optimal strategy to detect functional voice changes after thyroidectomy would be noninvasive, inexpensive, and easy to use both in terms of completion by patients and interpretation by surgeons<sup>7</sup>. Many tools already exist to assess voice changes comprehensively; videostroboscopic examination, patient self-evaluation, acoustic analysis, aerodynamic variables<sup>12</sup>. Voice Handicap Index (VHI), a self-questionnaire translated and validated in many languages (including French) remains the most popular and used tool for the evaluation of voice dysfunction<sup>1,12,14</sup>. It is a simple, but efficient and reliable tool which indicates clinically meaningful voice problems<sup>15</sup>. Objective evaluation of laryngeal mobility (vocal cord or videostroboscopic examinations) may differ from subjective evaluation<sup>8,16</sup>. The VHI questionnaires add value to the clinical assessment because their results are independent of acoustic and auditory perceptual measures<sup>14,15</sup>. Moreover, from the patient's point of view, his or her own voice perception is also essential and impacts quality of life more than objective results.

The aim of this study was to evaluate patients' voice self-perception after total thyroidectomy using the VHI questionnaire, and to identify predictive factors of postoperative voice perception impairment.

## **Material and Methods**

From September 2014 to December 2017, patients with benign or non-extensive malignant thyroid diseases, scheduled to undergo total thyroidectomy in seven French referral centers (Angers University Hospital, Limoges University Hospital, Nancy Regional University Hospital, Nantes University Hospital, Pitié-Salpêtrière Hospital

(Paris), South Lyon Hospital Complex, and Vendée Hospital Center (La Roche-sur-Yon)) were prospectively included in this single-arm study. All the centers involved in the study were high-volume centers in thyroid surgery (>150 procedures per year). Exclusion criteria were age under 18 years, pregnancy or breastfeeding, suspected or confirmed medullary thyroid cancer, clinically and/or radiologically enlarged cervical lymph node(s), and preoperative voice disorders with confirmed VCP (using laryngoscopy).

The national committee “Commission Nationale Informatique et Libertés” (CNIL) and local ethics committees, namely “Comité Consultatif sur le Traitement de l’Information en Matière de Recherche” (CCTIRS) and “Groupe Nantais d’Ethique dans le Domaine de la Santé” (GNEDS), approved this study (CNIL #914165; CCTIRS #14.105; GNEDS #2012-06-07). All patients provided signed informed consent before surgery. The study is registered with ClinicalTrials.gov number NCT02167529, as the “Quality of Life After Thyroidectomy (ThyrQoL)” study. Results regarding specifically quality of life have been submitted elsewhere.

## **Procedures**

Surgery was performed under general anesthesia with tracheal intubation. The surgical procedure consisted of extracapsular total thyroidectomy through a collar incision with a midline opening of the fascia. The strap muscles were not cut unless required. Accurate dissection close to thyroid capsule and single ligatures of superior lobe vessels were performed in order to preserve the external branch of superior laryngeal nerve (not routinely identified). RLN were routinely identified and preserved, possibly with the help of intraoperative neuromonitoring (IONM, Medtronic®, Jacksonville, FL, USA), the use of which was left to the surgeon’s choice. Lymph node dissection could be

performed if malignant disease was suspected on frozen section. Drainage was left to the discretion of the surgeons. Replacement therapy with levothyroxine was introduced on the day after surgery, according to each center standard protocol.

### **Outcome variables**

Demographic, clinical, and biological (calcium, TSH) data were prospectively collected during the preoperative period and 2 and 6 months after surgery.

Plasma levels of calcium were measured on the day after surgery. Measurements were repeated if serum calcium was  $<2$  mmol/L (80 mg/L) on postoperative day 2, along with measurement of parathyroid hormone level (PTH). Hypoparathyroidism was defined by postoperative serum calcium  $<2$  mmol/L and requirement for calcium and/or vitamin D supplementation. Hypoparathyroidism was defined as transient if resolved within 6 months after surgery, and permanent if persistent beyond 6 months after surgery.

Pre and postoperative laryngeal examinations were not systematic, but performed only in case of voice abnormality. VCP was defined as transient if solved within 6 months after surgery, and permanent if persistent beyond 6 months after surgery.

### **Subjective voice self-assessment**

Preoperative VHI self-questionnaires were given to the patient during the preoperative consultation and collected at admission for surgery; postoperative VHI self-questionnaires were sent to the patients and returned by mail 2 and 6 months after surgery.

The VHI includes 30 items, each scored on a 5-point scale ranging from “never” (0 point) to “always” (4 points)<sup>17</sup>. VHI score is therefore graded on a total of 120 points. Items are distributed in three 10-item subscales: “emotional” (e), “functional” (f), and “physical” (p) subscales. The higher the VHI score, the more impaired the voice quality is. A difference of 18 points or higher for the total score was considered to be clinically



significant, based on the values reported by Jacobson et al.<sup>17</sup>. Kletzien et al. defined a normal VHI score as <13 points<sup>11</sup>.

### **Statistics**

Variables were described using mean, standard deviation, and 95% confidence interval of the mean for continuous variables, median [first quartile, third quartile, and maximum] for discontinuous variables, and frequencies for qualitative variables.

Comparisons between groups were realized using Student's test for continuous variables, and chi-squared tests (or Fisher's exact test if required) for qualitative variables.

Variations of the VHI total score (between pre-operative visit and months 2 and 6) were modeled using linear models including continuous and qualitative variables as explaining variables. Presence of a large variation of the VHI total score (variation greater or equal to 18 points between pre-operative visit and months 2 or 6) were modeled using logistic models including continuous and qualitative variables as explaining variables.

In these models, all the non-significant variables at 5% were omitted one by one.

ROC curves were constructed using the results of the logistic models.

## **RESULTS**

### **Patient Characteristics and perioperative status**

Eight hundred patients were enrolled and included in the intention-to-treat analysis. Their perioperative characteristics are summarized in Table 1. The most frequent surgical indication was benign nodular goiter (69.5%). Patients with benign goiters underwent operation because of the size of the nodules (> 3cm) or because of symptoms related to goiter. Flow-chart of inclusions is shown in Figure 1.

Seven hundred and ninety-one patients (99%) underwent total thyroidectomy while 9 (1%) had lobectomy, because of IONM signal loss after resection of the first lobe (decision made intraoperatively by the surgeon). Three hundred and seventeen (41%) patients were operated on without IONM and 473 (59.1%) using IONM.

Thirty-seven patients (4.6%) had postoperative VCP; 18 had hypomobility and 19 had immobility (Table 1). At postoperative month 2 and month 6 respectively, 13 and 6 patients remained with VCP (Figure 2). There was no significant difference in postoperative VCP rates between patients operated on with IONM (4.0%) and without IONM (5%) ( $p=0.760$ ). The rates of VCP at 2 and 6 months were also similar in patients operated on with or without IONM.

### **Voice outcomes after surgery**

In total, 748 month-2 questionnaires and 740 month-6 questionnaires were collected. Median VHI scores were significantly higher at postoperative month 2 (4 [0;20;108];  $p<0.0001$ ) compared to preoperative values (2 [0;8;76]) (Table 2, Figure 3) and were unchanged at month 6 (2 [2;11;92];  $p=0.5100$ ) compared to preoperative values. Median VHI scores were also significantly higher at month 2 compared to month 6 ( $p<0.0001$ ).

The differences between preoperative and month-2 and between month-2 and month-6 were statistically significant for all VHI subscales.

At month 2, a clinically significant voice impairment (i.e. total score increase  $\geq 18$  points) was observed in 147 patients (19.7%), while 601 (80.3%) had a  $<18$ -point change. Ninety-five patients (12.8%) had persistent clinically significant voice impairment ( $\geq 18$  points) at month 6.

The comparison of postoperative VHI scores between patients with normal preoperative VHI score (i.e. preoperative VHI  $< 13$  points) and those with impaired preoperative VHI score (i.e. preoperative VHI  $\geq 13$  points) is shown in Table 3. VHI scores remained statistically different at month 2 and at month 6 between these two groups of patients. However, the rates of clinically significant impairment did not differ by preoperative VHI status at month 2 (20% vs. 17%) nor at month 6 (13% vs. 13%).

### **Effects of VCP on voice evolution after surgery**

Median VHI scores were significantly higher in patients with postoperative VCP compared to those without VCP, at postoperative month 2 (14 [0;3;39;107] versus 4 [0;0;20;108];  $p=0.0039$ ) and were not significantly higher at month 6 (5 [0;1;15;92] versus 2 [0;0;10;87];  $p=0.0702$ ).

At month 2, 38% of patients with postoperative VCP described clinically relevant voice impairment ( $\geq 18$  points) versus 19% of those without postoperative VCP ( $p=0.010$ ). At month 6, the difference was no longer statistically significant (19% and 13%, respectively,  $p=0.310$ ).

### **Predictive factors for postoperative voice impairment (VHI rise $\geq 18$ points)**

In univariate analysis, high BMI, increased weight of the thyroid gland, absence of IONM utilization, postoperative hypocalcemia, and postoperative VCP were significantly associated with clinically significant postoperative voice impairment at month 2 (Table 4). In multivariate analysis, thyroid weight, postoperative hypocalcemia, postoperative VCP and absence of IONM utilization were associated with an increased risk of a  $\geq 18$ -point increase in VHI score at month 2 (Table 5).

A VHI score increase at month 2 ( $p < 0.001$ ) was the only factor associated with an increased risk of a  $\geq 18$ -point VHI score increase at month 6 compared to preoperative value (area under the curve: 0.783, Figure 4).

## Discussion

This prospective multicenter study reports significant self-perceived changes in voice quality in patients who underwent total thyroidectomy. Due to the large number of patients, we can assume that these results reflect “real world” post-thyroidectomy course.

In this study, almost 20% of patients estimated that their voice was significantly impaired (VHI rise  $\geq 18$  points) 2 months after thyroidectomy and 12.8% had persistent clinically significant voice impairment at month 6. We confirmed that VCP was an essential predictive factor for postoperative voice impairment - at least when it was documented during selective laryngoscopy. This study provided new data and showed that other factors, such hypocalcemia, thyroid weight, and utilization of IONM were significant risk factors for postoperative voice impairment. VHI score variations observed between the preoperative period and postoperative month-2 was the only predictive factor for VHI impaired score at 6 months. We recently published a series of patients with systematic VHI auto-questionnaire evaluation, focusing on those with normal postoperative vocal cord examination<sup>1</sup>. At month 2, 20.5% of patients had significant voice impairment. At month 6, 5.7% still experienced significant discomfort. However, maybe due to the small sample size (160 patients at month 6), we failed to identify predictive factors for postoperative VHI score rise<sup>1</sup>. In the current study, we showed that about 20% of patients without VCP estimated that their voice was significantly impaired 2 months after surgery. In 13% of the patients, this impairment remained clinically significant at postoperative month 6.

Prior reports showed that voice impairment can persist beyond 6 months after thyroidectomy in up to 25% of patients who do not have objective evidence of vocal

cord paresis or paralysis<sup>15,18</sup>. Literature also reports that, apart from VCP, female sex, age, volume of the resected gland, tobacco consumption, difficulties in intubation, and professional voice users were predictive factor for voice impairment<sup>5,13,19-21</sup>. We acknowledge that we did not evaluate these additional potential factors for voice deterioration such as tobacco consumption, difficulties in endotracheal intubation, or profession. This study data did not confirm that female sex was a predictive factor for voice impairment. However, we described another potentially-important predictive factor, namely IONM use. Because IONM had no impact on postoperative VCP rate, we believe that underlying mechanisms between IONM use and postoperative voice improvement do not imply only RLN preservation. We hypothesize that IONM may have helped surgeons to preserve EBSLN. Because of the absence of videostroboscopic examination, we cannot validate this hypothesis. Lifante et al. have shown that IONM aids in the visualization of the EBSLN and may lead to an improvement in patient voice quality<sup>6</sup>. Furthermore, because IONM allows detecting intraoperatively a RLN dysfunction during thyroidectomy (loss of signal) the surgeon may lower the traction on the nerve resulting in less impact on the nerve function. However, available series never reported that IONM significantly preserves nerve function. We postulate that IONM may help some surgeons to operate more gently and precisely and to better understand nerve function intraoperatively <sup>22</sup>. We did not evaluate experience of surgeons. We did not know if IONM use was correlated to surgeon's experience, which could reduce the impact of IONM. Another important result is the predictive role of hypocalcemia on voice impairment. It is known that hypocalcemia leads to neuromuscular hyper reactivity. We hypothesize that neuromuscular disorders of laryngeal muscles may impair voice. It is also interesting to notice that preoperative voice impairment was not found as a risk factor for postoperative voice impairment.

Clinical research in the area of post-thyroidectomy functional assessment uses videostroboscopic, acoustic, and aerodynamic techniques<sup>15,23</sup>. The VHI questionnaire is included in many assessments and can be useful as a stand-alone screening tool<sup>7,15</sup>. VHI has high predictive values (88% positive predictive value and 97% negative predictive value) for short-term dysphonia<sup>15</sup>. Despite claims that the original description of VHI defined a change of more than 30 points to be clinically significant, no such interpretation was found in the original article<sup>17,24</sup>. Previous investigators have described many different change thresholds to be significant: 8, 12, 13, 15, 18, 20 points<sup>15</sup>. Most studies suggest that differences in VHI scores exceeding 18 points are likely to indicate clinically meaningful voice problems<sup>15</sup>.

We believe that VHI questionnaire has many advantages over objective tools. It is free, simple to complete, and surgeons have negligible influence over patient responses. Moreover, because postoperative visits were usually performed at 3-4 weeks, patients could freely respond at 2 and 6 months, with no “fear” to displease their surgeon. Finally, the level of personal ability to interpret subtle vocal dysfunction is inconsistent among thyroid surgeons. VHI scores do not need an expert to be interpreted. VHI is a practical and reliable questionnaire which allows identifying patients who may benefit from referral to a speech therapist.

We chose 2 and 6 months for VHI evaluation, which is later than in many other studies: 2 weeks for Solomon et al., 1 week and 3 months for Stojadinovic et al.<sup>15,23</sup>. We estimated that early postoperative discomfort has no major impact on quality of life as many patients are in off-work period. Furthermore, premature detection of transient vocal disorders may lead to unnecessary referral to a voice therapist since it is likely to resolve spontaneously.

Deterioration of voice quality is more pronounced after total thyroidectomy than after hemithyroidectomy; therefore, we decided to include only total thyroidectomy<sup>13</sup>.

Since we had no systematic vocal cord examination, nor systematic objective voice evaluation, we did not distinguish between objective and subjective voice disorders. We estimated that subjective ones are the most likely to impair the quality of life of patients.

Despite its large number of included patients, the present study has many limitations. Firstly, not all patients had postoperative laryngoscopy. Patients with a subtly abnormal voice and RLN palsy may not have been identified as VCP patients. The present study did not include a non-thyroidectomy group; therefore, the effect of endotracheal intubation could not be studied. Nevertheless, it has been shown that voice changes are more related to thyroidectomy than to endotracheal intubation<sup>12</sup>.

However, the present study provides additional data regarding post-thyroidectomy patients' self-perception of the voice. Clinically-apparent postoperative VCP, postoperative hypocalcemia, and increased thyroid size (weight) are predictive of an impaired voice quality at postoperative month 2. Absence of IONM utilization was also potentially associated with this finding. These data may help the surgeon clearly inform patients undergoing thyroidectomy about expected vocal outcomes.

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## References

1. Borel F, Christou N, Marret O, et al. Long-term voice quality outcomes after total thyroidectomy: a prospective multicenter study. *Surgery*. 2018;163(4):796-800. doi:10.1016/j.surg.2017.09.023
2. Blanchard C, Pattou F, Brunaud L, et al. Randomized clinical trial of ultrasonic scissors versus conventional haemostasis to compare complications and economics after total thyroidectomy (FOThyr). *BJS Open*. 2017;1(1):2-10. doi:10.1002/bjs5.2
3. Enomoto K, Uchino S, Watanabe S, Enomoto Y, Noguchi S. Recurrent laryngeal nerve palsy during surgery for benign thyroid diseases: Risk factors and outcome analysis. *Surgery*. 2014;155(3):522-528. doi:10.1016/j.surg.2013.11.005
4. Duclos A, Peix J-L, Colin C, et al. Influence of experience on performance of individual surgeons in thyroid surgery: prospective cross sectional multicentre study. *BMJ*. 2012;344:d8041.
5. Wojtczak B, Sutkowski K, Kaliszewski K, et al. Voice quality preservation in thyroid surgery with neuromonitoring. *Endocrine*. 2018;61(2):232-239. doi:10.1007/s12020-018-1614-4
6. Lifante J-C, McGill J, Murry T, Aviv JE, Inabnet WB. A prospective, randomized trial of nerve monitoring of the external branch of the superior laryngeal nerve during thyroidectomy under local/regional anesthesia and IV sedation. *Surgery*. 2009;146(6):1167-1173. doi:10.1016/j.surg.2009.09.023
7. Stojadinovic A, Henry LR, Howard RS, et al. Prospective trial of voice outcomes after thyroidectomy: evaluation of patient-reported and clinician-determined voice assessments in identifying postthyroidectomy dysphonia. *Surgery*. 2008;143(6):732-742. doi:10.1016/j.surg.2007.12.004
8. de Pedro Netto I, Fae A, Vartanian JG, et al. Voice and vocal self-assessment after thyroidectomy. *Head Neck*. 2006;28(12):1106-1114. doi:10.1002/hed.20480
9. Lombardi CP, Raffaelli M, D'Alatri L, et al. Voice and swallowing changes after thyroidectomy in patients without inferior laryngeal nerve injuries. *Surgery*. 2006;140(6):1026-1034. doi:10.1016/j.surg.2006.08.008
10. Sinagra DL, Montesinos MR, Tacchi VA, et al. Voice changes after thyroidectomy without recurrent laryngeal nerve injury. *J Am Coll Surg*. 2004;199(4):556-560. doi:10.1016/j.jamcollsurg.2004.06.020
11. Kletzien H, Macdonald CL, Orne J, et al. Comparison Between Patient-Perceived Voice Changes and Quantitative Voice Measures in the First Postoperative Year After Thyroidectomy: A Secondary Analysis of a Randomized Clinical Trial. *JAMA Otolaryngol-- Head Neck Surg*. 2018;144(11):995-1003. doi:10.1001/jamaoto.2018.0309

12. Papadakis CE, Asimakopoulou P, Proimos E, Perogamvrakis G, Papoutsaki E, Chimona T. Subjective and Objective Voice Assessments After Recurrent Laryngeal Nerve-Preserved Total Thyroidectomy. *J Voice*. 2017;31(4):515.e15-515.e21. doi:10.1016/j.jvoice.2016.12.011
13. Lee MC, Park H, Lee B-C, Lee G-H, Choi IJ. Comparison of quality of life between open and endoscopic thyroidectomy for papillary thyroid cancer. *Head Neck*. 2016;38 Suppl 1:E827-831. doi:10.1002/hed.24108
14. Woisard V, Bodin S, Puech M. [The Voice Handicap Index: impact of the translation in French on the validation]. *Rev Laryngol - Otol - Rhinol*. 2004;125(5):307-312.
15. Solomon NP, Helou LB, Henry LR, et al. Utility of the Voice Handicap Index as an Indicator of Postthyroidectomy Voice Dysfunction. *J Voice*. 2013;27(3):348-354. doi:10.1016/j.jvoice.2012.10.012
16. Lombardi CP, Raffaelli M, De Crea C, et al. Long-term outcome of functional post-thyroidectomy voice and swallowing symptoms. *Surgery*. 2009;146(6):1174-1181. doi:10.1016/j.surg.2009.09.010
17. Jacobson BH, Johnson A, Grywalski C, et al. The Voice Handicap Index (VHI): Development and Validation. *Am J Speech Lang Pathol*. 1997;6(3):66. doi:10.1044/1058-0360.0603.66
18. Pereira JA, Girvent M, Sancho JJ, Parada C, Sitges-Serra A. Prevalence of long-term upper aerodigestive symptoms after uncomplicated bilateral thyroidectomy. *Surgery*. 2003;133(3):318-322. doi:10.1067/msy.2003.58
19. Vicente DA, Solomon NP, Avital I, et al. Voice outcomes after total thyroidectomy, partial thyroidectomy, or non-neck surgery using a prospective multifactorial assessment. *J Am Coll Surg*. 2014;219(1):152-163. doi:10.1016/j.jamcollsurg.2014.03.019
20. Henry LR, Helou LB, Solomon NP, et al. Functional voice outcomes after thyroidectomy: an assessment of the Dysphonia Severity Index (DSI) after thyroidectomy. *Surgery*. 2010;147(6):861-870. doi:10.1016/j.surg.2009.11.017
21. Kim C-S, Park JO, Bae J-S, et al. Long-Lasting Voice-Related Symptoms in Patients Without Vocal Cord Palsy After Thyroidectomy. *World J Surg*. 2018;42(7):2109-2116. doi:10.1007/s00268-017-4438-0
22. Mirallié É, Caillard C, Pattou F, et al. Does intraoperative neuromonitoring of recurrent nerves have an impact on the postoperative palsy rate? Results of a prospective multicenter study. *Surgery*. 2018;163(1):124-129. doi:10.1016/j.surg.2017.03.029
23. Stojadinovic A, Shaha AR, Orlikoff RF, et al. Prospective functional voice assessment in patients undergoing thyroid surgery. *Ann Surg*. 2002;236(6):823-832.

24. Niebudek-Bogusz E, Woznicka E, Zamyslowska-Szmytko E, Sliwinska-Kowalska M. Correlation between Acoustic Parameters and Voice Handicap Index in Dysphonic Teachers. *Folia Phoniatr Logop.* 2010;62(1-2):55-60. doi:10.1159/000239064

**Table 1:** Patients characteristics and perioperative outcomes, n=800

	Characteristics	Value
Patients characteristics	Age at surgery, mean $\pm$ SD (years)	51.15 $\pm$ 13.48
	Gender	
	Male, n (%)	144 (18.0)
	Female, n (%)	656 (82.0)
	Surgical indication	
	Benign nodular goiter, n (%)	556 (69.5)
	Graves' disease, n (%)	112 (14.0)
	Nodule with Bethesda IV cytology, n (%)	54 (6.8)
Surgery	Other <sup>†</sup> , n (%)	78 (9.8)
	Total thyroidectomy, n (%)	791 (98.9)
	Unilateral lobectomy, n (%)	9 (1.1)
	Use of IONM, n (%)	473 (59.1)
	Unilateral IONM loss of signal, n (%)	43 (9.1)
	Associated lymph node dissection, n (%)	88 (11.0)
Histological diagnosis	Associated parathyroid procedure, n (%)	93 (11.6)
	Benign thyroid disease, n (%)	610 (76.3)
	Malignant tumor*, n (%)	190 (23.8)
	Papillary thyroid cancer, n (%)	161 (84.7)
	Vesicular thyroid cancer, n (%)	27 (14.2)
	Other <sup>Δ</sup> , n (%)	9 (4.7)
	Multiple malignant tumors, n (%)	71 (37.4)
	Tumor size <sup>¶</sup> , mean $\pm$ SD (mm)	13.2 $\pm$ 15.4
	N+, n (%)	26 (13.7)
	Associated thyroiditis, n (%)	207 (25.9)
Postoperative outcomes	Thyroid weight, mean $\pm$ SD (g)	43.6 $\pm$ 40
	Immediate postoperative complications	
	Reoperation for hematoma <sup>‡</sup> , n (%)	11 (1.4)
	Transient VCP <sup>§</sup> , n (%)	37 (4.6)
	Transient hypoparathyroidism <sup>‡</sup> , n (%)	87 (10.9)
	Hospital length stay, mean $\pm$ SD (days)	1.88 $\pm$ 3.7
	Long-term postoperative complications	
	Permanent VCP <sup>#</sup> , n (%)	6 (0.8)
	Permanent hypoparathyroidism <sup>§</sup> , n (%)	44 (5.5)

<sup>†</sup> Prophylactic thyroidectomy for familial history of medullary thyroid cancer, iatrogenic dysthyroidism, unspecified

IONM: Intraoperative neuromonitoring;

\* Seven patients had two different tumor types

<sup>Δ</sup> Medullary thyroid cancer (n = 3), Thyroid metastasis (n = 2), Solitary fibrous tumor (n = 1), Thyroid tumor of uncertain malignant potential (n = 1), Thyroid oncocytic tumor (n = 1), Unspecified tumor (n = 1)

¶ Mean tumor size considering the largest tumor

¢ Re-operation for bleeding or compressive hematoma during the first 24 hours postoperatively

VCP: vocal cord palsy

∫ Postoperative VCP solved within 6 months after the surgery

# Postoperative VCP persisting 6 months after the surgery

‡ Hypocalcaemia <2 mmol/L at hospital discharge

§ Need for calcium and/or vitamin D supplements on postoperative month-six

Table 2. VHI subscales and total scores. Values before surgery, 2 and 6 months after surgery (Median [1<sup>st</sup> quartile;3<sup>rd</sup> quartile;maximum])

VHI score	Preoperative, n=782	M 2, n=750	M2 vs. Pre	M 6, n=745	M6 vs. Pre	M6 vs. M2
VHI-f	0 [0;2;23]	1 [0;6;36]	< 0.0001	0 [0;3;29]	0.070	< 0.0001
VHI-e	0 [0;1;31]	3 [0;5;31]	< 0.0001	0 [0;1;33]	0.99	< 0.0001
VHI-p	1 [0;5;33]	3 [0;5;33]	< 0.0001	3 [0;11;38]	0.065	< 0.0001
<b>VHI</b>	<b>2 [0;8;76]</b>	<b>4 [0;20;108]</b>	< 0.0001	<b>2 [2;11;92]</b>	0.51	< 0.0001

VHI-f: Functional subscale of the VHI score

VHI-e: Emotional subscale of the VHI score

VHI-p: Physical subscale of the VHI score

VHI: Voice Handicap Index

Table 3. Outcomes according to initial VHI score.

	<b>Preoperative VHI &lt;13, n=640</b>	<b>Preoperative VHI ≥13, n=142</b>	<b>p value</b>
Preoperative VHI (Median [Min;1 <sup>st</sup> quartile;3 <sup>rd</sup> quartile;Max])	1 [0;0;4;12]	23 [13;18;36;76]	<b>&lt;0.001</b>
VHI month 2 (Median [Min;1 <sup>st</sup> quartile;3 <sup>rd</sup> quartile;Max])	2 [0;0;14;87]	19 [0;9;37;108]	<b>&lt;0.001</b>
VHI month 6 (Median [Min;1 <sup>st</sup> quartile;3 <sup>rd</sup> quartile;Max])	1 [0;0;7;86]	13.5 [0;4;27;92]	<b>&lt;0.001</b>
Patients with ≥18-point increase at month 2, n (%)	128 (20%)	24 (17%)	0.41
Patients with ≥18-point increase at month 6, n (%)	83 (13%)	18 (13%)	0.82

VHI: Voice Handicap Index

Table 4. Comparison of patients with and without significant ( $\geq 18$  points) VHI score increase (preoperative versus month 2). Univariate analysis.

	<18-point VHI increase n=612	$\geq 18$ -point VHI increase n=136	p value
Sex, females (%)	82	81	0.690
Age, years (mean $\pm$ SD)	51.1 $\pm$ 13.5	51.2 $\pm$ 13.5	0.990
BMI, kg/m <sup>2</sup> (mean $\pm$ SD)	25.7 $\pm$ 5.3	27.6 $\pm$ 7.4	<b>&lt;0.0001</b>
Preoperative TSH level, UI/mL (mean $\pm$ SD)	0.90 $\pm$ 0.45	0.88 $\pm$ 0.46	0.510
IONM utilization (%)	63	48	<b>&lt;0.001</b>
Thyroid weight, g (mean $\pm$ SD)	41.7 $\pm$ 35.7	49.7 $\pm$ 40.1	<b>0.011</b>
Postoperative hypocalcemia (%)	9	16	<b>0.024</b>
Postoperative VCP (%)	3	8	<b>0.004</b>
Preoperative VHI score	7.2 $\pm$ 12.0	7.1 $\pm$ 12.4	0.92

BMI: Body Mass Index; IONM: intraoperative neuromonitoring; TSH: thyreostimulin; VCP: vocal cord palsy; VHI: Voice Handicap Index;

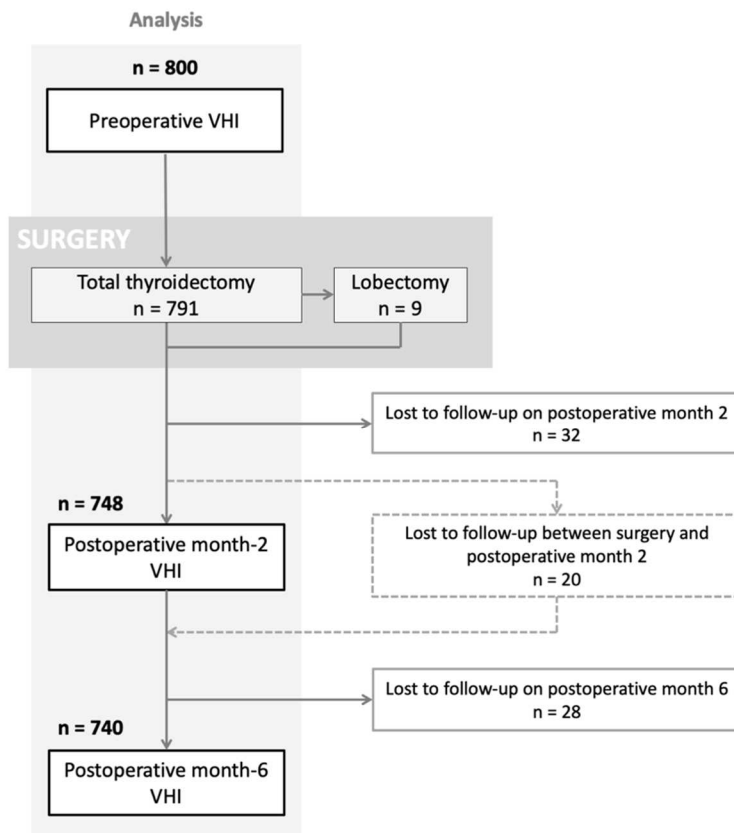
Table 5. Predictive factors for significant VHI score increase at month 2. Multivariate analysis.

	Odds ratio	Standard Deviation	95% Confidence Interval	p value
Thyroid weight	1.005	0.002	1.000; 1.010	<b>0.019</b>
Postoperative hypocalcemia	1.757	0.498	1.007; 3.064	<b>0.047</b>
Postoperative VCP	2.333	0.989	1.016; 5.356	<b>0.046</b>
IONM utilization	0.648	0.130	0.438; 0.961	<b>0.031</b>

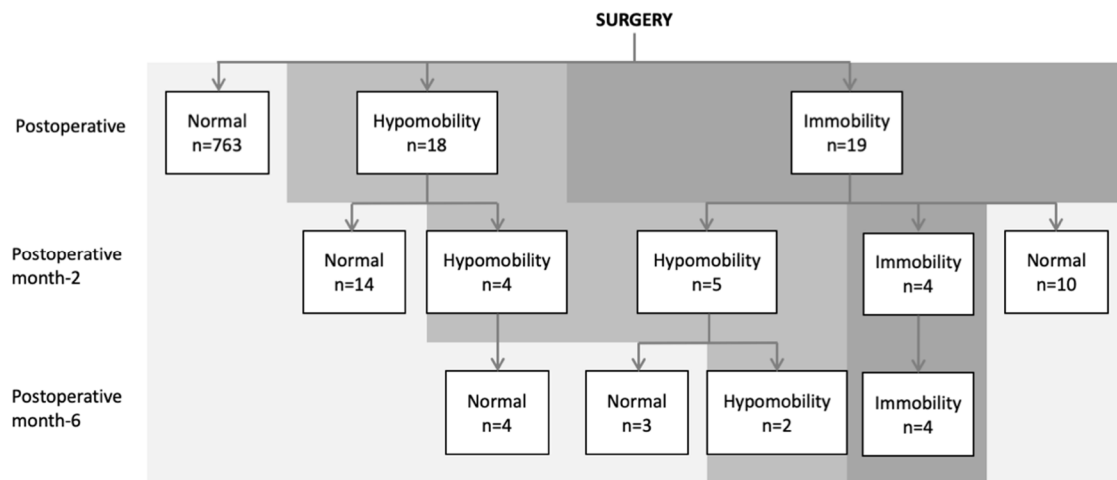
IONM: intraoperative neuromonitoring; VCP: vocal cord palsy; VHI: Voice Handicap Index



**Figure 1:** Flowchart of the trial.



**Figure 2:** Patients with VCP, immediately, and 2 and 6 months after thyroidectomy



**Figure 3:** Evolution of VHI scores before and after thyroidectomy ((Median [1<sup>st</sup> quartile;3<sup>rd</sup> quartile]))

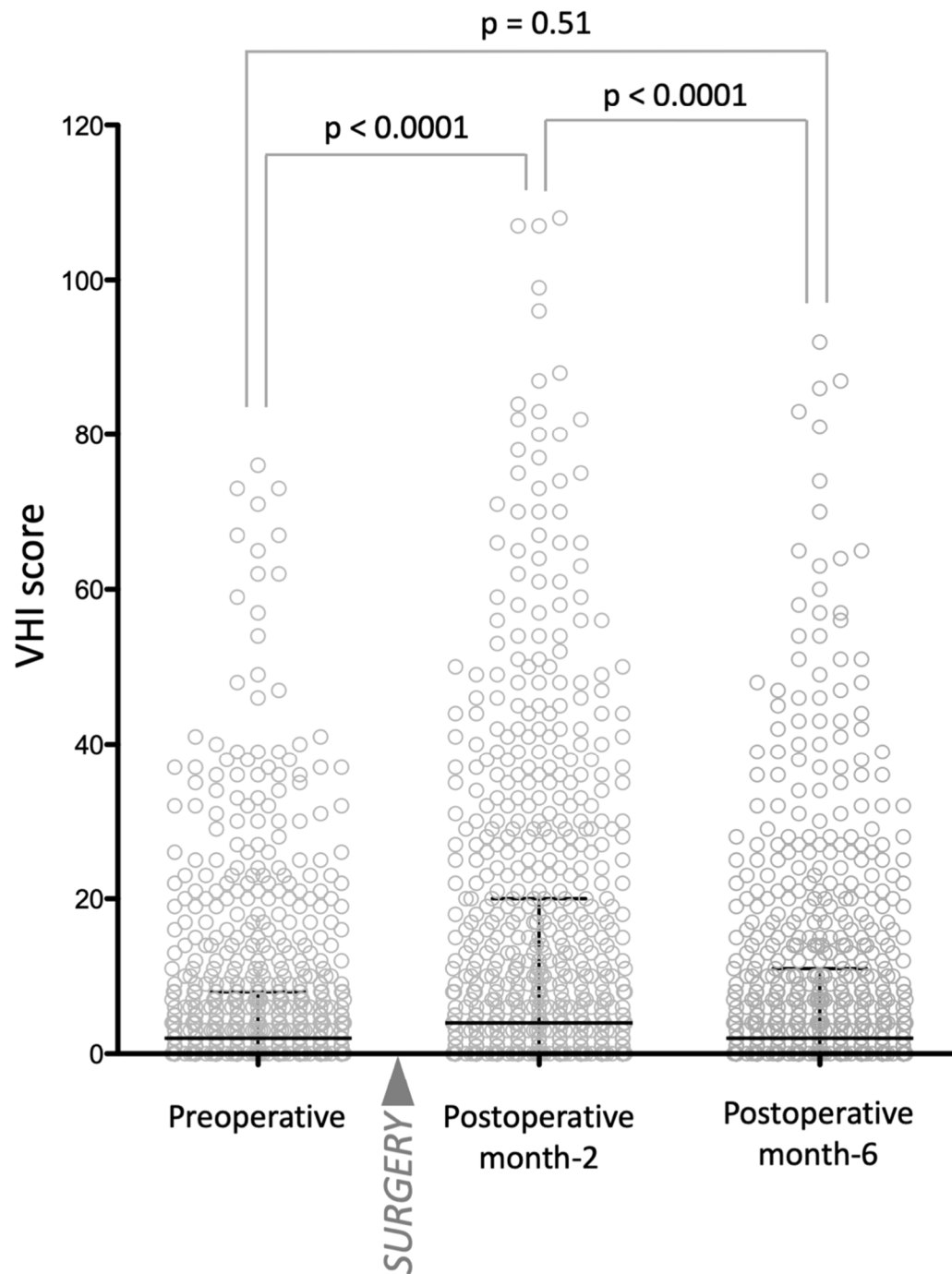


Figure 4. ROC curve using  $\Delta$  pre / month 2 VHI scores for predicting a  $\geq 18$ -point VHI score increase at month 6.

