

# Assessment of voice changes of patients after thyroidectomy without inferior and superior laryngeal nerves injury according to the intraoperative neuromonitoring

A Guillemaud<sup>1</sup>, G Buiret<sup>1a\*</sup>, M Fieux<sup>2</sup>, S Zaouche<sup>2a</sup>, JC Lifante<sup>3</sup>

<sup>1</sup>Service d'ORL et de chirurgie cervicofaciale, Centre Hospitalier de Valence, 179 Boulevard du Maréchal Juin, 26953 Valence, France.

<sup>2</sup>Service d'ORL et de chirurgie cervicofaciale, Centre Hospitalier Lyon Sud, Chemin du Grand Revoyet, 69495 Pierre-Bénite France.

<sup>3</sup>Service de chirurgie viscérale et endocrinienne, Centre Hospitalier Lyon Sud, Chemin du Grand Revoyet, 69495 Pierre-Bénite France.

\*Corresponding Author: G Buiret, Service d'ORL et de chirurgie cervicofaciale, Centre Hospitalier de Valence, 159 Boulevard du Maréchal Juin, 26953 Valence.

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## Abstract

**Objectives:** to assess voice changes of patients after thyroidectomy without inferior and superior laryngeal nerves injury according to the intraoperative neuromonitoring.

**Material and methods:** This monocentric study included all patients who underwent thyroidectomy with laryngeal nerves neuromonitoring between September, 2018 and December, 2019. The voice assessment was performed 1 month before and 3 months after surgery. It was both subjective (with Voice Handicap Index 10 and GRBAS scale) and objective (Dysphonia Severity Index). Voice was considered impaired if there was an increase  $\geq 4$  points of the Voice Handicap Index 10 score or  $\geq 1$  point of the GRBAS scale score or a decrease  $\geq 2$  points of the Dysphonia Severity Index score between the two vocal assessments. A composite score was created, combining both subjective and objective scores. Predictive factors of altered voice were seek.

**Results:** Fifty-nine patients were analyzed. Mean Voice Handicap Index 10 varied from  $3.39 \pm 5.40$  to  $2.90 \pm 5.29$  ( $p = 0.62$ ) before and after the surgery respectively, mean GRBAS from  $0.64 \pm 0.76$  to  $0.73 \pm 0.85$  ( $p = 0.57$ ) and mean Dysphonia Severity Index from  $8.47 \pm 1.15$  to  $8.31 \pm 1.03$  ( $p = 0.42$ ). Voice impairment composite score identified 14 patients with an impaired voice (23.7%). Age  $\geq 65$  years, preoperative Voice Handicap Index 10 score  $\geq 3$  and thyroidectomy past history were independent risk factors of voice impairment.

**Conclusions:** the voice quality 3 months after thyroidectomy was not significantly subjectively and objectively changed compared to before thyroidectomy. When grouping voice impairment scores, age  $\geq 65$  years, preoperative Voice Handicap Index 10 score  $\geq 3$  and thyroidectomy past history were independent risk factors of voice impairment.

**Key words:** thyroidectomy; inferior laryngeal nerve; superior laryngeal nerve; voice quality

## Introduction

In France, 49 477 thyroidectomies were performed in 2014 [1]. The main and specific risk of this procedure is post-operative dysphonia [2]. This procedure may be explained by a lesion of the lower laryngeal nerve resulting in vocal alteration by paralysis of the ipsilateral vocal cord. This complication incidence is estimated between 0 and 18.6% for an average value of 2.3% [3]. In the absence of injury to this nerve, post-operative vocal changes are regularly attributed to damage to the External Branch of the Upper Laryngeal Nerve (EBULN), whose incidence is estimated between 5 and 28% of thyroidectomies [2]. This branch, innervating the cricothyroid muscle, allows the vocal cords to be stretched during phonation. In case of injury, the symptoms described are variable and not specific: limitation or loss of singing voice, vocal weakness, decreased maximum phonation time, reduction of voice strength [4].

It is possible to monitor the laryngeal nerves (neuromonitoring) during the surgery. This tool is reliable. Indeed, the negative predictive value of intraoperative monitoring of lower laryngeal nerves is very high, between 92 and 100% [4]. Thus, a patient operated on from thyroidectomy should not have a post-operative laryngeal paralysis if the electrical signals of these nerves are preserved at the end of the procedure. In addition, this laryngeal monitoring can be used to help identify and preserve EBULN [5, 6]. Stimulation of this nerve branch results in a glottic electrical response in 70 to 80% of cases [7]. However, the correlation between the absence of electrical (lower and upper) laryngeal nerves injury and quality of voice is not absolute and if the laryngeal monitoring allows to know post-operative cordal mobility, it does not guarantee the absence of alteration of the patient's vocal quality. Indeed, other causes of post-thyroidectomy vocal impairment are classically advanced: laryngeal

edema, any other post-intubation complication, muscle lesions (section or resection of an infrahyoid muscle, lesion of one cricothyroid muscle), changes in the vascularization or the lymphatic drainage of the larynx, post-operative pain itself, psychological impact of this surgery or hormonal changes secondary to the thyroidectomy [8].

Few studies focused on the evolution of the voice after thyroidectomy in patients without laryngeal nerve lesion according to neuromonitoring. The main objective of this work was to analyze the evolution of patients' voices after thyroidectomy using subjective and objective tools. The secondary objective of the study was to identify predictive factors of voice impairment when intraoperative electrical responses were normal.

**Methods**

We conducted a single-center descriptive study from September 2018 to December 2019.

*Recruiting*

In the endocrine surgery unit, patients for whom thyroid surgery is scheduled has a consultation with an ENT one month prior to surgery to control laryngeal mobility.

All patients who volunteered during this period to receive a voice recording during this consultation as well as 3 months after surgery were analyzed.

The inclusion criteria were: patients ≥18 years-old, able to read French, and undergoing a thyroidectomy (partial or total, with or without associated recurrent or bilateral lymphadenectomy) with intraoperative monitoring of the lower and upper laryngeal nerves.

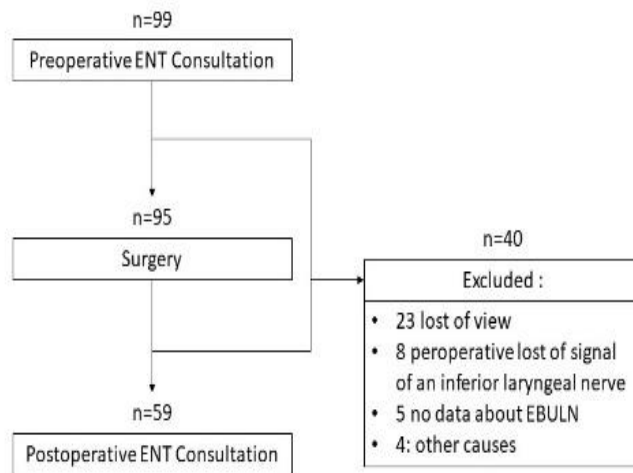
The non-inclusion criteria were: patients with preoperative laryngeal paralysis, an objectified cordal lesion at pre-surgical consultation or for whom an unrelated event interfered with speech-altering surgery occurred between preoperative consultation and surgery.

The exclusion criterion after surgery was the loss of the signal during lower laryngeal stimulation or the absence of a signal from one of the upper laryngeal nerves (true absence or missing signal data).

The study protocol was approved by the institutional review board and was conducted in accordance with the principles of the Declaration of Helsinki. All participants provided written informed consent before inclusion.

*Population*

Ninety-nine patients operated on from thyroid surgery received an ENT consultation with preoperative vocal check-ups. The flowchart of the study is shown in Figure 1. Among the eight patients with a lost of signal at the end of the surgery, only two had finally a laryngeal paralysis, all with thyroid carcinoma.



EBULN: External Branch of the Upper Laryngeal Nerve

**Figure 1.** Flowchart of the study.

The mean age was 54 years ±14. The sex-ratio was 3 women per 1 man, the mean body mass index was 26.05kg/m<sup>2</sup> ± 4.68 and the mean follow-

up time was 4 months. The population characteristics are presented in table 1.

Characteristics	n (%)
Sex:	
Females, n (%)	44 (74.6)
Males	15 (25.4)

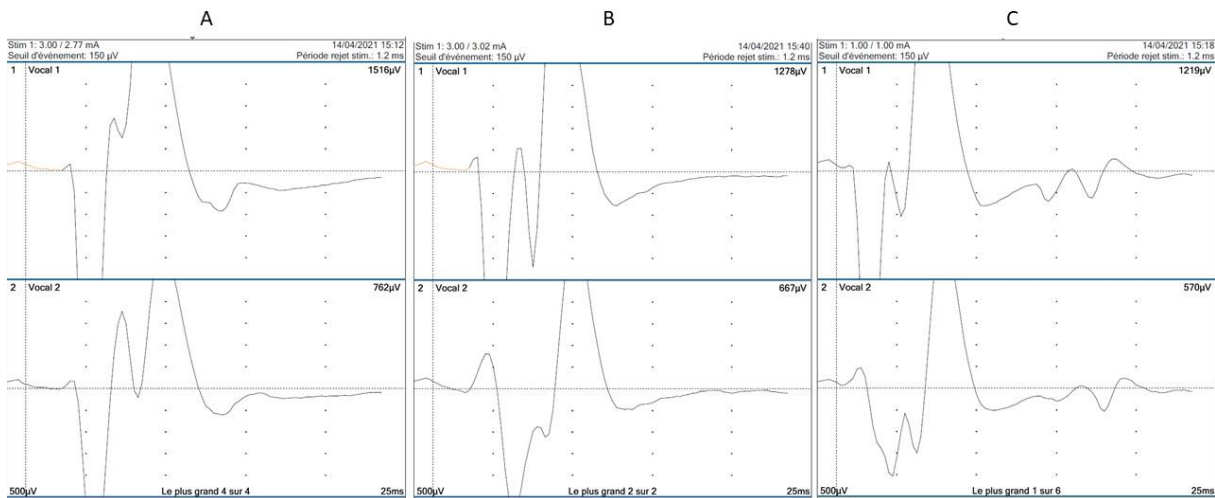
Intensive vocal use at work:	
Yes	34 (57.6)
No	5 (8.5)
No information	20 (33.9)
Smoking:	
Yes	12 (20.3)
No	47 (79.7)
Cervical surgery past history	6 (10.2)
Cause of surgery:	
Basedow	7 (11.9)
Benign nodular goiter	29 (49.2)
Goiter with thyrotoxicosis	7 (11.9)
Suspect nodule	10 (16.9)
Papillary carcinoma	5 (8.5)
Hematocele	1 (1.7)
Type of surgery:	
Total thyroidectomy	36 (61.0)
Lobo-isthmectomy	11 (18.6)
Thyroidectomy and lymphadenectomy	8 (13.6)
Associated muscle resection	
Yes	4 (6.8)
No	55 (93.2)
Associated muscle section:	
Yes	13 (22.0)
No	46 (78.0)
Final pathological diagnosis:	
Benign	40 (67.8)
Malignant	15 (25.4)
Other <sup>a</sup>	4 (6.8)
Iodine therapy:	
Yes	5 (8.5)
No	54 (91.5)

**Table 1.** Population characteristics and perioperative data.

<sup>a</sup> Non-invasive vesicular tumour with papillary-type nuclei (n=3) and thyroid metastasis of a neuroendocrine tumour (n=1).

Nerve monitoring was carried out using Medtronic's NIM-Response 3.0 (Medtronic Xomed, Jacksonville, Florida, USA) in intermittent stimulation. The figure 2 presents the NIM and the expected responses.

*Surgical procedure*



**Figure 2:** Medtronic NIM® and the expected laryngeal responses.

A: stimulation of vagus nerve before the inferior laryngeal nerve dissection; B: stimulation of vagus nerve after the inferior laryngeal nerve dissection; C: stimulation of the superior laryngeal nerve with collection of the signal of the inferior laryngeal nerve

The lower laryngeal nerve in the resected lobe was considered functional at the end of the procedure if it was macroscopically intact and its stimulation direct to 1 mA as well as that at 3 mA of the ipsilateral vagus nerve resulted in a normal-shaped glottic electrical response (biphasic curve), intensity and latency on neuromonitoring. The EBULN was considered functional if its direct stimulation at 1 mA resulted in a glottic electrical response on neuromonitoring or if a contraction of the cricothyroid muscle was observed with the naked eye.

If one of the four nerve branches (bilateral lower and upper laryngeals) was not considered intact, the patient was excluded from the study.

#### Voice assessment

The voice recording allowed subjective and objective analyses of the subjects' voices.

The subjective assessment of the voice was carried out by:

- A auto-assessment questionnaire: the Voice Handicap Index 10 (VHI 10) [9] that the patient had to complete after reading the text "The Wind and the Sun" (Annex 1). The VHI 10, a simplified version of the Voice Handicap Index in 30 questions (VHI 30), is a validated tool that allows the rapid and simple assessment of the quality of the voice and the impact of the voice on the patient's quality of life, as perceived by the patient. It is a questionnaire in 10 questions, from 0 to 4 points for each of them, with a total score ranging from 0 to 40 depending on the vocal discomfort. An asymptomatic patient will have a VHI 10 near 0 while a patient experiencing permanent vocal discomfort will have a score approaching 40.
- An hetero-assessment questionnaire: the GRBAS [10]. This acronym takes 5 characteristics of a voice: its "Grade", its raucous ("Rough"), its veiled character ("Breathy"), its hypotonic aspect ("Asthenic") and conversely its hypertonic, tight character ("Strained"). For each characteristic, its appreciation is between 0 (normal) and 3 (very altered). After reading the adaptation of Aesop's fable, "Boree and the sun", recorded on the PRAAT software (version 6.1.03), two blind investigators who assessed the voice with a full number score between 0 and 15.

The objective assessment of the voice was made by an acoustic recording of the patient's voice. To do so, he/she was first asked to produce a [a] on his normal voice, without forcing, holding this phoneme for as long as possible. Then he/she was asked to perform an upward siren on a [or] few seconds in order to get the most acute voice possible. This recording collected the following data: the mean (Fo) and maximum (Fo-max) fundamental frequency in Hz, the maximum phonation time (MPT) in s, the Jitter (change in the average fundamental frequency on the [a]) in %, the Shimmer (variation of the fundamental intensity of the [a]) in % and the Harmonic/Noise Ratio (HNR). We have also chosen to use the Dysphonia Severity Index (DSI) [11] whose formula is calculated from the objective parameters for the study of the voice:  $DSI = (0.13 \times MPT) - (0.0053 \times Fo\text{-max}) - (0.26 \times k) - (1.18 \times Jitter) - 12.4$ . We chose to use a

constant (k) as a minimum intensity for all patients (k = 50 dB, classically encountered intensity). Indeed, we did not want the possible differences between pre- and postoperative DSI to be correlated only with the variation in intensity-minimum, a highly variable acoustic parameter. A poor quality voice leads to a  $DSI \leq -5$ ; a good quality voice  $\geq +5$ .

All the variables were collected during the preoperative consultation and repeated three months after surgery.

The distribution of patients between normal and impaired voice was achieved after construction of a composite score. The voice was considered impaired if there was an increase of at least 4 points of the VHI 10 and/or an increase of at least 1 point of the GRBAS scale score and/or a decrease of at least 2 points of the DSI.

#### Statistical considerations

Comparisons of means were made using Wilcoxon test based on validation of the conditions of completion.

Comparisons of proportions were made by chi-2 tests.

The identification of predictors of voice quality was made by multivariate logistic regression after verification of the absence of collinearity and the stability of the model. Age was included in categorical form because of a non-linear relationship with voice quality.

A  $p < 0.05$  was considered significant. All statistical analyses were conducted using the R software (v. 3.5.3, [www.r-project.org](http://www.r-project.org)).

## Results

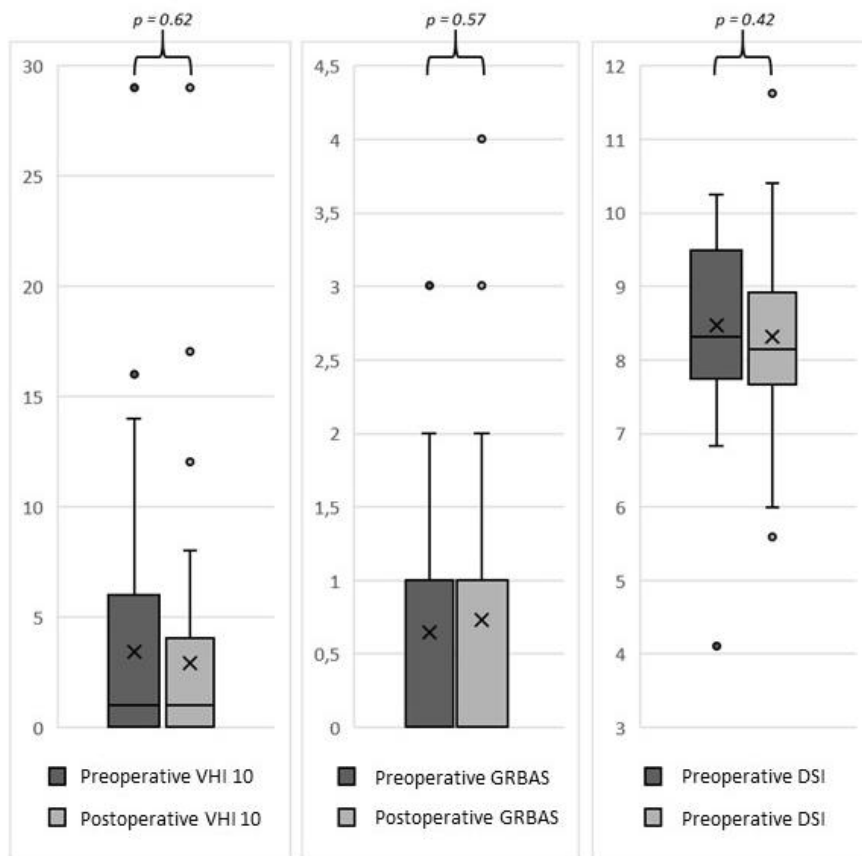
#### Comparisons of voice assessments before/after surgery.

The mean VHI evolved from  $3.39 \pm 5.40$  in preoperative to  $2.90 \pm 5.29$  ( $p=0.62$ ) in postoperative. The mean GRBAS score increased from  $0.64 \pm 0.76$  in preoperative to  $0.73 \pm 0.85$  in postoperative ( $p=0.57$ ). Finally, the mean DSI evolved from  $8.47 \pm 1.15$  before surgery to  $8.31 \pm 1.03$  after ( $p=0.42$ ).

The mean of the postoperative values of the 59 patients with the different acoustic measurements were not significantly different from those preoperative: Fo had evolved from 157.06 Hz to 164.01 ( $p=0.36$ ), the mean Jitter from 0.66 to 0.54% ( $p=0.19$ ), the mean Shimmer from 8.70 to 7.70% ( $p=0.19$ ), the Fo-max from 495.35 to 471.93 Hz ( $p=0.37$ ) and the TMP from 15.56 to 14.19 seconds ( $p=0.19$ ). Only HNR was significantly different in postoperative ( $15.31 \pm 4.52$  dB) compared to its preoperative measure ( $13.62 \pm 4.36$  dB) ( $p=0.04$ ).

The figure 3 represents changes in scores at the VHI10, GRBAS and DSI scales of our population after thyroid surgery.

Of the 59 patients included, 12 patients (20.3%) answered in the affirmative to the question asked during the 3-month post-operative vocal check-up "Is your voice degraded compared to the pre-surgical one?"



**Figure 3.** Evolution of VHI 10, GRBAS and DSI.

*Distribution of patients in altered/unaltered voice groups*

The distribution of patients using the composite vocal impairment score identified 14 patients with an impaired voice (23.7%) three months after surgery. Of these 14 patients, one met all three outcomes (VHI 10, GRBAS and DSI), one patient two of the three criteria (VHI 10 and

GRBAS). The other 12 patients met only one criterion (one patient had an increase VHI 10  $\geq$  2, 10 an increase in GRBAS  $\geq$  2 and finally the last patient had a decrease in his DSI score  $\leq$  2). The characteristics of patients with and without voice impairment objectified by the chosen composite judgment criterion are listed in Table 2.

	Unaltered voice N = 45	Altered voice N = 14	p
Mean age $\pm$ SD (yrs)	52.04 $\pm$ 13.45	61.53 $\pm$ 15.25	<b>0.046</b>
Age by categories (yrs) n (%)			<b>0.047</b>
< 45	15 (33.3)	3 (21.4)	
45 – 55	12 (26.7)	1 (7.1)	
55 – 65	10 (22.2)	2 (14.3)	
> 65	8 (17.8)	8 (57.1)	
Sex			0.483
Females	32 (71.1)	12 (85.7)	
Males	13 (28.9)	2 (14.3)	
Body mass index (kg/m <sup>2</sup> )			0.717
< 25	19 (42.2)	8 (57.1)	
$\geq$ 25 and < 30	18 (40.0)	4 (28.6)	
$\geq$ 30	8 (17.8)	2 (14.3)	
Intensive vocal use at work:			0.563
Yes	27 (84.4)	7 (100.0)	
No	5 (15.6)	0 (0.0)	
Smoking:			0.052
Yes	12 (26.7)	0 (0.0)	
No	33 (73.3)	14 (100.0)	
Mean preoperative VHI 10 $\pm$ SD	2.24 $\pm$ 3.80	7.07 $\pm$ 7.89	<b>0.014</b>

Mean postoperative VHI 10 ± SD	1.44 ± 2.48	7.57 ± 8.56	<b>0.003</b>
Mean preoperative GRBAS ± SD	0.71 ± 0.73	0.43 ± 0.85	0.088
Mean postoperative GRBAS ± SD	0.49 ± 0.66	1.50 ± 0.94	<b>&lt; 0.001</b>
Mean preoperative DSI ± SD	8.37 ± 1.13	8.77 ± 1.22	0.392
Mean postoperative DSI ± SD	8.42 ± 1.01	7.95 ± 1.02	0.129
Postoperative Fo-max (Hz) ± SD	490.47 ± 145.52	412.35 ± 118.19	0.06
High preoperative VHI 10 (≥3) n (%):			<b>0.007</b>
Yes	12 (26.7)	10 (71.4)	
No	33 (73.3)	4 (29.6)	
High preoperative GRBAS (≥1) n (%):			0.109
Yes	26 (57.8)	4 (28.6)	
No	19 (42.2)	10 (71.4)	
Voice Fatigue			<b>0.008</b>
Yes	6 (13.3)	7 (50.0)	
No	39 (86.7)	7 (50.0)	
« Has your voice deteriorated?»			<b>&lt; 0.001</b>
Yes	3 (6.7)	9 (64.3)	
No	42 (93.3)	5 (35.7)	

**Table 2.** Comparison of populations "Unaltered Voice" and "Altered Voice" according to the composite judgment criterion.

SD: standard deviation

The other acoustic variables studied did not show a significant difference between the two groups (Fo, Jitter, Shimmer, MPT).

The surgical history, surgical indication, type of surgery, size of the larger thyroid nodule, resection or section of infra-hyoid muscles, pathological analysis and follow-up duration were not significantly different between the "unaltered voice" and "impaired" group.

Of the 59 patients included, 12 patients (20.3%) answering in the affirmative to the question asked during the 3-month post-operative vocal check-up "Is your voice degraded compared to the pre-surgical one?", 9 (75.0%) voice impairment objectified by the composite judgment test chosen in this work. The only patient with an alteration of his voice objectified by all the elements of the composite judgment criterion did not complain of having a "degraded" voice at 3 months of surgery compared to his preoperative voice.

In the group of patients who answered negatively to the question "Is your voice degraded compared to pre-surgical?", 5 (10.6%) of these 47 patients had vocal impairment using our composite endpoint as an endpoint. Thus, between these two groups, the difference in vocal alterations highlighted by the composite judging criterion was significant ( $p < 0.001$ ).

#### *Multivariate determination of predictive factors of altered/unaltered voice*

Table 3 shows the results of the multivariate logistic regression model performed with age, sex, body mass index, preoperative VHI 10 score in categorical form, and type of surgery. Age  $\geq 65$  (Odds ratio (OR): 17,4; 95% Confidence Interval (IC) [1,6; 560,0],  $p=0.04$ ), preoperative VHI  $\geq 3$  (OR: 9,5; IC [1,9; 66,4],  $p=0.011$ ) and thyroid re-intervention (OR: 75,8; IC [2,1;9777,8],  $p=0.037$ ) therefore emerged in our population as significant independent risk factors for vocal impairment.

## Discussion

Our subjective and objective study of the voice showed that the vocal quality at 3 months of thyroid surgery with a complete neuromonitoring response at the end of the surgery was not significantly impaired compared to the preoperative situation. Our composite judgment criterion identified 14 patients (23.7%) vocal impairment after surgery. The three independent risk factors for postoperative vocal impairment identified in our work were age  $\geq 65$  years, AHI 10  $\geq 3$  in preoperative and thyroid reintervention.

Very few studies presented results with intraoperative monitoring of lower and upper laryngeal nerves in such a population with subjective and objective evaluation criteria [12-14]. Grouping three scores including subjective and objective evaluation variables allowed us to prioritize sensitivity to specificity. The vocal degradation might therefore be overestimated allowing us to identify patients with an altered voice, whereas it was considered to be of good quality by the averages at VHI 10, GRBAS and DSI scores analyzed separately. Among the risk factors identified in our model, age was also described by Sahli et al. [15], as well as thyroid reintervention [16]. Calcifications of laryngeal cartilage, alteration of the laryngeal lining, or atrophy of laryngeal muscles accompanying aging have all been suggestions advanced to explain that age is an independent risk factor for vocal impairment after thyroid surgery [17]. Other studies have shown that sex, body mass index, lack of use of laryngeal neuromonitoring, thyroid tumor size, thyroid gland weight or postoperative hypocalcemia were risk factors for altering vocal quality at a distance from surgery [18, 19], which we did not find in our work.

According to our composite score, 14 patients (23.7%) had altered their voices at 3 months of their thyroid surgery, which is classically found at a distance from thyroid surgery [2, 20]. However, unlike these studies, these vocal changes did not appear to be possible to be attributed to lesions of the lower or higher laryngeal nerves. To explain this large number of patients with altered voices but functional nerves according to the neuromonitoring, several reasons could be put forward (that can be limitations of our study). The combination of subjective and objective variables to detect impaired voices further improved sensitivity, compared to other studies using only subjective evaluation criteria may be one possible explanation [2, 8, 12, 13]. The short time between surgery and postoperative ENT evaluation at 3 months also overestimated the percentage of post-thyroid vocal impairment. This interval had been retained in order to minimize the number of patients lost of view. In addition, selection bias related to the inclusion of surgically operated patients in a referral hospital could explain this high percentage of impaired voices. Indeed, the preoperative mean VHI 10 was measured at 3.39, knowing that a normal VHI 10 according to the scientific literature is less than 2.83 [21]. However, we have shown that a preoperative VHI 10  $\geq 3$  was a risk factor of vocal impairment. Thus our population did not have a voice considered normal in preoperative. Finally, the method of assessing the functional integrity of EBULN could be discussed. The

electromyography of the cricothyroid muscle is the gold standard to ensure the proper functioning of the ipsilateral EBULN. However, this difficult-to-access technique is invasive and EBULN neuromonitoring at 1 mA, according to the scientific literature, is reliable for highlighting a complete nerve injury [7, 22]. But enough for a slight impairment?

No significant differences were found between the acoustic data before and after surgery other than an increase of HNR. This increase would even suggest an improvement in the patient's voice. Other studies have found alterations in Fo, Fo-max, Shimmer, MPT or but none monitored the EBULN [23, 24]. Thus, these acoustic changes could be attributed to damage to this nerve branch [25, 26]. The Engelsman et al. study monitoring the lower and upper laryngeal nerves did not object to any significant difference between the different acoustic parameters studied [14].

The perspective of this study is to find out if the voice impairment is linked with an EBULN injury that can't be seen with the neuromonitoring or with another reason. Performing a perioperative electromyography of the cricothyroid muscle is too difficult but the technological improvement of the NIM with lower level of detection of the cricothyroid muscle May precise it.

## Conclusions

In the absence of laryngeal nerve injury (lower and upper) objectified by intraoperative neuromonitoring, post-thyroidectomy vocal quality was not significantly impaired compared to preoperative. However, in our more sensitive model (combined score), 23.7% of patients undergoing thyroid surgery would have an alteration of their voice. The three independent risk factors for postoperative vocal impairment found in our work were age  $\geq 65$  years, VHI 10  $\geq 3$  in preoperative and thyroid reintervention.

## Conflict of interests

None

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