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Original article Complications of voice prostheses and analysis of tracheoesophageal voice after total laryngectomy.

> Complicaciones de las prótesis fonatorias y análisis de la voz traqueoesofágica tras laringectomía total.

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## Resumen

**Introducción:** La fístula traqueoesofágica ha demostrado ser un método efectivo para la rehabilitación vocal tras laringectomía. El objetivo de este estudio es evaluar las complicaciones derivadas de la fístula traqueoesofágica y analizar la calidad de la voz.

**Material y métodos:** Estudio descriptivo ambispectivo realizado en pacientes laringectomizados y rehabilitados mediante fístula traqueoesofágica, entre enero de 2010 y diciembre de 2017 en un hospital terciario. Se analizaron complicaciones como la fuga protésica, y su asociación con otros factores. Se consideró un valor p<0.05 como estadísticamente significativo. De forma prospectiva, se realizó un análisis acústico de la voz en un subgrupo de pacientes.

**Resultados:** La prótesis fonatoria se colocó de forma primaria en un 88.2% de los casos. Un 39% de los pacientes presentó fuga protésica. El promedio de recambios al año fue de 1,6. La asociación entre estadío tumoral y fuga protésica, fue estadísticamente significativa (p=0.015), por el contrario, la radioterapia no fue estadísticamente significativa (p=0.67). Un 89% de los pacientes usan la fístula traqueoesofágica como su método de comunicación habitual.

**Conclusiones**: La voz traqueoesofágica es un método muy efectivo, sin embargo, conlleva un alto índice de complicaciones que exigen un seguimiento estrecho de los pacientes. En la mayoría de las ocasiones, estas complicaciones pueden resolverse de forma sencilla en la consulta.

<u>**Palabras claves:**</u> Laringectomía; Fístula Traqueoesofágica; Voz Protésica; Rehabilitación de las Alteraciones Vocales y del Lenguaje; Calidad Vocal; Acústica Vocal.

# Abstract

**Introduction:** Tracheoesophageal puncture (TEP) has been shown to be an effective method for speech restoration after laryngectomy. This study aims to evaluate the TEP-related complications and to assess the voice quality outcomes.

**Material and methods:** Descriptive-ambispective study of laryngectomee rehabilitated by TEP between 2010 and 2017 in a tertiary hospital. Complications, such as salivary leakages, and their association with other factors were analyzed. A p-value <0.05 was considered statistically significant. Prospectively, we performed an acoustic analysis of voice in a subgroup of patients.

**Results**: TEP was placed primarily in 88.2%. Thirty-nine percent of patients had salivary leakage. The average number of replacements per year was 1,6. Tumor stage and salivary leakage were significantly associated found (p=0.015), but radiotherapy was not (p=0.67). Eighty-nine percent of patients used TEP as their usual communication method.

**Conclusions:** Tracheoesophageal voice is highly effective method but entails frequent complications, requiring close monitoring, although most are fixed easily in clinic.

**Keywords:** Laryngectomy; Tracheoesophageal Puncture; Voice Prosthesis; Rehabilitation of Speech and Language Disorders; Voice Quality; Speech Acoustics.

## Introduction

Total laryngectomy continues to be one of the treatments of choice for advanced laryngeal and hypopharyngeal carcinoma<sup>1–3</sup>, alongside organ-preservation protocols with chemotherapy and radiotherapy. However, this surgery has a functional, physiological and psychological<sup>4</sup> impact on patients, being the loss of voice one of its most traumatic sequel<sup>5,6</sup>. Laryngectomee patients may suffer adjustment disorders associated with the emotional burden of the disease, which more often appears during vocal rehabilitation<sup>7</sup>.

Voice rehabilitation seeks to provide a communication method that compensates for the absence of the larynx<sup>2,8</sup>. Currently, this is done using an electrolarynx device, esophageal voice, or tracheoesophageal puncture (TEP)<sup>3,5</sup>. However, a TEP is the most effective method with success rate of 70-90%<sup>9,11</sup>. Also, the acoustic parameters of tracheoesophageal voice are more similar to laryngeal voice than the achieved by erigmophonia<sup>3</sup>. It provides a greater air reservoir<sup>5,12</sup> allowing air passage from the trachea to the esophagus; the air then vibrates in the pharyngoesophageal segment and finally is modulated in the oral cavity<sup>3</sup>.

However, one of the main inconvenient of voice prosthesis is their lifetime variability<sup>12</sup>, as well as complications related to their use, such as salivary leakage, enlargement of the shunt, prosthesis fall, among others<sup>13</sup>. Radiation has been related to the occurrence of these complications. Still, only few contraindications for a TEP have been described<sup>13</sup>.

This study aimed to determine complications associated with TEP during the rehabilitation of speech after laryngectomy, their relationship with radiotherapy, and the time of placement of the voice prosthesis; to assess the patient's subjective degree of vocal disability, and to analyze voice quality.

# **Material and methods**

An ambispective descriptive study of patients who underwent total laryngectomy from January 2010 to December 2017 in a tertiary hospital.

Inclusion criteria were: total laryngectomy and placement of a voice prosthesis (Provox® Vega, Atos Medical, Hörby Sweden) through a tracheoesophageal puncture—both primarily, at the time of the total laryngectomy surgery, and secondary, as a separate procedure after laryngectomy— follow-up of at least 12 months. Patients who never underwent a tracheoesophageal puncture were excluded.

Data were obtained through electronic medical records, including surgical intervention sheets, medical examination sheets, complementary tests performed, and follow-up clinical courses. Variables studied were: demographic data, tumor staging according to the 8th edition of the American Joint Committee on Cancer TNM classification system<sup>14</sup>, treatment before surgery, radiotherapy, time of placement of the voice prosthesis, vocal rehabilitation effectiveness (percentage of patients that use tracheoesophageal voice as their usual communication method), complications such as salivary leakage, granulomas, fungal colonization, extrusion, incarceration, fall, closure, among others. Additionally, we studied the relationship between the occurrence of complications and radiotherapy and the time of prosthesis placement.

## Severity of Illness Index and, speech acoustics analysis

Assessment of vocal disability was performed prospectively using the Voice Handicap Index-10 (VHI-10) questionnaire translated and validated into Spanish<sup>15</sup>. An acoustic analysis of voice was performed in only 12 of these patients—ten men and two women—, because the other 8 refused to participate in this part of the study. Also, we completed a perceptual evaluation of the voice using Hirano's<sup>16</sup> GRBAS scale, simplified to GRB. Patients who participated in this part of the study gave their informed consent.

Acoustic signal was analyzed using PRAAT software, version 6.0.46 for MacBook Pro, MAC OS HIGH SIERRA 10.13.6. Voice was recorded with a Behringer XM8500 unidirectional microphone, 20 cm from the mouth and, a TUBE MP preamplifier. The sampling frequency was 44,100 Hz. The phonation of vowels /e/, /a/, monosyllables, short sentences and, reading of a paragraph were collected. Variables analyzed were F0 (fundamental frequency), MPT (maximum phonation time), jitter, shimmer and, harmonic-noise ratio. A narrowband spectrogram analysis was performed for the sustained vowel /a/, according to Yanagihara's classification<sup>17</sup>.

## Statistical analysis

Statistical analysis was performed using the SPSS software, version 23 for Mac (IBM Corporation, Chicago, Il.). A Chi-square test was used to analyze the dichotomous qualitative variables. Fisher's exact test was used for the 2x2 tables. A p-value of <0.05 was considered statistically significant. Patient survival was calculated using the Kaplan-Meier survival analysis, while the comparison between curves was performed through the log-rank test.

# Results

## **Demographic characteristics**

A total of 118 total laryngectomee patients were registered in the period studied. Exclusion of 36 patients in whom voice prosthesis was never placed was made; also 6 patients with missing follow-up information were excluded. This resulted in 76 subjects to analyze. Sixty-eight were men (89.5%) and eight women (10.5%). The mean age at the time of diagnosis was 64.32 years (range 40.6-97.3).

Table 1 summarizes the demographic, pathological, and therapeutic data. Fifty-seven percent of patients had tumor stage IVa at the time of diagnosis, and almost a third had a tumor stage III. Twenty-seven (35.4%) patients received oncologic treatment before total laryngectomy, while 47 patients (61.8%) received adjuvant treatment afterward.

The mean patient survival rate was 2.06 years  $\pm$  1.84 DS (range 0.18-8.04 years). The analysis of patient survival by subgroups of adjuvant treatment lacked statistically significant differences ( $\chi^2 = 3.97$ , p = 0.26).

### Complications with voice prostheses

Sixty-seven (88.2%) voice prostheses were placed primarily, and nine (11.8%) as a secondary procedure. The average number replacement per year was 1.6 (range 0-5.54), and the mean duration of the prostheses was 5.67 months  $\pm$  3.90 DS. Salivary leak was the most frequent complication present in 82.9% of the patients - fifty-eight patients (76.3%) had an endoprosthetic leak and thirty-four patients (44.7%) had a periprosthetic leak. Of these patients, 30 (39.5%) suffered both types of leaks during follow-up, although not synchronously in all cases. For the treatment of periprosthetic leaks various devices were used in 26 patients - fifteen patients received a silicone flange customized to the size of their shunt, 19 had the homologous Xtraflange® silicone washer and seven had the Xtraseal® special prosthesis. Only one patient wore a plug during a transprosthetic leakage because prosthesis replacement had to be postponed.

The analysis between radiotherapy and salivary leakages showed no statistically significant differences (p = 0.169), see Table 2; neither did a subgroup analysis between pre-surgical radiotherapy, adjuvant radiotherapy, and salivary leakages; (58.3%, p = 0.35) and (44%, p = 1), respectively.

All the secondary prostheses developed salivary leaks, in contrast to primary prostheses, which had salivary leakage in 80.6% of cases. A post hoc power analysis using G\*power<sup>17</sup> revealed that for an effect of this size to be detected as significant, a sample of 117 participants would be required. As secondary prostheses were placed in patients with advanced tumoral stage, a subgroup analysis was performed: statistical analysis showed that patients with tumoral stage III and IV had a higher frequency of salivary leakage than those with stage I and II ( $\chi 2= 25.054$ , p=0.015, V=0.33).

On the other hand, a statistically significant relation was found between secondary placement of the prostheses and the occurrence of extrusion p=0.05 (RR=1.39, 95% CI: ,87-2.12), fall p=0.021 (RR=1.61, 95% CI: ,89-2.90) and, permanent shunt closure p=0.023 (RR=1.09, 95% CI: ,89-2.90). Also, procedures like infiltration of hyaluronic acid (due to persistent periprosthetic leak), placement of a nasogastric tube for secondary shunt closure, and usage of proton pump inhibitors to treat granulomas were more frequent in the secondary prostheses (see Table 4).

The second most common complication was fungi colonization (32.9%)—mostly treated with topical Nystatin. Other complications were granulomas (managed with proton pump inhibitors and other treatments such as chemical cauterization), extrusion, incarceration and fall of prosthesis. Table 4 displays complications encountered and their treatment modalities.

### Assessment of voice usage, severity of illness index and, speech acoustics.

To calculate the effectiveness of vocal rehabilitation, only 64 patients were taken into account since this information did not appear in the medical records of 12 patients and they had died before this study was carried out. Fifty-seven patients (89.1%) used tracheoesophageal voice to communicate regularly, and seven of these fifty-seven patients also talked effectively by esophageal voice. Two subjects (3.1%) only spoke through esophageal voice and, five patients (7.8%) could not communicate at all. Nevertheless, only one requested permanent closure of the shunt.

The VHI-10 questionnaire was completed by a subgroup of 20 patients (26.3%) since 37 subjects (48.7%) had died at the time of the study, and 19 patients (25%) refuse to collaborate. The mean value of this questionnaire was 15.8 (range 5-39), showing moderate vocal disability in most patients (45%), mild inability in 35% and, reporting both severe and grievous voice impairment by the minority (10% each). The F2 item "People have difficulty understanding me in a noisy room" had the highest score. Also, no statistically significant differences were found in the VHI-10 score of patients receiving adjuvant radiotherapy, compared with those only undergoing laryngectomy (p = 0.191) statistical power= 0.5 (a post hoc analysis showed that to reach a statistical power of 0.8 we would need at least 31 subjects). The score was also similar in primary and secondary prostheses (p = 0.296), statistical power= 0.5, to reach a statistical power of 0.8 at least 47 subjects are needed.

Finally, Table 5 compiles the results of both acoustic and perceptual analysis of the voice. The mean F0 (fundamental frequency) was 119.65 Hz and, the mean MPT (maximal phonation time) was 4.94 seconds. Nine patients showed a Yanagihara type 4 spectrogram and, the remaining three, a spectrogram type 3. The perceptual evaluation of voice with the GRB scale, the G (grade) and R (roughness) parameters showed a severe alteration, in 66.7% and 58.4% of the patients, respectively; parameter B (breathiness) revealed a grave alteration only in 25% of subjects, and a moderate alteration in 41.7% (see Table 6).

# **Discussion**

Tracheoesophageal puncture is a simple and effective method of voice rehabilitation for the laryngectomee. In our study, 89.1% of patients used tracheoesophageal voice as their main method of communication—in line with other studies reporting an effectiveness of more than 70%<sup>18,19</sup>.

Voice prosthesis placement entails frequent complications, most commonly salivary leakage, that can be handled successfully and quickly in clinic<sup>11</sup>. Intraprosthetic leaks imply prosthesis replacement due to valve insufficiency, but the number of changes that each patient requires varies greatly. The average number of replacements per year in our study was 1.6, similar to what reported González *et al.*<sup>20</sup>. However, periprosthetic leak management entails other procedures. In our review, 57.8% of periprosthetic leaks were treated using accessories—like the Xtraflange, plugs and, customized flanges — or reinforced prostheses like the Xtraseal. Also, two patients received an infiltration of hyaluronic acid in the tissue around the shunt.

In our sample, secondary prostheses placement was preferred in patients with advanced tumor stages, yet finding that these suffered more complications: all secondary prostheses suffered salivary leaks, compared to 80.6% of the primary prostheses. In this last group, 8 patients had a short follow-up due to premature death (in the first year after surgery), in two patients the fistula was closed due to fall of the prosthesis and two patients had incarceration of the prosthesis that conditioned the replacements; all these complications can explain the absence of leakage. These findings are similar to those of Scherl *et al.*<sup>11</sup> —who recently found a significant association between secondary prosthesis placement and complications of the shunt; and with reduction of the complication-free period. However, these complications can be related to an advanced tumoral stage. The study of Barauna-Neto *et al.*<sup>21</sup> describes that salivary leakage is less frequent in secondary prostheses, and a metanalysis performed by Chakravarty *et al.*<sup>22</sup> concludes that secondary prostheses are preferred in patients at risk of developing a pharyngocutaneous fistula, although statistical significance was not reached.

On the other hand, eighty-three percent of the patients treated with radiotherapy developed salivary leakage, although this association was not statistically significant (p=0.169), which follows what described Gonzalez-Poggioli *et al.*<sup>20</sup>. However, the recently published study of Scherl *et al.*<sup>11</sup> uncovered that placement of voice prosthesis after receiving radiotherapy increases the risk of complications.

Placement of a nasogastric tube and waiting for secondary closure of a dilated shunt was more frequent in secondary prosthesis. As well as extrusions, falls, and permanent closure of the shunt — those late complications could be the reason why secondary fistulas dilated more. Several articles point to the conservative attitude of place a nasogastric tube as the most effective method for managing them<sup>23</sup>.

Other complications include granuloma formation around the shunt and fungi colonization of the prosthesis. Granulomas relate to gastroesophageal reflux but, while Pepsin is present in the tracheoesophageal tract of laryngectomee patients, no statistically significant association relates this to TEP complications<sup>24</sup>. Hadzibegovic *et al.*<sup>25</sup> studied the use of proton pump inhibitors and concluded the same. In our department, we do not use PPIs systematically in all the laryngectomy patients with voice prosthesis. However, 14.5% of the patients had granulomas — most frequently those with secondary prosthesis (see Table 3) —, and all of them received such treatment. On the other hand, thirty-three percent of the patients suffered from fungi colonization, and most of them cleaned the prosthesis with a brush soaked in nystatin (see Table 2). Somogyi-Ganss *et al.*<sup>26</sup> pointed that colonization is a frequent cause of valve failure, but prolonged treatments with antifungals are not usually effective. We choose the VHI-10 questionnaire to assess vocal disability as it is widely validated, fast, and easy to perform. We found a moderate severity of illness index in most of the patients studied — in line with other series<sup>3</sup>. Other authors<sup>27</sup> obtained equal results using the VHI-30 questionnaire: in patients with esophageal voice and with tracheoesophageal voice —without significant differences between them. However, Allegra *et al.*<sup>28</sup> used various questionnaires (VHI-10, V-RQOL, and VPQ) to compare those voice training methods and reported a significant difference for the functional subscale, with better performance of tracheoesophageal voice.

Acoustic analysis of the voice is a convenient, non-invasive method to evaluate vocal functionality<sup>12,29</sup>. We found that the tracheoesophageal voice has a lower F0 and MPT than the normal laryngeal voice, as other authors have published<sup>30</sup>. However, these values are still better than those obtained in patients using esophageal voice<sup>18,28</sup>. Tracheoesophageal voice is less aperiodic, which improves patient's fluency, prosody, and intelligibility.

The inability to speak after total laryngectomy, regardless of the rehabilitation method used, is related to a lower quality of life<sup>30</sup>. Tracheoesophageal voice is easy to learn, and patients can achieve it almost immediately after surgery<sup>1</sup>. On the other hand, at least five voice-training sessions are needed to learn esophageal voice, as concluded by Del Rio-Valeiras *et al.*<sup>6</sup> which also reported that the patient's socioeconomic status is one of the factors influencing the learning process.

Finally, the rehabilitation program in our hospital begins almost immediately after surgery, with the transition from a feeding tube to eating by mouth. The first visit by the speech and language therapist takes place while the patient is still hospitalized and continues with speech rehabilitation sessions at discharge. Thus, many patients manage to speech soon. Also, patients are taught the basic care of the prosthesis and what to do if a complication occurs.

This study meets several limitations. The risk of bias is difficult to control in retrospective observational studies like this one. Also, our sample is not balanced between groups. Some of the variables analyzed have minimal representation, like secondary prostheses, vocal disability and, speech acoustic analysis. Likewise, the patient's socioeconomic status and family support were not measured.

## Conclusions

The most effective method for speech rehabilitation in laryngectomee patients is a tracheoesophageal puncture. Tracheoesophageal voice improves fluency and intelligibility compared to esophageal voice. However, we must remember that voice prosthesis usage entails several complications, which can decrease the half-life of the device. Knowledge of these complications and their treatment is essential for an adequate follow-up. The association of radiotherapy and the development of complications, such as saliva leakage, is controversial, as previous studies reported opposite findings. Also, there is no consensus on the profit of primary prostheses over secondary ones. Our study lacks the statistical power to find strong relationship between the time of prosthesis placement and the development of complications, and a recent metanalysis could not confirm this either, although it suggested a significantly increased risk of fistula in primary compared to secondary tracheoesophageal puncture. Larger studies are needed to confirm these findings. We conclude that assessment of each case is needed, taking into account previous treatments received by the patient and tumor size.

# **Compliance with ethical standards**

The authors declare that the procedure followed in this research conform to the ethical standards in accordance with the World Medical Association and the Declaration of Helsinki. The study was approved by Galicia's Ethics Committee, code 2019/583.

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# **Conflict of interest**

Authors declare no conflict of interest.

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# **Tables**

Features	<u>n (%)</u>	
Sex, n (%)		
Male	68 (89.5%)	
Female	8 (10.5%)	
Age, median (range).	64.32 (range 40.6-97.3)	
TNM, n (%)		
Stage I	2 (2.6%)	
Stage II	7 (9.2%)	
Stage III	21 (27.6%)	
Stage IVa	44 (57.9%)	
Stage IVb	2 (2.6%)	
Treatment before laryngectomy, n (%)		
None	49 (64.5%)	
Radiotherapy	8 (10.5%)	
Chemotherapy	2 (2.6%)	
Combined chemo-radiotherapy	2 (2.6%)	
Chemo-radiotherapy and surgery	2 (2.6%)	
Surgery	13 (17.1%)	
Adjuvant treatment, n (%)		
None	29 (38.2%)	
Radiotherapy	27 (35.5%)	
Chemotherapy	2 (2.6%)	
Combined chemo-radiotherapy	14 (18.4%)	
Chemo-radiotherapy and surgery	4 (5.3%)	
Follow-up, years (range).	3.14 (0-11.95)	

 Table 1. Baseline demographic, pathological and treatment features.

	None	Transprosthetic salivary leakage	Periprosthetic Salivary leakage	Both	Total
Radiotherapy n (%)					
No	4 (19.0)	8 (38,1)	4 (19.0)	5 (23,8)	21 (100)
Yes	9 (16.4)	18 (32,7)	3 (5,5)	25 (45,5)	55 (100)
Total	13 (17,1)	26 (34,2)	7 (9,2)	30 (39,5)	76 (100)

**Table 3.** Events related to the time of prosthesis placement.

	Sex	Tumoral stage	RT	Granulomas	PPIs	Fungi
Primary	F:11.9%	I:3%	70.1%	11.9%	11.9%	32.8%
	M:88.1%	II:10.4%				
		III:28%				
		IV:58.2%				
Secondary	F:0%	I:0%	88.9%	33.3%	33.3%	33.3%
	M:100%	II:0%				
		III:22.2%				
		IV:77.8%				
+P value		0.59	0.43	0.12	0.12	1.00

+Differences between primary and secondary placement of the prostheses.

	Nystatin	Incarceration	Extrusion	Fall	Nasogastric tube	Hyaluronic Acid Infiltration	Closure
Primary	29.9%	26.9%	7.6%	10.4%	6%	1.5%	10.4%
Secondary	33.3%	33.3%	33.3%	44.4%	55.6%	11.1%	44.4%
+P value	1.00	0.70	0.05%*	0.02%*	0.001*	0.22	0.02*

+*Differences between primary and secondary placement of the prostheses.* F: female; M: male; RT: radiotherapy; PPIs: Proton pump inhibitors.

\* p-value ≤0,05 in Fisher's exact test.

Table 4. Complications encountered with voice prosth	heses and its treatment strategies.
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Complication	n (%)	Treatment	n (%)
Salivary leakage	64 (84.2%)		
Endoprosthetic leakage	58 (76.3%)	Xtraflange <sup>®</sup> washer	19 (29.7%)
Periprosthetic leakage	34 (44.7%)	Xtraseal® prosthesis Customized silicone flanges Plug Hyaluronic acid infiltration Nasogastric tube and secondary shunt closure	7 (10.9%) 15 (23.4%) 1 (1.6%) 2 (3.1%) 5 (7.8%)
Granulomas	11 (14.5%)	Proton pump inhibitors	100%
		Cauterization, nasogastric tube and secondary shunt closure	2 1
Fungi	25 (32.9%)	Topical Nystatin	23(93.3%)
Incarceration	21 (27.6%)	Replacement	100%
Extrusion	8 (10.5%)	Replacement	100%
		Nasogastric tube and secondary shunt closure.	1
Prosthesis loss	11 (14.5%)	Replacement	100%
Closure	11 (14.5%)		
<u>Causes</u>		Nasogastric tube and	
Granuloma	2 (2.6%)	secondary shunt closure.	5 (55.6%)
Tumor persistency	2 (2.6%)		
Fistula enlargement	1 (1.3%)		
Patient request	4 (5.3%)		
Fall	1 (1.3%)		

Table 5. Acoustic analysis and perceptual evaluation of voice.

### \*Patient 1

Age: 76; Female; MPT: 3.5; F0: 119.72; Jitter: 2.61%; Shimmer: 10.27%; HNR: 4.54; Spectogram: 3; GRB: 3 3 2.

### \*Patient 2

Age: 62; Male; MPT: 3.1; F0: 109.81; Jitter: 1.48%; Shimmer: 8.86%; HNR: 3.67; Spectogram: 3; GRB: 1 1 0.

### \*Patient 3

Age: 58; Male; MPT: 3.2; F0: 122.27; Jitter: 0.45%; Shimmer: 4.82%; HNR: 10.75; Spectogram: 4; GRB: 2.2.1.

#### \*Patient 4

Age: 71; Male; MPT: 2; F0: 136.59; Jitter: 2.97%; Shimmer: 2.61%; HNR: 1.97; Spectogram: 4; GRB: 3 3 2.

### \*Patient 5

Age: 70; Male; MPT: 5.4; F0: 123.36; Jitter: 2.41%; Shimmer: 13.73%; HNR: 1.59; Spectogram: 4; GRB: 3 2 3.

### \*Patient 6

Age: 78; Male; MPT: 6.57; F0: 112.68; Jitter: 1.40%; Shimmer: 12.81%; HNR: 1.42; Spectogram: 4; GRB: 2.2.1.

### \*Patient 7

Age: 70; Male; MPT: 13.3; F0: 125.48; Jitter: 1.46%; Shimmer: 7.70%; HNR: 7.01; Spectogram: 3; GRB: 3 3 2.

#### \*Patient 8

Age: 72; Male; MPT: 4.9; F0: 131.39; Jitter: 2.89%; Shimmer: 12.47%; HNR: 2.02; Spectogram: 4; GRB: 3 3 2.

#### \*Patient 9

Age: 62; Male; MPT: 4.75; F0: 109.38; Jitter: 1.31%; Shimmer: 8.90%; HNR: 3.77; Spectogram: 4; GRB: 3 3 3.

### \*Patient 10

Age: 61; Male; MPT: 5.5; F0: 86.12; Jitter: 0.92%; Shimmer: 5.74%; HNR: 8.82; Spectogram: 4; GRB: 2.2.1.

### \*Patient 11

Age: 56; Female; MPT: 5.9; F0: 107.04; Jitter: 0.93%; Shimmer: 6.59%; HNR: 5.16; Spectogram: 4; GRB: 3 3 2.

### \*Patient 12

Age: 61; Male; MPT: 1.2; F0: 151.98; Jitter: 3.49%; Shimmer: 12.98%; HNR: 2.64; Spectogram: 4; GRB: 3 3 3.

### Patient: Mean +/-SD

MPT: 4.94+/-3.09; F0: 119.65+/-16.67; Jitter: 1.86+/-0.97%; Shimmer: 8.96+/-3.60%; HNR: 4.44+/-3.01.

MPT: maximal phonation time (seconds); F0: fundamental frequency; HNR: harmonic-noise ratio; GRB: grade roughness and breathiness scale of voice; SD: standard deviation of the mean.

Parameter	Alteration degree n (%)			
	Normal (0)	Mild (1)	Moderate (2)	Severe (3)
G	0 (0)	1(8.3)	3 (25)	8(66.7)
R	0 (0)	1(8.3)	4(33.3)	7(58.4)
В	1(8.3)	3 (25)	5(41.7)	3(25)

Table 6. GRB	(grade, roughness an	d breathiness) scale.
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