Longitudinal vocal outcomes and voice-related quality of life after selective bilateral laryngeal reinnervation: a case study

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Abstract

Purpose: Bilateral vocal fold paralysis (BVFP) is a severe disorder that can result in respiratory, swallowing and voice-related problems. Most surgical treatments do not restore laryngeal function and often need to compromise voice quality to preserve respiratory function. Laryngeal reinnervation (LR) may offer a solution to this problem, but literature on longitudinal outcomes of this procedure is scarce. This study aims to report the longitudinal vocal outcomes of BVFP after laryngeal reinnervation and subsequent voice therapy.

Methods: The case of a 23-year-old man with BVFP after traumatic dissection of both recurrent laryngeal nerves is described. Selective bilateral laryngeal reinnervation of both adductors and abductors was performed five months after the onset of BVFP. Voice therapy was provided after the LR procedure. Multidimensional voice assessments including acoustic, perceptual and patient-reported outcome measures (PROMS) were conducted 2, 5, 6.5, 8, and 31 months after LR.

Results: An improvement of vocal capabilities and voice quality was noticed 6.5 months after LR, after 4.5 months of voice therapy, with normative values after 2.5 years. PROMS showed an improvement of voice-related quality of life, but some limitations to activities of daily life were still present. Inspiratory arytenoid abduction was not observed on laryngeal videostroboscopic findings in this patient, but tracheostomy was not required.

Conclusion: Voice therapy after LR helps establish healthy and efficient voice use without increasing compensatory hyperfunctional behavior. More research is needed to examine potential merits of voice therapy in the rehabilitation of vocal and respiratory functions after LR.

INTRODUCTION

Bilateral vocal fold paralysis (BVFP) is an uncommon but severe disorder caused by reduced or absent function of both recurrent laryngeal nerves, often leaving the vocal folds in a paramedian position (Li et al., 2017; Sapundzhiev et al., 2008). This in turn causes respiratory insufficiency and in some cases a decrease in voice quality due to immobility of the vocal folds and subsequent glottal insufficiency (Hillel et al., 1999; Sapundzhiev et al., 2008). The greatest concern is usually dyspnea, which can necessitate an emergency intubation or tracheotomy in order to preserve respiration (Zealear & Billante, 2004).

Etiologies of BVFP are similar to those of unilateral vocal fold paralysis and include thyroidectomy, other surgical or nonsurgical trauma, nonlaryngeal malignancy, idiopathic, systemic or neurological causes, and intubation (Benninger et al., 1998; Hillel et al., 1999; Salik & Winters, 2022). The incidence of BVFP remains relatively unknown (Rubin & Sataloff, 2007), but according to Benninger et al. (1998), BVFP comprises one third of all cases of vocal fold paralysis.

Dysphonia in BVFP due to glottal insufficiency manifests as a variety of vocal symptoms, including an altered voice quality, such as hoarseness and/or breathiness, pitch changes, vocal fatigue, changes in volume and pitch range, etc. (Nawka et al., 2015; Rubin & Sataloff, 2007; Salik & Winters, 2022). The severity of dysphonia is usually influenced by the position of the paralyzed vocal folds. When the vocal folds exhibit an intermediate or lateral position, voice and swallowing may be significantly impaired. However, when the vocal folds rest in a paramedian position, voice quality may be largely preserved (Rubin & Sataloff, 2007). In this case, airway obstruction and stridor may occur. This often forces the patient and health care provider to choose between a good voice quality and a good airway (Rubin & Sataloff, 2007).

These vocal and respiratory problems can have an important negative impact on the patients' quality of life (Harnisch et al., 2008), but finding a satisfactory treatment for BVFP is difficult. Common surgical treatments include tracheostomy, arytenoidectomy, cordotomy and suture lateralization (Li et al., 2017). However, these techniques do not restore laryngeal function and usually compromise voice quality due to potential vocal fold damage or expansion of the glottis (Li et al., 2017; Nawka et al., 2015; Rubin & Sataloff, 2007; Salik & Winters, 2022). In the past, tracheostomy was the most common treatment in BVFP patients to secure the airway, but it requires continuous wound care by the patients and has an important negative effect on quality of life (Li et al., 2017; Salik & Winters, 2022). Irreversible procedures such as arytenoidectomy and cordotomy usually impair voice quality, may put patients at a certain risk for aspiration, and may need revision interventions if granulation or formation of scar tissue narrows the glottal opening again (Li et al., 2017). A more dynamic approach, selective bilateral reinnervation of adductor and abductor laryngeal muscles, developed by Marie (1999), aims to restore functional vocal fold mobility by reinnervating both posterior cricoarytenoid (PCA) muscles with one right upper phrenic nerve root through an interposition-free nerve graft. The adductor muscles are reinnervated with thyrohyoid branches of the hypoglossal nerve (Marie, 2009). Successful results of this total motor reinnervation were obtained in canine larynxes (Marie, 1999; Marie et al., 2000). Outcomes of this procedure in humans have been reported since 2003. By 2017, long-term follow-up results of 40 cases performed in Rouen University Hospital in France were reported by Marie and Heathcote (2018), showing decannulation in 35 of these cases and improved respiratory parameters in 30. Voice preservation or improvement was observed in almost all cases, although it is not clear how this was measured. Likewise, different authors report preservation or improvement in vocal parameters after LR in case series and clinical studies based on auditory-perceptual and/or acoustic measurements (Lee et al., 2020; Li et al., 2013, 2019).

However, extensive reports of vocal outcomes based on a multidimensional voice assessment are often lacking in the current literature on LR after BVFP. To the best of our knowledge, objective multiparametric indices of overall dysphonia severity, such as the Dysphonia Severity Index (DSI; Wuyts et al., 2000) and Acoustic Voice Quality Index (AVQI; Maryn et al., 2010), and patient-reported outcome measures (PROMS) were never included in assessments of vocal function. Nevertheless, these measurements allow for standardized follow-up of voice quality and evaluation of the psychosocial impact of the patient’s voice disorder. Additionally, information on the application and effect of behavioral voice therapy after LR has not been reported before. Still, voice therapy may offer a valuable contribution to voice rehabilitation after LR because it facilitates an optimal breathing pattern with sufficient abdominal support and improves intrinsic laryngeal muscle strength and agility while avoiding incorrect voice use and compensatory hyperfunctional behavior (Remacle & Eckel, 2010; Rubin & Sataloff, 2007).

Therefore, the aim of this case study is to offer a detailed and comprehensive report of the long-term multidimensional voice outcomes after LR and subsequent voice therapy in a patient with BVFP.

METHODS

The study was approved by the Ethics Committee of Ghent University Hospital (BC-09508).

Participant and etiology of bilateral vocal fold paralysis

The participant was a 23-year-old Belgian man at onset, who was admitted to the Ghent University Hospital in October 2018 after a work-related incident with a chain saw. A traumatic transection of the throat with transverse transection of the platysma, strap musculature, thyroid cartilage, a total transection of the trachea at the level of the second tracheal ring, and a partial (80%) transection of the esophagus was observed. Both recurrent laryngeal nerves were completely transected, while the carotid arteries and jugular veins were intact. A primary reanastomosis of the trachea, platysma, strap musculature, thyroid and esophagus was performed, as well as a tracheostomy (Shiley tube 8 with cuff) and gastrostomy. A primary reanastomosis of the recurrent nerves was impossible due to severe laceration. After the surgery, the patient was shortly admitted to intensive care due to acute respiratory insufficiency and aspiration pneumonia.

Initial status and evolution before LR procedure

Due to the retrospective nature of most assessments, it should be noted that all laryngovideostroboscopic (LVS) examinations happened in clinical setting. Not all LVS recordings were available for blinded evaluation, so the results from clinical reports are described below. Images from LVS recordings that were available to us of the vocal folds at rest and during phonation are provided in Appendix A. Approximately two weeks after the primary surgery, an extensive ENT (ear, nose and throat) assessment was performed. LVS showed BVFP with vocal folds in paramedian position and no activity of the ad- or abductor muscles, and limited saliva stasis in the larynx. Sensory innervation of the larynx was preserved bilaterally. The patient also presented with dysphagia initially but recovered after a month of functional swallowing therapy.

Three months post-onset, no vocal fold mobility was observed during phonation. The patient communicated in writing and with gestures, since even whispering was considered difficult at that time. Four months post-onset, a more paramedian position of the vocal folds was observed with supraglottic adduction during phonation, resulting in a weak and high-pitched voice. No active adduction or abduction was observed. The patient reported that some form of phonation returned suddenly over the course of a few days.

Laryngeal reinnervation procedure

The surgical procedure was performed at the University Hospital in Rouen at the end of April 2019, 6 months post-onset of BVFP. After confirming the neurological nature of the BVFP through laryngeal electromyography (LEMG), a selective bilateral LR procedure was performed according to Marie (2009). This procedure is described in detail by Marie and Heathcote (2018). The right phrenic nerve was explored, and a retrograde dissection of a branch originating from C4 was performed. The thyrohyoid branches of the hypoglossal nerve were localized, with placement of vascular slings around the nerves. Then, intra- and retrolaryngeal dissection of the recurrent laryngeal nerves was performed bilaterally with creation of a retrocricoid tunnel, followed by reinnervation of the PCA muscles with the phrenic nerve. A Y-shaped, free nerve graft from the left superficial cervical plexus (great auricular nerve) was utilized and passed through the retrocricoid tunnel, after which the single end was attached to the identified root of the right phrenic nerve, while its double ends were implanted one into each

PCA muscle. The adductors were reinnervated by interposition of a free nerve graft between the distal stumps of the transected recurrent laryngeal nerves and ipsilateral thyrohyoid branches of the hypoglossal nerve. No nasogastric feeding tube was placed, but a cuffed tube was placed in the tracheostomy site. The patient was decannulated four days after the LR procedure. Follow-up was planned primarily at Ghent University Hospital, with sporadic consultations at Rouen University Hospital, since it was closer to the patient's residence. Due to the severe dysphonia following LR, the patient received voice therapy at the Ghent University Hospital. The content of the voice therapy program, as well as the evolution of vocal fold mobility, respiration and vocal outcomes are described below. Additionally, a comprehensive overview of the most important LVS findings, vocal outcomes and other clinical complaints over time following BVFP and the LR procedure can be found in Appendix B.

Voice therapy program

To improve the patient's voice quality by training the intrinsic laryngeal musculature and to avoid compensatory hyperfunctional behavior, voice therapy was started in July 2019, 9 months post-onset and 8 weeks after the LR procedure. In total, the patient followed voice therapy for 6 months. During the first three months, 30-minute sessions were planned twice per week, which reduced to once per week during the last three months.

The last author (I.M.) provided voice therapy, and its content was similar to the voice therapy program described by Meerschman et al. (2019). An overview of vocal techniques is described in Table 1. Specific attention was paid to respiration exercises to stimulate the diaphragm and consequently the PCA muscle reinnervation and body building, and to resonant voice exercises and semi-occluded vocal tract exercises (SOVTEs) to increase effective and efficient voice use, while avoiding any form of excessive supraglottic hyperfunction. The latter two techniques were provided in increasing difficulty, starting at phoneme level with phonation at a comfortable pitch, and pitch and loudness variations.

Generalization and transfer of the vocal techniques were stimulated by increasing vocal demands to reading tasks on word, sentence, text level, and eventually exercises on (semi)spontaneous speech.

At the start of the voice therapy program, while the patient was still aphonic, no home training exercises were provided to avoid overcompensation or overworking the voice. When the voice recovered over the course of voice therapy and the patient showed motivation to practice at home, he was encouraged to repeat the SOVTEs and resonant voice exercises that were offered during the therapy sessions. No strict home training program was imposed, and the patient was free to choose the frequency of home exercise. However, an exercise duration of five to ten minutes was advised based on previous literature about the optimal duration of SOVTEs (Bassetto & Constantini, 2021; Gillespie et al., 2022; Kang et al., 2019; Pozzali et al., 2021; Tulunoğlu et al., 2022), and he was instructed not to fatigue his voice during these exercises.

Table 1: overview of techniques utilized in voice therapy

Technique	**Description**
Education and counselling	Explanation of anatomy and physiology of the larynx and current pathology
Vocal hygiene program	Selection and discussion of vocal hygiene measures
Posture	Correct and eutonic posture for phonation in sitting and standing position
Relaxation	Local relaxation of neck, shoulders, larynx and pharynx
Respiration	Costo-abdominal respiration type and adequate breath support for phonation
SOVTE	Improving glottal closure through improved source-filter interaction - Water-resistance therapy - Resonant voice exercises
Voice placing, forward focus	Often combined with resonant voice exercises: gradual reduction of excessive resonance but maintenance of forward focus
Laryngeal manipulation	Relaxing tense (peri)laryngeal musculature
Pitch and loudness exercises	Strengthening and balancing the laryngeal musculature by exercises on pitch and loudness combined with SOVTE - Pitch glides: low to high, high to low, and alternating - Loudness exercises: swelling tones and alternating
Generalization and transfer	Combination of all learned techniques at different levels: word, sentence, text level, (semi)spontaneous speech

Abbreviations: SOVTE: semi-occluded vocal tract exercises

Multidimensional voice assessment

Before and after voice therapy, a multidimensional voice assessment was performed in an acoustically isolated room to determine the patient's objective voice quality and the severity of dysphonia. The duration of this assessment was approximately 30 minutes. At two points in time over during voice therapy, a shorter voice assessment was performed. The patient only provided speech samples of a sustained /a:/ and the Dutch phonetically balanced reading passage 'Papa en Marloes' (Appendix C) to perform an acoustic analysis and calculate the patient's AVQI (see further information below). Since this assessment took approximately five minutes, it was possible to conduct it during a therapy session, which would not be feasible for a multidimensional voice assessment. The complete voice assessment consisted of the procedures described below.

Acoustic and aerodynamic parameters

Maximum performance task. The patient's maximum phonation time (MPT, in s), which is considered an objective measure of respiratory efficiency during phonation (Neiman & Edeson, 1981), was determined. In adult Flemish men, the normative MPT is 21.8 seconds (De Bodt et al., 2015). The patient was asked to sustain the vowel /a:/ as long as possible at his habitual pitch and loudness, after a maximal inspiration.

Frequency and intensity range. This was determined by the Computerized Speech Lab (model 4500, KayPENTAX, Montvale, NY), using a Shure SM-48 microphone at 15 cm from the mouth. The patient was instructed to sustain the vowel /a:/ for several seconds, using respectively a habitual pitch and loudness, a minimal pitch, a minimal intensity, a maximal pitch and a maximal intensity (Heylen et al., 1998). Lowest and highest fundamental frequency (f-low, f-high), as well as lowest and highest intensity (I-low, I-high) were obtained.

Acoustic analysis. The patient was instructed to sustain the vowel /a:/ for several seconds at a comfortable pitch and loudness in a Samson C01U microphone, positioned at 30 cm from the mouth. The voice was recorded using the software program Praat (version 6.1.56, Boersma & Weenink, 2013) at a sampling frequency of 44.1 kHz. The middle three seconds were extracted from the sample to perform the acoustic analysis in Praat. Average fundamental frequency (f_o, in Hz), jitter (in %), shimmer (in %), and noise-to-harmonics ratio (NHR) and smoothed cepstral peak prominence of the vowel /a:/ ($CPPS_{vowel}$) were determined through this analysis. Additionally, the CPPS on continuous speech ($CPPS_{speech}$) was analyzed using the first two sentences from the Dutch phonetically balanced reading passage 'Papa en Marloes' (see Appendix C) (van de Weijer & Slis, 1991).

Signal typing of the samples (see Table 2) was performed by the first author in consensus with the last author, and was based on the classification of Titze (1995) and Sprecher et al. (2010).

Dysphonia Severity Index. The DSI is an objective and quantitative correlate of voice quality and is based on a weighted combination of the parameters MPT (in s), f-high (in Hz), I-low (in dB) and jitter (in %), according to the formula 'DSI = 0.13 MPT + 0.0053 f-high –0.26 I-low – 1.18 jitter(%) + 12.4' (Wuyts et al., 2000). The obtained score usually varies from -5 to +5, although lower and higher scores are possible in extreme cases. The cut-off score between a normophonic and pathological voice quality was determined at +1.6 (Raes et al., 2002), in which a higher score corresponds to a better voice quality, while a lower score indicates an increasingly severe dysphonia.

Acoustic Voice Quality Index. The AVQI is a 6-factor, multivariate acoustic model to objectively assess dysphonia severity based on both the sustained vowel /a:/ and continuous speech (Maryn et al., 2010). The score ranges from 0 to 10, with a lower score indicating better voice quality. The cut-off score between a normophonic and pathological voice quality is 2.95; a higher score corresponds to a dysphonic voice (Maryn et al., 2010). In order to determine the patient's AVQI, he was instructed to sustain the vowel /a:/ for several seconds at a comfortable pitch and loudness, and to read aloud the Dutch phonetically balanced reading passage 'Papa en Marloes' (see Appendix C) (van de Weijer & Slis, 1991). The middle three seconds from the sustained vowel and the first two sentences from the reading passage were used for the calculation of the AVQI in the software program Praat (version 6.1.56, Boersma & Weenink, 2013).

Patient-reported outcome measures

Patient-reported outcome measures (PROMs) consisted of several questionnaires, described below, and information from clinical reports.

Voice Handicap Index. The Voice Handicap Index (VHI) is a self-assessment tool for measuring the psychosocial impact of voice disorders, developed by Jacobson et al. (1997). It consists of 30 statements, equally distributed over 3 domains: functional, physical, and emotional. On a 5-point rating scale (0 = never, 1 = almost never, 2 = sometimes, 3 = almost always, 4 = always), the patient indicates their response, achieving a minimum score of 0 and a maximum of 120. The higher the score, the more severe the perceived impact of the voice disorder on a patient's activities of daily life (ADL). For the Dutch version of the VHI, a score below 20 indicates that the voice does not impose limitations on the patient's ADL, while a score of 20-40 suggests the presence of some limitations. A score of 40-60 indicates substantial limitations of ADL, and a score higher than 60 suggests that the voice disorder is considered a handicap.

Additional questionnaires. At the long-term follow-up assessment, three additional questionnaires were completed by the patient: the Dutch version of the Vocal Tract Discomfort Scale (VTDS; Luyten et al., 2016; Mathieson et al., 2009), Corporal Pain Scale (Van Lierde et al., 2010), and Vocal Fatigue Index (VFI; Nanjundeswaran et al., 2015). The VTDS is a self-rating instrument to measure the frequency and intensity of eight different types of discomfort in the throat: burning, tightness, dryness, aching, tickling, soreness, irritability, and globus sensation. Frequency and intensity of these sensations are rated separately on a seven-point Likert scale, with higher scores indicating more frequent and intense sensations of discomfort in the throat. The Corporal Pain Scale is a tool to quantify the frequency of 13 corporal pain symptoms during and after voice use on a 5-point Likert scale. Symptoms of proximal corporal pain (mandible pain, tongue pain, sore throat, shoulder pain, neck pain, diffuse pain) and distal corporal pain (headache, back pain, chest pain, arm pain, hand pain, earache) are investigated. The VFI is a self-assessment tool for measuring vocal fatigue, consisting of 19 statements distributed over 3 domains: (1) tiredness of voice and voice avoidance, (2) physical discomfort associated with voicing, and (3) improvement of symptoms with rest. Responses are indicated on a 5-point Likert scale (0 = never, 1 = almost never, 2 = sometimes, 3 = almost always, 4 = always), with higher scores in domain 1 and 2 and a lower score in domain 3 reflecting more self-perceived symptoms of vocal fatigue. These questionnaires were not provided during previous assessments and offer a more qualitative analysis of patient-reported vocal complaints.

Auditory-perceptual voice assessment

After completion of the follow-up, two speech-language pathologists (SLPs) with experience in voice diagnostics (A.A. and T.P.) rated all voice samples (continuous speech) blindly on the GRBASI scale (Dejonckere et al., 1996; Hirano, 1981). The GRBASI scale is a widespread tool to assess voice quality perceptually using six components: Grade (G; i.e. overall dysphonia severity), Roughness (R), Breathiness (B), Asthenia (A), Strain (S), and Instability (I). All components are rated on a four-point Likert scale, with 0 indicating a normal value, and 1, 2 and 3 a mild, moderate, and severe presence of the component, respectively. All voice samples were presented in a randomized order, and 25% of the samples were repeated to determine intra-rater reliability. First, the SLPs rated all samples individually, and during a second listening session, a consensus evaluation was performed. A two-way mixed, single measures, consistency Intraclass Correlation Coefficient (ICC(3,1)) was used to analyze inter- and intra-rater reliability, which has been shown to be identical to a weighted kappa with quadratic weights for ordinal scales, and the two may be substituted interchangeably (Norman & Streiner, 2008). Guidelines described by Koo and Li (2016) were used for interpretation of inter- and intrarater reliability. An ICC below .50 was considered poor, between .50 and .75 moderate, between .75 and .90 good, and above .90 excellent. Rater 1 achieved excellent intra-rater reliability for all parameters (ICC = 1), and rater 2 achieved excellent intra-rater reliability for G, R, A, S, I (ICC = 1) and B (ICC = .923). Interrater reliability was good for G (ICC = .776) and B (ICC = .800), moderate for S (ICC = .727), but poor for R (ICC = .258), A (ICC = .444) and I (ICC = .211). Differences in individual ratings were discussed until a consensus evaluation was reached. The consensus evaluation achieved an excellent intra-rater reliability for all parameters (ICC = 1).

RESULTS

Laryngovideostroboscopic findings

Two weeks after the LR, a more intermediate position of the vocal folds, with an associated increased dysphonia and dysphagia, was noted during clinical evaluation (see Appendix B for a comprehensive overview of LVS findings and vocal outcomes). This intermediate position was unchanged without any movement of the vocal folds two months after LR. At this point, voice therapy was started, which is described below. Four months post LR, LVS showed a slightly more paramedian position of the vocal folds without active ad- or abduction.

During a follow-up consultation in October 2019, 6 months after LR, a paramedian position of the vocal folds was observed at rest with minimal tonus of the left vocal fold and a present but asynchronous mucosal wave during phonation. Eight months after the LR procedure, LVS showed good tonus and activity in both vocal folds during phonation, although more apparent in the left, but minimal to no abduction during inspiration. In January 2020, LVS revealed minimal to no abduction, with a glottal opening of 2-3 mm on inspiration, and mild edema of the vocal folds, which was attributed to a potential respiratory infection.

One year and two months after the LR procedure, in June 2020, LVS showed an unaltered paramedian position of the vocal folds at rest without active abduction of the vocal folds on inspiration. During deep inhalation or inhalation through the mouth, minimal medialization of the vocal folds was observed, with stridor or mild inspiratory phonation as a result. LVS revealed a normal mucosal wave and normal vocal fold closure during phonation, as reported on the clinical record. The same observations were made in November 2020, one year and a half after the LR procedure, and in November 2021, two and a half years post LR (see Appendices A and B). Partial arytenoidectomy to improve the airway was proposed over the course of the rehabilitation process due to the ongoing respiratory complaints, but the patient was informed that this could potentially cause a decrease in voice quality. Because of this concern, the patient did not undergo the procedure and wished to preserve his current voice quality.

Evolution of acoustic, aerodynamic and auditory-perceptual vocal parameters after LR

The results from the first voice assessment, shortly before the start of voice therapy, showed severe deviations of all parameters (see Table 2). The MPT was extremely short due to the existing glottal insufficiency caused by the paralysis. An acoustic analysis showed that the patient's average fundamental frequency (211.631 Hz) deviated strongly (higher) from normative values in Flemish men, which range from 78 Hz to 166 Hz (De Bodt et al., 2015). Other acoustic parameters were also pathological, and the patient's frequency and intensity range were limited (Table 2). Consequently, his vocal capabilities (DSI -8.2) and voice quality (AVQI 7.68) indicated severe dysphonia. Cepstral analysis showed decreased CPPS values, both based on the vowel /a:/ and on continuous speech, which are illustrated in Table 2.

During the voice therapy program, a shorter voice assessment was performed twice to evaluate the evolution of the AVQI and CPPS. As can be seen in Table 2, the AVQI and CPPS values showed a large improvement between the first and the second intermediate evaluation.

After completion of the voice therapy program (8 months post LR), the patient had a fundamental frequency within normative range (132.164 Hz) and normal jitter and NHR values, as well as a normalized frequency range and cepstral measures. Additionally, intensity range and MPT were very limited, which had an impact on the DSI: although a strong improvement could be observed between the pre-assessment and post-assessment, the DSI (-2.5) indicated moderate to severe limitations in vocal capabilities. The AVQI (3.21) showed a clinically significant improvement in comparison to the pre-assessment (difference of 4.47) based on Barsties and Maryn (2013), but it was still suggestive of a mild dysphonia. Although vocal capabilities and voice quality still deviated from the norms, voice therapy was concluded at this time in dialogue with the patient due to work resumption.

The patient was invited for a long-term follow-up voice assessment approximately two years after the completion of voice therapy (ca. 31 months after the LR procedure). Nearly all parameters showed further improvement, as can be seen in Table 2, leading to a normalization of DSI to +2.3 (i.e. above the cut-off score of +1.6, Raes et al., 2002) and an AVQI of 2.35 (i.e. below the cut-off score of 2.95, Maryn et al., 2010). A visual representation of these improvements can be found in Figure 1 and 2. Only the MPT and lowest intensity still deviated from normative values.

Table 2: evolution of vocal parameters after LR

Parameter	**95% PI** ***(cut-off value)***	**Pre VT (24/06/19)**	**During VT (25/09/19)**	**During VT (08/11/19)**	**Post VT (19/12/19)**	**LT follow-up (22/11/21)**
Time after LR		*2 months*	*5 months*	*6.5 months*	*8 months*	*31 months*
Aerodynamic parameters						
MPT (s)	6.7 – 37.0 *(21.8)*	3.5*			5.0*	12.1*
Acoustic analysis						
Average f_o (Hz)	78 – 166	211.631* (high)	189.709* (high)	140.186	132.164	120.152
Jitter (%)	0 – 2.1 *(0.81)*	3.602*	1.989*	0.409	0.404	0.571
Shimmer (%)	0.7 – 6.4 *(3.6)*	13.075*	14.636*	3.409	4.744*	3.715
NHR	0.1 – 0.2 *(0.133)*	0.202*	0.104	0.030	0.035	0.031
$CPPS_{vowel}$	11.76 – 22.61	5.60*	5.21*	15.30	15.55	17.02
$CPPS_{speech}$	5.91 – 8.99	4.54*	4.97*	11.22	13.68	13.07
Signal type		IV	IV	II	I	I
Frequency and intensity range						
Lowest f (Hz)	51 – 118	185.00*			87.31	98.00
Highest f (Hz)	229 – 944	330.00			416.30	698.46
f range (ST)	21 – 45	10*			27	34
Lowest I (dB)	43 – 58	72*			67*	57
Highest I (dB)	81 – 114	84			84	107
I range (dB)	26 – 67	12*			17*	50
Multiparametric indices						
DSI	*(+1.6)*	-8.2*			-2.5*	+2.3
AVQI	*(2.95)*	7.68*	7.60*	3.37*	3.21*	2.35
Questionnaire						
VHI	*(20)*	51*			27*	33*

Abbreviations: PI: prediction interval; VT: voice therapy; LT: long-term; LR: laryngeal reinnervation; MPT: maximum phonation time; f_o: fundamental frequency; NHR: noise-to-harmonics ratio; CPPS: smoothed cepstral peak prominence; f: frequency; ST: semitones; I: intensity; DSI: Dysphonia Severity Index; AVQI: Acoustic Voice Quality Index; VHI: Voice Handicap Index
*Deviation from normative values (if available) of Flemish adult men, obtained from De Bodt et al. (2015) and Batthyany et al. (2019). 95% prediction intervals are provided in column 2. If a clinical cut-off value is available to determine whether the result is pathological, it is provided under the 95% PI.

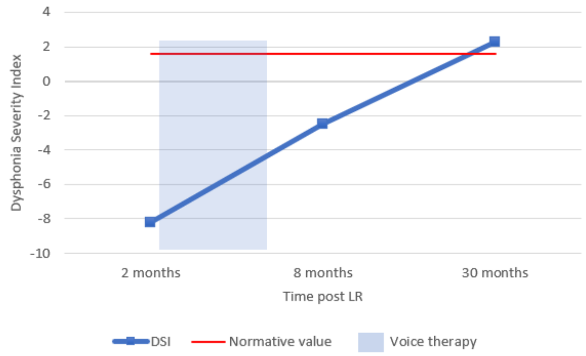

Figure 1: Evolution of the Dysphonia Severity Index after laryngeal reinnervation

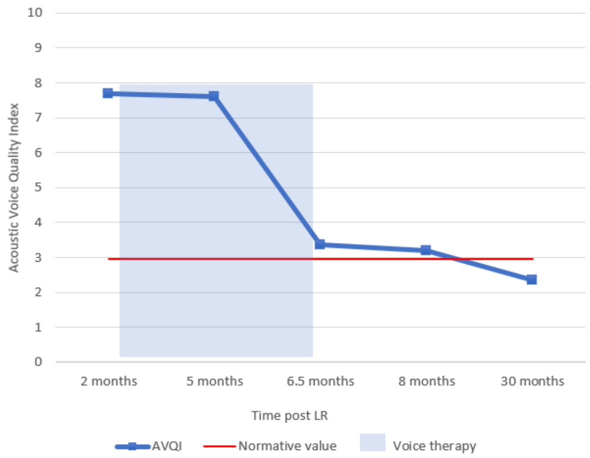

Figure 2: Evolution of the Acoustic Voice Quality Index after laryngeal reinnervation

The blinded consensus evaluation showed an improvement of overall Grade from 3 to 1 over the course of voice therapy. The sample from the long-term follow-up was rated as moderate (G2). Roughness was rated as mild in nearly all samples, except for the long-term follow-up, where the patient received a moderate R score. The most notable improvements were observed in breathiness and asthenia, which started at severe scores and ameliorated to normal to mild values after voice therapy. Strain showed variable scores and remained mild to moderate, while instability was scored as mild and eventually as normal in the long-term follow-up sample.

Table 3: Consensus evaluation of the GRBASI scale

Parameter	**Pre VT (24/06/19)**	**During VT (25/09/19)**	**During VT (08/11/19)**	**Post VT (19/12/19)**	**LT follow-up (22/11/21)**
Time after LR	*2 months*	*5 months*	*6.5 months*	*8 months*	*31 months*
Grade	3	3	2	1	2
Roughness	1	1	1	1	2
Breathiness	3	3	1	0	0
Asthenia	3	2	1	0	1
Strain	2	1	2	1	2
Instability	1	1	1	1	0

Abbreviations: LR: laryngeal reinnervation, VT: voice therapy, LT: long-term

Patient-reported vocal and respiratory outcomes

Information from clinical reports

Four months post LR, dyspnea on exertion, especially during warm weather, was reported by the patient, for example after climbing stairs or during long conversations. These complaints remained present over the course of the rehabilitation. In December 2019, the patient reported a sudden normalization of habitual pitch after a night out, approximately eight months post LR. However, pitch was still subjectively higher than before onset of the BVFP, and respiratory symptoms remained unchanged. An episode of increased dyspnea and stridor was reported by the patient in January 2020, nine months post LR, especially on exertion but also during sleep. When paying attention to respiration through the nose, some improvement was noticed. Respiratory complaints decreased during the following months, although exertional tolerance remained low.

During the long-term follow-up assessment in November 2021, the patient reported no respiratory problems at rest, but dyspnea still occurred sometimes on exertion. During sleep, stridor was sometimes observed by the patient’s partner, and if nasal breathing was hindered (e.g. in case of rhinitis), respiratory difficulties occurred more frequently. Dyspnea during conversations was not reported, although the patient had to breathe between phrases more often than before the onset of BVFP. He did report a subjective normalization of voice quality and pitch, but voice projection was still limited. This was occasionally problematic while performing his profession (construction work), especially in loud environments. Vocal fatigue did not occur according to the patient.

3.3.2 Questionnaires

At the start of the voice therapy program (June 2019), the patient scored 51 on the VHI, suggesting that the voice disorder caused substantial limitations to his ADL (see Table 2). However, this score reduced greatly to 27 after completion of voice therapy (December 2019), which indicated only some limitations of ADL. During the long-term follow-up assessment in November 2021, the VHI was slightly elevated compared to the post-assessment in December 2019, with a score of 33, still indicating some limitations of ADL.

The VFI, which was administered only at the long-term follow-up assessment, showed low scores in the first two domains. This corresponds to the patient's own report of not experiencing vocal fatigue. Only the statement 'I experience more effort while speaking' in the first domain received a score of 3 (almost always). The VTDS, also only completed during the long-term follow-up assessment, indicated a frequently occurring globus sensation with high intensity, but other sensations of discomfort occurred rarely or never. Lastly, according to the Corporal Pain Scale, the patient sometimes experienced a sore throat during or after voice use, but no other corporal pain symptoms were reported.

DISCUSSION

The clinical focus of BVFP treatment is usually improvement of respiration and securing the airway, which can be achieved through several techniques. However, in most techniques, such as cordotomy, arytenoidectomy and suture lateralization, laryngeal function is not restored and voice quality may be compromised (Li et al., 2017; Rubin & Sataloff, 2007). With selective bilateral laryngeal reinnervation, the aim is to restore functional vocal fold mobility, thus improving both respiration and voice quality (Li et al., 2017; Marie, 2009). Previous case reports and clinical studies have documented promising results of LR on respiratory and vocal function in both adults and children (Lee et al., 2020; Li et al., 2013; Marie & Heathcote, 2018), but extensive results of multi-dimensional vocal assessments are often lacking. The objective of the current case study was to report the longitudinal vocal outcomes of selective bilateral laryngeal reinnervation in an adult patient with BVFP.

LVS findings during follow-up ultimately showed complete adduction to a small posterior gap of the vocal folds during phonation (see Appendices A and B), but active abduction on inspiration remained absent throughout the rehabilitation process. One year and a half after LR, no recovery of the PCA muscles was expected, but the patient showed relatively adequate adaptation to the situation. Reinnervation of the PCA muscles has always been a challenge in LR, and results from previous clinical studies show a variable success. Out of 40 patients, Marie and Heathcote (2018) described successful arytenoid abduction on at least one side on inspiration in 27, and bilateral abduction in 16. Li et al. (2013) reported an 87% recovery rate of vocal fold abduction after LR in a series of 44 patients. Potential reasons for failure of PCA muscle reinnervation may be synkinesis through a communicating branch between the PCA and interarytenoid (IA) muscles or delay between onset of the BVFP and LR (Su et al., 2015; van Lith-Bijl et al., 1998). Since no LEMG assessments were performed, it is impossible to determine whether a minimal PCA reinnervation was still achieved or not.

Although inspiratory arytenoid abduction was not visible in the current case study, active adduction was still achieved after an initial increase of aspiration and dysphonia after the LR procedure, due to a more intermediate position of the vocal folds. This temporary degradation of voice was expected until axonal growth was achieved (Marie, 2009). A gradual but ultimately clinically significant improvement of voice quality, acoustic parameters and patient-reported outcomes were observed afterwards. The most noticeable clinical improvements of vocal parameters were detected approximately six months after the LR procedure, which lies within the expected time frame of nerve recovery from the muscle reinnervation (Marie, 2009). At that moment, voice therapy had been ongoing for four months. Furthermore, our patient reported a normalization of voice quality and pitch to pre-onset level between eight months and one year after LR, soon after completion of voice therapy, which is reflected in the results from the vocal assessment of December 2019 and November 2021.

Our results are in line with reports from previous studies, who reported an amelioration of vocal parameters in nearly all cases (Lee et al., 2020; Li et al., 2019; Marie & Heathcote, 2018). Lee et al. (2020) reported improved GRBAS scores, with a decrease of at least one component with one or two points, in six out of eight pediatric patients. The two remaining patients already showed normal to mildly disturbed GRBAS scores preoperatively. Our patient showed similar improvements of auditory-perceptual voice quality after voice therapy, but no preoperative auditory-perceptual evaluation was possible. In a larger study with 44 participants, Li et al. (2013) found improvement in jitter (from 1.19% to 1.07%), shimmer (7.92% to 7.19%) and MPT (8.93 s to 9.21 s) 12 months after LR of the PCA muscles, but none of the investigated vocal parameters showed statistically significant changes. Likewise, auditory-perceptual parameters from the GRBAS scale remained stable, with median differences of 0.2 points or less, after the procedure. It is important to note that the authors of the latter study did not perform adductor reinnervation, which may explain the lack of significant improvements. Additionally, acoustic and auditory-perceptual parameters at the preoperative assessment were already closer to normative values than in the current case study. Marie and Heathcote (2018) described preservation or improvement of the voice in almost all cases out of 49, but no specific measurements are provided, which renders comparison to the current case study difficult.

This case study is the first to use a holistic multidimensional voice assessment to evaluate vocal outcomes after LR in a BVFP patient at multiple time intervals, with inclusion of PROMS and multiparametric indices to objectively quantify voice quality. This allowed for a standardized and objective follow-up of voice quality and offered an insight in the timespan of this evolution. As previously mentioned, a notable improvement of DSI and AVQI was observed after approximately 6 months post LR, but even after two years, further advancement of vocal capabilities and quality could be expected. Still, the blinded perceptual evaluation revealed a moderate grade and roughness of the voice at the last follow-up, which were rated mild immediately after voice therapy. Similarly, asthenia and strain received higher scores for the sample of the last follow-up. A potential explanation for this seeming deterioration of auditory-perceptual voice quality is that voice therapy was completed approximately two years ago by then; application of the vocal techniques, such as speaking with abdominal breath support and forward focus of the voice, may have diminished somewhat. Nevertheless, objective vocal outcome measures were suggestive of a normal voice quality, and the patient reported that his voice quality was nearly identical to his voice before the onset of BVFP. The PROMS, and more specifically the VHI, showed that BVFP caused significant limitations to the voice-related quality of life of our patient at the start of voice therapy, which is similar to findings from related studies investigating psychosocial impact of the voice in BVFP after surgical treatment that reported mean VHI scores of 55 and VHI-10 scores of 14.25 (Bosley et al., 2005; Harnisch et al., 2008). However, surgical treatment in those studies consisted of arytenoidectomy and cordotomy, which usually have an adverse effect on voice quality (Marie, 2009; Rubin & Sataloff, 2007). The VHI score obtained before start of voice therapy in the current study corresponded to a more intermediate position of the vocal folds in our patient, while adduction was functionally restored during the follow-up assessments. Interestingly, even though a normal objective voice quality and vocal capabilities were obtained 31 months after LR, the VHI still showed some limitations in the patient's ADL due to his voice. This could potentially be explained by the self-perceived inability to project the voice and to speak long sentences, since certain statements on the VHI are related to these issues (e.g. 'I run out of air when I talk', 'People have difficulty understanding me in a noisy room'). Additionally, the VHI showed a slightly higher score at the long-term follow-up assessment in November 2021 compared to the post-therapy assessment of December 2019 (increase of 6 points), but according to Jacobson et al. (1997), a difference of at least 18 points between two administrations represents a significant change in psychosocial function.

To the best of our knowledge, none of the studies reporting vocal outcomes after LR described the use of voice therapy after the procedure. Nonetheless, voice therapy may positively influence vocal outcomes of BVFP after LR by teaching the patient how to correctly use the newly innervated larynx and by eliminating compensatory hyperfunctional behavior (Marie, 2009; Rubin & Sataloff, 2007). In our patient, LVS before LR showed supraglottic compensation during phonation, which resulted in a weak and high-pitched voice. One objective of voice therapy after LR was to avoid this compensatory hyperfunctional activity to obtain a healthy and efficient phonation. This goal was achieved after six months of voice therapy and with recovery of the adductory musculature, since no supraglottic compensation was observed during follow-up LVS. Special attention was also given to breathing technique and adequate breath support in voice therapy to stimulate the diaphragm and PCA reinnervation. No formal respiratory outcome measures are available, but an increase in MPT was noticed during the last follow-up assessment. Although PCA recovery was not accomplished, voice therapy may have aided in compensation of respiratory issues. Harnisch et al. (2008) reported that voice therapy that had a positive effect on breathing technique and speaking habits subsequently improved subjective physical capacity (e.g. exertion tolerance) and voice quality in several patients. Since scientific literature is still inconclusive about the contribution of voice therapy in BVFP, this case study offers a first insight in the potential merit of voice therapy in BVFP, both for rehabilitation of the voice and respiration. More research is needed to determine the extent of the efficacy of voice therapy in BVFP, and to identify exercises that provide the greatest benefits to vocal and respiratory recovery after LR. It would be interesting to explore whether voice therapy invokes a better outcome of laryngeal activity, voice quality and respiration compared to a more conservative approach after LR.

The current study has its limitations. First, the report is retrospective in nature, except for a prospective follow-up assessment two and a half years after LR. Not all data from before the LR procedure were available, and videos from LVS assessments were not always saved, which impeded a blinded evaluation of LVS findings. Additionally, the two first voice samples were classified as a type IV acoustic signal, which is less reliable for perturbation analyses (Sprecher et al., 2010). It has been suggested that cepstral and spectral analyses, as well as auditory-perceptual evaluation may be more accurate in measuring dysphonia severity in these severely dysphonic voices (Choi & Choi, 2014; Sprecher et al., 2010). These latter evaluations were included in the multidimensional voice assessment of the current study to offer a complete and more reliable report of the patient's voice quality over time. Based on these considerations, it is highly recommended that future studies also conduct a multidimensional voice assessment in all patients with BVFP. Lastly, LEMG was not used to evaluate neuromuscular activation of the vocal folds after LR, since the patient did not wish to undergo these assessments. Therefore, it is not possible to ascertain the status of reinnervation after the LR procedure. This in turn makes it difficult to transfer our findings to other similar cases. Functional LVS findings were also not always described in clinical reports. Future studies should include LEMG assessments and standardized extensive reports of LVS findings to provide a complete overview of physiological, functional, and structural outcomes after LR. Nevertheless, the study offers new insights on the long-term vocal outcomes and potential contribution of voice therapy after LR, which merits further investigation.

Data availability statement

All data generated or analyzed during this study are included in this published article.

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Data availability statement

All data generated or analyzed during this study are included in this article.

6. TABLES AND FIGURES

Table 1: overview of techniques utilized in voice therapy

Technique	**Description**
Education and counselling	Explanation of anatomy and physiology of the larynx and current pathology
Vocal hygiene program	Selection and discussion of vocal hygiene measures
Posture	Correct and eutonic posture for phonation in sitting and standing position
Relaxation	Local relaxation of neck, shoulders, larynx and pharynx
Respiration	Costo-abdominal respiration type and adequate breath support for phonation
SOVTE	Improving glottal closure through improved source-filter interaction - Water-resistance therapy - Resonant voice exercises
Voice placing, forward focus	Often combined with resonant voice exercises: gradual reduction of excessive resonance but maintenance of forward focus
Laryngeal manipulation	Relaxing tense (peri)laryngeal musculature
Pitch and loudness exercises	Strengthening and balancing the laryngeal musculature by exercises on pitch and loudness combined with SOVTE - Pitch glides: low to high, high to low, and alternating - Loudness exercises: swelling tones and alternating
Generalization and transfer	Combination of all learned techniques at different levels: word, sentence, text level, (semi)spontaneous speech

Abbreviations: SOVTE: semi-occluded vocal tract exercises

Table 2: evolution of vocal parameters after LR

Parameter	**95% PI *(cut-off value)***	**Pre VT (24/06/19)**	**During VT (25/09/19)**	**During VT (08/11/19)**	**Post VT (19/12/19)**	**LT follow-up (22/11/21)**
Time after LR		*2 months*	*5 months*	*6.5 months*	*8 months*	*31 months*
Aerodynamic parameters						
MPT (s)	6.7 – 37.0 *(21.8)*	3.5*			5.0*	12.1*
Acoustic analysis						
Average f_o (Hz)	78 – 166	211.631* (high)	189.709* (high)	140.186	132.164	120.152
Jitter (%)	0 – 2.1 *(0.81)*	3.602*	1.989*	0.409	0.404	0.571
Shimmer (%)	0.7 – 6.4 *(3.6)*	13.075*	14.636*	3.409	4.744*	3.715
NHR	0.1 – 0.2 *(0.133)*	0.202*	0.104	0.030	0.035	0.031
$CPPS_{vowel}$	11.76 – 22.61	5.60*	5.21*	15.30	15.55	17.02
$CPPS_{speech}$	5.91 – 8.99	4.54*	4.97*	11.22	13.68	13.07
Signal type		IV	IV	II	I	I
Frequency and intensity range						
Lowest f (Hz)	51 – 118	185.00*			87.31	98.00
Highest f (Hz)	229 – 944	330.00			416.30	698.46
f range (ST)	21 – 45	10*			27	34
Lowest I (dB)	43 – 58	72*			67*	57
Highest I (dB)	81 – 114	84			84	107
I range (dB)	26 – 67	12*			17*	50
Multiparametric indices						
DSI	*(+1.6)*	-8.2*			-2.5*	+2.3
AVQI	*(2.95)*	7.68*	7.60*	3.37*	3.21*	2.35
Questionnaire						
VHI	*(20)*	51*			27*	33*

Abbreviations: PI: prediction interval; VT: voice therapy; LT: long-term; LR: laryngeal reinnervation; MPT: maximum phonation time; f_o: fundamental frequency; NHR: noise-to-harmonics ratio; CPPS: smoothed cepstral peak prominence; f: frequency; ST: semitones; I: intensity; DSI: Dysphonia Severity Index; AVQI: Acoustic Voice Quality Index; VHI: Voice Handicap Index

*Deviation from normative values (if available) of Flemish adult men, obtained from De Bodt et al. (2015) and Batthyany et al. (2019). 95% prediction intervals are provided in column 2. If a clinical cut-off value is available to determine whether the result is pathological, it is provided under the 95% PI.

Table 3: Consensus evaluation of the GRBASI scale

Parameter	**Pre VT (24/06/19)**	**During VT (25/09/19)**	**During VT (08/11/19)**	**Post VT (19/12/19)**	**LT follow-up (22/11/21)**
Time after LR	*2 months*	*5 months*	*6.5 months*	*8 months*	*31 months*
Grade	3	3	2	1	2
Roughness	1	1	1	1	2
Breathiness	3	3	1	0	0
Asthenia	3	2	1	0	1
Strain	2	1	2	1	2
Instability	1	1	1	1	0

Abbreviations: LR: laryngeal reinnervation, VT: voice therapy, LT: long-term

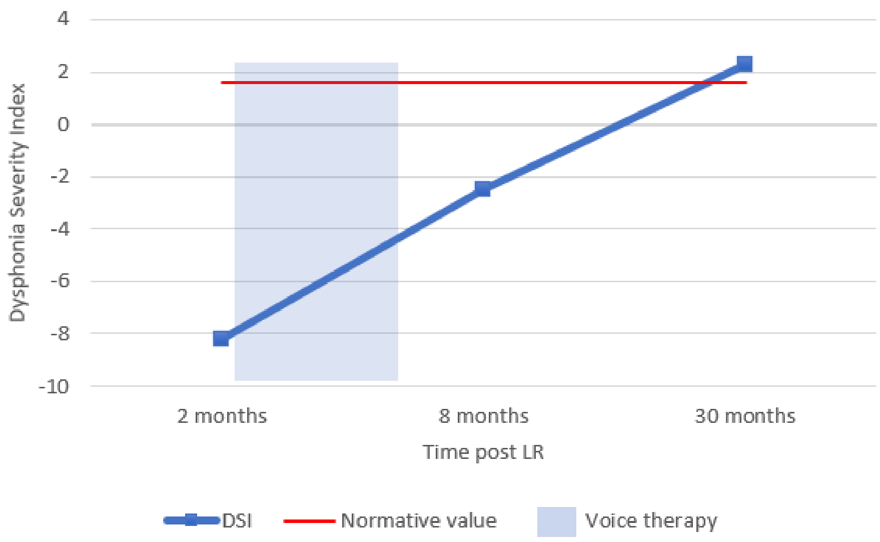

Figure 1: Evolution of the Dysphonia Severity Index after laryngeal reinnervation

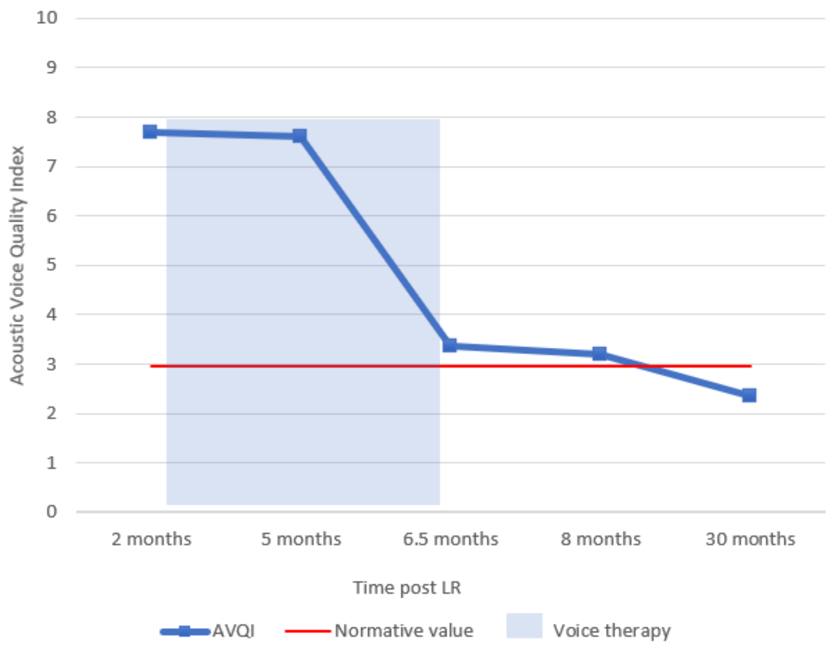

Figure 2: Evolution of the Acoustic Voice Quality Index after laryngeal reinnervation

7. APPENDICES

Appendix A: Images from laryngovideostroboscopic recordings of the vocal folds at rest and during phonation

Time	At rest	During phonation
November 19 2018		
April 2019	Laryngeal reinnervation procedure	
June 24 2019		
August 19 2019		
June 15 2020		
November 22 2021		

Appendix B: Time frame of LVS findings, vocal outcomes, and other reported complaints following traumatic BVFP and LR

Time	LVS	Voice	Other clinical reports
October 19, 2018 Onset of BVFP	- Paramedian position of VF - No mobility	Aphonia	Dysphagia (improvement after 1m of swallowing therapy)
January 4, 2019 3m post onset	- Paramedian position of VF - No mobility - Supraglottic adduction	Aphonia	
February 4, 2019 4m post onset	- More paramedian position of VF - No mobility - Supraglottic adduction	Weak and high-pitched voice	
LR procedure at the end of April 2019			
May 13, 2019 7m post onset 2 weeks post LR	- Intermediate position of VF - No mobility - No MW	Increased dysphonia (clinical report)	Temporary increase of aspiration
June 24, 2019 8m post onset 2m post LR	- Intermediate position of VF - No mobility - No MW	- Pathological MPT and acoustic parameters - Reduced frequency and intensity range - DSI: -8.2 and AVQI: 7.68 - VHI: 51	
Start of voice therapy			
August 19, 2019 10m post onset 4m post LR	- Slightly more paramedian position of VF - No mobility		Dyspnea on exertion
October 7, 2019 12m post onset 6m post LR	- Paramedian position of VF - Minimal tonus of left VF during phonation - Asynchronous MW		
December 23, 2019 14m post onset 8m post LR	- Good tonus and some degree of activity of VF during phonation - Minimal to no abduction	***December 19, 2019*** - Pathological MPT - Normative acoustic parameters (except for shimmer) - Normative frequency range - Reduced intensity range - DSI: -2.5 and AVQI: 3.21 - VHI: 27	Sudden decrease of pitch after a night out Dyspnea on exertion
	End of voice therapy		
January 7, 2020 15m post onset 9m post LR	- Minimal to no abduction - Mild edema of VF		Episode of dyspnea and stridor on exertion and at rest
June 15, 2020 20m post onset 14m post LR	- Unaltered situation - More tonus in the left VF than right		
November 23, 2020 25m post onset 19m post LR	- Paramedian position of VF - No abduction - Normal MW and GC		
November 22, 2021 37m post onset 31m post LR	- Paramedian position of VF - No abduction - Normal MW and GC	- Pathological MPT - Normative acoustic parameters - Normative voice range - DSI: +2.3 and AVQI: 2.35 - VHI: 33	Dyspnea on exertion

Abbreviations: LVS: laryngeal videostroboscopy, BVFP: bilateral vocal fold paralysis, VF: vocal folds, m: months, LR: laryngeal reinnervation, MPT: maximum phonation time, DSI: Dysphonia Severity Index, AVQI: Acoustic Voice Quality Index, VHI: Voice Handicap Index, MW: mucosal wave, GC: glottal closure

Appendix C: Dutch oronasal reading passage ‘Papa en Marloes’

Papa en Marloes staan op het station.

Ze wachten op de trein.

Eerst hebben ze een kaartje gekocht.

Er stond een hele lange rij, dus dat duurde wel even.

Nu wachten ze tot de trein eraan komt.

Het is al vijf over drie, dus het duurt nog vier minuten.

Er staan nog veel meer mensen te wachten.

Marloes kijkt naar links, in de verte ziet ze de trein al aankomen.