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Laryngology

Bilateral selective laryngeal reinnervation in patients with bilateral vocal cord palsy

Reinnervazione selettiva bilaterale della laringe nei pazienti con paralisi bilaterale delle corde vocali

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SUMMARY

Objective. Bilateral selective reinnervation of the larynx aims to restore both vocal cord tone and abductor movements in patients with bilateral vocal cord palsy.

Methods. Four females and one male treated by bilateral selective reinnervation of the larynx were included in the present study. In all cases, both posterior cricoarytenoid muscles were reinnervated using the C3 right phrenic nerve root through the great auricular nerve graft, while adductor muscle tone was bilaterally restored using the thyrohyoid branches of the hypoglossal nerve through transverse cervical nerve grafts.

Results. After a minimum follow-up of 48 months, all patients were successfully tracheostomy free and had recovered normal swallowing. At laryngoscopy, the first patient recovered a left unilateral partial abductor movement, the second had complete bilateral abductor movements, the third did not show improvements of abductor movements, but symptomatology was improved, the fourth recovered partial bilateral abductor movements and the fifth case did not show improvements and needed posterior cordotomy.

Conclusions. Bilateral selective laryngeal reinnervation, although a complex surgical procedure, offers a more physiologic recovery in the treatment of bilateral vocal fold paralysis. Selection criteria still needs to be precisely defined to avoid unexpected failures.

KEY WORDS: recurrent laryngeal nerve, selective reinnervation, vocal fold paralysis, functional results

RIASSUNTO

Obiettivo. *La reinnervazione bilaterale della laringe ha lo scopo di ripristinare sia il tono delle corde vocali che i movimenti degli abduttori in pazienti con paralisi glottica bilaterale.*

Metodi. *Quattro donne e 1 uomo, sottoposti a reinnervazione bilaterale della laringe, sono stati inclusi nello studio. In tutti i casi entrambi i muscoli crico-aritenoidei posteriori sono stati reinnervati con la radice C3 del nervo frenico. Il tono dei muscoli adduttori è stato ripristinato bilateralmente utilizzando il nervo per il muscolo tiro-ioideo, con l'interposizione di un innesto prelevato dal nervo cervicale trasverso.*

Risultati. *Dopo 48 mesi, tutti i pazienti hanno potuto chiudere il tracheostoma e recuperare una alimentazione orale fisiologica. All'ultimo controllo fibrolaringoscopico, il primo paziente ha recuperato una abduzione parziale della corda vocale sinistra, il secondo movimenti abduttori bilaterali nei limiti della norma, il terzo non ha mostrato miglioramenti della motilità volontaria ma riferisce un miglioramento soggettivo della sintomatologia, il quarto paziente ha recuperato movimenti abduttori parziali e il quinto caso non ha avuto alcun beneficio ed è stato sottoposto a cordotomia posteriore.*

Conclusioni. *La reinnervazione bilaterale selettiva della laringe consente un recupero di una funzione laringea più fisiologica in selezionati pazienti con paralisi delle corde vocali. Le modalità di selezione dei pazienti devono ancora essere ben definite attraverso casistiche più ampie, al fine di evitare fallimenti inattesi.*

PAROLE CHIAVE: *nervo laringeo ricorrente, reinnervazione selettiva, paralisi delle corde vocali, risultati funzionali*

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Introduction

Bilateral vocal fold paralysis (BVFP) in adults is most frequently observed after total thyroidectomy, due to the bilateral lesion of the recurrent laryngeal nerve (RLN), although head and neck trauma can be a further aetiology [1-3]. From 4% to 14% of patients tolerate this condition, which can be managed with conservative speech and swallowing therapy [1,2]. Botulinum toxin injections can be used in low-symptomatic cases to reduce synkinesis, while gene and stem cell therapy are only in the experimental phase of research [3].
When BVFP considerably compromises the airway, it represents a dramatic and potentially life-threatening condition [4-6]. Surgical techniques through external and endoscopic approaches are indicated in cases of symptomatic BVFP [7]. Numerous procedures have been described and targeted to improve the airway without major voice disruption [8].
Usual treatments for BVFP are mainly based on a static enlargement of the airway at the glottic level. Static glottic enlargement procedures consist in removal of laryngeal tissue (cordectomy plus or minus partial arytenoidectomy) or shifting anatomic structures (latero-fixation of the vocal fold or arytenoid abduction) [7]. Enlargement of the airway is inevitably achieved with the worsening of voice and risk of aspiration on swallowing.
The current challenge of treating BVFP is to restore both vocal folds tone and abductor movements while preventing synkinesis and swallowing impairment, without the need to perform tissue resection [4].
The physiological restoration of laryngeal function could be attempted with bilateral reinnervation techniques. The key to restoring inspiratory laryngeal abduction is to provide an inspiratory trigger to the posterior cricoarytenoid (PCA) muscles while preventing synkinetic respiratory vocal adduction [9].
Different methods of bilateral reinnervation of the larynx have been proposed in the literature, varying on the basis of the donor nerves [4]. In 2014, Marie reported promising results in BVFP patients treated with bilateral selective laryngeal reinnervation (BSLR), reporting a decannulation rate of 92.5% in 40 patients with more than 1 year of follow-up [10].
To date, this BSLR technique has been reproduced in only a few centers [11-13]. Since these promising reports, our group performed this technique in a series of patients with BVFP and the results are reported herein.

Materials and methods

Five patients (4 females, 1 male) with BVFP (identified as CA1, CA2, CA3, GE4 and GE5) underwent BSLR from October 2017 to February 2019.
The inclusion criteria for BSLR were diagnosis of BVFP for more than 6 months (23, 8, 84, 12, and 96 months, respectively) with no sign of reinnervation of the PCA muscles detected at pre-operative evaluation and good health status (patients were fit and well, and no neuromuscular pathologies or respiratory diseases were present).
Two of 5 patients were tracheostomy dependent when referred to our team; tracheostomy was performed at other ENT departments due to acute respiratory distress.
A multidisciplinary team was established during both pre-operative and post-operative work-up: neurologists, speech and language therapists and pneumologists were considered necessary for the correct assessment of patients.
Pre-operative evaluations included fibrelaryngoscopy, videostroboscopy, voice perceptual analysis, laryngeal electromyography (EMG), contrast-enhanced head and neck and chest computed tomography (CT), and respiratory function tests.
In patients CA1, GE4, and GE5, pre-operative fibrelaryngoscopy showed BVFP in a complete adduction position during inspiration with complete glottic closure during phonation. Patient CA2 had BVFP in the paramedian position. In patient CA3, fibrelaryngoscopy showed a near complete closure of the glottic space due to tight median position of the vocal folds associated with some sporadic synkinetic movements.
Speech and language assessment consisted of the evaluation with Grade, Roughness, Breathiness, Asthenia, and Strain (GRBAS), Voice Handicap Index (VHI) 10, Airway-Dyspnea-Voice-Swallow (ADVS) scales, maximum phonation time (MPT), and Eating Assessment Tool (EAT) 10 scores, collected pre- and post-operatively [14-16]. In the present study, the most descriptive parameter of the GRBAS scale was the grade of hoarseness [G] (rating scale: 0 = normal; 1 = slight; 2 = moderate; 3 = severe hoarseness). The ADVS has already been used for assessment of quality of life in patients with BVFP [7] and evaluates four laryngeal functions, scoring each domain on a 1-5 scale. The EAT-10 is a self-administered, symptom-specific outcome scoring system for the evaluation of dysphagia [15,16]. The physiological MPT usually ranges from 15 to 25 seconds and from 25 to 35 seconds in women and men, respectively.
Pre-operative laryngeal EMG was always performed under local anaesthesia under fibrelaryngoscopy with the ENT and a dedicated neurophysiologist. The needle electrode positioning must be accurate, because the insertion into adjacent pharyngeal musculature could show inspiratory muscle activity even in case of BVFP, producing a false positive result. EMG helps to objectively assess the absence of functional PCA movements, and to determine degrees of denervation, spontaneous reinnervation and muscle atrophy [9].
Pre-operative spirometry was performed on every patient. Direct laryngoscopy under general anaesthesia was always

performed before reinnervation, and bilateral crico-arytenoid joint movements were evaluated to confirm that patients were not affected by ankylosis or posterior stenosis and, consequently, were suitable for BSLR.

Surgical procedure

All patients underwent standard general anaesthesia and ventilation through the tracheostomy performed after intubation if not already present. Laryngeal access was achieved through a horizontal neck incision made approximately 2-4 cm above the suprasternal notch at the level of the cricoid. A standard subplatysmal flap was elevated. Sternocleidomastoid muscles, the anterior belly of the digastric muscles, the neurovascular bundle and the accessory nerve were bilaterally isolated. Before any further laryngeal dissection, the great auricular nerve (GAN) and the transverse cervical nerve were both isolated. A Y-shaped free nerve graft and two linear free nerve grafts were harvested for subsequent use (Fig. 1).

Ten cm of the external jugular vein was harvested and divided equally into 5 segments for subsequent protection of the nerve sutures. The right phrenic nerve was dissected and traced retrogradely until its roots were found; its roots (C3-C5) were identified using a disposable nerve stimulator, and the nerve was isolated for later use (Fig. 1).

Under a microscopic view (ZEISS S7 Microscope, Carl Zeiss, USA; focal length 250 mm), the inferior constrictor muscles were released from the posterior margins of the thyroid alae to visualise both RLNs and the posterior crico-arytenoid muscles. The RLNs were traced proximally to the site of RLN injury. The distal stump of the bilateral RLNs were exposed, removing the scar tissue or neuroma. The postero-inferior portion of the thyroid lamina was partially removed to allow exposure of the intra-laryngeal branches of the RLNs. The main trunk of the RLN was sectioned distant from the scar. The hypoglossal nerve was dissected to expose its thyrohyoid branch, easily identified using a disposable nerve stimulator, and then transected as distally as possible. The main trunk of the RLN was linked to the thyrohyoid branch of the hypoglossal nerve with interposition of the transverse cervical nerve free graft bilaterally. The proximal end of the right phrenic nerve, sectioned after the C3 root, but before C4-C5, was anastomosed with the main trunk of the Y-shaped free nerve graft, whereas each distal branch of the Y-shaped free nerve graft was implanted into the main body of each PCA muscle. Neurorrhaphies were made using 8/0-9/0 Ethilon sutures under magnification of surgical microscope. In Figure 2 a schematic representation of the neurorrhaphies of BSLR is shown.

A vein sheath segment previously harvested from the external jugular vein was used to cover each nerve suture. Finally, the wound was closed in layers. A passive drain (Penrose) was used to avoid any negative pressure on the anastomoses. A cuffed tracheal tube was positioned in all patients.

Post-operative care was ward-based and did not require any intensive care monitoring. Nevertheless, 48-hour continu-

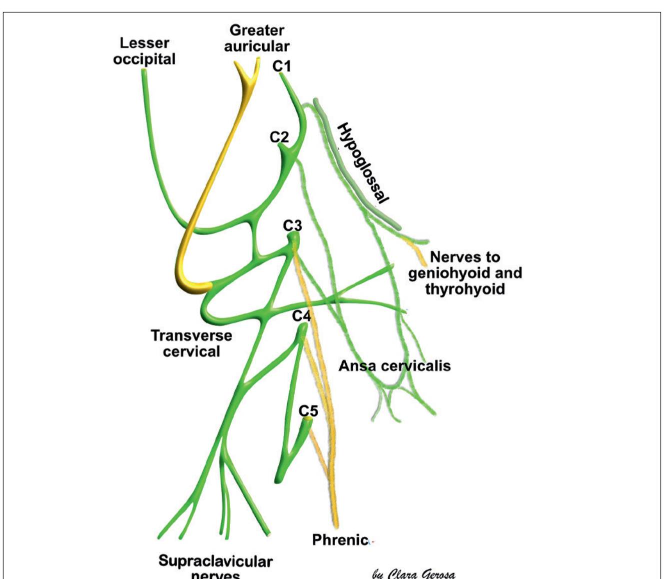

Figure 1. Scheme of the anatomy of the nerves (drawn in yellow) used during surgery for the BSLR.

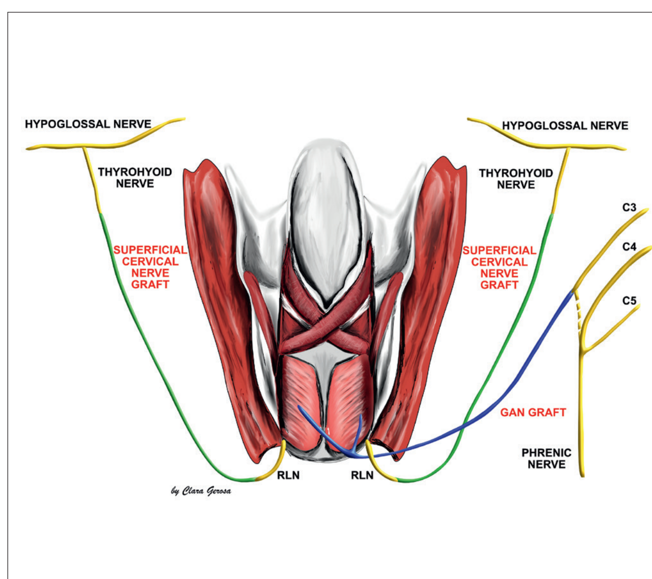

Figure 2. Schematic representation of the neurorrhaphies performed during BSLR: donor and recipient nerves are drawn in yellow, while grafts are shown in green (grafts harvested from the superficial cervical plexus) and blue (the Y-shaped GAN graft).

ous monitoring of vital signs was performed for every patient. Antibiotics were administered daily for 7 days. Proton pump inhibitors were used to prevent gastric reflux and potential aspiration. In addition, all patients were kept on total parenteral nutrition for two post-operative days, and nasogastric tube feeding was subsequently started. Pain control was achieved using continuous morphine infusion for the first 48 hours.

All patients were followed-up after surgery by fibrelaryngoscopy. All endoscopic procedures were recorded to better evaluate any "new acquired movements" (NAM): the outcomes were codified as abduction (Ab) and adduction (Ad). The decannulation rate and the time of decannulation were considered as parameters of surgical success in patients who were tracheostomised before the procedure.

Results

Four patients had BVFP after thyroid surgery (cases: CA1, CA3, GE4 and GE5), and one patient (CA2) had BVFP after trauma. Patient CA2 had a percutaneous gastrostomy before BSLR, and two patients were tracheostomy dependent before surgery (patients CA1 and CA2). Patients CA3, GE4 and GE5 underwent tracheostomy at the time of the surgical procedure to avoid post-operative life-threatening complications. All patients underwent BSLR using the phrenic nerve on the right and the thyrohyoid branch of the hypoglossal nerve bilaterally as donors. Post-operatively, four of five patients were fed by nasogastric feeding tube, and one (CA2) was fed by percutaneous gastrostomy. Speech and swallowing therapy were started at 3 days after surgery in all cases. Nasogastric feeding tubes were removed within 7 days in four patients, while patient CA2 continued feeding through percutaneous gastrostomy for 3 months after surgery until he recovered complete oral feeding. Patients did not experience post-operative complications. Chest X-ray showed unilateral palsy of the right diaphragm in all cases, but it was always asymptomatic, and recovery was confirmed in all cases at one year after surgery.

Endoscopic findings

During the first months after surgery, glottic movements were impaired and after bilateral transection of the RLN the cadaveric position reached by the vocal folds improved the airways, although tracheostomy was still needed. After long-term follow-up of at least 48 months, all patients were successfully tracheostomy free and recovered normal swallowing. At fibrelaryngoscopy/videostroboscopy, three of five patients showed a "new acquired movement" (NAM): patient CA1 recovered left unilateral Ab movements, patient CA2 recovered bilateral Ad and Ab movements (Figs. 3A, 3B), patient CA3 did not show NAM, but her original dyspnoea was improved; patient GE4 recovered bilateral Ab movements, and patient GE5 did not show any improvements and needed posterior cordotomy.

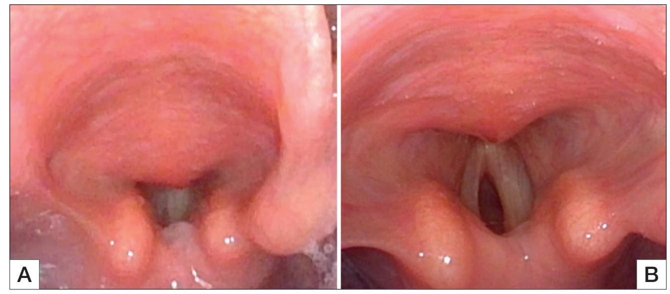

Figure 3. Post-operative fibrelaryngoscopy of patient CA2 showing a bilateral Ad during phonation (**A**) and Ab during inspiration (**B**).

Functional achievements

None of our patients experienced pneumonia during swallowing training or during follow-up: the post-operative EAT 10 score was normal (score of 2 in all patients). Voice analysis showed a decreased post-operative G score in comparison with pre-operative values in cases CA1, CA2 and GE4 and remained steady in cases CA3 and GE5 (score of 3 in both cases). The ADVS score improved in all patients. All the patients were tracheostomy-free: the mean decannulation time was 10.4 months (24, 2, 3, 8 and 15 months, respectively). Spirometry performed 12 months after surgery showed that FVC and FEV1 were not significantly different from the normal reference values in all patients: even though an overall reduction in the expiratory volumes was detected due to fixed upper airway alterations in all the patients, on average, a post-operative improvement was detected. Patient features and outcomes are detailed in Tables I and II.

Discussion

Until the 1920s, tracheotomy was the only treatment that was routinely applied for the treatment of nonreversible symptomatic BVFP. In 1922, Chevalier Jackson was the first surgeon to perform open ventriculocordectomy with the intent of improving the airway while preserving the voice [17]. During the seventies, arytenoidectomy by a cervical approach, which was proposed by Woodman et al. [18], obtained general agreement. Afterward, transoral approaches were progressively developed, and currently, transoral laser-assisted posterior cordotomy is frequently used due to its lower complication rate, absence of an external scar, and shorter surgical and hospitalisation times [7]. However, airway improvement after static glottic-widening

Table I. Pre-operative features of patients treated with selective laryngeal reinnervation for BVFP.

Patients/sex/age	BVFP etiology	Duration of BVFP	Pre-op. PEG dependence	Pre-op. tracheostomy dependence	Pre-op. ADVS	Pre-op. EAT10	Pre-op. VHI	Pre-op. GIRBAS
CA1/female/44 years	Thyroid surgery (2015)	23 months	No	Yes	4,4,2,2	13	106	3, 1, 1, 0, 1, 0
CA2/male/33 years	Cervical injury (2017)	8 months	Yes	Yes	4,4,2,5	28	110	3, 1, 1, 2, 2, 0
CA3/female/46 years	Thyroid surgery (2011)	84 months	No	No	1,3,2,2	14	22	2, 0, 2, 0, 1, 0
GE4/female/59 years	Thyroid surgery (2018)	12 months	No	No	1,4,3,2	23	18	2, 2, 1, 1, 1, 1
GE5/female/29 years	Thyroid surgery (2010)	96 months	No	No	1,5,3,3	18	25	3, 2, 1, 1, 1, 1

BVFP: bilateral vocal fold paralisis; PEG: percutaneous endoscopic gastrostomy; ADVS: airway dyspnoea voice swallowing; EAT 10: eating assessment tool; VHI: voice handicap index; GIRBAS: grade, roughness, breathiness, asthenia, strain.

Table II. Post-operative features of patients treated with selective laryngeal reinnervation for BVFP.

Patients	Post-op. PEG dependence	Post-op. tracheostomy dependence	Post-op. ADVS	Post-op. EAT-10	Post-op. VHI	Post-op. GRBAS	Post-op. spirometry outcomes
CA1	No	No	1, 2, 2, 1	8	80	1, 1, 0, 1, 1, 0	Improved
CA2	No	No	1, 2, 2, 1	2	35	1, 1, 0, 0, 1, 0	Improved
CA3	No	No	1, 2, 2, 2	10	15	2, 0, 2, 0, 1, 0	Unchanged
GE4	No	No	1, 1, 2, 1	1	11	1, 0, 1, 0, 0, 0	Improved
GE5	No	No	1, 2, 2, 1	1	18	3, 2, 1, 1, 1, 1	Unchanged

BVFP: bilateral vocal fold paralisis; PEG: percutaneous endoscopic gastrostomy; ADVS: airway dyspnoea voice swallowing; EAT 10: eating assessment tool; VHI: voice handicap index; GIRBAS: grade, roughness, breathiness, asthenia, strain.

procedures is often incomplete, and is at the expense of poorer voice quality and increased aspiration risk [7,9].
Selective reinnervation of the larynx has been progressively optimized to restore the function of the PCA muscles, overcoming the limits of static glottic-widening procedures [10-13,19]. Tucker described a nerve–muscle pedicle technique using ansa hypoglossi with an island of strap muscle embedded into the PCA [20]. He reported a 74% success rate, but deterioration was noticed in 17% of patients [20]. Currently, the technique with free nerve grafting between the upper root of the right phrenic nerve and the bilateral PCA and between the thyrohyoid branch of the hypoglossal nerve and adductor branches of the RLN has been proposed as a promising technique [9], although very few centres have been able to reproduce the promising results of Marie and Li [10-13] (Tab. III).

Selection criteria

Reinnervation procedures can be indicated when patients with BVFP are fit for general anaesthesia and when the palsy has a traumatic aetiology with a denervation period between the onset of RLN injury and reinnervation surgery within 18 months as suggested by Grinsell et al. [21], without a clinical history of neurologic and/or neoplastic disorders. Pre-operative laryngeal EMG is generally performed in

Table III. Literature review of patients who underwent BSLR using the phrenic nerve for the PCA and the thyrohyoid branch of the hypoglossal nerve for the adductors muscles.

Authors	Year of publication	Age of patients	Number of cases	Outcomes
Lee et al. [12]	2020	Children	8	100% of patients were decannulated
Li et al. [11]	2019	Adults	7	86% of patients were decannulated
Marie et al. [10]	2014	Adults and children	49	92.5% of patients with a follow-up longer than 1 year were decannulated
Li et al. [13]	2013	Adults	44	87% of patients were decannulated

the literature before BSLR [9,11,12,22]. EMG can confirm the neurogenic lesions of both RLNs, shows spontaneous reinnervation, and can exclude severe atrophy, a condition that is associated with irreversible muscular fibrotic changes which prevent them from regaining tone and bulk with reinnervation [9]. Moreover, as reported by Song and Marie, we believe that objective assessment of the absence of any inspiratory PCA laryngeal EMG activity should be recommended, because, if EMG shows the presence of brisk inspiratory activity of the PCA, the patient is not a candidate for reinnervation [22].

Previous head and neck surgery could complicate the identification of anatomical landmarks, while the presence of neoplastic lesions or neuromuscular disease preclude reinnervation [9]. Patients suitable for BSLR should show pathologic VHI-10 scores and should demonstrate high demand for laryngeal function restoration. An endoscopic evaluation under general anaesthesia is mandatory to assess the mobility of the cricoarytenoid joints. Failure to recognise interarytenoid scarring or cricoarytenoid joint fixation will result in inappropriate patient selection and consequently poor results after BSLR [22]. In cases of interarytenoid scar or cricoarytenoid joint fixation, an endoscopic approach (such as arytenoidectomy/posterior cordotomy) may be indicated [7,23].

EMG obtained serially over time can detect recovery and identify neuropraxic or axonotmetic lesions [21]. The lack of spontaneous clinical or EMG recovery after three to six months warrants reinnervation. Theoretically, there should be an accepted window period of 12-18 months for muscle reinnervation to be performed after the nerve injury, before irreversible motor end plate degeneration occurs (chronic axotomy and muscular fibrosis), in order to achieve functional recovery [21]. The effects of chronic axotomy and muscle denervation render the tissue environment suboptimal for successful axonal regeneration; as a consequence, delays introduced by "wait-and-see" diagnostics can be costly [24], since severe atrophy, and irreversible fibrotic changes in the muscles could prevent regain tone and bulk with reinnervation [9]. Mackinnon [25] demonstrated that early nerve repair results in improved functional outcomes. Usually, 12 months are allowed for spontaneous recovery, although recent studies suggest that 6 months may be enough, avoiding the risk of developing pathologic synkinetic movements [9]. This delay between RLN bilateral injury and BSLR could be unnecessary if there is clear evidence of RLN injury without any chance of spontaneous recovery. We believe that chronic axotomy and muscular fibrosis may have been the cause of the failure in the PCA movement recovery in CA3 and GE5.

Treatment

As described by Marie et al. [10], BSLR is based on the ansa – adductor anastomoses and C3 – bilateral abductor (using nerve graft) implantations [9,10]. Baldissera [24] first identified the phrenic nerve as an ideal candidate for the reinnervation of the abductor muscles, and in the literature, it has been effectively associated with positive outcomes [9]. Selective reinnervation of PCAs is achieved using a Y-shaped free nerve graft harvested from the GAN with the single end of the Y attached to the root (usually C3) of the right phrenic nerve (in humans, the phrenic nerve roots come from C3, C4, C5 or even C6) [4]. The double ends of the Y-shaped graft are directly implanted, one on each side, into a small pocket created within each PCA [9]. Orestes et al. [6] reported a different procedure based on the reinnervation of the PCA with the external branch of the superior laryngeal nerve through a direct anastomosis to the distal end of the RLN, avoiding the risk of hemidiaphragm paralysis [6]. However, a significant disadvantage of this procedure is the risk that the superior laryngeal nerve may not be available in patients who have undergone thyroid surgery [3], and the abductor movement is not triggered by the inspiratory mechanism.

According to Marie [10], the adductors are reinnervated by transecting the main trunks of the RLNs with the aim of denervating all the intrinsic muscles before neurorrhaphy. The adductors could be reinnervated with the ansa hypoglossi, but more recently, the nerve for the thyrohyoid muscle has been identified as the best choice [9]. This nerve is a branch of the anterior cervical plexus that travels with and branches off the hypoglossal nerve. It is active during phonation and deglutition but not during respiration. It is therefore an ideal candidate to supply laryngeal adductors, principally to prevent aberrant inspiratory reinnervation but perhaps also to provide a measure of movement during phonation and deglutition [9]. In this way, the precise identification of abductor fibers of the RLN within the larynx is not necessary [9]. In addition, the transection of the RLNs will create a complete paralysis of the vocal cords, allowing for the early removal of the tracheostomy since the airways are immediately improved with the induced cadaveric position of the vocal cords. In our experience, although time consuming, the nerve dissections and grafting are straightforward.

In our series, the post-operative palsy of the right diaphragm due to the section of the phrenic nerve was temporary and asymptomatic.

Post-operative outcome

The time of recovery is strictly related to the denervation course. Axonal regeneration occurs from the most distal node of Ranvier. As many as 50-100 nodal sprouts appear, mature into a growth cone, and elongate in response to directing signals from local tissue and denervated motor receptors (neurotrophic and neurotropic factors) [21]; as a consequence, the interval between surgery and recovery cannot be earlier than 6 months and eventually correlated to the length of the graft.

In our series, we observed a clear correlation between a shorter denervation interval time from surgery and better outcomes: patients CA2 and GE4 were treated within one year after the RLN injury and experienced an initial recovery of laryngeal function within 6-8 months. Patient CA1 was treated 24 months after the palsy and experienced unilateral partial recovery of laryngeal motility without any pathologic synkinetic movements. Patients CA3 and GE5 were treated 7 and 8 years after the RLN injury, respectively, and did not recover NAM. However, patient CA3 had improved symptomatology for the reduction of pathologic synkinetic movements. Although our experience is limited, our failures could be related to a delayed reinnervation (more than 24 months from RLN injury), as already described in other regions [21]. The recovery of abductor function could be related not only to the timing of the injury but also to the characteristics of the grafting. Li et al. [11] reported that the free nerve graft between the phrenic nerve and PCA should be 1 to 2 cm shorter in length than the free nerve graft between the thyrohyoid branch and adductor branch of the RLN such that the regenerating axons from the different donor nerves would grow into the laryngeal adductor and abductor muscles at approximately the same distance. According to Li et al. [11], another important surgical detail is the section of the interarytenoid branch of the RLN adductor into the larynx to prevent fibers from the phrenic nerve from regenerating into the laryngeal adductors. Furthermore, for primary nerve repair, approximately 50% of the original axons will successfully regenerate through the repair site. For a nerve graft with two sutures, 25% of axons will successfully regenerate through the graft. Depending on the distance to the motor target, there will then be additional axonal loss because of chronic axotomy and muscle fibrosis [24]; as a consequence, the results could be negatively affected by unpredictable and not clearly preoperatively identifiable definitive neuromuscular changes.

The aim of BSLR for BVFP is to relieve airway compromise, preserve voice function as much as possible and avoid aspiration [9-11]. An 8 to 10 mm glottic opening is considered necessary to ensure a safe and secure airway [1]. In our patients, the main purpose to relieve airway compromise was achieved in all cases: the two patients who were tracheostomy-dependent before surgery could be decannulated after laryngeal reinnervation, while one patient who was non-tracheostomy-dependent before surgery improved respiratory function. No further treatments were necessary to improve breathing and voice in our three successful patients.

In the case of anatomic and functional failure of the procedure, BSLR does not preclude the possibility of delayed or later laryngeal static widening surgeries, as performed in patient GE5.

Conclusions

Although it is a complex surgical procedure, BLSR offers a valid option in the treatment of BVFP. Selective reinnervation of the PCAs is achieved using a Y-shaped free nerve graft harvested from the GAN with the single end of the Y attached to the C3 root of the right phrenic, while the adductors are rightly reinnervated with the nerve to thyrohyoid muscle. The choice of the timing to perform the procedure is probably crucial: when reinnervation is performed within one year after RLN injury, the patient has the highest chance of recovery, while delayed reinnervation of more than 18-24 months is associated with a lower recovery of laryngeal motility (as observed in CA3 and GE5). Although our findings are still limited and the technique is somewhat complex, we believe that BSLR represents the first-choice option for the treatment of selected patients with BVFP who request the attempt to restore laryngeal physiology.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

RP, KH, GPE: performed the surgeries; RP, GPE, FC, VM: designed and wrote the manuscript with support from CM, CG, MF, FM, GPA, SMV, and MT. All the authors read and approved the final version of the manuscript.

Ethical consideration

This study was approved by the Institutional Ethics Committee of our University Hospital (PG/2018/11694). The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki. Written informed consent was obtained from each participant/patient for study participation and data publication.

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