

Therapeutic Outcomes of Vocal Fold Botulinum Toxin Injections for Exercise-Induced Laryngeal Obstruction[☆]

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SUMMARY: Objective. To investigate the effectiveness of vocal fold botulinum toxin injection (BTI) for treating patients with the glottic form of exercise-induced laryngeal obstruction (EILO).

Methods. The outcomes of 13 patients treated with BTI for a confirmed diagnosis of EILO between May 2017 and July 2024 were retrospectively analyzed. Electromyography-guided bilateral BTI (1.5 IU Xeomin) was administered through the cricothyroid membrane approach. The BTI effectiveness was assessed at 3-month follow-up on the dyspnea and stridor. The number of BTIs, mean doses, and adverse events were collected.

Results. The cohort included nine females and four males (mean age of EILO onset: 21 years), predominantly runners ($n = 7$), with all having reduced or stopped their high-intensity sport activities. Twelve patients (92.3%) reported symptom improvement after a single BTI, with the remaining patient responding to a second BTI with an increased dose. The mean duration of BTI effectiveness was 90 days (range: 30-180 days) for a mean follow-up period of 14 months. The mean number of BTI to reach a sustained symptom relief was 4.38. Transient mild aphonia occurred in 53.8% of patients following initial treatment.

Conclusion. Single or repeated BTIs into vocal folds are an alternative, safe, and effective procedure for treating isolated glottic EILO. Future large-cohort studies are needed to investigate its effectiveness on the long-term with comparison with voice therapy through multidimensional subjective and objective evaluations.

Key Words: Voice–Otolaryngology–Head neck surgery–Exercise induced laryngeal obstruction–Laryngology–Botulinum toxin.

INTRODUCTION

Exercise-induced laryngeal obstruction (EILO) is a subtype of induced laryngeal obstruction (ILO) with sport as the primary trigger.^{1,2} The prevalence of EILO may reach 5 to 10% of adolescents or young adults, with a female predominance.^{3,4} The primary symptoms of EILO occur during exercise and include dyspnea, stridor, chest tightness, cough, and dysphonia.² EILO can substantially limit the sport activity of patients, especially professional athletes, due to severe respiratory distress, hyperpnea, or panic attacks.^{2,5} The pathophysiology of EILO is poorly understood, with several hypotheses supporting a role of airway anatomy, congenital laryngomalacia, airway hyperresponsiveness to neuronal stimuli, associated asthma, and reflux disease.⁶ To date, the treatment of EILO consists of a multidisciplinary approach involving otolaryngologists, pulmonologists, psychologists, and speech therapists.⁷ The first-line treatment remains voice therapy (breathing

techniques, biofeedback, and behavioral therapy), which is particularly effective for the glottic EILO pattern.^{7,8} Supraglottoplasty surgery has been proposed for the treatment of isolated supraglottic forms of EILO,⁹ with careful management of associated conditions (eg, asthma, laryngopharyngeal reflux disease, and allergy). Among conservative therapeutic approaches, the injection of botulinum toxin (BTI) into the vocal folds is an effective treatment for ILO.¹⁰ To date, the effectiveness of BTI in EILO is, however, poorly investigated, with only two papers available in the literature.^{11,12} The objective of this retrospective study was to investigate the effectiveness of vocal fold BTI for treating patients with the glottic form of EILO.

MATERIALS AND METHODS

This is a retrospective study of 13 consecutive EILO patients who underwent BTI into the vocal folds in the Department of Otolaryngology-Head and Neck Surgery of Foch Hospital (Paris, France) and in a private setting between May 2017 and July 2024. The EILO diagnosis was based on patient history and videolaryngostroboscopy examination during exercise on a home bike (continuous laryngoscopy exercise). EILO signs, such as vocal fold adduction during respiration, were documented. Only patients with glottic narrowing due to vocal fold adduction were included in the series. Patients with supraglottic narrowing were excluded.

After the diagnosis of the isolated glottic form of EILO, the first author of the paper (MM) performed electromyography-guided BTI into both vocal folds through a cricothyroid approach in all patients. Initial BTIs were

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administered bilaterally with a starting dose of 1.5 IU of Xeomin® (Merz, Pharmaceuticals GmbH, Frankfurt am Main, Germany) in the thyroarytenoid (vocal) muscles. Patients were followed for at least 3 months with consultation follow-up after 1 and 3 months. Patients requiring additional care were followed for a longer period. The occurrence of adverse events and the effectiveness of BTI were evaluated at 3 months post treatment through a semi-structured interview listing potential adverse events and the postinjection physical activity features of patients. To assess patient perception accurately, BTI effectiveness was evaluated with a binary question: "Do you have a substantial reduction of your symptoms-Yes/No." At that time, patients with recalcitrant symptoms or symptom recurrence received a second BTI. The dosage was titrated based on duration and degree of improvement in dyspnea and the presence and severity of any adverse events. Note that the patients were not addressed in voice therapy due to the lack of specialized voice therapists for such disorders.

Patients consented to participate. The institutional review board approval was obtained despite the retrospective design of the study (P2022-039).

RESULTS

The data of 13 patients were collected. There were nine females (69.2%) and four males (30.8%). The mean age of symptom onset was 21 years (range: 14-39 years). Patients practiced the following sports: running ($n = 7$), cycling ($n = 2$), boxing ($n = 1$), swimming ($n = 1$), gymnastics ($n = 1$), and judo ($n = 1$). Four patients were professional athletes. All patients had stopped practicing their sport at high intensity or level (professional athletes) because of EILO.

Among comorbidities, three patients reported a childhood history of asthma, and one patient had suspected gastroesophageal reflux disease. According to patient-reported outcomes, they reported the following symptoms: dyspnea ($n = 13$), stridor ($n = 13$), dysphonia ($n = 2$), and cough ($n = 1$). Twelve patients (92.3%) were previously evaluated by pulmonologists who prescribed beta-2 agonists or inhaled corticosteroids, without improvement of their EILO. One individual received proton pump inhibitors without reporting significant improvement. No patient underwent voice therapy treatment before receiving BTI because lack of voice therapists specialized in this field.

BTIs were performed in all patients without complications. The mean follow-up was 14 months (range: 6-80 months). The mean number of BTI was 4.38. Three patients (23.1%) received a single BTI, four (30.8%) patients required two BTIs, one (7.7%) had three injections, two (15.4%) had four injections, one (7.7%) had nine injections, one (7.7%) had 12 injections, and the last one (7.7%) had 14 injections. The average dose of BTI was 1.75 IU of Xeomin per vocal fold. Among the three patients who received one BTI, one continued the BTI closed from its home, one stopped the BTI because stop sport, and the last one had a

TABLE 1.
Demographic, Clinical, and Therapeutic Outcomes

Outcomes	N (%)
<i>Demographics</i>	
Gender	
Females	9 (69.2)
Males	4 (30.8)
Mean age (years, SD)	
<i>Sports</i>	
Running/Athletic tracks	7 (53.8)
Cycling	2 (15.4)
Boxing	1 (7.7)
Swimming	1 (7.7)
Gymnastic	1 (7.7)
Judo	1 (7.7)
<i>Symptoms</i>	
Dyspnea	13 (100)
Stridor	13 (100)
Dysphonia	2 (15.4)
Cough	1 (7.7)
<i>Therapeutic Outcomes</i>	
Mean number of BTI per patient	4.38
Total number for symptom reduction	
Single BTI	12 (92.3)
Two BTIs	1 (7.7)
Total number for sustained symptom relief	
Single BTI	3 (23.1)
Two BTIs	4 (30.8)
Three BTIs	1 (7.7)
Four BTIs	2 (15.4)
Nine BTIs	1 (7.7)
Twelve BTIs	1 (7.7)
Mean botulinum toxin doses (mean, SD; IU)	1.7 (0.75-3.0)
Duration of effect (mean, range, days)	90 (30-180)
Follow-up (mean, range, months)	14 (6-80)

Abbreviations: BTI, botulinum toxin injection; SD, standard deviation; IU, international units; N, number.

recurrence of symptoms and planned a second injection just before its marathon. Twelve (92.3%) patients had partial or total relief of dyspnea after the first BTI. The remaining patient (7.7%) experienced benefits after increasing the dose of BTI during the second injection. The mean duration of BTI effectiveness was 90 days (range: 30-180 days). The patient-reported adverse event evaluation revealed that seven patients (53.8%) had transient mild aphonia after the first BTI. The results are summarized in [Table 1](#).

DISCUSSION

The findings of the present case series support that BTI is a safe therapeutic approach for EILO, with no major adverse events and a high proportion of sustained dyspnea reduction or complete relief after a mean of 4.38 BTIs. In a retrospective review of 46 patients with paradoxical vocal fold movement disorder, including ILO and EILO, Marcinow et al successfully treated two recalcitrant

athletes unresponsive to voice therapy with a single BTI without reporting major adverse events.¹¹ The safety and effectiveness of BTI in EILO was similarly supported by Rebours et al in the case of a 22-year-old healthy female professional cyclist with a 1.3 IU of Xeomin BTI into the vocal folds, which corroborates our observations.¹² Because Marcinow et al injected two patients,¹¹ and Rebours et al only one patient,¹² this case series is the largest one in the literature describing BTI outcomes for EILO. While both teams reported effectiveness of BTIs on dyspnea relief, it remains difficult to compare our results with the current literature given the limited literature. Considering paradoxical vocal fold movement disorder, DeSilva et al reported that BTI in both vocal folds was an effective treatment in 13 patients with refractory dyspnea to appropriate medical therapy and respiratory retraining protocols.¹³ The average BTI dose in the study of DeSilva et al was 2.55 IU, whereas an average of 1.7 IU was used in the present study.

While these studies support the effectiveness and safety of single or repeated BTIs, the primary treatment remains voice therapy.⁷ However, there is a substantial shortage of speech therapists in some rural European regions, while very few speech therapists are trained for the management of breathing and laryngological disorders. Moreover, most studies suggested that speech therapy is effective after several sessions,^{5,7} whereas BTI can be effective a few days after the injection in most patients.¹⁴ In this study, 92.3% ($n = 12$) of patients were relieved of their primary symptoms (dyspnea and stridor) 30-90 days after the first BTI, and one patient was relieved after a second BTI with increased doses. All patients resumed normal sporting activity, at an intensity comparable to that prior to the onset of EILO. Importantly, professional athletes were able to continue their careers, making BTI an alternative safe and effective therapeutic approach to speech therapy for high-performance athletes who need to achieve their goals in a short period of time.

A potential pathophysiological hypothesis underlying the development of certain forms of EILO is that they may represent an atypical manifestation of laryngeal dystonia. Traditionally, laryngeal dystonias are classified as "function-specific," occurring exclusively during either speaking, singing, or respiratory activities. We propose that some EILO presentations may exist at the intersection of respiratory dystonia and singer's dystonia. This conceptual framework is supported by several points: In singer's dystonia, professional vocalists experience highly specific and predictable voice dysfunction at precise points in their vocal range despite intensive technical training. Similarly, EILO affects athletes in a systematic, reproducible manner that persists despite appropriate respiratory training interventions. This theoretical model could explain why certain cases of glottic EILO respond favorably to BTI yet remain fundamentally incurable, reflecting the underlying neurologic dysregulation characteristic of focal dystonias.

Although this study is the largest case series of BTI for glottic EILO, the low number of patients, the lack of sample size calculation, validated patient-reported outcome questionnaire for documenting ILO/EILO/paradoxical vocal fold movement disorder symptoms and findings, and objective respiratory and laryngeal examinations (eg, lung measurements, laryngeal electromyography, or aerodynamic/acoustic measurements) are the primary limitations of the study. Moreover, our findings cannot be reproduced for other forms of paradoxical vocal fold movement disorders, including ILO or supraglottic EILO, which have different pathophysiological and clinical patterns than glottic EILO.

CONCLUSION

Single or repeated BTIs into vocal folds are an alternative, safe, and effective procedure for treating isolated glottic EILO. Future large-cohort studies are needed to investigate their long-term effectiveness with comparison to voice therapy through multidimensional subjective and objective evaluations.

CRedit authorship contribution statement

Marie Maily: Contributions: design, acquisition of data, data analysis & interpretation, drafting, final approval, and accountability for the work; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. **Stéphane Hans:** Contributions: final approval and accountability for the work; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. **Jérôme R. Lechien:** Contributions: data analysis & interpretation, drafting, final approval, and accountability for the work; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

1. Milstein CF, Patel RR, Laurash E, Kampert M. Identification of breathing pattern disorder in athletes with exercise-induced laryngeal obstruction: a novel assessment tool. *J Voice*. 2023. <https://doi.org/10.1016/j.jvoice.2023.01.006>. S0892-1997(23)00006-1.
2. Shembel AC, Hartnick CJ, Bunting G, et al. Perceptual clinical features in exercise-induced laryngeal obstruction (EILO): toward improved diagnostic approaches. *J Voice*. 2019;33:880-893. <https://doi.org/10.1016/j.jvoice.2018.05.006>.
3. Johansson H, Norlander K, Berglund L, et al. Prevalence of exercise-induced bronchoconstriction and exercise-induced laryngeal obstruction in a general adolescent population. *Thorax*. 2015;70:57-63.
4. Røksund OD, Maat RC, Heimdal JH, Olofsson J, Skadberg BT, Halvorsen T. Exercise induced dyspnea in the young. Larynx as the bottleneck of the airways. *Respir Med*. 2009;103:1911-1918.
5. Vos DJ, Milstein CF. Long-term outcomes of respiratory retraining therapy for exercise-induced laryngeal obstruction. *J Voice*. 2024. <https://doi.org/10.1016/j.jvoice.2024.06.005>. S0892-1997(24)00177-2.
6. Zalvan C, Yuen E, Geliebter J, Tiwari R. A trigger reduction approach to treatment of paradoxical vocal fold motion disorder in the pediatric population. *J Voice*. 2021;35:323.e9-323.e15. <https://doi.org/10.1016/j.jvoice.2019.08.013>.
7. Mahoney J, Vertigan A, Hew M, Oates J. Exploring factors impacting engagement in speech pathology intervention for inducible laryngeal obstruction. *J Voice*. 2024. <https://doi.org/10.1016/j.jvoice.2024.03.008>. S0892-1997(24)00079-1.
8. Shaffer M, Litts JK, Nauman E, Haines J. Speech-language pathology as a primary treatment for exercise-induced laryngeal obstruction. *Immunol Allergy Clin North Am*. 2018;38:293-302. <https://doi.org/10.1016/j.iac.2018.01.003>.
9. Christen A, O'Connell A, Mayer I, Tona G, Hilland M, Clemm H. Understanding speech-language pathology and surgical interventions for exercise-induced laryngeal obstruction. *Immunol Allergy Clin North Am*. 2025;45:29-38. <https://doi.org/10.1016/j.iac.2024.09.002>.
10. Koh J, Phyland D, Baxter M, Leong P, Bardin PG. Vocal cord dysfunction/inducible laryngeal obstruction: novel diagnostics and therapeutics. *Expert Rev Respir Med*. 2023;17:429-445. <https://doi.org/10.1080/17476348.2023.2215434>.
11. Marcinow AM, Thompson J, Chiang T, Forrest LA, deSilva BW. Paradoxical vocal fold motion disorder in the elite athlete: experience at a large division I university. *Laryngoscope*. 2014;124:1425-1430. <https://doi.org/10.1002/lary.24486>.
12. Rebours C, Brasnu D, Le Garrec S, Ayache D, Mailly M. Laryngeal electromyography and botulinum toxin injection in exercise-induced laryngeal obstruction. *Mov Disord Clin Pract*. 2019;6:708-710. <https://doi.org/10.1002/mdc3.12836>.
13. deSilva B, Crenshaw D, Matrk L, Forrest LA. Vocal fold botulinum toxin injection for refractory paradoxical vocal fold motion disorder. *Laryngoscope*. 2019;129:808-811. <https://doi.org/10.1002/lary.27471>.
14. Fujiki RB, Olson-Greb B, Braden M, Thibeault SL. Therapy outcomes for teenage athletes with exercise-induced laryngeal obstruction. *Am J Speech Lang Pathol*. 2023;32:1517-1531. https://doi.org/10.1044/2023_AJSLP-22-00359.