Vocal cord paralysis as a rare complication of bronchoscopic lung volume reduction

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Vocal cord paralysis as a rare complication of bronchoscopic lung volume reduction: a case series of five patients

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To the Editor:

Lung volume reduction is now standard of care for symptomatic hyperinflated patients with COPD and emphysema whenever significant breathlessness persists despite maximal bronchodilation and pulmonary rehabilitation [1]. Since treatment options are limited in this context, removal of the most emphysematous parts of the lungs was initially validated surgically. Nonetheless, the benefits of surgical resection are tempered by significant morbidity [2]. Therefore, several endoscopic techniques were developed for lung volume reduction using minimally invasive bronchoscopic approaches, such as the endobronchial valves that reduce the airflow to the most damaged lobes, endobronchial coils that mechanically reduce the lobe volume, and other techniques such as vapour ablation or use of polymer foam. Most randomised controlled trials have studied endobronchial valves and coils [3–6], demonstrating improvement in forced expiratory volume in 1 s (FEV_1), 6-min walk distance and quality of life. Endobronchial valve therapy is now the most used technique worldwide with more than 25 000 patients treated globally (according to numbers provided by the manufacturer). The most common complication of these procedures remains, by far, pneumothorax (up to 25% of the procedures in the IMPACT trial). Other, more rare, complications include pneumonia, COPD exacerbation, respiratory failure, valve migration and haemoptysis [7].

Since our involvement in the development of these techniques, starting in the early 2000s, two cases of left recurrent laryngeal nerve (LRLN) paralysis after bronchoscopic lung volume reduction (BLVR) (one treated with valves and the other with coils) came to our attention. Extensive workup in both patients eliminated any expansive mediastinal process on the course of the LRLN. After an extensive literature review, we found only one report of a similar situation, in which a side-effect of valve implantation was noted without providing further explanation [4]. We therefore contacted the principal investigator of this study and the manufacturer of the Zephyr valves (Pulmonx Corp., Redwood City, CA, USA), and were able to collect three additional cases of left recurrent paralysis, all of which occurred after left upper lobe (LUL) volume reduction. We report herein the clinical presentation of these five cases as well as the evolution of this rare complication. We discuss its pathophysiology and propose a course of action for clinical practice.

The patients are described in table 1. Four of the five patients had LUL Zephyr valve implantation and one (patient 1) had LUL and right upper lobe (RUL) coil implantation. The time between the bronchoscopic procedure and the occurrence of hoarseness was variable, ranging from 48 h to 7 months. All patients underwent ear-nose-throat (ENT) evaluation to confirm the diagnosis of LRLN paralysis. Chest computed tomography (CT) showed mediastinal and bronchial tree remodelling associated with complete LUL atelectasis in all cases, without any organic lesion on the LRLN pathway.

In patients 1, 2 and 3, the procedure was clinically and functionally beneficial. Therefore, the valves/coils were left in place and interventional ENT treatment of vocal cord palsy was undertaken and was successful in reversing significantly the hoarseness. Patient 4 underwent valve removal because of his LRLN paralysis. Patient 5 presented with hoarseness 7 days after valve implantation. FEV_1 had improved from 0.97 L to 1.38 L (+42%) and residual volume dropped from 4.04 L to 2.70 L (−1340 mL) with chest CT showing LUL atelectasis. Valve removal did not reverse dysphonia, but speech therapy did so over the course of 6 months.

Shareable abstract (@ERSpublications)
This is the first description of a case series of left recurrent nerve paralysis as a complication of left upper lobe bronchoscopic lung volume reduction, a complication that pulmonologists should be familiar with https://bit.ly/3FlECzx

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TABLE 1 Patients characteristics

Centre	Gender	Age (years)	Type of BLVR	Lobe	Onset of dysphonia	Valve removal	Outcome of dysphonia if valve removed	ENT treatment	Outcome after ENT treatment	FEV_1 before BLVR (L and %)	Best FEV_1 after BLVR (L and %)
Nice	Male	67	Coils	LUL and RUL	7 months	No	NA	Vocal fold medialisation	Partial improvement	0.7 (22%)	1.47 (47%)
Nice	Male	60	Valves	LUL	48 h	No	NA	Vocal fold medialisation	Partial improvement	0.73 (20%)	0.8 (23%)
Atlanta	Male	84	Valves	LUL	60 h	No	NA	LBTI and vocal fold medialisation	Partial improvement	0.95 (29%)	1.31 (41%)
Heidelberg	Female	71	Valves	LUL	3 weeks	Yes	Improved	NA	NA	0.54 (18%)	0.68 (27%)
Groningen	Female	68	Valves	LUL	7 days	Yes	No improvement	Speech therapy	Resolved after 6 months	0.97 (44%)	1.38 (64%)

BLVR: bronchoscopic lung volume reduction; ENT: ear-nose-throat; FEV_1: forced expiratory volume in the first second; LUL: left upper lobe; RUL: right upper lobe; NA: not applicable; LBTI: laryngeal botulinum toxin injection.

The LRLN courses postero-medially beneath the aortic arch, and then through the aorticopulmonary window posterior to the ligamentum arteriosum. It then ascends vertically to reach the tracheoesophageal groove [8]. Cervical and thoracic surgery is the first cause of LRLN [9]. Traction and compression are the common mechanisms during thyroid surgery [10]. Mediastinal tumours, especially of the aorto-pulmonary window are the second cause of LRLN palsy [11]. Stretch or compression by enlarged vascular structures such as thoracic aortic aneurism, pulmonary hypertension or dilated left atrium was described at the end of the 19th century and referred to as Ortner's or cardio-vocal syndrome [12, 13]. Lastly, complete LUL collapse related to benign conditions (cystic fibrosis [14], pulmonary tuberculosis with fibrotic changes in the left lung apex [8], or coal workers' pneumoconiosis with progressive massive fibrosis pneumoconiosis [15]) have also been reported as a cause of LRLN palsy most probably *via* mediastinal remodelling and stretch-induced nerve injury. The only autopsy-documented finding related to a case of Ortner's syndrome [13] was thinning of the nerve within the sheath at the point where it passes between the aorta and left pulmonary artery, with complete loss of axons and myelin on microscopic examination.

This complication seems to be very rare and specific to LUL-BLVR. In Groningen, more than 600 patients had received BLVR before this adverse event was first experienced.

In conclusion, endoscopists should be familiar with this rare, nonetheless significant adverse event of LUL-BLVR. Whenever it happens, vocal cords should be immediately checked. Valve removal should be discussed with the patient based on the clinical and functional benefit obtained with LUL-BLVR, and the possible alternatives. Otherwise, ENT treatment such as medialisation thyroplasty and speech therapy should be proposed. In patients with bilateral upper lobe emphysema, in whom a similar benefit is expected from treating a LUL or RUL, and where both lobes are eligible targets, one should probably prefer the RUL to avoid this seemingly LUL-specific complication.

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Data sharing statement: Data that underlie the results reported in this article, after de-identification (text, tables) is made available to researchers who provide a methodologically sound proposal to achieve aims in the approved proposal on request to the corresponding author.

Ethics statement: The study was determined not to require ethics committee or institutional review board review since it is a retrospective collection of de-identified cases.

Conflict of interest: K. Klooster reports lecture honoraria from PulmonX and Chiesi, outside the submitted work. F.J.F. Herth reports advisory board participation with and lecture fees from PulmonX, Uptake Medical and Olympus Medical, outside the submitted work. D-J. Slebos is an advisor and principal investigator for PulmonX Corp., Redwood City, CA, USA. The remaining authors have no potential conflicts of interest to disclose.

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