



# Vocal cord dysfunction/inducible laryngeal obstruction cannot be diagnosed from symptoms

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## To the Editor:

The diagnosis of vocal cord dysfunction/inducible laryngeal obstruction (VCD/ILO) is challenging, with ephemeral symptoms and varied clinical expressions [1, 2], which may overlap with asthma. To date, it is not firmly established if individual symptoms articulated by patients, or combinations thereof, can function as sensitive and specific indicators of the disorder and help to distinguish it from asthma. In this study, we assessed patient-reported symptoms and questionnaires in patients with suspected VCD/ILO confirmed by gold-standard laryngoscopy.

We audited the prospectively maintained Monash Health VCD/ILO Multidisciplinary Team (MDT) Clinic database (n=164) between September 2014 and September 2021. Ethics approval was granted by Monash Health HREC (RES-084L). Individuals with a clinical suspicion of VCD/ILO were initially reviewed by respiratory or ear, nose and throat (ENT) specialists who subsequently referred people to the MDT Clinic if the diagnosis was considered feasible on the basis of clinical features such as throat tightness, atypical response to asthma treatment and throat prominent wheeze. The MDT is comprised of respiratory physicians, ENT surgeons, a respiratory clinical nurse consultant, a speech pathologist and a radiologist [3]. On the same day, questionnaires (Vocal Cord Dysfunction Questionnaire (VCDQ) [4], Pittsburgh Questionnaire [5], Nijmegen Questionnaire [6], and Hospital Anxiety and Depression Scale (HADS) [7]) were completed, detailed symptom evaluation was done and laryngoscopy was performed.

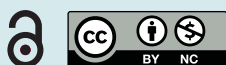
Symptoms were routinely assessed by direct inquiry, and included shortness of breath, cough, subjective voice changes, throat tightness, chest tightness, globus, dysphagia and wheezing. Triggering factors were dichotomised as exercise (54 out of 164, 33%) or other (weather, chemicals, odours, stress, talking, *etc.*; 65 out of 164 (40%)) (figure 1). Fisher's exact test and univariate logistic regression were used to explore relationships between clinical measures and laryngoscopy-confirmed VCD/ILO.

Mean±SD age was 57.2±15.1 years and 83% (136 out of 164) identified as female. Mean body mass index was 32.3±7.7 kg·m<sup>-2</sup>. Asthma was diagnosed by specialist respiratory physicians following confirmation of clinical history and, 12% and 200 mL bronchodilator response or abnormal bronchoprovocation. There was no association between having asthma and a diagnosis of VCD/ILO (p=0.37, Fishers' exact test), although asthma prevalence was high (106 out of 164, 65%).

After laryngoscopy, 45% (73 out of 164) received a definitive diagnosis of VCD/ILO as defined by ≥50% inspiratory vocal fold closure [1]. Provocation was performed with continuous laryngoscopy using sequential stimuli: the patient's usual stimuli (if known), and a sequence of hyperventilation (~30–45 s) and phonation followed by the patient's nominated chemical/odour irritant.

Most individuals were polysymptomatic. Figure 1 illustrates that there were multiple overlapping symptom patterns and, importantly, that many combinations of symptoms can be present with or without laryngoscopy-confirmed VCD/ILO.

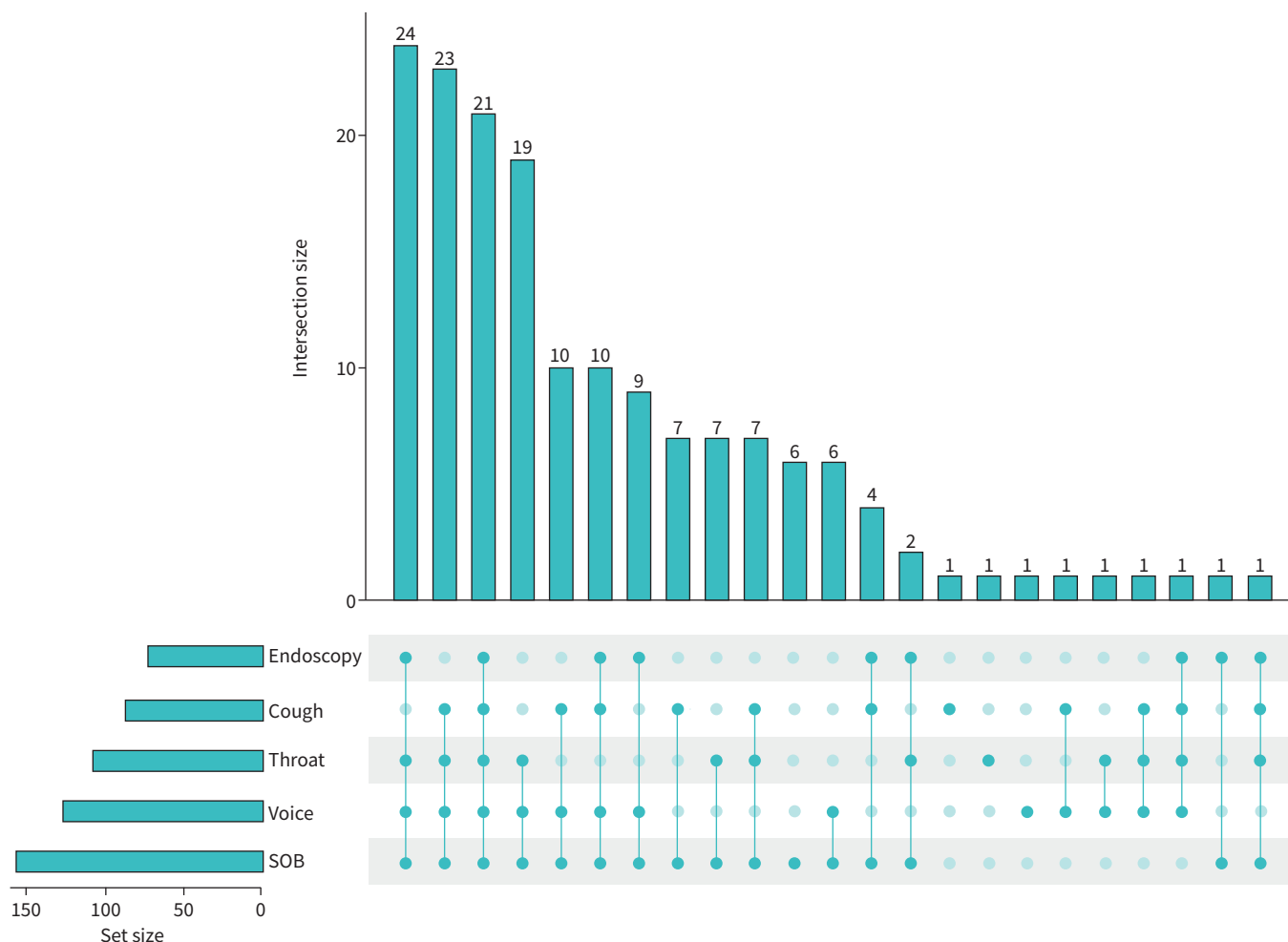
Dysphonia (the report of subjective voice change) was more common in the group with laryngoscopy-confirmed VCD/ILO (65 out of 73, 89%) than in people with negative laryngoscopy (62 out



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Vocal cord dysfunction/inducible laryngeal obstruction is highly variable. Standard clinical symptoms and questionnaires cannot predict laryngoscopic diagnosis in a “lung disease” population. <https://bit.ly/3QUtsbB>

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**FIGURE 1** Symptom combinations of vocal cord dysfunction/inducible laryngeal obstruction (VCD/ILO) participants. The vertical bars represent the frequency of the combinations of findings indicated on the lower portion of the chart. Endoscopy: laryngoscopy-proven VCD/ILO; throat: throat tightness; voice: subjective vocal alteration; SOB: shortness of breath.

of 91, 68%;  $p=0.031$ ). Logistic regression indicated that dysphonia was associated with an odds ratio of 2.30 (95% CI 1.08–4.92) for laryngoscopy-confirmed VCD/ILO.

The Pittsburgh Questionnaire was 1.4 units higher (mean 8.5 *versus* 7.1,  $p=0.003$ ) in individuals with positive laryngoscopy; however, the overall mean score of 7.6 exceeded the cut-off  $\geq 4$  suggested in the initial validation [5]. A score  $\leq 3$  was uncommon and those individuals usually had negative laryngoscopy (seven out of nine, 78%), but this cut-off could not be recommended to definitively rule out the diagnosis clinically as it would miss the remaining two out of nine (22%). In logistic regression, for every unit higher on the Pittsburgh, the odds ratio of laryngoscopy-diagnosed VCD/ILO rose by 1.31 (95% CI 1.09–1.58).

When the Nijmegen score was  $\geq 19$ , laryngoscopy-proven VCD/ILO was present relatively frequently 49 out of 104 (47%). When the Nijmegen was  $< 19$ , laryngoscopy was negative in 66% (25 out of 38) of individuals. These were insufficiently predictive to warrant clinical rule-in or rule-out usage for VCD/ILO. The VCDQ and HADS (overall and subscales) showed no consistent association with the diagnosis.

Our main findings were that dysphonia is associated with VCD/ILO and that other symptoms sometimes considered typical (*e.g.* a tight throat) were not helpful individually or in combination. The observations that symptoms of laryngeal dysfunction are not specific to a single diagnosis mirror the findings of others [8] and dysphonia could be contextualised as part of the laryngeal dysfunction concept [9]. Disappointingly, other candidate symptoms, such as globus, dysphagia and throat tightness, did not emerge as important in this comorbid population, suggesting the asthma population may experience VCD/ILO

differently to individuals with asthma alone or VCD/ILO alone. Questionnaires were insufficient for accurate diagnosis, performing poorly in this symptomatic “lung disease” population, and combinations were present with or without laryngoscopy-confirmed VCD/ILO. Results were not unexpected since symptoms of VCD/ILO are highly subjective, nonspecific (breathlessness), overlap with asthma (wheeze and others), may fluctuate over time and occur intermittently. Furthermore, questionnaires were administered outside of their initial derivation and validation contexts (the Nijmegen [10] was intended for dysfunctional breathing, the VCDQ [4] for VCD symptom monitoring, and Pittsburgh [5] for differentiation of asthma and VCD).

The study has caveats. The study population was drawn from a single-centre, selected population with a high prevalence of asthma, initially screened by specialists, and do not reflect general practice settings. However, previous studies found a prevalence of 30–50% in this patient population and setting, and a positive diagnosis in 47% of people is consistent with these reports [11]. Formal exercise protocols were not used to provoke VCD/ILO and our patient population chiefly reflects the classic and lung disease-associated phenotypes [12].

In summary, these findings provide evidence that the diagnosis of VCD/ILO cannot be confidently made based on clinical symptoms and questionnaires, and laryngoscopy remains essential. Dysphonia may be a useful clue but can be found in asthma with inhaled corticosteroid treatments. Taken together, it seems unlikely that further refinement of symptom-based strategies and the development of other questionnaires will provide a validated methodology to confidently rule VCD/ILO in or out. However, further screening tools, perhaps technology-based or otherwise, are required as recognition of the importance of VCD/ILO continues to grow and the need to conserve sophisticated diagnostic tools, including laryngoscopy, becomes more important.

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