Clinical and Lung-Function Variables Associated With Vocal Cord Dysfunction

Maura A Watson DO MPH CPT MC USA, Christopher S King MD CPT MC USA, Aaron B Holley MD MAJ MC USA, David L Greenburg MD MPH CPT MC USA, and Jeffrey A Mikita MD MAJ MC USA

BACKGROUND: Vocal cord dysfunction (VCD) is difficult to diagnose. Laryngoscopy while the patient is symptomatic is the accepted standard method to establish a diagnosis of VCD, but patient characteristics and spirometry values are thought to be useful for predicting VCD. We sought to identify clinical and spirometric variables that suggest VCD. METHODS: We performed 2 parallel studies. First, 3 staff pulmonologists (who were blinded to the laryngoscopy results), scored 3 flow-volume loops from each PFT session on the likelihood that the inspiratory curve indicated VCD. We also performed a cross-sectional study of clinical characteristics and spirometric data from all patients who underwent laryngoscopy for any indication, including suspected VCD, over a 3-year period. We compared the laryngoscopy findings to the clinical characteristics, spirometry results, and the pulmonologists' assessments of the flow-volume loops. We used multivariate logistic regression to identify independent predictors of VCD. RESULTS: The pulmonologists agreed about which flow-volume loops predicted VCD (quadratic kappa range 0.55–0.76), but those ratings were not predictive of laryngoscopic diagnosis of VCD. During the study period, 226 patients underwent laryngoscopy. One hundred (44%) were diagnosed with VCD. Independent predictors of VCD included female sex (odds ratio 2.72, 95% confidence interval 1.55–4.75) and obesity (body mass index > 30 kg/m^2) (odds ratio 2.06, 95% confidence interval 1.12–3.80). With spirometric data from the effort that had the best forced-vital-capacity, multivariate analysis found the ratio of the forced inspiratory flow at 25% of the inspired volume to forced inspiratory flow at 75% of the inspired volume ($FIF_{25\%/75\%}$) predictive of VCD (odds ratio 1.97, 95% confidence interval 1.12–3.44). The diagnostic performance of these characteristics was poor; the area under the receiver-operating-characteristic curve was 0.68. With the spirometric data from the effort that had the subjectively determined best inspiratory curve, and after controlling for the reproducibility of the inspiratory curves, multivariate analysis found none of the spirometric variables predictive of VCD. CONCLUSIONS: VCD remains difficult to predict with spirometry or flow-volume loops. If VCD is suspected, normal flow-volume loop patterns should not influence the decision to perform laryngoscopy.
Key words: vocal cord dysfunction, paradoxical vocal cord motion, flow-volume loop, spirometry, laryngoscopy. [Respir Care 2009;54(4):467–473]

Introduction

Vocal cord dysfunction (VCD) is a respiratory condition characterized by paradoxical closure of the vocal cords, resulting in wheezing, stridor, shortness of breath, and exertional dyspnea.[1-7] The prevalence of VCD in the general population is hard to quantify because of difficulties in diagnosis. Patients with VCD are frequently misdiagnosed as having exercise-induced asthma, but generally respond poorly to asthma therapies.[1-4,8,9] Failure to diagnose VCD may lead to unnecessary health care utilization, inappropriate medication use, and hospitalization.[10]

SEE THE RELATED EDITORIAL ON PAGE 448

Maura A Watson DO MPH CPT MC USA, Christopher S King MD CPT MC USA, Aaron B Holley MD MAJ MC USA, David L Greenburg MD MPH CPT MC USA, and Jeffrey A Mikita MD MAJ MC USA are affiliated with Walter Reed Army Medical Center, Washington DC.

The authors report no conflicts of interest.

Though laryngoscopy with direct visualization of the vocal cords is the accepted standard for VCD diagnosis, patient characteristics and spirometry results are thought to be useful for predicting VCD. Clinical findings associated with VCD include abnormal exercise test results, previous asthma diagnosis, and comorbid psychiatric disorders.[1,4,8,9,11]

Spirometry has also been used to support the diagnosis of VCD. Isolated flattening of the inspiratory curve of the flow-volume loop while the patient is symptomatic is consistent with a variable extrathoracic obstruction, which is the abnormality most commonly described in VCD.[2,6] Diagnosis based on the flow-volume loop can be misleading, though, because asymptomatic VCD patients may have normal findings. When an asymptomatic patient has blunting of the inspiratory flow-volume curve, many physicians believe the likelihood of VCD is increased, but that relationship is not well defined.

Our goal was to evaluate patient characteristics, spirometry values, and flow-volume-loop appearance to assess the strength of their associations with VCD. VCD symptoms occur episodically, which makes VCD difficult to diagnosis when the patient is asymptomatic. We hypothesized that clinical or subtle spirometric alterations due to subclinical symptoms would be predictive of VCD. Identification of such predictors might help tailor the workup for the patient with unexplained dyspnea and avoid inappropriate therapy or treatment delay.

Methods

We performed a cross-sectional study of all patients referred to the pulmonology clinic at the Walter Reed Army Medical Center who underwent a laryngoscopy for any reason, including suspected VCD, from July 1, 2003 through June 30, 2006. At our hospital all individuals suspected of having VCD undergo spirometry and laryngoscopy. The population served by this clinic includes both active and retired members of the military, and their dependents. This project was approved by our institutional review board.

Each patient underwent direct laryngoscopy with a flexible rhinolaryngoscope (VNL 1130, Pentax, Tokyo, Japan). The choice of topical anesthesia (viscous, aerosolized, or liquid lidocaine for numbing the nares, posterior pharynx, and vocal cords, respectively) and VCD provocations (deep or rapid breathing, smelling salts, methacholine, or exercise) was at the discretion of the laryngoscopist. From the laryngoscopy reports we obtained the VCD diagnosis and the presence of other abnormalities.

We performed 2 parallel studies. The first was to determine pulmonologists' ability to predict VCD solely by reviewing flow-volume loops. Three staff pulmonologists (who were blinded to the laryngoscopy results) graded the likelihood that flow-volume loops indicated VCD. Each inspiratory curve was scored with the following Likert scale: 1 = normal, 2 = minimally suggestive of VCD, 3 = moderately suggestive of VCD, and 4 = highly suggestive of VCD. We gave no instruction as to what inspiratory-curve appearance suggests VCD. The loops from all patient efforts were available for evaluation. Agreement between the pulmonologist raters was measured with the quadratic kappa statistic.

Two other physicians (CSK and JAM), who were also blinded to the laryngoscopy results, then classified each inspiratory flow-volume curve into one of 5 patterns: parabolic, with 1 or 2 inflection points; smooth (flattened); jagged (sawtooth); truncated; or other (Fig. 1).

In both analyses, the raters were limited to viewing only the loop from the effort with the largest forced vital capacity (FVC). We evaluated the relationship between pattern identification and laryngoscopic diagnosis of VCD.

In the second portion of the study we looked for clinical and spirometric predictors of VCD. From each patient record we obtained age, height, weight, race, spirometry values, flow-volume loops, laryngoscopy indication(s), and laryngoscopy results. We had access to all the flow-volume loops and spirometry values, including forced expiratory volume in the first second (FEV_1), FVC, forced inspiratory volume in the first second (FIV_1), forced inspiratory flow at 25% of the inspired volume ($FIF_{25\%}$), forced inspiratory flow at 50% of the inspired volume ($FIF_{50\%}$), forced inspiratory flow at 75% of the inspired volume ($FIF_{75\%}$), and the various ratios of those values. All spirometry (Vmax 6200 Autobox DL, SensorMedics, Yorba Linda, California) was performed according to American Thoracic Society standards.[12] For FEV_1 and FVC we used the percent-of-predicted normal values determined by Crapo et al.[13]

Our laboratory, like many others, provides physicians with only the loop from the effort with the largest FVC, so those were the loops used in our initial univariate and multivariate analyses. However, the effort with the best FVC is not necessarily the one with the best (or even adequate) inspiratory effort,[14] so we also analyzed the loop with the best inspiratory curve, which was subjectively chosen by a blinded reviewer. We also assessed the reproducibility of the inspiratory curves. There are no standard-

---

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Army, Department of Defense, or the United States Government.

Correspondence: Christopher S King MD CPT MC USA, Pulmonary and Critical Care Medicine, Walter Reed Army Medical Center, 3831 Rodman Street NW, F30, Washington DC 20016. E-mail: christopher.king@amedd.army.mil.

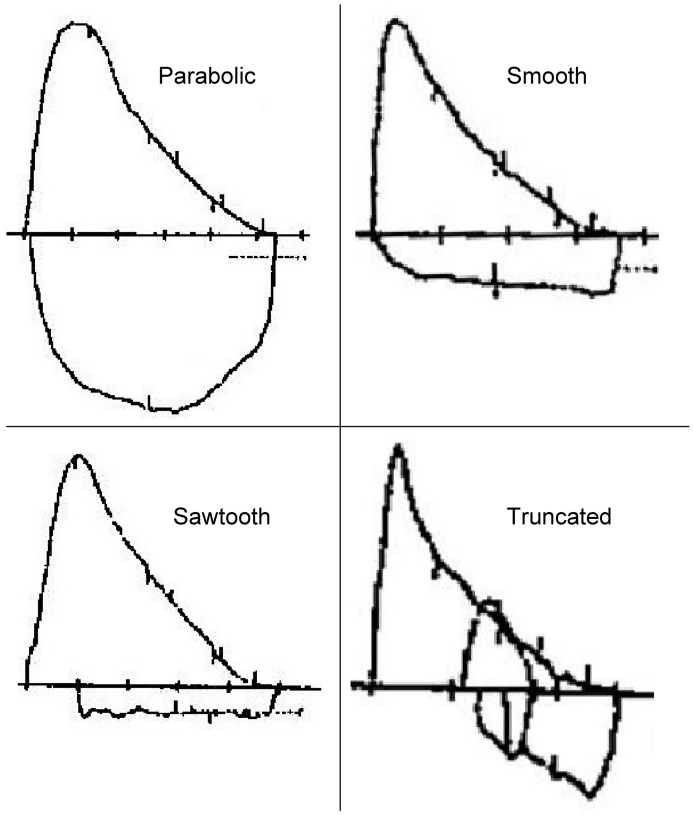

Fig. 1. Flow-volume loop patterns.

ized criteria for assessing inspiratory curves, so a blinded reviewer subjectively assessed 3 inspiratory curves from each PFT session as normal or abnormal.

Statistical Analysis

We compared the means of continuous variables with Student's *t* test with normally distributed variables, and with the Mann-Whitney U test with non-normally distributed variables. We analyzed categorical variables with the chi-square test, except if $\geq$ 20% of the expected cells contained values $<$ 5, in which case we used Fisher's exact test. We assessed the agreement between nominal and ordinal classifications with the kappa and quadratic kappa statistics, respectively. We used multivariate logistic regression to identify independent predictors of VCD and to calculate the adjusted odds ratios for VCD predictors. Candidate variables selected for regression modeling included laryngoscopy indication, prior literature support of the variable as a predictor of VCD, and observation of a univariate relationship between the variable and a VCD diagnosis with a P value $<$ .20. Colinear variables (as assessed with a Pearson's or Spearman's correlation coefficient $\geq$ 0.60) were not simultaneously included in regression models. Variables were retained in the regression models if the Wald test suggested they were independent predictors of VCD, based on a P value $<$ 0.10 or if there was confounding between variables. All analyses were done with statistics software (Stata 9.2, StataCorp, College Station, Texas).

Results

Two hundred twenty-six patients underwent laryngoscopy between July 1, 2003, and June 30, 2006 (Table 1). The most common indications for laryngoscopy were evaluation for suspected VCD (n = 120, 53%), unexplained dyspnea (n = 48, 21%), abnormal flow-volume loops (n = 41, 18%), chronic cough (n = 33, 15%), and hoarseness (n = 20, 10%). There were no statistically significant differences in mean age, body mass index (BMI), or laryngoscopy indication between those who were and were not found to have VCD via laryngoscopy. Women (risk ratio 1.7, 95% confidence interval [CI] 1.3–2.3) and nonwhites (risk ratio 1.36, 95% CI 1.00–1.8) were more likely to be diagnosed with VCD than were men or whites. After controlling for the effects of sex, obesity (BMI $>$ 30 kg/m^2) predicted a diagnosis of VCD (Mantel-Haenszel odds ratio 2.8, 95% CI 1.6–4.9).

Table 1. Subject Characteristics Relative to Presence of Vocal Cord Dysfunction ($n = 226$)

	VCD Absent ($n = 126$)	VCD Present ($n = 100$)	P
BMI (mean ± SD kg/m^2)	27.3 ± 4.9	28.2 ± 5.7	.15
Age (mean ± SD y)	39.7 ± 16.7	39.6 ± 13.4	.98
Sex (n and %)			< .001
Male	80 (67)	40 (33)	
Female	46 (43)	60 (57)	
Race (n and %)			.04
White	86 (61)	55 (39)	
African American	25 (45)	30 (55)	
Hispanic	8 (38)	13 (62)	
Asian	7 (78)	2 (22)	
Laryngoscopy indication (n and %)*			
Dyspnea	27 (56)	21 (44)	.94
Evaluation for VCD	70 (58)	50 (42)	.41
Abnormal PFT	19 (46)	22 (54)	.18
Hoarseness	9 (45)	11 (55)	.72
Chronic cough	15 (45)	18 (55)	.20
Stridor or wheeze	1 (17)	5 (83)	.20
Evaluation for stenosis	3 (75)	1 (25)	.63
Refractory asthma	2 (100)	0	.50

* The totals exceed the number of subjects because some subjects had more than one indication for laryngoscopy.
VCD = vocal cord dysfunction
BMI = body mass index
PFT = pulmonary function test

Table 2. Pulmonologists' Interpretation of Likelihood That the Flow-Volume Loop Represented a Patient With Vocal Cord Dysfunction

Pulmonologist	Likert Scale Rating* (mean ± SD)		P
	VCD Absent† (mean ± SD)	VCD Present† (mean ± SD)	
1	2.5 ± 1.3	2.8 ± 1.2	.10
2	2.2 ± 1.0	2.4 ± 1.0	.15
3	1.9 ± 1.1	2.0 ± 1.0	.45

* Likert scale: 1 = normal, 2 = minimally suggestive of vocal cord dysfunction (VCD), 3 = moderately suggestive of VCD, and 4 = highly suggestive of VCD.
† Diagnosed via laryngoscopy.

The 3 pulmonologists agreed on which inspiratory curves predicted VCD (quadratic kappa range 0.55–0.76), but those predictions were not correct; none of the physicians correctly differentiated the loops from patients with VCD from those without VCD (Table 2). Even with only the loops that all 3 raters considered either normal or highly suggestive of VCD, the raters still did not reliably predict VCD. Among the 37 patients with loops rated normal by all 3 pulmonologists, 14 were diagnosed with VCD. Of the 18 patients with loops graded highly suggestive of VCD, only 5 were diagnosed with VCD.

Table 3. Pulmonologists' Assessment of Inspiratory-Curve Truncation Versus Vocal Cord Dysfunction Diagnosed Via Laryngoscopy

	VCD Diagnosis (n and %)		Total (n)
	VCD Absent	VCD Present	
Pulmonologist 1			
Truncated	11 (32)	23 (68)	34
Not truncated	115 (60)	77 (40)	192
Pulmonologist 2			
Truncated	25 (45)	31 (55)	56
Not truncated	101 (59)	69 (41)	170
Total	126	100	

VCD = vocal cord dysfunction

Two physicians categorized the inspiratory curves (see Fig. 1). Their agreement was good (kappa 0.61). $FIF_{25\%/75\%}$ was significantly higher with the loops that were categorized as truncated, which suggests that this classification system may identify patients with elevated $FIF_{25\%/75\%}$. Table 3 compares the pulmonologists' assessments of inspiratory-curve truncation to the VCD diagnoses. Truncated inspiratory curves were associated with a laryngoscopic diagnosis of VCD for both raters (for pulmonologist 1 the odds ratio was 3.1, 95% CI 1.4–7.5, and for pulmonologist 2 the odds ratio was 1.8, 95% CI 0.94–3.5), but the test characteristics of truncated inspiratory curves were poor for both raters (Table 4).

With the values from the effort with the best FVC, the univariate spirometric predictors of VCD were $FIF_{50\%}$, $FIF_{75\%}$, FEV_1/FIV_1, and $FIF_{25\%/75\%}$ (Table 5). There was significant colinearity between $FIF_{25\%}$ and $FIF_{50\%}$ (rho 0.94, $P < .001$), $FIF_{25\%}$ and $FIF_{75\%}$ (rho 0.81, $P < .001$), and $FIF_{50\%}$ and $FIF_{75\%}$ (rho 0.94, $P < .001$). When univariate analysis was repeated with the data from the effort that was subjectively determined to have the best inspiratory curve, only $FIF_{75\%}$ and $FIF_{25\%/75\%}$ were predictive of VCD (Table 6). Fifty-seven (25%) of the 226 patients had inspiratory curves graded as nonreproducible (ie, only one of the 3 inspiratory curves was abnormal). Univariate analysis when the data from those patients were excluded found none of the spirometric variables predictive of VCD.

The following potential predictors were evaluated via multivariate logistic regression: age, sex, race, obesity (BMI > 30 kg/m^2), indication for laryngoscopy, ratio of FIV_1 to forced inspiratory vital capacity, $FIF_{25\%}$, $FIF_{50\%}$, $FIF_{75\%}$, FEV_1/FIV_1, $FIF_{25\%/75\%}$, and findings from flow-volume-loop analysis. When the spirometric variables were taken from the effort with the largest FVC, independent predic-

Table 4. Test Characteristics in Pulmonologists' Assessments of Inspiratory-Curve Truncation

	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Positive Likelihood Ratio (%)	Negative Likelihood Ratio (%)	Area Under the ROC Curve (%)
Pulmonologist 1	23	91	68	60	2.6	0.84	0.57
Pulmonologist 2	31	80	55	59	1.6	0.86	0.56

ROC = receiver operating characteristic

Table 5. Spirometry and Vocal Cord Dysfunction Assessed Based on the Effort With the Highest Forced Vital Capacity

	VCD Diagnosis		*P*
	VCD Absent	VCD Present	
FVC (mean ± SD % predicted)	92.0 ± 15.6	89.0 ± 18.5	.20
FEV_1 (mean ± SD % predicted)	87.2 ± 17.7	85.2 ± 19.5	.41
FEV_1/FVC (mean ± SD %)	0.77 ± 0.9	0.79 ± 0.0.9	.27
FIV_1/FIVC (mean ± SD %)	0.75 ± 0.19	0.72 ± 0.19	.19
$FIF_{25\%}$ (mean ± SD L/min)	3.7 ± 1.8	3.3 ± 1.6	.12
$FIF_{50\%}$ (mean ± SD L/min)	3.6 ± 1.9	3.1 ± 1.7	.04
$FIF_{75\%}$ (mean ± SD L/min)	3.1 ± 1.7	2.5 ± 1.6	.01
$FEF_{50\%}/FIF_{50\%}$ (mean ± SD)	1.3 ± 0.8	1.6 ± 1.3	.15
FEV_1/FIV_1 (mean ± SD)	1.2 ± 0.5	1.6 ± 2.0	.04
$FIF_{25\%/75\%}$ (mean ± SD)	1.3 ± 0.5	1.5 ± 0.5	.007

VCD = vocal cord dysfunction
FVC = forced vital capacity
FEV_1 = forced expiratory volume in the first second
FIV_1 = forced inspiratory volume in the first second
FIVC = forced inspiratory vital capacity
FIF_{25} = forced inspiratory flow at 25% of the inspired volume
FIF_{50} = forced inspiratory flow at 50% of the inspired volume
FIF_{75} = forced inspiratory flow at 75% of the inspired volume
FEF_{50} = forced expiratory flow at 50% of the inspired volume
$FIF_{25/75}$ = ratio of FIF_{25} to FIF_{75}

Table 6. Spirometry and Vocal Cord Dysfunction Assessed Based on the Subjectively Determined Best Inspiratory Curve

	VCD Diagnosis		*P*
	VCD Absent	VCD Present	
FVC (mean ± SD % predicted)	89.6 ± 15.9	85.6 ± 19.0	.09
FEV_1 (mean ± SD % predicted)	85.4 ± 18.2	83.2 ± 19.8	.40
FEV_1/FVC (mean ± SD %)	76.8 ± 9.5	78.8 ± 19.8	.11
FIV_1/FIVC (mean ± SD %)	78.8 ± 16.1	77.7 ± 13.5	.63
$FIF_{25\%}$ (mean ± SD L/min)	3.8 ± 1.7	3.4 ± 1.4	.07
$FIF_{50\%}$ (mean ± SD L/min)	4.5 ± 1.8	3.3 ± 1.5	.10
$FIF_{75\%}$ (mean ± SD L/min)	3.2 ± 1.6	2.6 ± 1.5	.005
$FEF_{50\%}/FIF_{50\%}$ (mean ± SD)	1.2 ± 0.6	1.3 ± 1.1	.12
FEV_1/FIV_1 (mean ± SD)	1.1 ± 0.4	1.2 ± 0.5	.12
$FIF_{25\%/75\%}$ (mean ± SD)	1.2 ± 0.4	1.5 ± 0.9	.002

VCD = vocal cord dysfunction
FVC = forced vital capacity
FEV_1 = forced expiratory volume in the first second
FIV_1 = forced inspiratory volume in the first second
FIVC = forced inspiratory vital capacity
FIF_{25} = forced inspiratory flow at 25% of the inspired volume
FIF_{50} = forced inspiratory flow at 50% of the inspired volume
FIF_{75} = forced inspiratory flow at 75% of the inspired volume
FEF = forced expiratory flow at 50% of the inspired volume
$FIF_{25/75}$ = ratio of FIF_{25} to FIF_{75}

tors of diagnosing VCD at laryngoscopy included female sex (adjusted odds ratio 2.72, 95% CI 1.55–4.75), obesity (adjusted odds ratio 2.06, 95% CI 1.12–3.80), and $FIF_{25\%/75\%}$ (adjusted odds ratio 1.97, 95% CI 1.12–3.44). The performance of this model was poor; the area under the receiver-operating-characteristic curve was 0.68. After adjusting this model for inspiratory-curve reproducibility, $FIF_{25\%/75\%}$ was no longer predictive of VCD. When the multivariate analysis was repeated with the spirometric variables from the effort that had the subjectively determined best inspiratory curve, $FIF_{25\%/75\%}$, again, was not predictive of VCD.

Discussion

VCD is difficult to diagnose and frequently confused with other diseases. We studied whether pulmonologists could predict VCD based solely on examination of flow-volume loops. Three blinded physicians rated the likelihood of VCD on a Likert scale, and we gave no instruction about what flow-volume loop findings suggest VCD. Although there was good agreement between the pulmonologists about which inspiratory curves probably indicated VCD, these pulmonologists did not accurately identify which patients had VCD. When 2 physicians classified the loops based on predefined patterns, predictive ability also was limited.

In our second analysis, independent predictors of a laryngoscopic VCD diagnosis included higher $FIF_{25\%/75\%}$, obesity, and female sex. In practice, an abnormally high $FIF_{25\%/75\%}$ correlates with an initially normal flow followed by rapid flow tapering, which is consistent with paradoxical vocal cord motion during inspiration. $FIF_{25\%/75\%}$ was not predictive in the analysis of the spirometric data from the effort with the best inspiratory curve or when we controlled for inspiratory-curve reproducibility. This implies

that the elevated $FIF_{25\%/75\%}$ was related to an inadequate or inconsistent effort, rather than functional pathology due to VCD. In the future, more focus on adequate inspiratory effort might help to define appropriate reproducibility criteria. Inability to consistently reproduce inspiratory volumes may suggest VCD.

Truncation of both the inspiratory and expiratory curves has been described in symptomatic VCD, but the inspiratory curve is thought to be more commonly affected.[1,8,15,16,17] All of our patients underwent spirometry as part of the clinical workup for unexplained symptoms, and they were unlikely to have been acutely symptomatic at the time of testing. In laryngoscopy, several provocative maneuvers are used to attempt to precipitate VCD and make the diagnosis, but no provocation is undertaken prior to spirometry. Previous attempts to establish a provocation that induces spirometric changes and inspiratory-curve truncation have yielded inconsistent results.[2]

To our knowledge, we are the first to identify obesity as a risk factor for VCD. Multiple studies have reported an association between asthma and high BMI in women.[18-20] Gastroesophageal reflux disease and obesity frequently coexist, which led some to suggest that reflux predisposes obese patients to airway hyperreactivity and asthma.[21] Gastroesophageal reflux disease has also been reported with VCD, and may be a causal link between obesity and VCD.[22-24]

A higher prevalence of VCD in women was previously documented. Newman and Dubester reported on 95 patients who were diagnosed with VCD at National Jewish Medical Center for Immunology and Respiratory Medicine. Eighty (84%) of those 95 patients were women.[8] A retrospective review at our hospital found that 80 (66%) of the 122 patients diagnosed with VCD were female.[25] In the present study, of the 110 patients diagnosed with VCD, 64 (58%) were women. The challenges to identifying the true prevalence of VCD in a population makes it difficult to determine the distribution of VCD by sex. Although several studies have found VCD more common in females than males, those studies may have suffered referral bias.

Limitations

The most important limitation of the present study is the absence of documented symptoms. Our goal was to help tailor the workup for a patient who presents with unexplained symptoms, as opposed to a patient who is acutely dyspneic in the emergency department. Had we evaluated a population that presented acutely and performed spirometry on them, we may have seen a more consistent relationship between laryngoscopically confirmed VCD diagnosis and flow-volume-loop abnormalities, identified either subjectively or objectively with $FIF_{25\%/75\%}$.

Our findings are applicable to patients who present to a specialty clinic for existing symptoms. Although laryngoscopy is the accepted standard to diagnose VCD, a patient with VCD may have a normal laryngoscopy. Furthermore, provocations to increase laryngoscopy's sensitivity for detecting VCD may sacrifice specificity, because these provocations may cause paradoxical vocal cord movement in patients who do not have VCD. Also, those provocations are not standardized. Unfortunately, this limitation applies to the majority of current VCD research.

Finally, the criteria we used to identify the best inspiratory curve and reproducibility were somewhat subjective. We hoped that blinding the reviewers to the diagnosis eliminated any bias that may have been introduced in those assessments.

Our subjects probably had prior workup to rule out pathology. The percentage of patients diagnosed with VCD is significantly higher than would be expected in a typical population presenting with unexplained symptoms.[26] Our results are subject to selection bias, which again limits generalization to other settings.

Conclusions

We sought clinical and spirometric predictors of VCD in patients who presented with unexplained symptoms. We found 3 independent predictors of VCD. The combined performance of these tests was limited, based on assessment of the receiver operating characteristic. VCD remains challenging to diagnose. The appearance of the flow-volume loops should not strongly influence the decision to perform laryngoscopy.

REFERENCES

1. Morris MJ, Deal LE, Bean DR, Grbach VX, Morgan JA. Vocal cord dysfunction in patients with exertional dyspnea. Chest 1999;116(6):1676-1682.
2. Perkins PJ, Morris MJ. Vocal cord dysfunction induced by methacholine challenge testing. Chest 2002;122(6):1988-1993.
3. Brugman SM, Newman K. Vocal cord dysfunction. Med Sci Update 1993;11(5):1-5.
4. Christopher KL, Wood RP, Eckert RC, Blager FB, Raney RA, Souhrada JF. Vocal-cord dysfunction presenting as asthma. N Engl J Med 1983;308(26):1566-1570.
5. Maschka DA, Bauman NM, McCray PB, Hoffman HT, Karnell MP, Smith RJH. A classification scheme for paradoxical vocal cord motion. Laryngoscope 1997;107(11):1429-1435.
6. Soto FJ, Guntupalli KK. All that wheezes is not asthma: diagnosing the mimics. Emerg Med 2001;33(11):40-56.
7. Shusterman D. Review of the upper airway, including olfaction, as mediator of symptoms. Environ Health Perspect Supplements 2002;110(4):649-653.
8. Newman KB, Dubester SN. Vocal cord dysfunction: masquerader of asthma. Semin Respir Crit Care Med 1994;15:162-167.
9. McFadden ER Jr, Zawadski DK. Vocal cord dysfunction masquerading as exercise-induced asthma. Am J Respir Crit Care Med 1996;153(3):942-947.

10. Mikita J, Parker J. High levels of medical utilization by ambulatory patients with vocal cord dysfunction as compared to age and gender matched asthmatics. Chest 2006;129(4):905-908.
11. Vlahakis NE, Patel AM, Maragos NE, Beck KC. Diagnosis of vocal cord dysfunction: the utility of spirometry and plethysmography. Chest 2002;122(6):2246-2249.
12. American Thoracic Society. Standardization of spirometry, 1994 update. Am J Respir Crit Care Med 1995;152(3):1107-1136.
13. Crapo RO, Morris AH, Gardner RM. Reference spirometric values using techniques and equipment that meet ATS recommendations. Am Rev Respir Dis 1981;123(6):659-664.
14. Hnatiuk OW, Sierra A, Chang AS. Evaluation of the normal inspiratory flow-volume curve. Respir Care 1998;43(12):1058-1063.
15. Bahrainwala AH, Simon MR, Harrison DD. Atypical flow volume curve in an asthmatic patient with vocal cord dysfunction. Ann Allergy Asthma Immunol 2001;86(4):439-443.
16. Kivity S, Bibi H, Schwarz Y, Grief Y, Topilsky M, Tabachnick E. Variable vocal cord dysfunction presenting as wheezing and exercise induced asthma. J Asthma 1986;23(5):241-244.
17. Alpert SE, Dearborn DG, Kercsmar CM. On vocal cord dysfunction in wheezy children. Pediatr Pulmonol 1991;10(2):142-143.
18. Gennuso J, Epstein LH, Paluch RA, Cerny F. The relationship between asthma and obesity in urban minority children and adolescents. Arch Ped Adol Med 1998;152(12):1197-1200.
19. Young SY, Gunzenhauser JD, Malone KE, McTiernan A. Body mass index and asthma in the military population of the northwestern United States. Arch Intern Med 2001;161(13):1605-1611.
20. Nathell L, Jensen I, Larsson K. High prevalence of obesity in asthmatic patients on sick leave. Respir Med 2002;96(8):642-650.
21. Parker JM, Guerrero ML. Airway function in women: bronchial hyperresponsiveness, cough, and vocal cord dysfunction. Clin Chest Med 2004;25(2):321-330.
22. Powell DM, Karanfilov BI, Beechler KB, Treole K, Trudeau MD, Forrest LA. Paradoxical vocal cord dysfunction in juveniles. Arch Otolayngol Head Neck Surg 2000;126(1):29-34.
23. Perkner JJ, Fennelly KP, Balkissoon R, Bartelson BB, Ruttenber AJ, Wood RP II, Newman LS. Irritant associated vocal cord dysfunction. Journal of occupational and environmental medicine 1998;40(2):136-143.
24. Koufman JA, Wiener GJ, Wu WC, Cooper JB, Richter JE, Castell DO. Reflux laryngitis and its sequelae: the diagnostic role of ambulatory 24-hour pH monitoring. J Voice 1988;2:78-89.
25. Perrello MM, Gurevich J, Fitzpatrick T, Berg BW, Parker JM. Clinical characteristics of vocal cord dysfunction in two military tertiary care facilities (abstract). Am J Respir Crit Care Med 2003;167:A788.
26. Morris MJ, Grbach VX, Deal LE, Boyd SY, Morgan JA, Johnson JE. Evaluation of exertional dyspnea in the active duty patient: the diagnostic approach and the utility of clinical testing. Mil Med 2002;167(4):281-288.