Comparative analysis of clinical profile: Chronic cough vs paradoxical vocal fold motion

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ABSTRACT

Background: Ongoing contention surrounding typical demographic and clinical attributes of chronic cough (CC) and paradoxical vocal fold motion (PVFM) impedes timely diagnosis and optimum patient care. Designed to reduce preventable patient morbidity through improved recognition and differentiation, the current study aimed to determine representative clinical profiles for CC and PVFM, with identification of distinctive attributes from the general population and risk factors associated with each diagnosis.
Methods: Self-reported medical questionnaires, demographic and lifestyle attributes of CC and PVFM cases from a disease-specific outcomes database were compared to US population data and published normative values. Univariate comparison and multivariate regression modelling of age, sex, alcohol intake, smoking, Reflux Symptom Index (RSI), Voice Handicap Index (VHI), and Generalized Anxiety Disorder 7-item Scale (GAD-7) determined distinguishing features between the clinical groups, including odds ratios for presenting with CC versus PVFM.
Results: Clinical profiles developed from 283 (128 CC, 155 PVFM) adults (18–91years) were significantly different from the general population across each demographic, lifestyle and clinical variable (all $p < .01$), with the exception of obesity. Age (55.39 ± 13.54 vs 45.07 ± 16.51years, $p < .01$) and mean RSI score (21.5 ± 9.02 vs 18.1 ± 9.08, $p < .01$) most reliably distinguished CC from PVFM, with those aged 60–69 years ($OR = 9.45$) most likely to be diagnosed with CC.
Conclusions: Standard clinical profiles of CC and PVFM are distinct from the general population, aiding determination of relative probabilities and risk factors in the differential diagnostic process. Variations between CC and PVFM were subtle, reliably distinguished by age and relative severity of laryngopharyngeal reflux symptomatology.

1. Introduction

Reported to have wide ranging implications for patients (physical, social, occupational, financial) and the health care system, chronic cough (CC) and paradoxical vocal fold motion (PVFM) represent significant clinical problems in ambulatory care settings that share many common signs and symptoms, yet many patients do not receive timely or appropriate management (each is treated differently by numerous disciplines) [1–5]. Considerable contention surrounds each diagnosis, resulting in lengthy differential diagnostic procedures involving multiple consultations with a range of specialists (and often a series of medical trials) in order to eliminate other causes of airway disturbance (e.g. asthma, infection, allergies, or neurological change) [6,7]; recognition impeded by lack of consensus surrounding typical clinical presentation.

Clinical profiles of CC and PVFM have largely developed in parallel, yet are markedly similar in terms of demographic (sex disparity, obesity) and clinical attributes (reflux, dysphonia, mental health). Initial attempts have been made to compare the two diagnoses [6,8], however limited sample sizes, the inclusion of heterogeneous diagnoses, and absence of direct comparison between PVFM and CC with population data have left uncertainty as to

whether or not demographic and associated factors differ between the two disorders, and how individuals with CC and/or PVFM compare to the population at large.

The primary objective of the current study was to determine distinguishing characteristics for self-reported medical questionnaires in addition to demographic and lifestyle attributes of individuals diagnosed with PVFM and CC, in comparison to the general population and between the disorders. Through this analysis, we aim to provide clinicians with a reference for typical attributes of individuals with CC and PVFM, assisting in disorder recognition, differential diagnosis and ultimately improved patient care.

2. Methods

This study was conducted using the University of Wisconsin–Madison Voice and Swallow Outcomes Database, established and accessed with approval by the University of Wisconsin–Madison School of Medicine and Public Health Institutional Review Board. At the time of access, the database contained health information of more than 3000 current or previous patients of the Division of Otolaryngology Head and Neck Surgery Voice and Swallow Clinics. To identify potential participants, a search of the database records was conducted using the following terms: International Classification of Disease, Clinical Modification (ICD-9-CM) codes 478.5 (other diseases of the vocal cords) and 786.2 (cough), "VCD", "vocal cord dysfunction", "PVFM", "paradoxical vocal fold", and "cough". Patients diagnosed with co-existing neurological conditions, both CC and PVFM or significant vocal pathology were excluded from the study to ensure clarity of pathophysiology. To be included in the study, patients needed to be 18 years or over and diagnosed with either CC or PVFM by a physician and/or speech-language pathologist. Those in the CC group needed to present with chronic refractory cough as the primary complaint and report onset at least eight weeks prior to date of visit (no co-existing PVFM). Patients on ACE inhibitor medications were excluded from the CC group, with the exception of one patient who had already completed a cessation trial with no change in cough symptoms.

Key demographic details and lifestyle attributes for the CC and PVFM cohorts were extracted from the database for analysis, with United States population data for age, sex, BMI, smoking status and alcohol consumption gleaned from the US Census (2010) [9] and National Health Interview Survey (2012) [10] (NHIS) publications. Demographic categorization for age, sex, BMI, smoking and alcohol consumption for those with PVFM and CC matched that from the US Census [9] and NHIS [10]. To allow for statistical comparison to published normative values, the following self-report measures were chosen: Voice Handicap Index (VHI, a 30-item scale measuring the impact of voice disorders on patient quality of life; scores − 0–17 WNL, 18–39 mild, 40–59 moderate and >60 severe) [11]; Reflux Symptom Index (RSI, a nine-item scale measuring the clinical symptoms of laryngopharyngeal reflux, LPR, a score less than 11.6 indicates no LPR) [12]; and the 7-item Generalized Anxiety Disorder Assessment (GAD-7, a seven-item scale identifying the presence or absence of Generalized Anxiety Disorder, scores 0–4 minimal, 5–9 mild, 10–14 moderate, 5–21 severe) [13]. The Leicester Cough Questionnaire [14] (a 19-item health-related quality of life questionnaire specific to CC whose total score ranges from 3 to 21; a higher score indicates a better health-related quality of life, with minimal important difference of 1.3.) was included as a standard measure for the CC group, allowing comparison to previously published data.

Differences in demographics between the general population, CC and PVFM cohorts were determined using Chi-square statistics,

with statistical significance set at p < .05. Laryngopharyngeal reflux (RSI), dysphonia (VHI), and anxiety (GAD-7) measures were compared between the CC and PVFM groups, and to published normative values, using two-sample t-tests. Relative odds ratios for presenting with CC (as opposed to PVFM) were determined through a multivariate regression model. All statistical analyses were conducted using SAS software (version 9.2; SAS Institute, Cary, NC).

3. Results

A total of 283 patients met the eligibility criteria for the study, 128 participants with CC (18–82 years) and 155 participants with PVFM (18–91 years). The demographic profile of the clinical groups was significantly different from US population norms (p < .01), with the exception of BMI. The majority of both PVFM (n = 111, 72%) and CC (n = 94, 73%) patients were female, who have never smoked (n = 83, 65% CC; n = 102, 66% PVFM), who were overweight or obese (n = 80, 74% CC; n = 75, 63% PVFM). Alcohol consumption was less prevalent in both CC and PVFM compared to the US population, with half (n = 61, 50%) of the CC group and 54% (n = 66) of the PVFM group abstaining (Table 1). Scores for the CC and PVFM groups on the RSI, VHI, and GAD-7 were significantly higher (p < .01) than normative values, indicative of elevated levels of LPR, dysphonia, and generalized anxiety within the clinical cohort (Table 2). LCQ mean scores for the CC group (13.76 ± 3.46) were similar to previously published mean values for individuals with CC (12.2 ± 4.91) (p = .071).

Univariate and multivariate statistical analyses determined distinguishing demographic and clinical attributes for CC versus PVFM (Tables 2 and 3). Patients with CC (55.39 ± 13.54 years) were, on average, 10 years older than those with PVFM (45.07 ± 16.51 years, p < .01), and had significantly higher RSI scores (21.5 ± 9.02 vs 18.1 ± 9.08, p < .01). Mean BMI (29.81 ± 6.79, CC; 29.27 ± 7.98, PVFM; p = .584), VHI (20.1 ± 20.6, CC; 19.4 ± 20.4, PVFM; p = .806) and mean GAD-7 scores (4.02 ± 5.1, CC; 5.34 ± 5.45, PVFM; p = .067) did not differentiate between the two groups (Table 2). Multivariate regression modelling revealed the strongest predictor (p < .05) of having CC rather than PVFM to be age (Table 3). Compared with individuals less than 30 years old, patients 40–49 years were 3 times more likely to have CC, those 50–59 years and over 70 years 4 times more likely, with individuals 60–69 years found to be at greatest risk with an odds ratio of 9.45. While the remaining demographic (sex, BMI, smoking status, alcohol and smoking history) and clinical attributes (GAD-7, RSI, VHI scores) were not found to be independently predictive of diagnosis (p > .05), in general the relative odds for presenting with CC rather than PVFM were higher for those who were overweight/obese (OR = 1.73), female (OR = 1.16), currently consumed alcoholic beverages (OR = 1.18), with elevated levels of laryngopharyngeal reflux symptomatology (RSI score, OR = 1.74) and self-reported mild impairment in voice-related quality of life (VHI, OR = 1.38). Current drinkers (OR = .597) and those with severe levels of generalized anxiety (GAD-7, OR = .489) were more likely to have PVFM.

4. Discussion

At their core, CC and PVFM share an underlying adduction of the vocal folds for no obvious physiologic purpose that is presently known. While sharing a common locus, however, research has tended to follow separate paths, with independent descriptions of patient presentation, alongside parallel evolution of attempts to elucidate underlying processes. A recent multinational investigation [7], for example, proposed CC to represent 'the most striking