*The Laryngoscope*

ORIGINAL REPORT

# Effects of Daily Electronic Cigarette Use on the Vocal Mechanism: A Multimodality Study

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## ABSTRACT

**Objectives:** To compare self-reported voice, cough, and dyspnea symptom impacts, aerodynamics, and laryngeal kinematics in young adults who do and do not use electronic cigarettes.

**Methods:** A total of 26 electronic cigarette users (EC group; 10 male, 16 female) and 39 nonusers (control group; 10 male, 29 female) completed the study. Standardized questionnaires related to voice, dyspnea, and cough symptoms were completed. Aerodynamic measures of peak expiratory flow and volume for cough, subglottal pressure, and vital capacity were obtained. Laryngeal kinematics were evaluated during tasks of sustained /i:/ and /hi-hi/ from high-speed videoendoscopy. Comparisons between EC and controls were examined, and regression analyses were calculated to evaluate how characteristics of use (e.g., duration, frequency, co-use with marijuana) were related to outcome measures.

**Results:** The EC group reported significantly greater voice and cough symptoms on standardized questionnaires compared to controls, with a longer duration of use significantly related to greater symptoms. Use of marijuana was related to greater cough symptoms as well. The EC group also exhibited significantly smaller vocal fold adductory velocities during /hi-hi/ productions as well as significantly lower amplitude quotient variability and phase asymmetry.

**Conclusion:** This study provides preliminary evidence of the negative effects of daily electronic cigarette use in young adults, with users reporting more voice/cough symptoms, along with subtle changes to laryngeal kinematics. However, voice and cough aerodynamics were not affected. Future studies should investigate how factors of duration and use of marijuana influence voice and cough in electronic cigarette users.

**Level of Evidence:** III.

## 1 | Introduction

Electronic cigarettes (e-cigarettes, EC), often called "vapes" or "mods" [1, 2], heat e-liquids containing solvents, like propylene glycol, along with nicotine and other additives to produce an inhaled aerosol. First introduced to the US market in 2006 as an alternative to conventional cigarettes and a smoking cessation tool [3], ECs are frequently perceived as a safer option [4, 5]. However, growing evidence suggests that ECs contain harmful chemicals, such as heavy metals and carcinogens [6], that can increase physical health risks [7]. An estimated 50% of all EC users are under the age of 35 years [8], with many first trying

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them as teenagers, and the 18- to 24-year-old age group having the highest incidence of EC use as of 2021 [9].

### 1.1 | Effects of ECs on Voice and Upper Airway

A recent scoping review evaluated the effects of ECs on otolaryngological symptoms in adults [10]; with 17 studies reporting cough accompanied by either mouth/throat irritation, dry mouth/throat, or sore throat. Reduced lung functions and vital capacities are also evidenced in users [11–13]. These reports are unsurprising, as propylene glycol—an ingredient in e-liquid—activates chemosensory channels [14] that promote asthmatic inflammation and contribute to disorders of the upper airway, such as chronic cough [15], and further generates toxic carbonyl compounds [16], which are known to irritate upper and lower airways [17].

Studies have demonstrated negative impacts on vocal fold tissues after short-term exposure, including increased hyperplasia and metaplasia in rats [18], damage to apical epithelial cells and mucosal inflammation in engineered tissues [19], and cytotoxic effects on human vocal fold fibroblasts [20]. Yet, the evidence for an impact on clinical voice outcomes is more limited. Hua et al. [21] reported a "harsh" vocal quality for some users; however, Tuhanioğlu et al. [22] revealed no differences between users and nonusers for acoustic measures related to pitch and roughness. An unpublished thesis evaluated vocal fold vibrational features by comparing a small number of EC users ($n=7$) with conventional cigarette users and nonsmokers [23]. EC users showed reduced mucosal wave, abnormalities in the vocal fold edge (typically convex or irregular), and a predominant closed phase likely due to increased edema in the vocal folds compared to nonusers.

## 2 | Purpose

To our knowledge, no studies have reported the impact of ECs on the aerodynamics of voice and cough, nor on objective laryngeal kinematics. The paucity of research on the impacts of ECs on the vocal mechanism does not provide sufficient knowledge to inform our clinical practice amidst the growing trend of EC use. We hypothesized (a) greater degrees of dyspnea, cough, and voice symptoms [10], (b) changes to aerodynamics and laryngeal kinematics (vibratory and adductory) consistent with vocal fold edema [23, 24], and (c) that the characteristics of EC use (e.g., duration, frequency) would be significantly related to outcome measures.

## 3 | Methods

Data were collected prospectively at the University of Cincinnati (UC; IRB#2021-0994) and Indiana University (IU; IRB#2020-0105-001), according to the institutional review board approval at both sites. All participants provided informed consent prior to participation.

### 3.1 | Participants

Participants met the following inclusion criteria: (i) adults aged 18–45 years, (ii) no current history of speech, voice, or hearing disorder, (iii) no professionally trained singing experience, and (iv) no current or history of neurogenic or pulmonary disease (e.g., asthma). The EC group included individuals who vaped daily for a minimum of 3 months. Users who also concurrently smoked conventional cigarettes were enrolled as long as vaping was their primary means of nicotine delivery, as reports show ~50% of those who vape also smoke [6]. Controls were defined as those who had not used ECs or conventional cigarettes within the past 5 years.

Participants were screened for dysphonia via auditory-perceptual analysis using the Consensus Auditory-Perceptual Evaluation of Voice [25] by a trained speech–language pathologist, with ratings $<10$ mm indicating normal vocal quality [26]. Participants were screened for tolerance of rigid laryngoscopy and vocal fold pathology. A total of 77 participants were screened; however, 9 could not tolerate the rigid laryngoscope, and 3 female EC users had bilateral pre-nodule swelling that excluded them from the study. A total of 65 participants qualified for the study: 26 EC and 39 controls (Table 1).

### 3.2 | Data Collection and Analysis

#### 3.2.1 | Questionnaires

Participants completed questionnaires to assess their voice and respiratory symptoms, including: (1) the Voice Handicap Index (VHI) [27], a 30-item questionnaire that assessed Functional, Physical, and Emotional domains of voice; (2) the Vocal Fatigue Index's (VFI) [28] Tiredness and Avoidance, Physical Discomfort, and Improvement with Rest factors; (3) the University of Cincinnati Dyspnea questionnaire (UCD) [29] that assessed the degree of dyspnea during daily speech and physical activities; (4) the Leicester Cough Questionnaire (LCQ) [30], which assessed the impact of cough on Physical, Psychological, and Social domains; and (5) the Modified Medical Research Council Dyspnea scale (MMRC) [31], which is a single question for the level of dyspnea during physical activities. All questionnaires were summed and/or averaged using standardized methods outlined in each survey.

#### 3.2.2 | Case History

The EC group completed an additional intake exploring the duration (years), frequency (number of puffs per day), and recency of use (within 1 h of the research session), along with use of additional substances (i.e., marijuana) and other characteristics (Table 1).

#### 3.2.3 | Aerodynamics

The phonatory aerodynamic system (PENTAX, model 6600) was used to collect aerodynamic measures. Subglottal pressure ($cmH_2O$) was estimated from pressure peaks obtained via an intraoral pressure tube during /pi-pi-pi-pi-pi/ productions at comfortable pitch and volume [32]. Vital capacity (L) was elicited up to three times, and the maximum capacity was reported. Participants were cued to cough to gather peak expiratory airflow (L/s) and expiratory volume (normalized to vital capacity; %) [33].

**TABLE 1** | Demographic information.

| Variable | Value |
|---|---|
| EC group | |
| Male vs. female (*n*) | 10, 16 |
| Age (years) | 22.62 ± 4.52 |
| Control group | |
| Male vs. Female (*n*) | 10, 29 |
| Age (years) | 23.38 ± 3.75 |
| Race | |
| White | 71% |
| Two or more races | 9% |
| Asian | 8% |
| Black | 8% |
| Not reported | 4% |
| Ethnicity | |
| Hispanic | 14% |
| Non-Hispanic | 86% |
| Enrollment location | |
| UC | 37% |
| IU | 63% |
| EC use | |
| Duration (years) | 3.0 ± 1.7 |
| Puffs per day | 71.4 ± 41.8 |
| Concentration | |
| > 18 mg/mL | 27% |
| 2–6 mg/mL | 46% |
| Unsure | 27% |
| Within 1 h of session | 58% |
| Marijuana added | 46% |
| Flavors added | 100% |
| Conventional cigarettes | |
| Past | 46% |
| Current | 8% |

#### 3.2.4 | Laryngeal Kinematics

Participants underwent rigid high-speed videoendoscopy (HSV) at 4000 frames per second [34] while producing sustained /i:/ and the laryngeal diadochokinetic gesture of /hi-hi-hi/ at typical pitch and loudness. HSV data were captured via a Phantom high-speed camera (VEO-340 L; 512 × 512 spatial resolution) or by the PENTAX Medical system (9710; 512 × 256 spatial resolution). Concurrent acoustic information was captured using a headset or lapel microphone, at a sampling rate of 40,000 Hz, further calibrated to vocal intensity (dB SPL) at 30 cm [32].

**3.2.4.1** | **Vibratory Kinematics.** The Glottis Analysis Tool (ver. 2020) was used to segment and analyze HSV recordings [35, 36]. A segment of 100 cycles during the mid-portion of the vowel /i:/ steady-state was selected to extract the glottal area waveform. Outcome measures included those that reflected glottal dynamics (closing quotient, glottal area index), mechanics (amplitude quotient), and symmetry (phase asymmetry index), as well as their standard deviations (SD) across the 100 cycles.

**3.2.4.2** | **Adductory Kinematics.** Glottic angles during the transition from the voiceless consonant /h/ to the onset of the /i/ vowel during /hi-hi/ were automatically identified using a custom MATLAB algorithm (Figure 1A). The glottic angle identification process was repeated iteratively over the adductory gesture for each frame. Data points were smoothed using a low-pass filter, followed by a sigmoidal regression [37]. The absolute value of the maximum adductory angular velocity was calculated from the fitted sigmoidal data (Figure 1B). A kinematic estimate of laryngeal stiffness was determined as the ratio of the maximum adductory velocity to the maximum abductory angle during the /h/ production [38, 39]. Kinematic estimates of laryngeal stiffness are impacted by thyroarytenoid (TA), lateral cricoarytenoid, and posterior cricoarytenoid muscle activation [39]. The motivation to study vocal fold adduction measures like stiffness was due to our hypothesis that EC use increases vocal fold edema that impacts TA muscle activation and subsequent coordination with aerodynamic forces for phonatory onset. Measures of maximum glottic angle (°), maximum adductory velocity (°/s), and kinematic estimate of laryngeal stiffness (1/s) were used as outcome measures in this study (Table 2).

### 3.3 | Statistical Analysis

Nonparametric Mann–Whitney *U* tests were calculated to compare questionnaires and vocal fold adductory kinematic measures due to non-normal distributions and uneven sample sizes between the two groups. Effect size was calculated using a rank-biserial correlation ($r_{rb}$) for nonparametric tests [40] and interpreted like a Pearson's correlation coefficient [41, 42].

General linear models with fixed effects of group (EC, control), sex (male, female), and their interaction were computed for each vibratory kinematic measure (mean, SD) and aerodynamic measure. Sex was added as a factor to these models to account for known sex differences in these measures [43]. Effect sizes were calculated using Hedges *g*, which accounted for the unequal sample sizes between groups [44].

To investigate how EC use and health behaviors impacted outcome measures, multiple regression models were calculated for statistically significant variables (symptom impact questionnaires, aerodynamics, and laryngeal kinematics) for only the EC group. Model predictors included the duration of EC use (years), frequency of use (number of puffs per day), recency of use (yes/no to whether they used within 1 h of the research session),

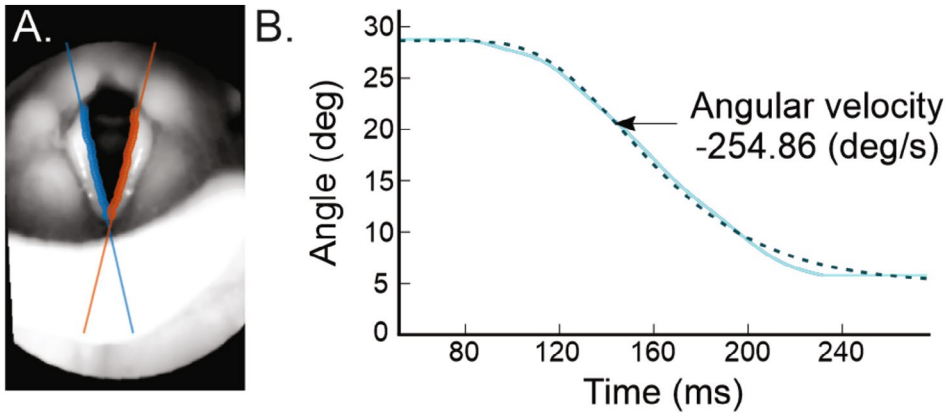


**FIGURE 1** | (A) Image captured through high-speed videoendoscopy with automated glottic angle identification (26.75°) for a female EC user. (B) A segment of the smoothed data (solid line) and a sigmoidal fit (dashed line) from the adductory gesture used to determine laryngeal adductory kinematic measures.

**TABLE 2** | List of vibratory and adductory laryngeal kinematic measures.

| Task | Measure | Description |
|---|---|---|
| Sustained /i:/ | Closing quotient (range = 0–1) | Ratio of the closing duration to the overall duration of the glottal cycle. Smaller ratios indicate a shorter closing time compared to opening |
| | Glottal area index (range = 0–∞) | Ratio of the glottal area dynamic range divided by the open quotient. A smaller ratio indicates a larger glottal gap |
| | Amplitude quotient (range = 0–∞) | Amplitude of the glottal area dynamic range normalized by the maximum closing velocity. Larger values indicate an increased duration of closing phase |
| | Phase asymmetry (range = −1 to 1) | Subtracting the time point of the maximum glottal area of the right side per cycle from the time point of the same event on the left side of the cycle, normalized to the duration of the entire glottal cycle. A value of 0 indicates symmetry and values closer to the extremes of −1 or 1 indicate one vocal fold is leading. A negative value indicates a leading left vocal fold and a positive value indicates a leading right vocal fold |
| Diadochokinetic /hi-hi/ | Maximum glottic angle (°) | Maximum abductory angle during the /h/ segment |
| | Maximum adductory velocity (°/s) | Absolute value of the maximum angular velocity from the adductory gesture from the /h/ to the onset of /i/ |
| | Kinematic estimate of laryngeal stiffness (1/s) | Ratio of the maximum adductory velocity to the maximum glottic angle |

history of conventional cigarette use (yes/no), and presence of additional substances (i.e., marijuana in addition to nicotine vs. nicotine alone). The coefficient of determination $\left(R^2_{adj}\right)$ was reported. All statistical analyses were completed in Minitab (ver. 20.3) statistical software, except for rank-biserial correlations, which were calculated in Jamovi (ver. 2.3.28). All variable significance was set to $p < 0.05$.

## 4 | Results

### 4.1 | Questionnaires

Significant differences were found between EC and controls for VHI-Physical ($W = 1017.5$, $p = 0.032$; $r_{rb} = 0.320$) and VHI-Emotional ($W = 1000.50$, $p = 0.008$; $r_{rb} = 0.357$), in which the EC group reported significantly higher scores. The LCQ subtests and total score all reached significance (LCQ-Physical: $W = 1558.50$, $p < 0.001$; LCQ-Psychological: $W = 1458.0$, $p = 0.017$; LCQ-Social: $W = 1486.0$, $p = 0.001$; LCQ-Total: $W = 1551.0$, $p < 0.001$), in which the EC group showed significantly lower scores, indicating greater cough symptoms (Table 3).

### 4.2 | Aerodynamics

Vital capacity was significantly higher in males compared to females ($F(1,61) = 34.67$, $p < 0.001$, $g = 1.61$; males = 5.37 ± 1.04 L, females = 3.93 ± 0.83 L), and likewise, cough peak expiratory airflow was significantly higher for males as well ($F(1,61) = 34.67$, $p < 0.042$, $g = 0.53$). There were no significant findings between the EC group and controls.

### 4.3 | Laryngeal Kinematics

#### 4.3.1 | Vibratory Kinematics

Phase asymmetry was significantly lower in the EC group compared to the control group ($M = -0.026 \pm 0.08$ and $M = 0.060 \pm 0.05$, respectively; $F(1,61) = 35.92$, $p = < 0.001$, $g = 1.35$) and negative, indicating a left-leading vocal fold asymmetry. Amplitude quotient SD was also significantly lower ($F(1,61) = 6.88$, $p = 0.01$, $g = 0.61$) in the EC group ($M = 0.000085 \pm 0.000073$) compared to the control group ($M = 0.000145 \pm 0.000111$).

Females showed larger closed quotients ($M = 0.38 \pm 0.10$) compared to males ($M = 0.32 \pm 0.07$; $F(1,61) = 5.33$, $p = 0.024$). Other measures were significantly smaller in females compared to males for glottal area index ($F(1,61) = 7.16$, $p = 0.010$; female: $M = 1.19 \pm 0.35$; male: $M = 1.45 \pm 0.34$), amplitude quotient ($F(1,61) = 26.0$, $p < 0.001$; female: $M = 0.00095 \pm 0.00023$; male: $M = 0.00138 \pm 0.00044$), and glottal area index SD ($F(1,61) = 6.39$, $p = 0.01$; female: $M = 0.057$; male: $M = 0.096$; Table 4).

#### 4.3.2 | Adductory Kinematics

Adductory kinematics were not captured in 10 participants (2 female EC, 2 male EC, 5 female controls, 1 male control) due to difficulty visualizing the vocal folds during the /hi-hi/ gesture (e.g., epiglottic obstruction) with a standard rigid endoscope. Maximum adductory velocity was significantly lower ($W = 1049.0$, $p = 0.032$, $r_{rb} = 0.344$) in the EC group (Mdn = 218.05°/s) compared to the control group (Mdn = 306.24°/s). Differences were not obtained for other adductory kinematic measures.

### 4.4 | Relationships Between Characteristics of Use and Outcome Measures for EC Group

Multiple linear regression analyses showed that as duration of use increased, both VHI-Physical ($t(19) = 3.18$, $p = 0.005$) and VHI-Emotional scores ($t(19) = 2.41$, $p = 0.026$) also significantly increased. Duration of EC use was significantly related to LCQ-Physical ($t(20) = -3.57$, $p = 0.002$), LCQ-Psychological ($t(20) = -2.58$, $p = 0.018$), LCQ-Social ($t(20) = -2.46$, $p = 0.023$), and LCQ-Total ($t(20) = -3.20$, $p = 0.005$). Results indicated that as the duration of EC use increased, the scores on the LCQ decreased (indicating greater degrees of cough symptoms). Reports of using marijuana-related products also resulted in significantly lower scores for LCQ-Physical ($t(20) = -2.73$, $p = 0.013$) and LCQ-Total ($t(20) = -2.42$, $p = 0.025$; Table 5).

## 5 | Discussion

We investigated the effects of ECs on voice, cough, and dyspnea symptoms; aerodynamics of voice and cough; and laryngeal kinematics in young adults. Our hypotheses were partially supported when we found evidence for increased voice and cough symptoms that were significantly related to a longer duration of EC use. Significantly lower phase asymmetry index (left-shifted asymmetry), vocal fold adductory velocity, and amplitude quotient variability were also found for the EC group.

The EC group exhibited significantly greater VHI-Physical and VHI-Emotional scores compared to the control group. Nevertheless, all VHI scores were still considered within normal ranges [27, 45] and were, on average, slightly lower than previously reported scores from young conventional cigarette smokers [46, 47]. Likewise, the LCQ subtests and total score were significantly lower (indicating a greater degree of symptoms) compared to the control group but also fell within normal limits (i.e., $\geq 17.64$) [48]. Thus, we were able to capture preclinical symptomology that was still significantly different from controls but would be unable to be identified through these questionnaires based on current clinical normative values. This may present a challenge when screening EC users.

The differences in vibratory kinematics between the EC and the control groups were observed for phase asymmetry and amplitude quotient variability, indicating left-leading vocal fold vibration and restricted vibrational movement in the EC group. The observed differences in vibratory kinematics may be related to the edema and changes to the vocal fold weight and cover. Watanabe et al. [49] used HSV to evaluate vibrational characteristics in Reinke's edema (often due to smoking) and found asymmetry in six of the seven participants and quasi-periodic vibration in three out of seven. Further, a large-scale study of conventional smokers revealed a greater incidence of abnormal symmetry and amplitude in smokers compared to nonsmokers [46]. Future studies could include a deeper delve into vibrational symmetry and amplitude abnormalities and include a comparison to these changes observed in conventional cigarette smokers.

Further, the EC group showed significantly lower vocal fold adductory velocities compared to controls, which could have been due to swelling. Vocal fold edema impacts viscoelastic [50] and biomechanical properties [51, 52] and modifies the underlying shape of the TA muscle [51], perhaps influencing TA contractile properties and subsequent adductory velocities [39]. While adductory velocities provide a window into the larger, dynamic laryngeal gestures during voiceless-to-voiced transitions, it may be fruitful to investigate co-occurring oscillatory onset behaviors as well [53–55]. Oscillatory onsets provide insights into vocal fold pliability and vibrational symmetry during the transition to the voicing steady-state [54].

Our hypothesis of reduced aerodynamics in the EC group was not supported. It may be that young EC users may not have yet developed significant changes in aerodynamics, as the effects of EC use on respiratory function may become more pronounced with longer-term use or higher levels of consumption. Or perhaps other measures that are more sensitive to edema, like phonation threshold pressure [52], could be investigated.

### 5.1 | Relationships Between Symptoms, Laryngeal Kinematics, and EC Use

As expected, a longer duration of use was associated with a greater degree of voice and cough symptoms. However, dosing

**TABLE 3** | Summary and inferential statistics ($p$ values, effect sizes) for each questionnaire and adductory kinematic measure by group (EC, control).

| Measure | | EC<br>*M* (SD)<br>Mdn (IQR) | Control<br>*M* (SD)<br>Mdn (IQR) | *p* | $r_{rb}$<br>(interpretation) |
|---|---|---|---|---|---|
| Questionnaire | | | | | |
| VHI | Functional | 4.76 (4.87)<br>4 (0, 8) | 2.87 (2.80)<br>2 (1, 4) | 0.294 | — |
| | Physical | 4.20 (3.38)<br>3 (1.5, 7) | 2.41 (2.33)<br>2 (0, 4.5) | 0.032* | 0.320<br>Small |
| | Emotional | 2.08 (3.35)<br>2 (0, 2) | 0.57 (1.12)<br>0 (0, 1) | 0.008* | 0.357<br>Small |
| | Total | 11.04 (10.21)<br>8 (2, 18.5) | 5.84 (4.61)<br>6 (2, 8) | 0.066 | — |
| UCD | Physical | 20.31 (5.31)<br>19 (17, 22.5) | 17.80 (3.41)<br>18 (16, 20) | 0.111 | — |
| | Speech | 12.54 (4.23)<br>11 (10, 13) | 12.05 (2.05)<br>12 (10, 13) | 0.779 | — |
| | Physical + Speech | 21.62 (5.25)<br>20 (18, 23.25) | 19.51 (4.71)<br>20 (16, 23) | 0.259 | — |
| | Total | 54.46 (12.28)<br>50.50 (45.75, 60.5) | 49.36 (8.55)<br>50.00 (43, 55) | 0.249 | — |
| VFI | Tiredness and avoidance | 4.85 (5.07)<br>4 (0, 8) | 4.33 (4.94)<br>2 (0, 6) | 0.755 | — |
| | Physical discomfort | 1.15 (2.05)<br>0 (0, 1.25) | 0.85 (1.42)<br>0 (0, 2) | 0.635 | — |
| | Improvement with rest | 4.12 (4.22)<br>2.5 (0, 8.25) | 5.49 (4.7)<br>6 (0, 9) | 0.241 | — |
| LCQ | Physical | 5.90 (0.74)<br>6.13 (5.56, 6.41) | 6.53 (0.37)<br>6.63 (6.25, 6.88) | < 0.001* | 0.536<br>Medium |
| | Psychological | 6.32 (0.88)<br>6.71 (6.14, 7) | 6.72 (0.44)<br>7.00 (6.43, 7) | 0.017* | 0.339<br>Small |
| | Social | 6.64 (0.60)<br>6.88 (6.5, 7) | 6.95 (0.14)<br>7.00 (7, 7) | 0.001* | 0.393<br>Small |
| | Total | 18.86 (2.05)<br>19.38 (18.42, 20.27) | 20.20 (0.80)<br>20.38 (20.02, 20.88) | < 0.001* | 0.521<br>Medium |
| MMRC | | | | | |
| | Score | 0.58 (0.50)<br>1 (0, 1) | 0.36 (0.49)<br>0 (0, 1) | 0.087 | — |
| Adductory kinematic | | | | | |
| Maximum glottic angle (°) | | 24.82 (11.45)<br>23.64 (15.57, 33.52) | 28.16 (10.75)<br>27.17 (19.24, 34.27) | 0.299 | — |
| Maximum adductory velocity (°/s) | | 224.4 (88.3)<br>218.0 (148.1, 268.5) | 308.1 (154.9)<br>306.2 (202.3, 388.0) | 0.032* | 0.344<br>Small |
| Kinematic estimate of laryngeal stiffness (1/s) | | 10.04 (4.25)<br>8.65 (7.34, 11.99) | 11.18 (4.82)<br>10.27 (8.09, 13.71) | 0.207 | — |

Abbreviations: —, not calculated due to nonsignificant finding; EC, electronic cigarette user; IQR, interquartile range; LCQ, Leicester Cough Questionnaire; *M*, mean; Mdn, median; MMRC, Modified Medical Research Council Dyspnea Scale; $r_{rb}$, rank-biserial correlation; SD, standard deviation; UCD, University of Cincinnati Dyspnea Questionnaire; VFI, Vocal Fatigue Index; VHI, Voice Handicap Index.
*Significant at $p < 0.05$.

**TABLE 4** | Summary information for acoustics, aerodynamics, and vibratory kinematics by group (EC, control) and sex.

| Measure | EC, *M* (SD) | | Control, *M* (SD) | |
|---|---|---|---|---|
| | Female ($n=16$) | Male ($n=10$) | Female ($n=29$) | Male ($n=10$) |
| Mean $f_0$ (Hz)[a] | 259.88 (34.51) | 145.59 (34.63) | 253.46 (24.15) | 153.35 (32.82) |
| Vocal intensity (dB SPL)[a] | 72.98 (4.33) | 74.35 (3.36) | 72.64 (4.9) | 73.65 (6.11) |
| Subglottal pressure ($cmH_2O$)[b] | 5.59 (1.52) | 5.08 (1.71) | 5.48 (2.00) | 6.03 (2.77) |
| Vital capacity (L) | 3.83 (0.66) | 5.43 (1.23) | 3.98 (0.91) | 5.31 (0.89) |
| Cough peak expiratory airflow (L/s) | 8.15 (1.94) | 10.99 (1.37) | 8.98 (2.834) | 9.73 (4.17) |
| Cough expiratory volume (%) | 52.43 (16.29) | 48.44 (21.69) | 50.96 (18.97) | 41.78 (24.18) |
| Closing quotient | 0.39 (0.10) | 0.32 (0.08) | 0.37 (0.10) | 0.32 (0.07) |
| Closing quotient SD | 0.034 (0.011) | 0.030 (0.011) | 0.042 (0.017) | 0.034 (0.012) |
| Glottal area index | 1.19 (0.36) | 1.41 (0.35) | 1.19 (0.36) | 1.49 (0.35) |
| Glottal area index SD | 0.048 (0.044) | 0.085 (0.071) | 0.062 (0.060) | 0.108 (0.074) |
| Amplitude quotient | 0.00094 (0.00022) | 0.00129 (0.00041) | 0.00097 (0.00024) | 0.00148 (0.00047) |
| Amplitude quotient SD | 0.00008 (0.00007) | 0.00009 (0.00008) | 0.00013 (0.00011) | 0.00018 (0.00011) |
| Phase asymmetry | −0.026 (0.077) | −0.026 (0.095) | 0.057 (0.046) | 0.068 (0.047) |
| Phase asymmetry SD | 0.032 (0.009) | 0.027 (0.019) | 0.031 (0.010) | 0.031 (0.022) |

Abbreviations: EC, electronic cigarette user; $f_0$, fundamental frequency; *M*, mean; SD, standard deviation; SPL, sound pressure level.
[a]Mean $f_0$ and vocal intensity were extracted from the middle 2–3 s of the sustained /i:/ production using the functionality of Praat.
[b]Smaller sample for analysis with 28 control females and 9 control males.

**TABLE 5** | Regression model results with EC use and health behaviors as predictors. *p* values and coefficient of determination $\left(R^2_{adj}\right)$ are provided.

| Outcome measure | | Regression predictor | | | | | |
|---|---|---|---|---|---|---|---|
| | | Duration | Frequency | Marijuana | Recency | Conventional cigarettes | $R^2_{adj}$ (%) |
| Questionnaires | | | | | | | |
| VHI | | | | | | | |
| | Physical | 0.005* | 0.767 | 0.769 | 0.496 | 0.898 | 22.6 |
| | Emotional | 0.026* | 0.051 | 0.077 | 0.494 | 0.417 | 26.1 |
| LCQ | | | | | | | |
| | Physical | 0.002* | 0.791 | 0.013* | 0.905 | 0.877 | 41.6 |
| | Psychological | 0.018* | 0.533 | 0.065 | 0.457 | 0.818 | 18.7 |
| | Social | 0.023* | 0.282 | 0.082 | 0.616 | 0.968 | 17.6 |
| | Total | 0.005* | 0.464 | 0.025* | 0.580 | 0.944 | 32.3 |
| Kinematics | | | | | | | |
| Phase asymmetry | | 0.091 | 0.939 | 0.346 | 0.464 | 0.534 | 0.9 |
| Amplitude quotient SD | | 0.940 | 0.077 | 0.120 | 0.151 | 0.776 | 4.1 |
| Adductory velocity (°/s) | | 0.915 | 0.591 | 0.457 | 0.742 | 0.111 | 0.9 |

Abbreviations: LCQ, Leicester Cough Questionnaire; SD, standard deviation; VHI, Voice Handicap Index.
*Significant at $p<0.05$.

measures were merely based on self-reports and did not include objective dose amounts, durations, or puff sizes. Puff topography profiles quantify use and may be beneficial for relating dosing data with measures of voice and cough in EC users as well.

We investigated the use of marijuana as a potential factor related to outcome measures due to the association between marijuana-based products and vaping-related lung injury [56–58]. Only the LCQ-Physical and LCQ-Total scores were significantly

associated with marijuana use, in which marijuana users showed more frequent cough-related symptoms compared to nonusers. These findings further support the existing evidence that EC use of nicotine and marijuana (combined) results in greater lung irritation than nicotine alone.

Recency of EC use was not associated with any measure, which was surprising given previous studies on recency effects of conventional and ECs [11, 23, 24]. Sandage and Patel [24] assessed vibratory kinematics in a single-case design immediately before and after smoking, finding greater vibrational amplitude immediately following use and increased asymmetry of vibration. Future work could quantify recency and upper airway temperature changes following vapor exposure [24, 59] as possible influences on physiological outcomes.

Because conventional cigarette use is associated with greater voice symptoms [60], vocal fold inflammation [61], and the development of Reinke's edema [62], we anticipated that a history of conventional cigarette use would contribute negatively to the outcome measures here. However, that was not the case. One reason could be the heterogeneous nature of the study sample, with 42% reporting using conventional cigarettes, with a variation of use from 6 months to 7 years. The dosing (duration and consistency) of conventional cigarette use is directly related to the development of adverse health outcomes—laryngeal and system-wide [63]—and may be a factor to investigate further.

### 5.2 | Limitations and Future Directions

Although we were able to enroll a relatively large sample that was able to detect small effect sizes, a larger group stratified by sex would be helpful to tease out sex differences. When examining females, it would be crucial to control for hormonal stage and hydration levels [64, 65]. Further investigations could also enroll a larger age range of users.

Our sample represented different durations, frequencies, and types of use. Although this is an ecologically valid approach to begin to investigate symptoms and physiological changes in users as a whole, a more controlled sample would help to understand how these factors influence laryngeal functions. Additionally, future studies should also consider specific voice-related risk factors (e.g., profession, voice use, hydration) when interpreting the risk for developing voice-related issues in EC users.

Finally, given that our study participants were "vocally healthy," future studies examining inspiratory phonation may provide a unique window to examine the vibratory kinematic differences between users and nonusers [66]. Inspiratory phonation has been shown to detect subtle changes to the vocal fold edge that may go unnoticed during expiratory phonation [67]. Further, evaluation of the vocal folds using in vivo 3D laser HSV [68–71] could provide additional insights into early changes to vertical components (e.g., vocal fold thickness for quantifying edema), enhancing our understanding of the risks associated with EC use.

## 6 | Conclusion

This study provided preliminary evidence of negative effects of EC use on voice and cough symptoms and laryngeal kinematics in young adults. Most notably, longer duration of use was significantly related to VHI-Physical, VHI-Emotional, and all domains of the LCQ, providing support for a potential dosing effect on patient-reported outcome measures. Further investigations should consider use characteristics, voice-related history, and potential sex differences to understand risks associated with EC use.


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#### Disclosure

The authors have nothing to report.

#### Conflicts of Interest

The authors declare no conflicts of interest.

#### Data Availability Statement

Data are available upon reasonable request to the authors.

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