ORIGINAL RESEARCH

Laryngoscope
Investigative Otolaryngology

Long-term upper aerodigestive sequelae as a result of infection with COVID-19

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Abstract

Objectives: Respiratory, voice, and swallowing difficulties after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may result secondary to upper airway disease from prolonged intubation or mechanisms related to the virus itself. We examined a cohort who presented with new laryngeal complaints following documented SARS-CoV-2 infection. We characterized their voice, airway, and/or swallowing symptoms and reviewed the clinical course of their complaints to understand how the natural history of these symptoms relates to COVID-19 infections.

Methods: Retrospective review of patients who presented to our department with upper aerodigestive complaints as sequelae of prior infection with, and management of, SARS-CoV-2.

Results: Eighty-one patients met the inclusion criteria. Median age was 54.23 years ($\pm$17.36). Most common presenting symptoms were dysphonia ($n = 58$, 71.6%), dysphagia/odynophagia ($n = 16$, 19.75%), and sore throat ($n = 9$, 11.11%). Thirty-one patients (38.27%) presented after intubation. Mean length of intubation was 16.85 days (range 1–35). Eighteen patients underwent tracheostomy and were decannulated after an average of 70.69 days (range 23–160). Patients with history of intubation were significantly more likely than nonintubated patients to be diagnosed with a granuloma (8 vs. 0, respectively, $p < .01$). Fifty patients (61.73%) were treated for SARS-CoV-2 without requiring intubation and were significantly more likely to be diagnosed with muscle tension dysphonia (19 vs. 1, $p < .01$) and laryngopharyngeal reflux (18 vs. 1, $p < .01$).

Conclusion: In patients with persistent dyspnea, dysphonia, or dysphagia after recovering from SARS-CoV-2, early otolaryngology consultation should be considered. Accurate diagnosis and prompt management of these common underlying etiologies may improve long-term patient outcomes.

Level of evidence: 4

1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, colloquially referred to as COVID-19) has now been demonstrated to affect all major organ systems.[1–6] The upper respiratory tract, which is considered a unified airway with the lower respiratory tract, serves as the initial nidus for SARS-CoV-2 infections and has been well-demonstrated by the now commonly known symptoms of anosmia, hyposmia, phantosmia, and dysgeusia.[7–9] The term "long COVID" has been devised to refer to the profound, enduring effects of COVID infections on those who survive the acute, and often harrowing, stages of the disease.[10] Interestingly, in the chronic, long-haul population, evidence is mounting that patients are commonly presenting with laryngological complaints to their health care providers.[11] It is clear that a large subset of these laryngeal sequelae, including laryngotracheal stenosis, laryngomalacia, ulceration, and tracheitis, have been found to be secondary to prolonged intubations.[11–15] However, although these laryngotracheal sequelae are deserving of attention and analysis,[16,17] they by no means constitute the sole laryngological consequences of SARS-CoV-2 infections. Additionally, the latter do not account for the patients who were never intubated and, in fact, may never even have sought medical care during their infections, yet now present with new laryngological symptoms such as dysphagia, globus, and vocal fold dysfunction.[18,19]

Being in New York City (NYC), one of the original epicenters of the pandemic, provides us with the unusual privilege of obtaining a greater understanding of the breadth of SARS-CoV-2 laryngeal manifestations. This is because at the height of the first wave of the pandemic in April 2020, an estimated 1 in 20 people in NYC were infected with SARS-CoV-2, and 1 in 11 of those in the United States who contracted the illness died from their infection.[20,21] Much of the current knowledge of the laryngeal manifestations of SARS-CoV-2 is either anecdotal or derived from individual case reports. To obtain a greater understanding of the breadth of laryngeal manifestations, our team retrospectively examined a large cohort of patients presenting with laryngeal pathologies following documented SARS-CoV-2. Since these patients were presenting after the resolution of their acute infections and with concern for subsequent sequelae of their infections, we categorized their clinical presentations under "long-term" effects of a COVID-19 infection. We characterized their new, primary presenting symptoms and then reviewed the clinical courses associated with their laryngeal complaints to gain a deeper understanding of the natural history of their symptoms as they related to their earlier SARS-CoV-2 infections. Awareness of how SARS-CoV-2 infections manifest in patients who have otherwise recovered from their infections is critical to understanding both how to treat and counsel patients. The diagnoses and patterns of presentations here should not be dismissed as idiopathic, but rather identified by the otolaryngologist through careful history and examination among the possible ramifications of COVID-19 infections.

2 | METHODS

2.1 | Protocol approvals

This study was reviewed and approved by the Icahn School of Medicine at Mount Sinai Institutional Review Board (IRB-20-04319).

2.2 | Study design

This was a retrospective chart review of patients seen by five Mount Sinai otolaryngologists from March 15, 2020 to August 21, 2020, encompassing the first peak of the COVID-19 pandemic in NYC. Patients with documented COVID-19 infections, either by polymerase chain reaction (PCR), antibody testing, or documented verbal confirmation of prior positivity, were included in analyses. Patients with preexisting laryngeal symptoms that continued after clinical suspicion of COVID-19 infection and patients below the age of 18 years were excluded.

2.3 | Variables, diagnoses, and data analysis

Patient charts were examined for demographic information (age, sex, and body mass index [BMI]), presenting symptom, ultimate diagnosis, interventions (if any), and medical comorbidities. To prevent confounding or bias, any patients previously seen by laryngologists in our clinic who presented to our clinic after sustaining infections with COVID-19 were excluded from our study. Multiple presenting symptoms were recorded, if elicited. Additional key variables related to COVID-19 symptoms, complications, and treatments (e.g., intubation history, endotracheal tube size, length of intubation, tracheostomy history, and ICU length of stay) were documented to characterize the severity of infection.

Arytenoid ankylosis was often suspected based on high clinical suspicion from concern for joint fixation based on history and laryngoscopy findings, as well as CT scan findings with fine cuts through the larynx (when possible) demonstrating loss of the cricoarytenoid joint space. Palpation of the joints in the operating room confirmed fixation and immobility of the joints. Vocal fold paralysis was diagnosed when there was complete immobility of the joint and vocal fold with bowing of the cord and ipsilateral tilt of the interarytenoid cleft. Vocal fold paresis was diagnosed when vocal fold mobility was noted to be asymmetric, with one fold hypomobile on endoscopy, and amplitude was noted to be larger on the paretic side on stroboscopy.

TABLE 1 Demographics of patients presenting with upper aerodigestive complications from COVID-19

Demographic	Intubated ($n = 31$)	Not intubated ($n = 50$)	*p*-value
Sex, % (*n*)			
Female	32.26% (10)	44.00% (22)	
Male	67.74% (21)	56.00% (28)	.21
Age, % (*n*)			
18–34	3.23% (1)	26.00% (13)	
35–54	19.35% (6)	34.00 (17)	
55–64	38.71% (12)	22.00% (11)	
65+	38.71% (12)	18.00% (9)	.01
BMI, % (*n*)			
<18.5	0% (0)	2.00% (1)	
18.5–24.9	35.48% (11)	32.00% (16)	
25–29.9	19.35% (6)	20.00% (10)	
30–34.9	9.68% (3)	14.00% (7)	
35+	16.13% (5)	10.00% (5)	.92
COVID confirmation, % (*n*)			
PCR alone	45.16% (14)	28.00% (14)	
Antibody alone	3.22% (1)	30.00% (15)	
Both PCR and antibody	35.48% (11)	20.00% (10)	
Verbal (unconfirmed)	16.13% (5)	22.00% (11)	.01
Smoking history, % (*n*)			
Never	74.19% (23)	74.00% (37)	
Former	12.90% (4)	10.00% (5)	
Current	6.45% (2)	14.00% (7)	
Unknown	6.45% (2)	2.00% (1)	.55
Time intubated (days, ± SD)	16.85 ± 7.44	—	
ETT size (median)	8	—	
Tracheostomy history, % (*n*)			
Yes	58.06% (18)	0% (0)	
No	41.94% (13)	100.00% (50)	<.001
Time with trach (days, ± SD)	70.69 ± 43.75	—	
Tracheostomy size (median)	7	—	
Comorbidities, % (*n*)			
Asthma	6.45% (2)	8.00% (4)	1.00
COPD	6.45% (2)	2.00% (1)	.55
Diabetes mellitus	16.13% (5)	8.00% (4)	.29
GAD	0% (0)	12.00% (6)	.08
GERD	9.68% (3)	14.00% (7)	.73
Hypertension	3.23% (1)	6.00% (3)	1.00
MDD	0% (0)	4.00% (2)	.52
Obesity	3.23% (1)	6.00% (3)	1.00
OSA	0% (0)	4.00% (2)	.52
Panic disorder	0% (0)	4.00% (2)	.52
Substance use disorder	0% (0)	2.00% (1)	1.00
None	54.84% (17)	30.00% (15)	1.00

Abbreviations: COPD, chronic obstructive pulmonary disease; GAD, generalized anxiety disorder; GERD, gastroesophageal reflux disease; MDD, major depressive disorder; *n*, number of subjects; OSA, obstructive sleep apnea; PCR, polymerase chain reaction; SD, standard deviation.

TABLE 2 Presenting symptoms of intubated and nonintubated COVID-19 patients with laryngeal manifestations

Presenting symptoms[a]	Intubated (n = 31)	Not Intubated (n = 50)	Adjusted p-value
Dysphonia	64.52% (20)	76.00% (38)	1.00
Dysphagia/odynophagia	29.03% (9)	14.00% (7)	1.00
Sore throat	0% (0)	18.00% (9)	.11
Shortness of breath	12.90% (4)	10.00% (5)	1.00
Cough	6.45% (2)	10.00% (5)	1.00
Globus sensation	0% (0)	12.00% (6)	.77
Tracheostomy dependence	12.90% (4)	0% (0)	.19
Hemoptysis	0% (0)	2.00% (1)	1.00
Laryngeal spasms	0% (0)	2.00% (1)	1.00
Stridor	3.23% (1)	0% (0)	1.00

[a]Many patients presented with more than one symptom.

TABLE 3 Laryngeal diagnoses of intubated and nonintubated COVID-19 patients

Diagnosis[a]	Intubated (n = 31)	Not intubated (n = 50)	Adjusted p-value
Muscle tension dysphonia	3.23% (1)	38.00% (19)	<.01
Laryngopharyngeal reflux	3.23% (1)	36.00% (18)	<.01
Vocal fold paresis	9.68% (3)	6.00% (3)	1.00
Vocal fold paralysis	16.13% (5)	6.00% (3)	1.00
Vocal fold atrophy	9.68% (3)	12.00% (6)	1.00
Vocal fold polyp	0% (0)	16.00% (8)	.34
Granuloma	25.81% (8)	0% (0)	<.01
Glottic insufficiency	12.90% (4)	6.00% (3)	1.00
Chronic laryngitis	3.23% (1)	10.00% (5)	1.00
Arytenoid ankylosis	16.13 (5)	0% (0)	.11
Posterior or subglottic stenosis	16.13% (5)	0% (0)	.11
Tracheal stenosis	16.13% (5)	0% (0)	.11
Laryngeal hypersensitivity	0% (0)	8.00% (4)	1.00
Deconditioned swallow	9.68% (3)	0% (0)	.84
Laryngeal edema	0% (0)	4.00% (2)	1.00
Tracheomalacia	3.23% (1)	0% (0)	1.00

[a]Many patients were ultimately given more than one diagnosis.

TABLE 4 Interventions performed on intubated and nonintubated COVID-19 patients

Intervention	Intubated (n = 31)	Not intubated (n = 50)	Adjusted p-value
Vocal fold injection (Restylane or steroid)	19.35% (6)	6.00% (3)	.63
SLP referral	9.68% (3)	8.00% (4)	1.00
PPI	9.68% (3)	4.00% (2)	1.00
Laser excision	9.68% (3)	2.00% (1)	1.00
Bronchoscopy and dilation	12.90% (4)	0% (0)	.15
Microdirect laryngoscopy	9.68% (3)	0% (0)	.42
Inhaled steroids	3.23% (1)	2.00% (1)	1.00
Tracheal resection	3.23% (1)	0% (0)	1.00
None	22.58% (7)	78.00% (39)	<.01

Abbreviations: PPI, proton pump inhibitor; SLP, speech-language pathologist.

TABLE 5 Characteristics of patients with arytenoid ankylosis, PGS/SGS, or tracheal stenosis

Characteristic	Arytenoid ankylosis ($n = 5$)	PGS/SGS ($n = 4$)	Tracheal stenosis ($n = 4$)	Adjusted p-value
Sex, % (n)				
Female	0% (0)	50.00% (2)	50.00% (2)	
Male	100.00% (5)	50.00% (2)	50.00% (2)	.16
Age (years, mean ± SD)	60.6 ± 4.88	59 ± 8.04	65 ± 13.88	.65
BMI (mean ± SD)	38.93 ± 12.44	33.87 ± 12.60	30.49 ± 8.04	.55
COVID confirmation, % (n)				
PCR alone	60.00% (3)	25.00% (1)	50.00% (2)	
Antibody alone	0% (0)	0% (0)	0% (0)	
Both PCR and antibody	20.00% (1)	25.00% (1)	50.00% (2)	
Verbal (unconfirmed)	20.00% (1)	50.00%(2)	0% (0)	.92
Smoking history, % (n)				
Never	80.00% (4)	75.00% (3)	50.00% (2)	
Former	0% (0)	0% (0)	25.00% (1)	
Current	0% (0)	0% (0)	0% (0)	
Unknown	20.00% (1)	25.00% (1)	25.00% (1)	.99
Intubation history, % (n)				
Yes	100.00% (5)	100.00% (4)	100.00% (4)	
No	0% (0)	0% (0)	0% (0)	1.00
Time intubated (days, ± SD)	17.60 ± 4.39	16.50 ± 3.54	23.50 ± 6.36	.14
ETT size (median)	8	7	7	.32
Tracheostomy history, % (n)				
Yes	60.00% (3)	75.00% (3)	100.00% (4)	
No	40.00% (2)	25.00% (1)	0% (0)	.72
Time with trach (days, ± SD)	44.00 ± 26.87	58.00 ± 20.95	93.25 ± 45.46	.12
Tracheostomy size (median)	8	7	6	.10
Comorbidities, % (n)[a]				
Asthma	40.00% (2)	0% (0)	0% (0)	1.00
COPD	0% (0)	0% (0)	25.00% (1)	1.00
Diabetes mellitus	20.00% (1)	25.00% (1)	50.00% (2)	1.00
GERD	20.00% (1)	25.00% (1)	0% (0)	1.00
Obesity	40.00% (2)	50.00% (2)	25.00% (1)	1.00
Myasthenia gravis	0% (0)	0% (0)	25.00% (1)	1.00

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; GERD, gastroesophageal reflux disease; n, number of subjects; PCR, polymerase chain reaction; SD, standard deviation.
[a]Some patients possessed multiple comorbidities.

Retrospective data were collected and stored in Microsoft Excel 2011 (Microsoft Corp) and descriptive statistics were obtained. Data are presented as mean ± standard deviation (SD) unless otherwise indicated.

Given our small sample sizes, Fisher exact test was used to determine the significance for categorical data. Fisher–Freeman–Halton exact test was used to determine the significance for larger contingency tables. To calculate differences between subgroups in our patient cohort, unpaired, two-tailed Student t-tests and analysis of variance were used. Bonferroni post hoc corrections were applied to determine significance in cases when multiple comparisons were made within subgroups of our patient cohort. All statistical analyses were performed using IBM Statistical Product and Service Solutions software (SPSS; IBM). Values where $p < .05$ were considered statistically significant.

3 | RESULTS

3.1 | Demographics

There were 81 patients (49M, 32F) that met our inclusion criteria, with 31 (38.27%) of these having been intubated (see Table 1). These patients were reviewed an average of 5 months and 6 days after their initial positive test (min: 1 month, 23 days; max: 6 months, 21 days), and presented to a laryngologist an average of 4 months after their initial positive test (min: 1 month, 22 days; max: 5 months, 28 days). In this group, there were more patients over the age of 55 compared with the nonintubated group ($p = .01$). Thirty-four percent of patients ($n = 28$) had COVID positivity confirmed with PCR results alone,

TABLE 6 Characteristics of patients with vocal fold paralysis or paresis

Characteristic	Vocal fold paresis ($n = 6$)	Vocal fold paralysis ($n = 7$)	Adjusted p-value
Sex, % (n)			
Female	33.33% (2)	14.29% (1)	
Male	66.67% (4)	85.71% (6)	.56
Age (years, mean ± SD)	51.83 ± 14.73	54.86 ± 14.71	.37
BMI (mean ± SD)	28.85 ± 4.87	28.29 ± 7.42	.16
COVID testing, % (n)			
PCR alone	50.00% (3)	57.00% (4)	
Antibody alone	0% (0)	29.00% (2)	
Both PCR and antibody	50.00% (3)	14.00% (1)	
Verbal (unconfirmed)	0% (0)	0% (0)	.98
Smoking history, % (n)			
Never	50.00% (3)	42.86% (3)	
Former	16.67% (1)	42.86% (3)	
Current	33.33% (2)	14.29% (1)	1.00
Intubation history, % (n)			
Yes	50.00% (3)	71.43% (5)	
No	50.00% (3)	28.57% (2)	.43
Time intubated (days ± SD)	19.00 ± 12.29	18.80 ± 5.07	.97
ETT size (median)	7.83 ± 0.29	8	1.00
Tracheostomy history, % (n)			
Yes	50.00% (3)	57.14% (4)	
No	50.00% (3)	28.57% (3)	.80
Time with trach (days ± SD)	59.00 ± 28.28	57.33 ± 30.50	.92
Tracheostomy size (median)	7	7	1.00
Comorbidities, % (n)			
Cardiomyopathy	0% (0)	14.29% (1)	1.00
COPD	0% (0)	14.29% (1)	1.00
Diabetes mellitus	16.67% (1)	14.29% (1)	1.00
GAD	16.67% (1)	0% (0)	1.00
Panic disorder	16.67% (1)	0% (0)	1.00
Sarcoidosis	0% (0)	14.29% (1)	1.00
Substance use disorder	16.67% (1)	0% (0)	1.00
None	33.33% (2)	42.86% (3)	1.00

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; GAD, generalized anxiety disorder; n, number of subjects; PCR, polymerase chain reaction; SD, standard deviation.

19.75% ($n = 16$) were confirmed by positive antibody testing alone, 25.9% ($n = 21$) were confirmed via both PCR and antibody testing, and 19.75% ($n = 16$) had positivity ascertained through verbal confirmation of outside test results. Approximately three-quarters of patients ($n = 60$, 74.07%) had never smoked.

3.2 | COVID symptoms

The overall most common presenting symptom was dysphonia ($n = 58$, 71.60%) in both those who had been intubated ($n = 20$,

64.25%) and not intubated ($n = 38$, 76.00%) (see Table 2). Certain presenting symptoms such as dysphagia, stridor, and tracheostomy dependence were more common in patients who had been intubated, however were not statistically significant on further analysis.

3.3 | Post-COVID diagnoses and interventions

The patients in our cohort were diagnosed with 17 different aerodigestive diagnoses (see Table 3). Muscle tension dysphonia

TABLE 7 Characteristics of patients with MTD, LPR, or laryngeal hypersensitivity

Characteristic	MTD (n = 20)	LPR (n = 19)	Laryngeal hypersensitivity (n = 4)	Adjusted p-value
Sex				
Female	50.00% (10)	47.37% (9)	50.00% (2)	
Male	50.00% (10)	52.63% (10)	50.00% (2)	1.00
Age (years, mean ± SD)	47.90 ± 14.24	45.84 ± 12.13	41 ± 21.49	.66
BMI (mean ± SD)	29.28 ± 7.10	27.94 ± 6.23	23.45 ± 3.55	.27
COVID confirmation, % (n)				
PCR alone	45.00% (9)	31.58% (6)	25.00% (1)	
Antibody alone	15.00% (3)	26.32% (5)	0% (0)	
Both PCR and antibody	15.00% (3)	21.10% (4)	50.00% (2)	
Verbal (unconfirmed)	25.00% (5)	21.10% (4)	25.00% (1)	.69
Smoking history				
Never	75.00% (15)	68.42% (13)	75.00% (3)	
Former	15.00% (3)	32.05% (4)	0% (0)	
Current	10.00% (2)	10.53 (2)	25.00% (1)	
Unknown	0% (0)	0% (0)	0% (0)	.80
Intubation history				
Yes	5.00% (1)	5.26% (1)	0% (0)	
No	95.00% (19)	94.74% (18)	100.00% (4)	.46
Time intubated (days, mean ± SD)	28 ± 0	13 ± 0	—	1.00
ETT size (median)	8	8	—	1.00
Tracheostomy history				
Yes	5.00% (1)	0% (0)	0% (0)	
No	95.00% (19)	100.00% (19)	100.00% (4)	1.00
Time with trach (days)	79 ± 0	—	—	
Tracheostomy size (median)	6	—	—	
Comorbidities				
Asthma	5.00% (1)	5.26% (1)	25.00% (1)	1.00
COPD	5.00% (1)	0% (0)	0% (0)	1.00
CRS	10.00% (2)	10.53% (2)	0% (0)	1.00
Diabetes mellitus	15.00% (3)	5.26% (1)	0% (0)	1.00
GAD	20.00% (4)	15.79% (3)	25.00% (1)	1.00
GERD	0% (0)	15.79% (3)	25.00% (1)	1.00
HCV	10.00% (2)	5.26% (1)	0% (0)	1.00
HIV	5.00% (1)	5.26% (1)	0% (0)	1.00
Hypertension	15.00% (3)	10.53% (2)	0% (0)	1.00
Hypothyroidism	10.00% (2)	10.53% (2)	0% (0)	1.00
MDD	10.00% (2)	5.26% (1)	0% (0)	1.00
Migraines	5.00% (1)	5.26% (1)	0% (0)	1.00
NF2	5.00% (1)	0% (0)	0% (0)	1.00
OSA	5.00% (1)	5.26% (1)	0% (0)	1.00
Obesity	15.00% (3)	10.53% (2)	0% (0)	1.00
Rheumatoid arthritis	5.00% (1)	5.26% (1)	0% (0)	1.00
SLE	5.00% (1)	5.26% (1)	0% (0)	1.00

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRS, chronic rhinosinusitis; GAD, generalized anxiety disorder; GERD, gastroesophageal reflux disease; HCV, hepatitis C virus; HIV, human immunodeficiency virus; MDD, major depressive disorder; n, number of subjects; NF2, neurofibromatosis type 2; OSA, obstructive sleep apnea; PCR, polymerase chain reaction; SD, standard deviation; SLE, systemic lupus erythematosus.

(MTD) and laryngopharyngeal reflux (LPR) were more commonly found in the group of patients that were not intubated ($p < .01$). Diagnoses such as granulomas, arytenoid ankylosis, posterior/subglottic stenosis (PGS/SGS), and tracheomalacia were found exclusively in intubated COVID patients; however, only granuloma was found to be statistically significant in this group ($p < .01$).

Vocal fold injections with either Restylane or steroids, depending on the diagnosis, were the most common procedure performed in both previously intubated ($n = 6$, 19.35%) and nonintubated ($n = 3$, 6.00%) patients (see Table 4). Bronchoscopy with endoscopic dilation was the second most common intervention in previously intubated patients ($n = 4$, 12.90%). Referral to a speech-language pathologist was the most common referral in patients without a previous intubation history ($n = 4$, 8.00%).

3.4 | Stenotic lesions

Stenotic airway lesions such as arytenoid ankylosis, SGS, PGS, and tracheal stenosis were only seen in patients with prior intubation history (see Table 5). Patients with arytenoid ankylosis on average were intubated with a size 8.0 Mallinckrodt endotracheal tube and possessed higher BMIs (38.93 ± 12.44) compared to SGS (7, 33.87 ± 12.60, respectively) and tracheal stenosis (7, 30.49 ± 8.04, respectively). Patients diagnosed with tracheal stenosis possessed histories of remaining intubated the longest (23.50 ± 6.36 days) when compared to patients with arytenoid ankylosis, PGS, and SGS. All patients diagnosed with tracheal stenosis had a history of prior tracheostomy as a result of their prolonged intubations due to their COVID-19 infections. None of the above characteristics were statistically significant on further analysis.

3.5 | Vocal fold paralysis/paresis

Sixteen percent of patients ($n = 13$) were diagnosed with either vocal fold paralysis or paresis (see Table 6). Vocal fold paralysis was more likely to be diagnosed in patients with a history of prior intubation. The majority of patients in both the paresis (66.67%) and paralysis cohorts (85.71%) were male, and both groups possessed comparable BMIs (28.85 vs. 28.29, $p = .16$).

3.6 | MTD, LPR, and laryngeal hypersensitivity

Diagnoses of MTD, LPR, and laryngeal hypersensitivity were more common in nonintubated post-COVID patients (see Table 7). Ninety-five percent ($n = 19$) of MTD patients had not been intubated previously. Similarly, 94.74% ($n = 18$) of LPR and 100% ($n = 4$) of laryngeal hypersensitivity patients had not been intubated. Patients diagnosed with MTD, LPR, and laryngeal hypersensitivity disorders were young (MTD: 47.90 ± 14.24 years, LPR: 45.84 ± 12.13, laryngeal hypersensitivity: 41.00 ± 21.49) and had normal/overweight but not obese BMIs (MTD: 29.28 ± 7.1, LPR: 27.94 ± 6.23, laryngeal hypersensitivity: 23.45 ± 3.55).

4 | DISCUSSION

Respiratory, voice, and swallowing difficulties presenting after recovery from COVID-19 are distressing sequelae of an already devastating infection. In this report, our team highlighted the experience of the outpatient setting treating a large volume of patients with laryngeal dysfunction after recovery from COVID-19. Within our cohort, the
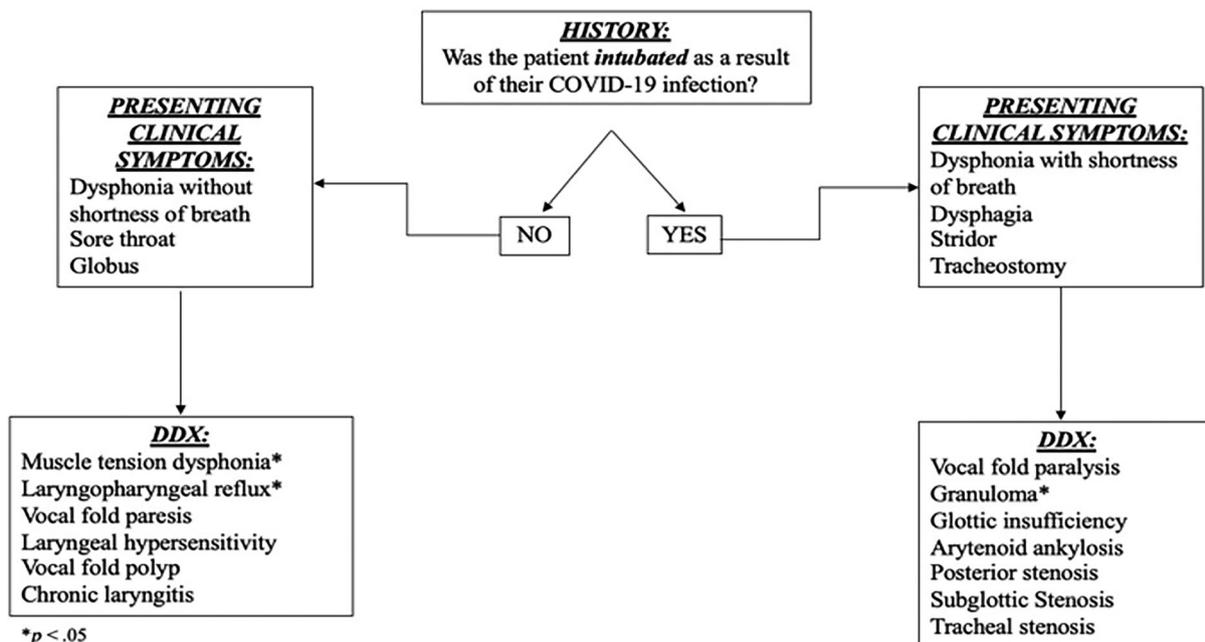

FIGURE 1 Algorithm for diagnosis of post-COVID patients presenting with laryngeal symptoms

largest such report to-date of laryngological manifestations, we noted a distinctive pattern in the symptoms and diagnoses when dividing patients into those who had been intubated as a result of their SARS-CoV-2 infections and those who had no history of intubation. Among the 31 patients who had been intubated, we noted that they were older when compared with the nonintubated group. We also found, within this previously intubated group, that the diagnoses were more likely to be related to structural and anatomic inflammatory changes of the upper airway and trachea: 16.13% were diagnosed with tracheal stenosis, 16.13% were diagnosed with arytenoid ankylosis, and 16.13% were diagnosed with PGS and/or SGS. However, only the clinical diagnosis of granuloma was found to be statistically significant upon comparison between the two cohorts. These results are consistent with data presented in recent literature demonstrating the prevalence of patients with a history of severely prolonged intubation as a consequence of COVID-related pneumonia who have presented with advanced stenotic airway lesions.[12,17,22,23]

The etiology of these laryngeal manifestations may be the inflammatory nature of COVID-19 infections or the intubation itself. The upper aerodigestive tract has long been considered to be part of a unified airway with the lower respiratory tract, the latter being the primary target of SARS-CoV-2.[24] It is well-known that the virus enters the cells of the respiratory tract by attaching to angiotensin converting enzyme 2 (ACE-2).[24] Current postmortem studies have mostly focused on the lower respiratory tract and why the disease causes severe lung injury and acute respiratory distress syndrome.[24,25] However, in two autopsy cases published thus far, tracheitis has been noted with chronic inflammation and edema.[6,24,25] Although it is difficult to ascertain whether this highly inflammatory nature of the infection is itself the cause or the effect of the resulting intubation, it is important to note that ACE-2 receptors are also found in the upper respiratory tract, likely establishing a predisposition to causality.[6,24,25] Furthermore, the inherent high viral load of SARS-CoV-2 in the oro- and nasopharynx, making it the most suitable and practical source for viral testing, is further evidence supporting causality for the upper aerodigestive complications we are seeing secondary to infection.

In contrast, among the patients in our cohort who had not been intubated, 76% presented to our laryngology clinics with dysphonia and 10% presented with shortness of breath as their chief complaints. Furthermore, 18% presented with a sore throat and 12% presented with globus, neither of which were chief complaints of any patients in our intubated cohort. In contrast to the patients in our cohort with history of intubation, the diagnoses in this nonintubated cohort had an underlying neurogenic etiology: 38% were diagnosed with MTD ($p < .01$), 36% were diagnosed with LPR ($p < .01$), and 6% were diagnosed with vocal fold paresis. We were intrigued by this trend, as it underscored the possibility of post-viral neurogenic complications of COVID-19, which has already been proposed as a complication of COVID-19.[5,24,26,27]

The diagnoses and patterns of patients' clinical laryngeal complaints after recovering from a SARS-CoV-2 infection should not be dismissed as idiopathic. Rather, through careful history and examination, the otolaryngologist should keenly evaluate these patients' symptoms to determine whether the patient is suffering from a ramification of their earlier SARS-CoV-2 infection. The algorithm (Figure 1) we present here can serve as a guide to the otolaryngologist or general clinician as they consider the possible underlying etiology for their patients' laryngeal symptoms after recovering from a COVID-19 infection. Considering each patient's clinical history during their COVID-19 infection—such as whether or not they required intubation for management of their infections—can improve a clinician's diagnostic insight. By deliberately diagnosing laryngeal symptoms such as shortness of breath or dysphonia, which may otherwise seem like vague and nonspecific clinical complaints, physicians can productively inform the course of these patients' anticipated treatments and recovery.

The present study is not without its limitations. Our data are limited by their retrospective nature and sample size. The small sample size risks a type II error that prohibits more robust statistical comparisons among subgroups within our cohort. As a result, the study relies on descriptive data and trends within the cohort for its conclusions. Still, such data are needed, particularly as the pandemic continues to unfold and recovering patients widely seek medical assistance from otolaryngologists. Lastly, 16 patients (19.7%) included in the present study did not have positive COVID PCR or antibody results on record within our institution's electronic medical record. These patients did report a positive outside test to their laryngologist, and documented positivity was not necessary for their subsequent treatment. As our study was retrospective, we were unable to retroactively contact those 16 patients who had been diagnosed outside of our institution for documentation. Future studies should explore the comparative incidences of intubation injuries in intubated patients with and without COVID-19, and should explore the degree to which these laryngeal injuries are caused by the inflammatory nature of COVID-19 infections rather than intubation itself. The observations noted from the data presented here provide a platform to delve into a critical, detail-oriented understanding of patients' constellations of symptoms and morbidities after suffering from COVID-19 infections. These trends serve as noteworthy starting points to further refine our understanding of how to accurately diagnose patients based on their intubation history and presenting clinical symptoms.

5 | CONCLUSION

Given that otolaryngologists will be grappling with the consequences of this pandemic for years to come, it is essential that they be aware of the diagnostic range of post-COVID-19 infection sequelae within the upper aerodigestive tract.[28] Moreover, it behooves otolaryngologists to understand how patient history and presenting symptoms can likely portend the patient's underlying diagnosis. Recognizing and managing these symptoms will allow otolaryngologists to reduce the burden of the sequelae from COVID-19.

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