Postacute COVID-19 Laryngeal Injury and Dysfunction

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Abstract

Objective. Patients with COVID-19 are at risk for laryngeal injury and dysfunction secondary to respiratory failure, prolonged intubation, and other unique facets of this illness. Our goal is to report clinical features and treatment for patients presenting with voice, airway, and/or swallowing concerns postacute COVID-19.

Study Design. Case series.

Setting. Academic tertiary care center.

Methods. Patients presenting with laryngeal issues following recovery from COVID-19 were included after evaluation by our laryngology team. Data were collected via retrospective chart review from March 1, 2020, to April 1, 2021. This included details of the patient's COVID-19 course, initial presentation to laryngology, and subsequent treatment.

Results. Twenty-four patients met inclusion criteria. Twenty (83%) patients were hospitalized, and 18 required endotracheal intubation for a median (range) duration of 14 days (6-31). Ten patients underwent tracheostomy. Patients were evaluated at a median 107 days (32-215) after their positive SARS-CoV-2 test result. The most common presenting concerns were dysphonia (n = 19, 79%), dyspnea (n = 17, 71%), and dysphagia (n = 6, 25%). Vocal fold motion impairment (50%), early glottic injury (39%), subglottic/tracheal stenosis (22%), and posterior glottic stenosis (17%) were identified in patients who required endotracheal intubation. Patients who did not need intubation were most frequently treated for muscle tension dysphonia (67%).

Conclusion. Patients may develop significant voice, airway, and/or swallowing issues postacute COVID-19. These complications are not limited to patients requiring intubation or tracheostomy. Multidisciplinary laryngology clinics will continue to play an integral role in diagnosing and treating patients with COVID-19–related laryngeal sequelae.

Keywords

COVID-19, laryngeal injury, prolonged intubation, delayed tracheostomy, postacute COVID-19 syndrome, laryngotracheal stenosis, muscle tension dysphonia

The rapid spread of COVID-19 led to an unprecedented surge in the number of patients requiring prolonged intensive care unit (ICU) stays for life-threatening sequelae.[1] As many as 5% of individuals with COVID-19 require endotracheal intubation and mechanical ventilation for acute hypoxemic respiratory failure.[2] A smaller subset undergoes tracheostomy due to the need for ongoing ventilatory support.[3]

It is generally accepted that for critically ill patients requiring prolonged intubation and mechanical ventilation, early tracheostomy may reduce rates of ventilator-associated pneumonia and laryngotracheal stenosis and decrease sedation needs, which can expedite ventilator weaning and ICU discharge.[4-6] Timing and practices regarding tracheostomy for intubated patients with COVID-19 were topics of much discussion early in the pandemic and have varied across institutions and countries.[7] At the start of the pandemic, most protocols advocated for delaying tracheostomy to minimize particle aerosolization and risk of viral transmission to health care providers.[8] In many situations, this led to patients remaining intubated for 3 to 4 weeks, much longer than prepandemic standards of 7 to 10 days.[9]

Experts warned of an impending surge of patients with new voice, airway, and/or swallowing concerns following COVID-19.[9] This rise was anticipated due to the foreseen effects of altered intubation and tracheostomy practices. These complications include laryngotracheal injury following prolonged intubation, leading to subglottic, tracheal, and/or

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posterior glottic stenosis (PGS).[10,11] Other unique sequelae of COVID-19 illness, such as pulmonary deconditioning and postviral inflammatory responses, were not as predictable. Similarly, the impact of the COVID-19 prothrombotic state upon laryngeal mucosal ischemia and resulting exacerbation of intubation-related scarring could not have been foreseen.

Limited series of patients with unique and anticipated laryngeal complications from COVID-19 have recently emerged.[12-15] These reports are crucial to understand the features, settings, and timeline of patients presenting with new voice, airway, and/or swallowing concerns following acute COVID-19. However, additional information is needed to help guide best practices for evaluating and caring for these patients.

Herein, we present the largest series of patients with postacute COVID-19 laryngeal injury and dysfunction. Our objectives are to outline the presentation and treatment of these patients and to highlight the importance of early and ongoing laryngologic evaluation.

Methods

This was a single-institution case series with data collection from March 1, 2020, to April 1, 2021. Patients were identified by 1 of the study authors (R.J.M., N.D.H., R.A.K., or A.P.S.) if they were evaluated for new voice, airway, and/or swallowing concerns postacute COVID-19 in the outpatient clinic, inpatient setting, or emergency department. Electronic medical records were then reviewed for inclusion criteria: at least 18 years of age; confirmed case of COVID-19 based on laboratory testing for SARS-CoV-2; and development or worsening of voice-, airway-, and/or swallowing-related issues following COVID-19. This study was determined to be exempt after review by the University of Michigan Institutional Review Board (HUM00190341).

Electronic medical records were reviewed to extract and collate the data. This included information regarding patients' demographics (age, body mass index, and comorbidities) and COVID-19 course (need for hospitalization, intubation, and/or tracheostomy). Characteristics of the laryngeal sequelae of COVID-19 were carefully evaluated: time to presentation with voice, airway, and/or swallowing concerns, as measured from time of initial positive SARS-CoV-2 test result; setting of presentation to laryngology team (inpatient, outpatient, or emergency department); presenting concerns and voice-related quality of life (V-RQOL) score[16]; and physical examination, including laryngeal videostroboscopy findings, treatment plan, and outcomes. Summary descriptive statistics were calculated with Microsoft Excel.

Results

Study Population and Management of COVID-19

We identified 31 patients presenting with voice, airway, and/or swallowing concerns after recovering from documented or suspected COVID-19. Six were excluded due to lack of confirmatory SARS-CoV-2 testing (5 developed symptoms when SARS-CoV-2 tests were not readily accessible). One patient had dysphonia that preceded the COVID-19 diagnosis and

Table 1. Characteristics of Study Population (N = 24).

	Median (range) or No. (%)
Age, y	50 (20-81)
Sex	
Female	12 (50)
Male	12 (50)
Race/ethnicity	
Caucasian	16 (67)
African American	3 (13)
Asian	3 (13)
Hispanic	2 (8)
Body mass index, kg/m^2	29.4 (20.9-61.2)
Comorbidities	
Asthma/chronic obstructive pulmonary disease	5 (21)
Coronary artery disease	2 (8)
Diabetes	9 (38)
Hypertension	9 (38)
Tobacco use history	
Never	16 (67)
Former	8 (33)
Current	0 (0)

was unchanged by this acute illness. Thus, our final study consisted of 24 patients.

This group had a median (range) age of 50 years (20-81), equal male:female ratio, and were predominantly Caucasian (67%; **Table 1**). Expected comorbidities associated with severe COVID-19 were relatively prevalent, such as obesity, hypertension, diabetes, and underlying lung disease.[17,18] Our cohort was biased toward patients with critical respiratory illness, with the majority requiring endotracheal intubation (**Table 2**). In hospitalized patients, the median duration of hospital and ICU admission was 38 days (1-95) and 21 days (10-76), respectively. Patients were intubated for a median 14 days (6-31). Ten patients had tracheostomies placed during their COVID-19 course after a median intubation duration of 18 days (8-31).

Presentation to Laryngology Team

Patients were most often evaluated in the outpatient clinic (n = 15, 63%) and less commonly as an inpatient (n = 6, 25%) or in the emergency department (n = 3, 13%). There was a natural delay from COVID-19 diagnosis to presentation with laryngeal concerns. Most patients were seen near the end of 2020 or beginning of 2021 (**Figure 1**). The median (range) time from initial positive SARS-CoV-2 test result to presentation to our laryngology team was 107 days (32-215). For previously hospitalized patients who were initially seen in clinic or the emergency department, the median time from discharge to evaluation by our team was 71 days (5-144). Also, 40% of hospitalized patients were treated at other hospitals before presentation to our institution. Of the 10 patients who required tracheostomy during their treatment for COVID-19, 5 had
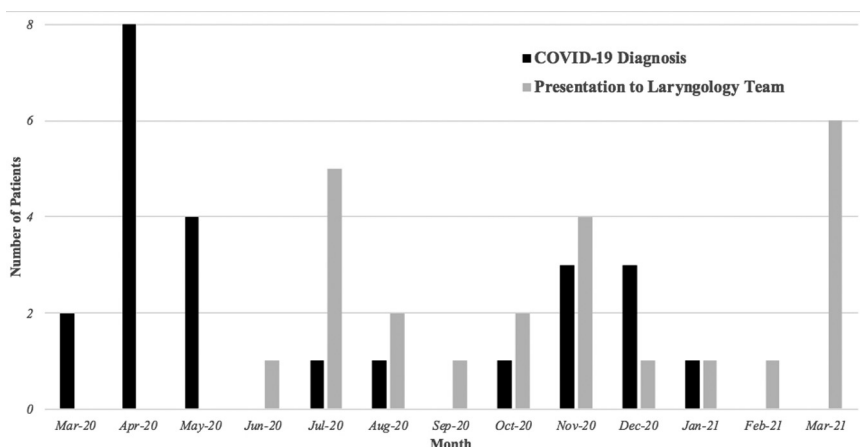
Figure 1. Frequency histogram of COVID-19 diagnosis and subsequent presentation to our multidisciplinary team.

Table 2. COVID-19 Treatment Characteristics for Hospitalized Patients (n = 20).

	Median (range) or No. (%)
Intensive care unit stay	
Yes	18 (90)
No	2 (10)
Intubation	
Yes	18 (90)
No	2 (10)
Endotracheal tube size, mm	8 (6-8)
Intubation duration, d	14 (6-31)
Tracheostomy	
Yes	10 (50)
No	10 (50)
Prone position	
Yes	10 (50)
No	10 (50)

Figure 2. Frequency histogram of individual chief complaints at initial presentation.

undergone decannulation prior to the initial laryngology evaluation.

Laryngeal Diagnoses and Treatment

Most patients (n = 18, 75%) presented with multiple chief complaints. Dysphonia and dyspnea were the most frequent concerns (**Figure 2**). Fourteen patients had V-RQOL questionnaire data available for analysis. The median (range) V-RQOL score at presentation for these patients was 73 (28-100) on a scale of 0 to 100.

Due to the connection between laryngotracheal injury and endotracheal intubation, patients were divided into groups based on their intubation status. Eighteen (75%) patients required intubation during management of COVID-19. Representative images from patients with intubation-related laryngeal injury are depicted in **Figure 3**. Diagnoses for this cohort included vocal fold motion impairment (n = 9, 50%), glottic injury (edema, erosion, and/or granulation; n = 7, 39%), subglottic or tracheal stenosis (n = 4, 22%), subglottic or tracheal granulation (n = 4, 22%), PGS (n = 3, 17%), and posterior glottic diastasis (n = 4, 22%; **Figure 4**). Most patients carried multiple diagnoses (n = 11, 61%; **Table 3**). Of the 9 patients with vocal fold motion impairment, 4 had unilateral immobility, 2 had unilateral hypomobility, and 3 had bilateral motion impairment from PGS.

Patients who did not require intubation (n = 6, 25%) were most often diagnosed with muscle tension dysphonia (MTD; n = 4, 67%). Additional diagnoses in this group were laryngitis (n = 1, 17%), glottic edema (n = 1, 17%), and unilateral vocal fold paresis (n = 1, 17%; **Figure 4**). Interestingly, 1 patient (No. 19) demonstrated new tongue tremor and fasciculations following COVID-19, which contributed to her dysphagia with a negative finding upon neurologic evaluation.

Of note, 7 patients in the entire cohort developed clinically significant pulmonary sequelae postacute COVID-19, which contributed to their dyspnea. Six of these patients had been hospitalized and intubated.

Treatment categories included multidisciplinary care with speech-language pathology or pulmonary rehabilitation, surgery, in-office procedures, medical management, and
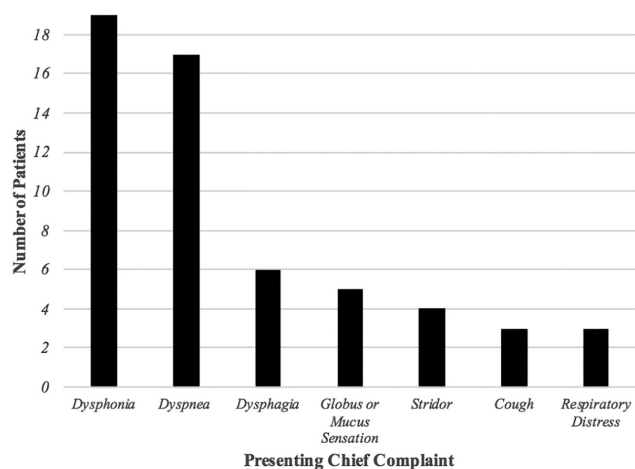
Table 3. Intubation Characteristics and Presenting Laryngeal Diagnoses.

Patient[a]	Endotracheal tube size, mm	Intubation time, d	Laryngeal diagnoses
1	7.5	20	Posterior glottic diastasis
2	8	19	Glottic edema and erosion, tracheal stenosis, tracheostomy dependence
3	Unknown	23	Glottic edema, posterior glottic diastasis
4	8	9	Bilateral vocal fold motion impairment, glottic granulation, tracheostomy dependence, posterior glottic stenosis
5	Unknown	17	Unilateral vocal fold immobility, glottic erosion, tracheostomy dependence
6	Unknown	14	Unilateral vocal fold immobility, posterior glottic diastasis
7	Unknown	18	Glottic erosion, tracheal stenosis
8	8	31	Unilateral vocal fold hypomobility, posterior glottic diastasis
9	6	24	Tracheal stenosis, tracheostomy dependence
10	Unknown	8	Tracheostomy dependence
11	8	13	Tracheal stenosis, tracheal granulation, tracheitis
12	Unknown	Unknown	Glottic granulation
13	8	6	Bilateral vocal fold motion impairment, glottic edema, subglottic granulation, posterior glottic stenosis
14	8	11	Subglottic granulation
15	8	15	Unilateral vocal fold hypomobility
16	8	12	Unilateral vocal fold immobility
17	7.5	13	Unilateral vocal fold immobility
18	8	14	Bilateral vocal fold motion impairment, subglottic granulation, posterior glottic stenosis

[a]Patients 1-10 also underwent tracheostomy during their treatment for COVID-19.
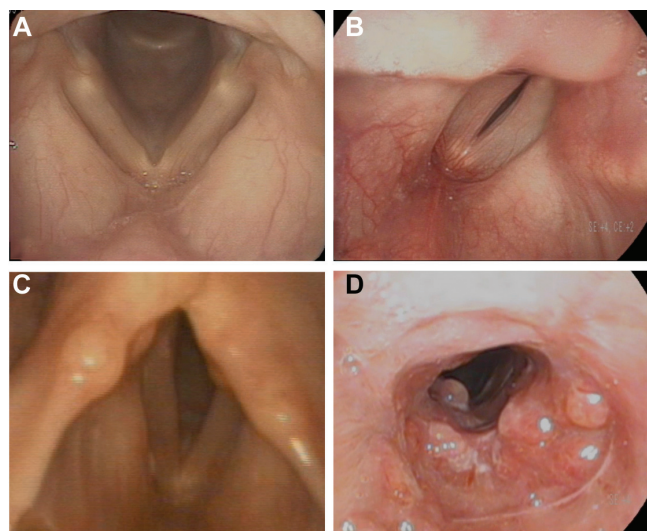
Figure 3. Representative images from intubated patients with COVID-19 and laryngotracheal pathology. (A) Posterior glottic diastasis. (B) Posterior glottic stenosis. (C) Left vocal fold immobility. (D) Tracheal stenosis.

observation (**Figure 5**). One-third of patients required multimodality treatment. Surgical treatments were injection augmentation, endoscopic management of posterior glottic or subglottic/tracheal stenosis (CO_2 laser, dilation, steroid injection, and mitomycin C application), tracheostomy, and cricotracheal resection. In-office procedures consisted of injection augmentation or postoperative steroid injections for patients with subglottic/tracheal stenosis. Voice and/or swallowing therapy was indicated for most of the nonintubated patients (n = 5, 83%).

Two patients had laryngeal issues prior to COVID-19 that were exacerbated by their illness. One patient had tracheal stenosis from an emergent tracheostomy performed over a year before she developed COVID-19. She had undergone decannulation but required a revision tracheostomy due to COVID-19. This led to worsening of her tracheal stenosis and development of subglottic stenosis, which precluded decannulation. She underwent a cricotracheal resection with revision tracheostomy and is working toward decannulation. The second patient had a history of vocal fold granulomas from prior traumatic intubations. Fortunately, this patient did not require intubation for COVID-19, but they presented with dysphonia and dyspnea secondary to laryngitis (prior granulomas had resolved).

Discussion

The COVID-19 pandemic has been ongoing for >1 year, and we are now routinely seeing patients with postacute COVID-19 laryngeal injury and dysfunction. A few initial case studies reviewed the presentation of airway complications following recovery from severe COVID-19.[13,19] Rouhani et al conducted a prospective study on patients with COVID-19 posttracheostomy and reported laryngotracheal pathology—primarily, vocal fold immobility and subglottic stenosis—in 19% of patients 2 months after discharge.[14] Naunheim et al
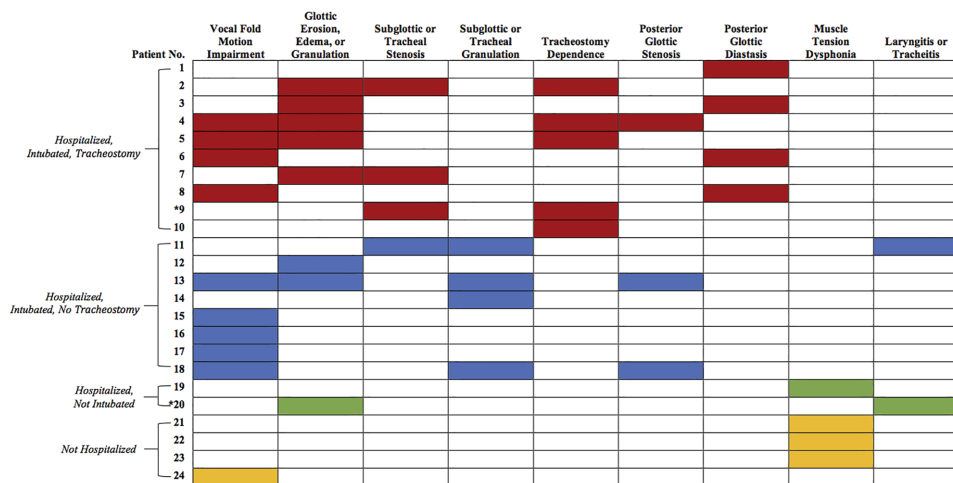
Figure 4. Profile of laryngeal diagnoses for patients postacute COVID-19. *Patients with laryngeal issues prior to COVID-19.
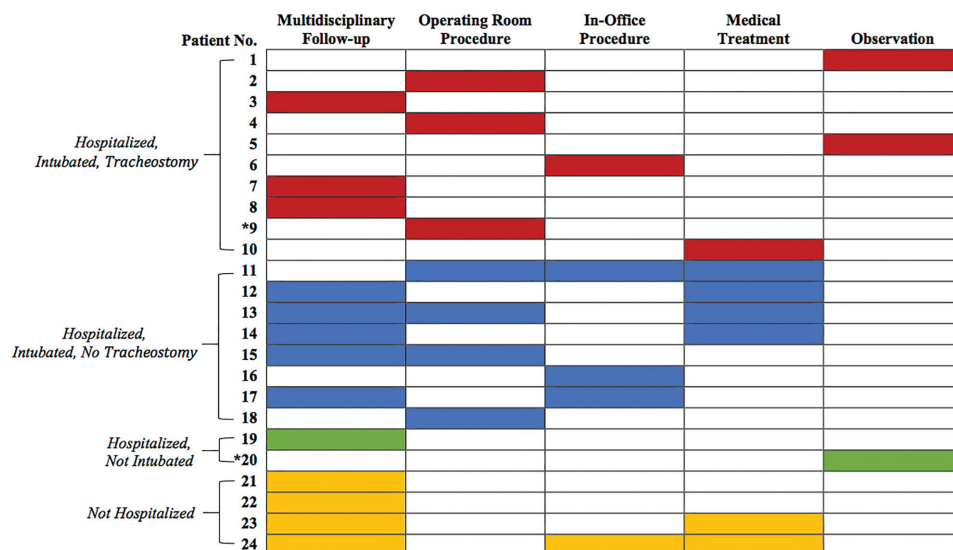

Figure 5. Management of postacute COVID-19 laryngeal complications. Multidisciplinary treatment involved voice and/or swallowing therapy or pulmonary rehabilitation. Medical treatment included steroids, bronchodilators, proton pump inhibitors, and antibiotics. *Patients with laryngeal issues prior to COVID-19.

performed a thorough analysis summarizing laryngeal complications in a cohort of 20 patients who recovered from COVID-19. This study focused on laryngoscopic and stroboscopic findings, and the authors noted abnormal mucosal wave in almost 88% of their patients.[15] It is becoming clear that the importance of fully understanding laryngeal sequelae of COVID-19 cannot be overstated, and ongoing research into characterization and treatment of these problems is essential. In this study, we describe the largest cohort of patients with voice, airway, and/or swallowing issues postacute COVID-19.

Complications related to endotracheal intubation in our cohort included glottic erosion and/or edema, granulomas/granulation tissue, vocal fold motion impairment, subglottic/tracheal stenosis, PGS, and posterior glottic diastasis. These are not necessarily specific to COVID-19, as these are known issues that can arise after intubation and/or tracheostomy.[10,11]

However, the rate at which these complications are occurring may be increased due to the unique characteristics of the virus and the circumstances of the pandemic. According to an anecdotal report and small case series, laryngeal edema caused by COVID-19 may increase intubation trauma and postextubation stridor.[12,20] Additionally, there is some evidence that the rate of tracheal complications following intubation for COVID-19 is higher.[12] This could be due to a unique combination of mechanisms causing tracheal damage, such as prone positioning, prothrombotic state leading to microvascular damage, proinflammatory cytokines induced by SARS-CoV-2, viral replication in the tracheal mucosa, systemic steroids causing mucosal atrophy, hypoxic damage, and health care worker fatigue.[21-23] Prospective studies evaluating the incidence of airway complications for intubated patients with COVID-19 as compared with other illnesses are needed to

understand the rate at which these complications occur as a result of COVID-19.

Our postintubation cohort had a prevalence of subglottic/tracheal stenosis (22% vs 15%) and PGS (17% vs 23%) similar to that of Naunheim et al,[15] although patients had a higher incidence of unilateral vocal fold immobility (22% vs 62%). However, our cohort had higher rates of early glottic injury (edema, granulation, and/or erosion) and subglottic/tracheal granulation (61% vs 15%). Presentation timeline is not outlined in their study, but it is possible that our evaluation of some patients earlier in their postacute COVID-19 course could account for a higher incidence of these findings.

The median intubation duration prior to tracheostomy in our group was 18 days, which is greater than the typical time before tracheostomy for respiratory failure (usually 7-10 days). This aligns with initial guidelines supporting avoidance of early tracheostomy in patients with COVID-19. This has changed with recent evidence showing benefits and safety of early tracheostomy with standardized protocols and personal protective equipment.[24-26] Thus, patients with extended intubation may be unique to hospitalizations in 2020, though many will require long-term management for laryngotracheal stenosis.

In June 2020, the European Laryngological Society predicted a growing number of patients with airway stenosis after COVID-19.[27] To prevent delayed diagnosis, the society suggested automatic follow-up by an otolaryngologist or airway specialist after severe COVID-19. The 24 patients in this study were evaluated by our laryngology team a median 107 days after their initial positive SARS-CoV-2 test result. Only 25% of patients were assessed in the inpatient setting, and hospitalized patients presented a median 71 days after discharge. This delay in initial assessment affects the patient's quality of life as one is recovering from COVID-19, and it may affect the ultimate treatment outcome.

PGS exemplifies this treatment paradigm well, as it is notoriously difficult to treat. Patients are frequently seen multiple months after initial injury and may already have mature scar formation and/or a tracheostomy in place. These patients often require multiple interventions, and despite best efforts they may remain tracheostomy dependent.[28] Lowery et al recently compared management and outcomes for patients with early intervention (≤45 days after intubation) versus late for posterior glottic injury or stenosis.[29] Patients who underwent early intervention had decreased duration of tracheostomy, increased frequency of decannulation, and fewer overall procedures. This likely reflects the impact of treating patients during the acute inflammatory healing phase as opposed to after the formation of mature scar and cricoarytenoid joint fixation. These concepts also apply to patients with subglottic and tracheal stenosis.[30] Ideally, patients with postacute COVID-19 voice, airway, and/or swallowing dysfunction would be evaluated by a otolaryngologist/laryngologist before discharge to determine if they may benefit from earlier intervention. Otolaryngologists should work in concert with their ICU teams to encourage awareness of these laryngeal issues and a low threshold for consultation to assess any potential concerns.

Laryngeal examination before discharge may not be viable in resource-limited communities. In our cohort, 40% of hospitalized patients were treated at outside hospitals, developed airway symptoms in a delayed fashion, and were then referred to our laryngology team. For these reasons, we expect volume increases for outpatient laryngology referrals to correspond to institutional and regional rates of COVID-19 hospitalizations.

A smaller number of patients (25%) presented with postacute COVID-19 laryngology issues without hospitalization and/or intubation. MTD, a suboptimal pattern of laryngeal and respiratory muscle coordination, was diagnosed in 67% of these patients. No patients in the intubated group were diagnosed with MTD. Dysphonia is a relatively common symptom of acute mild to moderate COVID-19, but the long-term functional manifestations are unclear.[31] Postviral laryngitis MTD has been described as compensatory dysphonia that persists despite resolution of inflammation.[32] No clear data exist to compare with other viral infections, but the incidence in our cohort suggests that MTD is a notable complication of mild COVID-19. Compensation associated with long-term dyspnea due to postacute COVID-19 syndrome should be considered a possible contributor to MTD.[33] Multidisciplinary care with speech-language pathology is critical for diagnosing and treating these patients.

Aside from MTD, patients who did not require intubation developed glottic edema, laryngitis, and unilateral vocal fold paresis. The patient who was diagnosed with unilateral vocal fold paresis is of particular clinical interest. It is unclear if this was coincidental or potentially related to an underlying inflammatory response to SARS-CoV-2, as there is an association between idiopathic unilateral vocal fold paresis and antecedent viral upper respiratory infection.[34] Another patient was diagnosed with tongue tremor/fasciculations, which contributed to the dysphagia. The patient did not have these symptoms prior to COVID-19, and the neurologic workup finding was negative. Again, it is unclear what role COVID-19 played in the development of this issue for our patient. Additional studies are needed to fully understand potential postacute COVID-19 laryngologic issues, particularly in patients who do not require intubation.

This study has important limitations. This is a retrospective analysis with a small sample size. Further studies will include a larger cohort to better understand the true incidence and impact of the laryngeal complications outlined in this article. Moreover, we did not have sufficient follow-up to determine if patients respond to standard interventions in an expected manner or if their underlying pathology reacts differently. Following these patients over time will also demonstrate how many require long-term follow-up for postacute COVID-19 laryngeal sequelae. Additionally, our patient cohort does not mirror the national distribution of racial, ethnic, and socioeconomic groups that have been affected by COVID-19, as we had a higher proportion of Caucasian patients and relatively fewer Hispanic patients. It is important to continue gathering data across the United States and the world to determine if different groups disproportionately develop postacute COVID-19 laryngeal injury and dysfunction.

Most patients presented to our team with dyspnea or dysphonia, including a combination of symptoms in 18 of 24 cases. A decreased median V-RQOL score of 73 on a scale from 0 to 100 illustrates the extended effect on a patient's quality of life and the importance of quantitative measures during follow-up. Furthermore, airway trauma and resulting symptoms contribute to post–intensive care syndrome—a common physical, cognitive, and neuropsychiatric decline leading to decreased quality of life after prolonged intubation.[35-37] Postacute COVID-19 syndrome is now an individually recognized combination of multiorgan and neuropsychiatric sequelae extending beyond 12 weeks after recovery.[33] As post–intensive care syndrome and postacute COVID-19 syndrome become more prevalent, recognition, diagnosis, and treatment of postintubation airway trauma will be important to address the associated decrease in quality of life and health disparities that extend far beyond recovery.[35-37] Early diagnosis is important and requires effective evaluation and prompt referral/consultation with otolaryngology, especially for any concerns related to fixed airway obstruction.[31,38]

Conclusion

This study describes the largest cohort of patients with postacute COVID-19 laryngeal injury and dysfunction. Prolonged intubation and tracheostomy during management of severe COVID-19 are major contributors to voice, airway, and swallowing dysfunction. However, we also identified notable laryngeal issues from mild disease. Multidisciplinary laryngology practices will continue to play an integral role in treating these patients in coordination with intensivists and primary care providers. Indeed early otolaryngology evaluation for voice, airway, and swallowing dysfunction remains critical as we seek to manage or prevent long-term laryngotracheal sequelae that could have lasting impacts on quality of life.

Author Contributions

Andrew J. Neevel, design, data collection, analysis, presentation; **Joshua D. Smith**, design, data collection, analysis, presentation; **Robert J. Morrison**, patient identification, manuscript review; **Norman D. Hogikyan**, patient identification, manuscript review; **Robbi A. Kupfer**, patient identification, manuscript review; **Andrew P. Stein**, patient identification, design, data collection, analysis, presentation.

Disclosures

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