

# Covid-19 impact on vocal and laryngeal sequelae: a literature review.

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## Abstract

SARS-CoV-2 disease is a new nosological entity with multiple repercussions on several anatomical districts. Many researchers have focused not only on lung damage but also on the laryngeal sequelae of the Covid-19 infection. To collate this information, this review analysed the literature published between March 2020 and May 2021. The findings seem to positively correlate Covid-19 and infection-related dysphonia, post-viral vagal neuropathy, inflammation and laryngeal oedema caused by cough and vomiting, and lesions of the vocal cords due to endotracheal intubation and tracheotomy. From analysis of the data, it is clear that ENT specialists and speech and language pathologists (SLP) will play a crucial role in the detection of dysphonia onset in patients reporting a previous Covid-19 infection. Further studies to assess the incidence and characteristics of dysphonia resulting from this disease are essential.

*Keywords: Covid-19, Voice, Dysphonia, Voice Disorders, Endotracheal Intubation*

## Introduction

In March 2020, following the cases identified in China and the rapid spread of the Sars-CoV-2 viral infection, the World Health Organization declared that there was a coronavirus pandemic. As we now know, the most serious forms of the so-called Covid-19 infection cause important repercussions, especially on the respiratory capacity of affected patients, necessitating an increasing number of intensive care unit (ICU) hospitalizations due to the need to practice procedures such as invasive mechanical ventilation, orotracheal intubation, and tracheostomy (Rouhani M.J. et al., 2021).

It has been widely reported in the literature that these procedures can lead to the onset of laryngeal lesions of various kinds, noted very frequently in ICU settings (Brodsky M. B. et al., 2018). In this regard, the Italian Guidelines on dysphonia recommend a thorough diagnostic assessment in cases of new onset dysphonia with a history of recent endotracheal intubation (Shindler A. et al., 2009). In

addition, it is also well known that most upper airway viral infections (URIs) are associated with laryngopharyngitis, the onset of which, as a result of Covid-19, may put the patient at increased risk of developing glottal and subglottal lesions or stenosis after a period of intubation (Rouhani M.J. et al., 2021).

It should also be pointed out that lung sequelae appear to be only part of the set of possible consequences of this new disease. Over the course of the last year there have been numerous studies and research carried out on Covid-19, aimed at describing and reporting its innumerable potential complications and consequences, including those related to the phonation system. It is known that severe compromise of lung function, as well as periods of endotracheal intubation can negatively impact vocal function. It is not yet clear, however, which other factors may be implicated, and how these could contribute to dysphonia onset as a result of Covid-19 infection. Hence, we thought it might useful

and timely to conduct a review of the literature currently available on complications affecting both the respiratory system and vocal production, to report the state of the art on dysphonia symptomatology following Covid-19 infection. We set out to assess the incidence, possible causes, and characteristics of the above, as well as to provide good clinical practice guidelines with a view to the early detection of these sequelae, ultimately to provide patients with adequate and targeted treatment pathways.

## Materials and Methods

This literature review focused on relevant scientific articles published from March 2020 to May 2021, identified using the major search engines (PubMed Central, Medline, Scopus, CINAHL). The research strategy was defined on the basis of the objectives of the study, examining specific clinical manifestations and laryngeal sequelae associated with Covid-19 infection. The search string included terms for the following three conceptual areas: voice disorders, Covid-19 disease, and endotracheal intubation procedures; within each area, the databases were searched for a series of synonyms of the above terms, including voice, dysphonia, speech therapy, SarsCov-2 and mechanical ventilation. The associated terms were systematically compared with each other to ensure precise selection of all relevant items and exclude irrelevant material. All the papers examined were published in English.

After an initial search, which yielded over 200 articles, we screened a total of 98, 74 of which were rejected on the basis of the title and abstract because they pertained to topics not strictly pertinent the aim of the review, such as risk of infection in vocal practice, the risk of contagion and discomfort related to the use of masks in the artistic and non-artistic field, risks related to fibre-optic laryngoscopy diagnostics, onset of dysphonia, and spectro-acoustic analysis of the voice in telemedicine. Also excluded were case reports and articles reporting repetitive studies, for which it was decided to examine the ones with the most statistically significant cohorts.

At the end of this selection process, 14 articles with the inclusion characteristics

described above remained for review, specifically those concerning voice disorders associated with Sars-Cov-2 infection that required endotracheal intubation procedures or not; a systematic review prior to the Covid-19 era (Brodsky M. B. et al., 2018) and cited by numerous studies was also included, as this would be fundamental for the definition of the laryngeal sequelae to be expected after said procedure.

## Results

In the pre-Covid-19 era, Brodsky and colleagues published a review of the literature highlighting an increased incidence of laryngeal lesions in intensive care unit (ICU) patients. Based on the existing data, the authors proposed a classification of post-intubation laryngeal lesions into 4 levels of severity: (1) absence of injury; (2) mild lesion (limited to the mucous membrane) i.e., oedema, erythema, hyperplasia or ecchymosis; (3) moderate lesion, including hematoma, ulceration, fibrin without narrowing of the glottis, mass lesions, granulation; and (4) severe injury, including stenosis, stenosis with glottic narrowing, hypomotility/immobility of the vocal cords and/or cricoarytenoid joint. The most frequently observed clinical symptoms reported in post-extubation studies were dysphonia (76%), pain (76%), hoarseness (63%) and dysphagia (49%) (Brodsky M. B. et al., 2018).

Covid-19 pathology is associated with a growing need for endotracheal intubation due to the well-known pulmonary symptomatology. A study by Rouhani and colleagues aimed to investigate the presence of dysphonia in a group of 41 patients suffering from Sars-Cov-2 who underwent orotracheal intubation and were subsequently tracheotomized. Following weaning from tracheal cannula and closure of the tracheal stoma, voice assessments were carried out, to detect the potential onset of dysphonia, through the administration of a self-assessment questionnaire (VHI-10) and the study of the vocal quality of patients carried out by experts using a perceptual voice assessment scale (GRBAS). According to the VHI-10, 13.2% of cases were potentially pathological, while according to the GRBAS scale, 53.7% of patients had scores indicative of impaired speech quality. Of the

patients undergoing flexible endoscopic examination of the larynx, 7.9% displayed unilateral vocal cord paralysis, 5.3% subglottic stenosis, 5.3% vocal cord ecchymosis, and 5.3% bilateral cord paralysis with subglottic granuloma (Rouhani M.J. et al., 2021). In another study, 95 out of 164 Covid-19 patients subjected to speech assessment presented dysphonia at the initial evaluation. Of these, 90 had been intubated, and 54 were still dysphonic at the time of hospital discharge. The vocal quality of these patients was assessed perceptually by experts via the GRBAS scale: at the initial evaluation the average value was 2 (range 0–3), while at the final evaluation the average score was 0 (range 0–1) (Archer S.K. et al., 2021).

As regards intubation, as reported by other authors, the Sars-CoV-2 virus can cause oedema of the airways, particular the larynx; a study conducted in the United Kingdom revealed that intensive care staff had to discontinue orotracheal intubation in a number of patients due to airway oedema (McGrath B.A. et al., 2020). The difficulty of emergency intubation in such cases, as well as the need for re-intubation, was also highlighted in a study by Castillo-Allendes and colleagues (Castillo-Allendes A. et al., 2020).

Naunheim and colleagues, on the other hand, stated that prolonged intubation adopted in patients with respiratory failure can lead to problems that inevitably affect not only swallowing but also the voice (Naunheim M.R. et al., 2020). Piazza and colleagues also report that patients with a history of prolonged intubation and/or tracheotomy and consequent dysphonia may exhibit laryngo-tracheal stenosis and granulomas (Piazza C. et al., 2021).

In terms of organic changes in the larynx following Covid-19 infection, a study by Saniasiaya and colleagues highlights that post-viral vagal neuropathy is among the possible aetiological factors, resulting from the neurotrophic and neuroinvasive characteristics of severe acute respiratory syndrome due to Sars-CoV-2. Vagal neuropathy may be associated with dysphonia, vocal fatigue, odynophagia, dysphagia, neuropathic pain, cough, laryngospasm, and continuous clearing of the throat (Saniasiaya J. et al., 2021). Other authors point out that vocal cords paresis and paralysis can

result from even short periods of endotracheal intubation, but also from vagus nerve lesion of viral aetiology, both potentially damaging the lower laryngeal nerve, responsible for motor innervation of the larynx (Helding L. et al., 2020). The same authors hypothesized that not only motor neuropathies of the larynx but also sensory ones, the most common manifestations of which are chronic cough and swallowing difficulties, can arise following Covid-19 infection, as with any other viral infection. A growing body of emerging data also implicates chronic fatigue, a common sequela of Covid-19 infection; although this does not directly interfere with vocal production, chronic fatigue can be associated with speech disorders and therefore significantly impact professional voice users in particular (Helding L. et al., 2020).

Analysing data on the correlation between Covid-19 and voice impairment, a multicentre study investigated the incidence of dysphonia in European patients with mild to moderate Covid-19 symptoms. In the cases under consideration (702 patients), dysphonia and otolaryngitis symptoms were assessed, revealing dysphonia in a quarter of such patients (188). In addition, it was shown that dysphonic patients were more symptomatic than non-dysphonic patients, and in most the symptomatology was characterized by the presence of cough, fatigue, nausea and vomiting. The study describes dysphonia of mild to moderate severity as an important symptom in Covid-19 patients, with a prevalence of 26.8% (Lechien J.R. et al., 2020).

This is considerably lower than that found in an Italian study by Cantarella and colleagues, which showed that dysphonia is a highly widespread and long-lasting symptom in subjects with Covid-19 (Cantarella G. et al., 2021). Their sample comprised 160 patients diagnosed with Covid-19, of whom 117 had moderate symptoms of the disease (73.1%), and 43 mild (26.9%). The exclusion criteria for this study were pre-existing dysphonia and a history of neck cancer. Dysphonia was reported in 70 of these patients (43.7%), and was associated with other symptoms such as voice fatigue, cough, rhinitis and dyspnoea; dysphonia was classed as being mild/moderate in 69 patients and severe in 1 patient alone. Vocal fatigue, due to the effort required to

produce vibration of the vocal cords and the decreased exhalation airflow, was also commonly reported by patients (43, i.e., 26.8%), and its severity was found to be related to dysphonia, cough, rhinitis, dyspnoea and loss of appetite.

In a study conducted by Iranian colleagues, the vocal quality of Covid-19 patients was evaluated using acoustic analysis, and compared with a group of controls. Statistical analysis of the data revealed significant differences between the two groups; in particular, differences in maximum phonation time (MPT) showed that Covid-19 patients mainly suffered from airflow failure due to lung involvement (Asiaee M. et al., 2020). As is well known, optimal air-pulmonary support is an essential prerequisite for efficient phonation, and when this is severely affected by Sars-Cov-2, it could cause new-onset dysphonia in Covid-19 patients (Saniasiaya J. et al., 2021). However, other changes in the acoustic characteristics of the voice are also attributable to laryngeal involvement, as Covid-19 patients displayed greater aperiodicity, irregularities and signal disturbance, and also an increase in noise levels in the voice, as compared to the control group (Asiaee M. et al., 2020). Laryngeal sequelae therefore require early detection in order to provide timely patient care, and therefore phonation specialists therefore need to be involved in the comprehensive diagnostic workup (Archer S.K. et al., 2021).

## Discussion

Covid-19 is a new disease, and as such little is yet known about its multi-organ sequelae. Research in this area is in progress, and in the near future we will certainly see the production of an increasing number of evidence-based studies assessing its post-viral effects. Thus far, however, it has been shown that the infection is associated with many and various respiratory complications that can negatively impact the voice. Furthermore, it should be noted that in addition to the direct respiratory sequelae, vocal production can be qualitatively and quantitatively impaired by laryngeal lesions resulting from endotracheal intubation (alterations and scarring of the vocal cord mucosa and mass, paralysis and hy-

potility of the vocal cords, residual laryngeal sensory neuropathy, and chronic fatigue.

The variations in Covid-19 symptomatology can lead to a hierarchical recognition of its effects by order of severity. Although correct from a diagnostic and rehabilitation point of view, this 'crisis management' approach often precludes assessment and management of the so-called 'minor' sequelae, among which speech impairment. However, knowledge, prediction and subsequent screening and treatment of such deficits should feature in a comprehensive approach to treatment of the disease.

Indeed, the articles included in this review of the literature point to the extent of respiratory sequelae, post-intubation laryngeal problems, post-viral vocal cord paralysis, dyspnoea, chronic vocal fatigue and post-viral laryngeal motor and sensory neuropathies associated with the Sars-Cov-2 infection. It appears that Covid-19 causes a significant incidence of dysphonia (26.8%–57.9%), albeit with different characteristics and severity levels in this patient population. As already pointed out in other reports (Naunheim M.R. et al., 2020), the prolonged intubation adopted in patients with respiratory failure can lead to problems that inevitably affect the voice and swallowing. Intubation, whether short or prolonged, causes a high incidence of phonatory insufficiency, which may be associated with laryngeal lesions, which are common, or a functional/compensatory deficit. Other risk factors are emergency intubation, tube size, and the need for reintubation (Castillo-Allendes A. et al., 2020). Presumably, the symptomatology could also be aggravated by the prone posture, often adopted in patients with Covid-19 infection to improve oxygenation and drainage of secretions. However, the correlation between pronation and a higher incidence of dysphonia is still controversial and needs further investigation.

A study by Cantarella et al. reveals not only the frequency with which vocal dysfunction occurs to varying degrees in association with Sars-Cov-2 infection, but also the prolonged duration of such symptomatology, as compared to common viral laryngitis. However, from the beginning of the pandemic, such issues have been widely underestimated (Cantarella G. et al., 2021). Nevertheless, it has

been observed that early detection of sequelae, i.e., vocal impairment and underlying laryngeal lesions, followed by targeted medical rehabilitation allows, in most cases, complete resolution of dysphonic issues resulting from Covid-19. This suggests that in the settings in which these patients are managed, it would be desirable to implement the routine consultation of specialists in the field in order to optimize patient rehabilitation outcomes, and in particular to meet the needs of patients with new-onset vocal disorders (Archer S.K. et al., 2021). In this scenario, SLP has a crucial role to play in the detection of the suspected onset of dysphonia in patients reporting a previous Covid-19 infection, as well as any underlying injuries. It would be desirable for self-assessment questionnaires to be administered to such patients, and for vocal output to be assessed over time using clinical tools such as measuring the maximum phonation time (useful for evaluating vocal cord defects) and perceptual evaluation scales (GRBAS). It is also important to provide patients with dedicated voice training and vocal hygiene habits, in order to prevent the onset of complications or spontaneous compensation (Castillo-Allendes A. et al., 2020). This suggests that in the coming months, otolaryngology specialists, voice scientists and SLP should be deployed to assess and manage potential vocal complications in patients with Covid-19.

Indeed, Covid-19 is a prime example of an infection that requires a multidisciplinary approach to manage multi-organ sequelae, and the phonation apparatus should not be overlooked in a thorough assessment of patient status. An article by Piazza and colleagues, in agreement with the European Laryngological Society, alerted the medical community to the potential increase in the number of Covid-19-related cases of laryngotracheal stenosis. Any such patient with a history of pro-

longed intubation and/or tracheotomy and persistent laryngeal symptomatology should be carefully evaluated, as this may conceal laryngotracheal stenosis and granulomas (Piazza C. et al., 2021). New-onset dysphonia therefore warrants an accurate history, accompanied by an objective examination. This is particularly important in professional voice users, as several known sequelae of Covid-19 infection, namely pulmonary issues and paralysis or paresis of even minor vocal cords, as well as chronic fatigue, can significantly impact not only the quality of life, but also the livelihoods of this patient population (Helding L. et al., 2020). Moreover, as previously pointed out by other authors, in the future it will be necessary not only to objectively evaluate the larynx but also to perform molecular research in all patients with new-onset vocal disorders to exclude Covid-19, as dysphonia could be a silent manifestation thereof (Saniasiaya J. et al., 2021).

## Conclusions

Further studies are essential to evaluate the incidence and characteristics of dysphonia resulting from Covid-19 infection. Meanwhile, the studies examined thus far highlight the need to perform objective assessment (preferably by fibre-optic laryngoscopy) of any organic or functional damage to the respiratory and phonation apparatus in patients who have contracted the coronavirus infection and present dysphonia, phonasthenia or hoarseness, in order to detect the source of the issue early and therefore ensure targeted and effective treatment. This is especially true for professional voice users, in whom even minor difficulties in this regard may have a catastrophic impact on their careers.

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